Separate evaluation of target facilitation and distractor suppression in the activity of macaque lateral intraparietal neurons during visual search

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Running head: Target facilitation and distractor suppression in LIP
ABSTRACT

During visual search, neurons in the lateral intraparietal area (LIP) discriminate the target from distractors by exhibiting stronger activation when the target appears within the receptive field than when it appears outside the receptive field. It is generally thought that such target-discriminative activity is produced by the combination of target-related facilitation and distractor-related suppression. However, little is known about how the target-discriminative activity is constituted by these two types of neural modulation. To address this issue, we recorded activity from LIP of monkeys performing a visual search task that consisted of target-present and target-absent trials. Monkeys had to make a saccade to a target in the target-present trials, whereas they had to maintain fixation in the target-absent trials, in which only distractors were presented. By introducing the activity from the latter trials as neutral activity, we were able to separate the target-discriminative activity into target-related elevation and distractor-related reduction components. We found that the target-discriminative activity of most LIP neurons consisted of the combination of target-related elevation and distractor-related reduction or only target-related elevation. In contrast, the target-discriminative activity composed of only distractor-related reduction was observed for very few neurons. We also found that on average, target-related elevation was stronger and occurred earlier compared with distractor-related reduction. Finally, we consider possible underlying mechanisms, including lateral inhibitory interactions, responsible for target-discriminative activity in visual search. The present findings provide insight into how neuronal modulations shape target-discriminative activity during visual search.

KEYWORDS: visual search, electrophysiology, lateral intraparietal area, nonhuman primate, saccade
INTRODUCTION

In a visual search, the target must be discriminated from distractors to direct covert attention and/or an overt saccade toward the target locus. Initial visual activity in the lateral intraparietal area (LIP), a crucial area involved in visual search (Liu et al. 2010; Wardak et al. 2002), does not discriminate the target. However, later activity involving stronger discharge rates when the target appears within the receptive field (target-related activity) than when it appears outside the receptive field (distractor-related activity) does discriminate the target (Balan et al. 2008; Buschman and Miller 2007; Ipata et al. 2006; Ogawa and Komatsu 2009; Thomas and Paré 2007). It is generally thought that such target–distractor discriminative activity is produced by the facilitation of target-related activity and the suppression of distractor-related activity. However, no systematic study has examined how these elevating and reducing modulations build the target-discriminative activity during the course of visual search. To address this issue, an ideal neutral activity must be used to separate the target-distractor discriminative activity into target-related elevating and distractor-related reducing components.

Model studies suggest that spatial competition mediated by mutual lateral inhibitory interactions is one possible mechanism to produce target–distractor discriminative activity during visual search (Deco et al. 2002; Itti and Koch 2000; Koch and Ullman 1985; Usher and McClelland 2001), and lateral inhibitory interactions are commonly found across visuomotor areas involving LIP (e.g. Cavanaugh et al. 2012; Dorris et al. 2007; Falkner et al. 2011; Munoz and Istavan 1998; Schall et al. 1995a, 2004; Suzuki and Gottlieb 2012). Under the existence of lateral inhibitory interactions, if the initial activation evoked by the target is slightly stronger than the activation evoked by distractors, spatial competition operates so that the stronger target-activation gains further strength, whereas, at the same time, the weaker distractor-activations are further suppressed (Fig. 1Da, b). In contrast, if only identical distractors were presented, such facilitation and suppression processes
according to spatial contrast would not proceed among the activations because all activations would have the same strength (Fig. 1Dc, d). Thus, the activity in target-absent (TA) trials, in which stimuli consist of only identical distractors, can be used as ideal neutral activity. By comparing the target-related/distractor-related activity in target-present (TP) trials with the activity in the TA trials, we could separately evaluate the elevating/reducing neuronal modulations in target-discriminative activity (Fig. 1De).

In this study, we recorded the activity of LIP visually responsive neurons while monkeys performed a singleton visual search task that involved both TP and TA conditions. The purpose of the present study was to decompose the target-discriminative activity into the target-related elevation and distractor-related reduction components and to qualitatively and quantitatively clarify the response properties of each neural modulation. The present results revealed the cell-to-cell variability in and the relationship between the properties of the elevating and reducing modulations. Additionally, to bridge our present results with the predictions of model studies, we also tested whether the observed properties of the activity modulations could be reproduced by the simulation using a simple network model with lateral inhibitory interactions.
METHODS

Animal preparation and apparatus

Data were obtained from two female macaque monkeys (*Macaca fuscata*, monkeys Y and S, 5.0 and 6.3 kg, respectively). A plastic head holder and recording chambers were secured to their skulls using dental acrylic resin (Unifast II, GC, Aichi, Japan) and ceramic screws (Thomas Recording, Geissen, Germany) under deep anesthesia and sterile conditions. The recording chambers (inner diameter, 22 mm) were placed at stereotaxic coordinates (P2 and L21.5 for monkey Y; P4.1 and L18, and P0 and L21 for monkey S) above the intraparietal sulcus (IPS) with the assistance of magnetic resonance imaging (MRI) performed before the surgery (see below). An eye coil was surgically implanted beneath the conjunctiva of one eye (Judge et al. 1980). The monkeys were allowed to recover for 2 weeks prior to training and recording. All procedures for animal care and all experimental protocols were in accordance with the Guide for the Care and Use of Laboratory Animals of the National Research Council (1996) and were approved by the Animal Care and Use Committee of Kyoto University.

The experiments were performed under the control of two Windows XP-based computers that presented stimuli, recorded neural signals and eye positions, and controlled the task schedule. They were developed using LabVIEW (National Instrument Japan, Tokyo, Japan) and C++ Builder (Borland Software Corporation, Scotts Valley, CA, USA). Visual stimuli were generated using a video-signal generator (ViSaGe; Cambridge Research Systems, Cambridge, UK) and presented on a video monitor with a 100-Hz refresh rate and 800 × 600 resolution (RDF223H; Mitsubishi, Tokyo, Japan). They were viewed binocularly from a distance of 42 cm in a dark room and subtended a visual angle of 51.5 × 40.0°. The color and luminance of visual stimuli were measured by a ColorCAL colorimeter (Cambridge Research Systems).

Single neurons were recorded using an epoxylite-insulated tungsten electrode (Frederick
Haer & Co., Bowdoinham, ME, USA) with an impedance >2 MΩ measured at 1 kHz (model IMP-1, Bak Electronics, Germantown, MD, USA). Extracellular activity was amplified using a microelectrode AC amplifier (Model-1800; A-M Systems, Carlsborg, WA, USA) and stored on a computer equipped with a multichannel analog-to-digital board at a sampling rate of 50 kHz (PCI-6143, National Instrument Japan). Eye position was monitored and recorded using the scleral search coil technique (Fuchs and Robinson 1966) (eye position detector DSC-2001; Datel, Tokyo, Japan). Precise spikes were discriminated off-line using a template-matching method. Eye-position signals were recorded at a sampling rate of 50 kHz but analyzed at a 1 kHz resolution.

The recording site was determined using a guide tube and a set of plastic grids that had holes spaced 1.0 mm apart and that were offset from each other by 0.5 mm. The guide tube (23 gauge) was lowered just above the dura mater surface, and the electrode penetrated the cortex through the dura using an oil hydraulic micromanipulator (MO-97A-S, Narishige, Tokyo, Japan). Under microscopic examination (OPMI-pico-i, Zeiss, Tokyo, Japan), a duratomy was made using fine forceps (Dumont No. 5) and a 25-gauge needle with the tip bent at a right angle. Only a small region of the tissue just below the selected grid hole was removed to avoid breaking the electrode. The chamber was filled with agarose (3%; A9793, Sigma, St. Louis, MO, USA) to promote recording stability. After each recording session, the dura matter surface was covered with anti-infective/anti-inflammatory ointment (Chlomy-P ointment, Daiichi-Sankyo, Tokyo, Japan).

**Behavioral paradigms**

Our behavioral task consisted of reaction-time and delayed-response visual search tasks. During these tasks, the activities of 122 visual neurons in LIP were recorded and examined.

**REACTION-TIME VISUAL SEARCH TASK**
In this task, two types of trials were interleaved: TP trials, in which a singleton target was embedded in five identical distractors (Fig. 1A), and TA trials, in which only distractors were presented (Fig. 1B). In each trial, after sustained fixation, usually for 1,000 ms [except for 23.8% (29/122) of recording sessions, which were for 1,500–2,000 ms] within a window (±1.2–1.8°), a six-element (circles of 2.24° in diameter) search array was displayed on a gray background (1 cd/m²). In TP trials, the monkeys were required to make a saccade toward the target after the array presentation. The target location was presented in the receptive field of the neuron under study or in the diametrically opposite location in the visual field with equal probability; hence, the target randomly appeared at just two fixed locations in each recording session. When the computer detected a saccadic eye movement, the visual stimuli and fixation spot were immediately extinguished. If the monkeys made a single saccade that landed inside a square window (±3.0 × 3.0°) centered on the target, another fixation point appeared at the target position. After 600 ms of fixation on this point, the monkey received a juice reward. In the TA trials, all six elements had the same stimulus features, and the monkeys received a reward if they maintained their fixation (600–1,800 ms) until the end of the trial. Erroneous saccadic responses to any element were regarded as false-alarm responses.

The luminance of each element was either 10 cd/m² ("Light") or 1 cd/m² ("Dim"). The color of each element was either orange (CIE chromaticity coordinate: x = 0.43, y = 0.47 for monkey Y; x = 0.44, y = 0.46 for monkey S), yellowish-orange (x = 0.41, y = 0.48 for monkey Y; x = 0.42–0.43, y = 0.47 for monkey S), green (x = 0.24, y = 0.41 for monkey Y; x = 0.23, y = 0.37–0.39 for monkey S), or bluish-green (x = 0.23, y = 0.38 for monkey Y; x = 0.22, y = 0.34 for monkey S). In the TP trials, target- and distractor-color pairs were selected so that their colors were either more different ("Easy:" target/distractor colors = orange/green, green/orange, yellowish-orange/bluish-green, or bluish-green/yellowish-orange) or more similar ("Hard:" yellowish-orange/orange, orange/yellowish-orange, bluish-green/green, or green/bluish-green). Each
color pair was presented with equal probability. In the TA trials, all elements were presented in one of the four colors with equal probability. Taken together, the TP trials had four stimulus conditions (Light–Easy, Light–Hard, Dim–Easy, and Dim–Hard TP conditions), and the TA trials had two stimulus conditions (Light and Dim TA conditions) (Fig. 1C). The TP and TA trials were pseudo-randomly presented at a ratio of 4:1 without any cue that discriminated between the two types of trials. In some recording sessions (71/122 = 58.2%), trials in which only an isolated target, instead of an array stimulus, was displayed were also interleaved (9.1% of trials). However, we did not use the data from these trials in the present study.

DELAYED-RESPONSE VISUAL SEARCH TASK

This task was a variation of a memory-guided saccade task (Hikosaka and Wurtz 1983). The procedure for this task was the same as that in the reaction-time visual search task except that a delay period was imposed, the number of color pairs in the array stimuli was decreased, and target-absent trials were eliminated. After a cue stimulus was displayed (500 or 700 ms), a variable-delay fixation was instituted (600–1,800 ms). When the fixation point was extinguished (“go” signal), the monkeys were required to make a saccade toward the location at which the target appeared during the cue period. A cue stimulus was either an isolated stimulus (isolated-stimulus trials) or an array stimulus (array-stimulus trials). Of 122 cells, 19 (15.6%) were recorded only in isolated-stimulus trials. The array stimuli were the same as those used in the Light–Easy trials during the reaction-time visual task.

Trials for the reaction-time (77–83%) and delayed-response (17–23%) visual search tasks were interleaved pseudo-randomly within a session, with the exception of the data from 20 neurons (16.4%), which were collected during separate sessions for each task. The eccentricity of the visual stimuli in both types of trials were fixed at 8.5° in the periphery to minimize inter-neuron differences.
in task difficulty across recording sessions because behavioral performance during visual search varies with retinotopical eccentricity (e.g., Carrasco and Yeshurun 1998; Meinecke and Donk 2002; Wolfe et al. 1998). The color or shape of the fixation spot identified the task type. A white circle (0.39–0.55° in diameter) was presented during the reaction-time task, whereas either a yellow circle or white square (0.39–0.55° in diameter) was presented during the delayed-response task. An inter-trial interval (300–2,000 ms) was inserted between the end of one trial and the beginning of the next.

Data collection

Single-cell activity was recorded by advancing an electrode into the lateral bank of the IPS, as verified by structural MRIs before the start of recordings. Once a neuron was isolated during recording sessions, we initially assessed the location of the receptive field in the memory-guided saccade task for all neurons studied. An isolated stimulus was presented at one of six evenly separated directions on an imaginary circle (eccentricity = 8.5°) because the target-location eccentricity was fixed at 8.5° during the visual search tasks. We manually adjusted these six directions so that one direction evoked the strongest activity. We then conducted the reaction-time and delayed-response visual search tasks.

RECORDING SITE

Before starting the present experiment, we specified the IPS location based on the response properties; the medial bank of the IPS tends to exhibit activity related to somatosensory stimuli, whereas the lateral bank exhibits visual and saccade-related responses (Barash et al. 1991b; Maimon and Assad 2006; Mountcastle et al. 1975). After specifying the IPS locus, we started to record neurons in the lateral bank of the IPS from a region, regarded as LIP, in which neurons exhibit
robust, spatially tuned responses during the delay period of a memory-guided saccade task (Barash et al. 1991a, 1991b; Colby et al. 1996; Gnadt and Andersen 1988; Shadlen and Newsome 2001). To ensure that our samples were in LIP rather than in area 7a, neurons recorded at a depth shallower than 3 mm from the dura surface were excluded from the present analysis (Andersen et al. 1990; Gifford and Cohen 2004; Linden et al. 1999). Neurons were typically recorded at a >5 mm depth from the dura surface (80.3%), and the majority of our neurons (54.1%) exhibited significant modulations in delay-period activity, as determined by whether activity 150–450 ms after the stimulus disappearance in the isolated-stimulus trials of the delayed-response task differed significantly according to target location (t-test, \( P < 0.05 \)). This fraction was comparable to that reported for LIP in previous studies (e.g., Barash et al. 1991a; Falkner et al. 2010; Maimon and Assad 2006).

To verify the recording positions, we acquired post-operative structural MRIs for both monkeys on a 0.2 Tesla open whole-body scanner (Signa Profile; General Electric, Milwaukee, WI, USA). The advantage of this low-magnetic field system is the reduced distortion of the original cortical structures (Petersch et al. 2004). We used a three-dimensional spoiled, gradient-recalled pulse sequence with the following parameters: \( TR = 29 \) ms, \( TE = 8.3 \) ms, flip angle = 40°, field of view = 16 cm, 256 x 256 matrix, 100 slices, voxel size = 0.63 x 0.63 x 1.0 mm. To improve image signal-to-noise ratio, we aligned and averaged two or three acquisitions during post-processing. Fig. 2 shows images from one monkey (monkey Y). We visualized five plastic tubes filled with an 84–87% glycerin solution (Glycerin P, Kenei, Tokyo, Japan) in the MRI to determine the plane and trajectory of the electrode penetrations (Fig. 2A). These tubes were embedded in a plastic base attached to the recording chamber so that one was at the center and the remaining four were arranged on the x–y coordinates (8 mm apart from the center) of the recording grid (Fig. 2B). The penetration sites on the brain surface were reconstructed based on the coordinates determined by the positions of
the reference tubes and recording grids. Fig. 2C shows coronal MRI s representing the most anterior to the most posterior recording positions. We similarly verified recording positions for another monkey (monkeys S) by acquiring post-operative MRI images. Thus, our samples were presumably recorded from LIP based on the physiological properties of the recorded neurons and verification by the MRIs.

Data analysis

Of the 122 neurons, datasets from 85 were examined for another purpose in our previous study (Nishida et al. 2013). Only neurons with visually responsive activity were used for the analysis in this study. A neuron was defined as exhibiting visually responsive activity when the activity occurring 50–150 ms after stimulus presentation was significantly greater than the pre-stimulus activity occurring 200–400 ms before the stimulus presentation ($t$-test, $P < 0.05$). When the datasets from the isolated-stimulus trials were obtained during fewer than five trials (18.9% = 23/122), the activity from the Light TA trials in the reaction-time visual search task were used to evaluate visually responsive activity. Unless otherwise indicated, data from only successful trials were analyzed.

Saccadic eye movements

Horizontal and vertical eye velocity signals were calculated by digitally differentiating horizontal and vertical eye position signals, respectively. Saccades were detected using a computer algorithm that identified the initiation and termination of each saccade based on a velocity-threshold criterion. Change in eye velocity was recognized as a saccade when it was greater than the threshold of 120°/s for at least 10 ms. Saccade initiation and termination were defined as the times at which the eye velocity was more and less than 30°/s, respectively. We excluded trials with unusually short or long
saccadic reaction times (more than two standard deviations [SDs] above or below the mean saccadic reaction time for correct trials under each trial condition; on average, 3.7% of trials were discarded).

SPIKE DENSITY FUNCTIONS

Spike density functions were constructed with 1-kHz resolution by convolving spike trains with a combination of growth (1-ms time constant) and decay (20-ms time constant) exponential functions that resembled a postsynaptic potential (Thompson et al. 1996). Because we wanted to remove the activity after saccade initiation, spikes occurring after saccade initiation during each trial were not included in the calculation. The responses for each neuron were calculated for durations starting from stimulus onset and continuing to the onset of the tenth longest reaction-time saccade under each condition. Normalized responses were calculated by subtracting the baseline activity (measured during a 200-ms period before stimulus onset) and dividing by the difference between the peak strength during all time points across stimulus conditions and that baseline strength.

Population-average responses were constructed by averaging the normalized responses across neurons.

In the TA trials of the reaction-time visual search task, the monkeys were not required to make a saccadic response. Hence, we used a bootstrap method to construct the virtual saccade-aligned responses for the TA trials using the saccadic reaction times derived from the TP trials. For each neuron, we randomly resampled the trial data, with replacement, from the TA trials so that the number of the samples matched the number of TP trials. The saccadic reaction times from the TP trials were assigned as the virtual reaction times for the TA trials, and the spike density function was calculated from these sampled TA trials. By repeating this procedure 1,000 times, we got the 1,000 spike density functions and averaged them to obtain the saccade-aligned response for each TA condition.
ACTIVITY IN THE TA TRIAL AS NEUTRAL BASELINE

We used the activity in the TA trial as "neutral" baseline to separately quantify the increase in target-related activity (target-related elevation) and the decrease in distractor-related activity (distractor-related reduction) in the TP trials. According to the generally accepted principle that lateral inhibitory interactions play a crucial role in forming target-discriminative activity (Deco et al. 2002; Itti and Koch 2000; Koch and Ullman 1985; Usher and McClelland 2001), we considered the activation in the TP and TA trials based on a conceptual network model with lateral inhibitory interactions. Fig. 1D illustrates why the activity in the TA trial can be regarded as neutral baseline.

Four color surface plots (Fig. 1Da–d) depict the possible LIP neuron activation map. For the sake of simplicity, we only consider the neuronal activations at the two locations where a singleton target appeared (filled arrowhead) and at the location diametrically opposite to that location (open arrowhead). Visual-area neurons exhibit stronger responses to a stimulus that differs from neighbor stimuli in some basic visual features than to a stimulus that is identical to surrounding stimuli (e.g., Kastner et al. 1999; Knierim and van Essen 1992; Nothdurft et al. 1999; Ogawa and Komatsu 2004; Schein and Desimone 1990). Therefore, in the TP trials (top row), the initial strength of LIP activations may be slightly stronger when a singleton target is presented in the neuron's receptive field (target-related activity; red outline in Fig. 1Da) as compared with when a distractor is presented in the receptive field (distractor-related activity; blue outline in Fig. 1Da). In contrast, in the TA trials (bottom row), because there is no feature contrast among the identical distractor stimuli, responses of the same strength may be evoked at all stimulus locations (black outline in Fig. 1Dc). As time elapses, under the TP condition, the distractor-related activations would be more strongly suppressed by the inhibitory influences due to the enhanced target-related activation (thick arrow in Fig. 1Db), whereas the target-related activation would be more weakly suppressed by those
influences due to the reduced distractor-related activation (thin dashed arrow in Fig. 1Db). Under the TA condition, although mutual inhibition would weaken the activations, the suppression strength would be intermediate relative to that under the TP conditions (thin arrows in Fig. 1Dd). As a result, the neutral activity under the TA condition would be intermediate between the target- and distractor-related activities under the TP condition (Fig. 1De). Thus, these considerations may justify the use of activation in the TA trial as "neutral" baseline to separate the target-related elevation and distractor-related reduction components in LIP activity.

TARGET DISCRIMINATION TIME

We identified the time point at which a single LIP neuron discriminated the target from distractors in terms of its activity (target discrimination time) using a modified version of the analytical method described in previous studies (e.g., Murthy et al. 2009; Ray et al. 2009). Using ROC analysis, we first computed the AUC between the distributions of the trial-based spike density functions derived from the target- and distractor-related activities. The AUC was calculated for successive 1-ms bins starting from stimulus onset and continuing to the onset of the tenth longest reaction-time saccade. The time sequence of the AUCs was fitted with a cumulative Weibull distribution function of the form $W(t) = \gamma - (\gamma - \delta) \exp[-(t/\alpha)^\beta]$, where $t$ is the time ranging from when the AUC attains its minimum value $\delta$ to when the AUC reaches its maximum value $\gamma$, $\alpha$ is the time at which the area under the ROC curve reaches the sum of 63.2% of its maximum, and $\beta$ is the slope. The target discrimination time was defined as the time when the curve fitted to the AUC reached a value of 0.7.

TARGET-RELATED ELEVATION AND DISTRACTOR-RELATED REDUCTION

The increase in target-related activity (target-related elevation) and the decrease in distractor-related activity (distractor-related reduction) in the TP trials relative to the neutral activity in the TA trials
were quantified using the area under receiver operating characteristic (ROC) curves (AUC) (Green and Swets 1966). For each trial, we computed the trial-based spike density function. Target-related elevation was evaluated by comparing target-related activity with neutral activity (target AUC), and distractor-related reduction was evaluated by comparing distractor-related activity with neutral activity (distractor AUC).

We quantified occurrence time at which substantial target-related elevation and distractor-related reduction emerged. At the population level, the time course of target and distractor AUCs was calculated by moving a 10-ms analysis window in 5-ms steps. The statistical significance of the difference between either target or distractor AUC and 0.5 was assessed using a t-test at $P < 0.01$, and the time point of the first significant window was considered the occurrence time of substantial neuronal modulations. When the significant difference did not continue for more than five consecutive steps ($\geq 25$ ms), target and distractor AUCs at such time points were not regarded as significant.

At the individual-neuron level, the occurrence time was defined as the time point at which the target AUC reached 0.6 or the distractor AUC reached 0.4 with the same method as that used for the target discrimination time (see above) except for the criterion level. Stimulus-aligned and saccade-aligned occurrence times were separately computed. For stimulus-aligned data, the AUC for each neuron were calculated for durations starting from stimulus onset and continuing to the onset of the tenth longest reaction-time saccade under each condition. For saccade-aligned data, the AUC for the same durations preceding saccade initiation was used.

It should be noted that although we examined the relationship between the strengths of target and distractor AUCs for individual neurons, comparisons of target-related elevation and distractor-related reduction are not available to the brain in real time because these two types of neural modulations do not occur in the activity of a single neuron at the same time. So, this analysis was performed under a previously proposed assumption (“antineuron”; Britten et al. 1992;
Thompson et al. 1996); that is, the activation of the neuron under study was compared with the activation of a hypothetical neuron that was identical except that its receptive field was located in the diametrically opposite direction.
RESULTS

Behavioral performance

Table 1 summarizes the behavioral results for the two monkeys under individual stimulus conditions. Average saccadic reaction times for correct responses in the TP trials were significantly delayed under the Dim condition relative to the Light condition for monkey Y \((t\text{-test; Dim–Easy vs. Light–Easy, } t_{70} = 48.0, P < 0.0001; \text{Dim–Hard vs. Light–Hard, } t_{70} = 26.7, P < 0.0001)\) and for monkey S \((\text{Dim–Easy vs. Light–Easy: } t_{50} = 36.9, P < 0.0001; \text{Dim–Hard vs. Light–Hard: } t_{50} = 18.8, P < 0.0001)\). Similar reaction-time prolongation was also observed under the Hard condition relative to the Easy condition for monkey Y \((\text{Dim–Hard vs. Dim–Easy, } t_{70} = 25.7, P < 0.0001; \text{Light–Hard vs. Light–Easy, } t_{70} = 30.6, P < 0.0001)\) and for monkey S \((\text{Dim–Hard vs. Dim–Easy, } t_{50} = 21.6, P < 0.0001; \text{Light–Hard vs. Light–Easy, } t_{50} = 22.8, P < 0.0001)\). Additionally, the proportion of correct responses was significantly greater under the Easy condition relative to the Hard condition for monkey Y \((\text{Light–Easy vs. Light–Hard, } t_{70} = 18.8, P < 0.0001; t_{70} = 13.6, P < 0.0001)\) and for monkey S \((\text{Light–Easy vs. Light–Hard, } t_{50} = 11.8, P < 0.0001; \text{Dim–Easy vs. Dim–Hard, } t_{50} = 7.8, P < 0.0001)\). Thus, saccadic reaction time was prolonged and the proportion of correct responses was reduced when stimulus luminance decreased and/or target–distractor similarity increased, reflecting changes in search difficulty (Bichot et al. 1999; Sato et al. 2001, 2003; Thompson et al. 2005; White and Munoz 2011).

Target-related elevation and distractor-related reduction in LIP activity during visual search

We recorded the activity of 122 well-isolated visually responsive neurons in LIP of two macaques (71 from monkey Y and 51 from monkey S) while they performed the reaction-time visual search task (Fig. 1). These neurons had sufficient trials under each stimulus–response condition (TP trials: 30–403 trials, mean ± SD = 99.5 ± 50.4 trials; TA trials: 16–204 trials, mean ± SD = 51.3 ± 26.3...
trials). Fig. 3A shows the activation of one representative LIP neuron in the Light–Easy TP and Light
TA trials aligned to stimulus onset (left panel) and to saccade onset (right panel). Data on the
target-related (red), distractor-related (blue), and neutral (black) activities were obtained from 70, 70,
and 73 trials, respectively. The ROC analysis to determine the timing at which this neuron reliably
discriminated the target from distractors revealed that the time of neuronal target discrimination
(AUC > 0.70) was 138 ms after stimulus onset (Fig. 3A, arrowhead above abscissa). After this time,
a difference between the target- and distractor-related activities gradually developed as the saccade
initiation time approached (Fig. 3A, right panel).

A key design feature of this study was the use of the activity during the TA trials as the
neutral reference activity. Comparison between target-related and neutral activity revealed that this
neuron increased its activity when the target appeared in the receptive field (red vs. black traces,
target-related elevation), whereas comparison between distractor-related and neutral activity
revealed that the activity decreased when a distractor appeared in the receptive field (blue vs. black
traces, distractor-related reduction), indicating that this cell exhibited both target-related elevation
and distractor-related reduction in its activity.

To quantitatively evaluate the strengths of target-related elevation and distractor-related
reduction in activity, we performed ROC analysis to compute target AUC (target-related vs. neutral
activities) and distractor AUC (distractor-related vs. neutral activities) by moving a 10-ms analysis
time bin in 5-ms steps (Fig. 3B). Target AUC became significant at 115 ms (110–120 ms bin) after
stimulus onset (permutation test, $P < 0.05$) and continually increased until the time of saccade onset.
On the other hand, distractor AUC became significant at 150 ms (145–155 ms bin) after stimulus
onset ($P < 0.05$) and gradually decreased in a push–pull manner relative to the target AUC increase.
Thus, the introduction of neutral activity enabled us to can successfully decompose target–distractor
discriminative activity (i.e., the difference between target-related and distractor-related activities)
into target-related elevation and distractor-related reduction. 

**Target-related elevation and distractor-related reduction in population responses**

Both target-related elevation and distractor-related reduction were observed at the population level. Fig. 4A shows the mean normalized spike density functions across all LIP neurons (n = 122) obtained from the Light–Easy TP and Light TA trials. The mean AUCs for target-related elevation and distractor-related reduction are shown in Fig. 4B. The statistical separation (absolute difference from 0.5) was greater for target AUC (~0.16) compared with distractor AUC (~0.07) in any time bin after 105 ms from stimulus onset (t-test, P < 0.01). This property was preserved for target AUC (~0.16) and distractor AUC (~0.08) when the activity was aligned at saccade onset.

At the level of the individual neuron, the degrees of target-related elevation and distractor-related reduction substantially varied across neurons. To illustrate this, the target and distractor AUCs measured during a 20-ms interval prior to saccade onset were plotted for each neuron (Fig. 4C). Overall, either target-related elevation or distractor-related reduction did not appear to form discrete clusters; instead, they were continuously distributed. Out of the 122 neurons, 27 (22.1%, back circles) exhibited significant response modulation for both target-related elevation and distractor-related reduction (permutation test, P < 0.05), 48 (39.3%, gray circles) had significant modulations for only target-related elevation, and only five (4.1%, white circles) had significant modulations for only distractor-related reduction. The ratios of these three types of neurons were not even. The ratio of the last type of neuron was significantly smaller relative to that of the former two types of neurons (McNemar's test, P < 0.0001). Very few LIP neurons exhibited either significant target-related reduction (n = 2 for target-related reduction only, upward gray triangles; n = 1 for target-related reduction with distractor-related reduction, downward black triangle) or significant distractor-related elevation (n = 1, white upward triangle) in their activity. The remaining 38 (31.1%,
crosses) neurons had no significant target-related or distractor-related modulation in their activity. Thus, our results show that both target-related elevation and distractor-related reduction were observed at the population response level, but the relative strengths of elevating and reducing modulations substantially varied across LIP neurons.

The main purpose of the present study was to investigate how the elevating and reducing modulations emerge in target–distractor discriminative activity of LIP neurons during visual search. To this end, it was appropriate to focus on the activity of those LIP neurons that exhibited sufficient target–distractor discrimination (AUC > 0.7) in their activity. Of the 122 neurons, 59 fulfilled this criterion and were the primary foci of the following analyses. Fig. 4D–F shows the results when the same analyses (Fig. 4A–C) were conducted for these 59 neurons. Aside from their modulation strengths, their basic response profiles were essentially the same as those of the entire sample of 122 neurons. Comparison of the results in Fig. 4F with those in Fig. 4C confirmed that the selected 59 neurons did not form a specific discrete cluster, but rather were a part of the continuous distribution of all 122 neurons, indicating that the criterion used for neuron selection was not essential for obtaining the present results.

The results illustrated in Fig. 4 were commonly observed under the other stimulus conditions. Fig. 5A–F shows the results from the same 59 LIP neurons during the Light–Hard TP and Light TA trials (Fig. 5A and B), the Dim–Easy TP and Dim TA trials (Fig. 5C and D), and the Dim–Hard TP and Dim TA trials (Fig. 5E and F). The visual response onset was around 50 ms under the Light conditions (Light–Easy and Light–Hard), but this was delayed and was around at 100 ms under the Dim condition (Dim–Easy and Dim–Hard). The earlier onset of LIP activity in response to a brighter stimulus is consistent with the results of our previous study (Tanaka et al. 2013). Following the response onset, the population responses evolved to discriminate the target from distractors. The difference in response strength between target- and distractor-related activities was
evident under the Easy condition compared with the Hard condition. Importantly, irrespective of these differences in response profiles, both target-related elevation and distractor-related reduction were consistently observed at the population level across stimulus conditions. Fig. 5G and H indicates target and distractor AUCs, respectively, measured during a 20-ms interval prior to saccade initiation under the four stimulus conditions. Comparison across stimulus conditions revealed that the strength of the target-related elevation and distractor-related reduction under the Easy (Light–Easy and Dim–Easy) conditions were significantly greater than those under the Hard (Light–Hard and Dim–Hard) conditions (t-test with Bonferroni’s correction, \( P < 0.0001 \)). Table 2 summarizes the number of neurons that exhibited significant target-related elevation and/or distractor-related reduction. We observed that although the majority of neurons exhibited significant response modulations for both target-related elevation and distractor-related reduction (20.3–61.0%; permutation test, \( P < 0.05 \)) or for only target-related elevation (28.8–62.7%), a small proportion of neurons had significant modulations for only distractor-related reduction (1.7–6.8%). This result again indicates that the ratio of the last type of neuron was significantly smaller relative to that of the former two types of neurons (McNemar’s test, \( P < 0.001 \)).

**Endogenous factors can evoke both target-related elevation and distractor-related reduction in LIP activity**

Target-absent trials occasionally resulted in false-alarm errors in which the monkeys made a saccade to one of the distractors before the trial ended. A previous study reported that frontal eye field (FEF) neurons exhibit increasing or decreasing activity when monkeys make such false-alarm errors in search trials (Heitz et al. 2010; Thompson and Schall 2000) or even in target-absent catch trials (Thompson et al. 2005). Does such increasing and decreasing activity evoked by endogenous factors in the absence of exogenous factors (i.e., a singleton target) also involve elevating and reducing
modulations? To address this issue, we compared the modulation in the activity of LIP neurons in the TA trials when the distractor that was the false-alarm saccade goal was located in the receptive field with that when it was located at the location opposite the receptive field. Of 59 neurons studied, 48 and 37 completed the criterion number of trials (≥10 trials for either saccade direction) for the Light TA and Dim TA conditions, respectively. Fig. 5I–J shows the pooled average activity in the correct and false-alarm trials under the Light TA condition. The results demonstrate that greater and lesser activity relative to neutral activity did indeed occur even though a singleton target was not presented in a given search array. Similar results were observed under the Dim TA condition (Fig. 5K–L). These results suggest that elevating and reducing modulations can be induced not only by exogenous factors but also by endogenous factors.

**Correlation between target-related elevation and distractor-related reduction**

As shown in Fig. 5G and H, there was a trend for stronger distractor-related reduction to be accompanied by stronger target-related elevation, whereas weaker distractor-related reduction tended to be accompanied by weaker target-related elevation. This raises the possibility that the magnitude of distractor-related reduction may vary in association with that of target-related elevation. To test this possibility, we compared the population-averaged values of target and distractor AUCs derived from sequential 10-ms time windows during the period in which either target and/or distractor AUCs were significant (t-test, P < 0.01). Of 59 neurons studied, 34 had sufficient neuronal data (≥10 trials) under the both TA conditions (false-alarm trials) in addition to the four TP conditions and were used for this analysis.

Fig. 6A–B shows the distribution of the data points of target and distractor AUCs across conditions, aligned by stimulus onset (Fig. 6A) and saccade onset (Fig. 6B). In both cases, target and distractor AUCs were significantly correlated (Pearson’s correlation: stimulus aligned, $r = -0.84$, $P <$
0.0001; saccade aligned, \( r = -0.83, P < 0.0001 \). Similar results were observed even when we
performed a correlation analysis on each stimulus condition (Pearson's correlation: stimulus aligned,
\( r = -0.96--0.50; P < 0.05 \); saccade aligned, \( r = -0.98--0.66; p < 0.0005 \)). The fact that the slopes of
both regression lines were negative and greater than -1 under all stimulus conditions (regression
slope: stimulus aligned, -0.63--0.30; saccade aligned, -0.67--0.23) indicates that the statistical
strength of target-related elevation was stronger than that of distractor-related reduction. Similar
results were observed when the relationship between target-related elevation and distractor-related
reduction was examined using the normalized firing rate instead of the AUC (Pearson's correlation:
stimulus aligned, \( r = -0.81, P < 0.0001 \); saccade aligned, \( r = -0.86, P < 0.0001 \); slope of regression
line: stimulus aligned, -0.36; saccade-aligned, -0.36).

To confirm the above results at the single-neuron level, we also compared target and
distractor AUCs measured in a 20-ms period prior to saccade initiation. For each of the same 34
neurons, the six pairs of target and distractor AUCs were computed (not shown). Figure 6D and E
shows the distributions of the slopes of the linear regression lines (line segments in Fig. 6C) and the
correlation coefficients calculated for the individual neurons, respectively. On average, both the
slope values and the correlation coefficients were significantly less than 0 (slope = -0.31 ± 0.50
\([\text{mean } \pm \text{SD}], t\)-test, \( t_{32} = -2.90, P < 0.01 \); Pearson’s \( r \) values = -0.26 ± 0.49, \( t_{32} = -3.03, P < 0.005 \)).
Similar results were also observed when the relationship between target-related elevation and
distractor-related reduction was examined in terms of the normalized firing rate during a 20-ms
interval prior to saccade initiation. Both the slope values of the regression line and the correlation
coefficients were significantly less than 0 (slope = -0.20 ± 0.17, \( t\)-test, \( P < 0.05 \); Pearson’s \( r \) values = -0.29 ± 0.45, \( P < 0.05 \)). Thus, these results indicate that, on average, the magnitude of
target-related elevation covaries with that of distractor-related reduction in LIP activity, raising the
possibility that elevating modulations act cooperatively with reducing modulations to produce the
target-discriminative activity.

Occurrence timing of substantial target-related elevation and distractor-related reduction

So far, we focused on the magnitude of and relationship between target-related elevation and distractor-related reduction. Next, we examined the temporal properties of these modulations in target-discriminative activity. First, we compared the times at which substantial target-related elevation and distractor-related reduction in LIP population activity occurred. The occurrence time in a population was defined as the time at which the population-averaged target or distractor AUCs, first significantly differed from 0.5 (see Materials and Methods). The results, summarized in Fig. 7A and B, revealed that the occurrence time of substantial neural modulation was 20–185 ms earlier for target-related elevation (90–160 ms after stimulus onset; 105–135 ms before saccade onset) than for distractor-related reduction (130–345 ms after stimulus onset; 30–80 ms before saccade onset) under all four TP conditions.

The earlier occurrence of target-related elevation was also observed at the single-neuron level. The occurrence time for individual neurons was defined as the time point at which the target AUC reached 0.6 or the distractor AUC reached 0.4 with the same method as that used for the target discrimination time except for the criterion level (see Materials and Methods). Of 59 neurons studied, we could determine the occurrence times for both target-related elevation and distractor-related reduction aligned to stimulus onset for 29, 8, 27, and 5 neurons and aligned to saccade onset for 22, 5, 22, and 7 neurons under the Light–Easy, Light–Hard, Dim–Easy, and Dim–Hard TP conditions, respectively. The neuronal data under the Light–Hard and Dim–Hard conditions were not analyzed because of the small sample. Fig. 7C and D shows the results under the Light–Easy and Dim–Easy conditions. The mean occurrence time for target-related elevation was significantly earlier than that for distractor-related reduction under both the Light–Easy condition (stimulus aligned, mean ± SD =
132.6 ± 28.2 ms vs. 169.0 ± 32.2 ms; saccade aligned, −52.7 ± 22.9 ms vs. −31.9 ± 27.8 ms; \( t \)-test, \( P < 0.005 \)) and the Dim–Easy condition (stimulus aligned, 149.4 ± 33.2 ms vs. 202.3 ± 42.3 ms; saccade aligned, −73.8 ± 26.6 ms vs. −48.0 ± 30.9 ms; \( t \)-test, \( P < 0.01 \)).

The earlier occurrence of target-related elevation was not explained by the difference in the saccadic reaction times between when the monkeys made a saccade toward the receptive field (target-related activity) and when they made a saccade away from the receptive field (distractor-related activity). In most cases (Light–Easy condition: 19/29 = 65.5%; Dim–Easy condition: 21/27 = 77.8%), the reaction times were not significantly different between the saccade directions (\( t \)-test, \( P > 0.05 \)) or significantly earlier when the monkeys made saccades away from the receptive field (\( t \)-test, \( P < 0.05 \)). Thus, the earlier occurrence of elevating modulations compared with reducing modulations was not due to the difference in saccadic reaction time.

### Persistent development of target-related elevation and distractor-related reduction

As another temporal property, we next examined the persistence of the development of elevating and reducing modulations. Target-related elevation and distractor-related reduction in the population average responses (Figs. 4 and 5) developed monotonically and gradually during the course of visual search under all stimulus conditions (Spearman’s correlation, \( \rho = 0.93–1.00 \) for target-related elevation, \( \rho = −0.93–−0.58 \) for distractor-related reduction, \( P < 0.0001 \)). To determine whether this was the case at the level of individual neurons, we computed the time sequences of target and distractor AUCs by moving a 10-ms analysis window in 5-ms steps from stimulus onset or saccade onset. Fig. 8 shows the time courses of target AUC (Fig. 8A–C) and distractor AUC (Fig. 8D–F) in terms of the activity of each of the 59 LIP neurons under the Light–Easy TP condition. A major portion of LIP neurons exhibited a significant monotonic increase in target AUC (stimulus aligned, 94.9%; saccade aligned, 91.5%; Spearman’s correlation, \( \rho > 0, P < 0.05 \)) and a significant decrease
in distractor AUC (stimulus aligned, 72.9%; saccade aligned, 69.5%; \( \rho > 0, P < 0.05 \)). On average, the mean correlation coefficients (Spearman’s \( \rho \)) for target AUC were significantly greater than zero (stimulus aligned, mean ± SD = 0.69 ± 0.27; saccade aligned, 0.83 ± 0.19), and those for distractor AUC were significantly less than zero (stimulus aligned, −0.48 ± 0.33; saccade aligned, −0.58 ± 0.35) (\( t \)-test, \( P < 0.0001 \)). This property was also observed under the other three TP conditions (target AUC: stimulus aligned, Spearman’s \( \rho = 0.52–0.71, P < 0.0001 \); saccade aligned, 0.72–0.77, \( P < 0.0001 \); distractor AUC: stimulus aligned, −0.44–−0.16, \( P < 0.05 \); saccade aligned, −0.63–−0.39, \( P < 0.0001 \)).

Similar results were observed even when the same analysis was conducted using the normalized firing rate instead of the AUCs for the Light–Easy condition. The mean correlation coefficients were significantly greater than zero for target-related elevation (stimulus aligned, mean ± SD = 0.71 ± 0.26; saccade aligned, 0.84 ± 0.19) and less than zero for distractor-related reduction (stimulus aligned, −0.47 ± 0.31; saccade aligned, −0.59 ± 0.35) (\( t \)-test, \( P < 0.0001 \)). Thus, these results suggest that target–distractor discriminative activity is composed of the monotonically developing elevating and reducing components in LIP activation. Such a monotonic development is repeatedly reported in decision-related activity in LIP during a moving-dot direction-discrimination task (Churchland et al. 2008; Roitman and Shadlen 2002), suggesting that the monotonically developing modulation might be a common property of LIP neurons across perceptual discrimination tasks.

**Relationship with target discrimination time**

Hitherto, our results show that distractor-related reduction in LIP activity was weaker compared with target-related elevation (Figs. 5 and 6). An important question is whether such weak reducing activity actually has a functional contribution to producing neuronal target discrimination in visual
search. To provide insight into this issue, we examined the relationship between target discrimination time and the strength of either target-related elevating or distractor-related reducing activity across conditions and neurons. Of the 59 neurons, 59, 24, 46, and 20 neurons (149 cases in total) exhibited substantial differences between target-related and distractor-related activities (AUC > 0.7) under the Light–Easy, Light–Hard, Dim–Easy, and Dim–Hard conditions, respectively (mean of target discrimination time: 148, 213, 176, and 274 ms, respectively). The strengths of elevating and reducing modulations were quantified by target and distractor AUCs measured in a 20-ms period prior to saccade initiation. To make an analysis across conditions and neurons, the target discrimination time and AUCs were separately normalized by subtracting the mean value and dividing by the standard deviation within each of conditions (z-score transformation), and were pooled across all cases (n = 149). The z-scored target discrimination time was negatively correlated with the z-scored target AUC (Fig. 9A; Pearson's correlation, \( r = -0.33, P < 0.0001 \)) and positively correlated with the z-scored distractor AUC (Fig. 9B; \( r = 0.24, P < 0.005 \)), indicating that on average target discrimination time became earlier with increase in the strength of not only target-related elevation but also distractor-related reduction. Similar results were obtained even when we performed a partial correlation analysis between target discrimination time and target AUC factoring out the effect of distractor AUC (\( r = -0.35, P < 0.0001 \)), and that between target discrimination time and distractor AUC factoring out the effect of target AUC (\( r = 0.27, P < 0.001 \)). Thus, these results suggest that distractor-related reduction as well as target-related elevation may contribute to accelerating the timing of neuronal target discrimination during visual search.

**Target discrimination in the reaction-time and delayed-response tasks**

In this study, we also recorded the responses of LIP neurons in the delayed-response visual search tasks. A previous study of LIP reported that decision process in a delayed-response
motion-discrimination task may terminate when the accumulated information reaches a critical level, even when the termination is long before the end of stimulus (Kiani et al. 2008). To test whether this was the case in our samples, we compared the neuronal target discrimination between the reaction-time and delayed-response tasks. Of the 59 neurons under study, 42 had sufficient neuronal data (≥5 trials for either target location) in the delayed-response task. Fig. 10A shows the mean spike density functions across the 42 neurons aligned to stimulus array presentation under the Light–Easy condition in the two tasks. The baseline activity measured during a 200-ms period before array presentation was significantly higher in the reaction-time task (black traces, mean = 19.0 Hz) compared with the delayed-response task (gray traces, 14.1 Hz) (t-test, \(P < 0.0005\)). However, the activity in the two tasks seems to show a small difference in the timing at which target-related activity (solid traces) was separated from distractor-related activity (dashed traces). To quantitatively examine this, we calculated target discrimination time (see Materials and Methods) for individual neurons in each of the two tasks. Of the 42 neurons, 35 substantially discriminated the target from the distractor in their activity (AUC > 0.7) in both tasks. We found that although the mean target discrimination times were significantly different between the two task conditions (t-test, \(P < 0.01\), target discrimination time in the delayed-response task (mean = 153 ms) was very close to that in the reaction-time task (mean = 143 ms) and occurred long before the end of visual stimulus (cue stimulus period = 500 or 700 ms) (Fig. 10B), suggesting that target discrimination processes may be governed by similar neural mechanisms regardless of whether the monkey or the environment determines the viewing time.

**Effects of fixation-related activity**

Previous studies reported the existence of tonically active neurons during active fixation in FEF and the superior colliculus (SC) (Bizzi 1968; Bruce and Goldberg 1985; Burman and Bruce 1997;
Everling et al. 1998; Izawa et al. 2009; Munoz and Wurtz 1993; Suzuki and Azuma 1977). Similar fixation-related activity was found in LIP (Ben Hamed and Duhamel 2002). If such neurons were included in our samples, the distractor-related activity in the TP trials would have been weaker than the activity in the TA trials due to fixation cessation rather than active suppressive modulations. To assess this possibility, we used a conventional method to test whether our samples exhibited fixation-related activity (Izawa et al., 2009; Suzuki and Azuma, 1977). A neuron was defined as having fixation-related activity when its mean firing rate during an 800-ms fixation period before stimulus onset was >2 SDs above the activity during the last 300-ms period of the inter-trial interval. For each neuron, trials were pooled across the four TP conditions (177–2,025 trials, mean = 610 trials, SD = 318 trials) and examined. We found that only four of 59 neurons exhibited fixation-related activity. Even after excluding these four neurons, distractor AUCs in the population responses during a 20-ms period prior to saccade onset were significantly smaller than zero under all stimulus conditions (t-test, \( P < 0.0001 \)). Thus, the distractor-related reduction observed in this study is unlikely to be explained by fixation-related activity.

**Effects of saccade-burst activity**

As mentioned above, the magnitudes of target-related elevation and distractor-related reduction reached their maximum values prior to saccade initiation. One might argue that these neural modulations play a role in saccade generation rather than target selection. To provide insight into this issue, we separated the neurons under study into two groups according to whether saccade-burst activity was exhibited and examined neural modulations separately for each group. Manifestation of saccade-burst activity was examined using datasets from the isolated-stimulus trials during the delayed-response visual search task. A neuron was defined as exhibiting saccade-burst activity if its activity during a 100-ms interval prior to saccade initiation was significantly greater than its
preceding delay-period activity during a 100-ms interval starting 300 ms before the initiation of a saccade ($t$-test, $P < 0.05$) (Lawrence et al. 2005).

Of the 59 neurons studied, 50 had a sufficient number of trials ($\geq 5$ trials) in the isolated-stimulus trials of the delayed-response visual search task. Of these 50 cells, 20 and 30 were verified as neurons with and without saccade-burst activity, respectively. We evaluated target and distractor AUCs during a 20-ms interval prior to saccade initiation separately for each group (Table 3). The mean value of either the target or the distractor AUC was not significantly different between these groups under all stimulus conditions ($t$-test, $P > 0.05$), suggesting that elevating and reducing modulations are not associated with the manifestation of saccade-burst activity. Thus, it is unlikely that these modulations are linked with saccade generation rather than target selection.

**Computer simulations**

Model studies have posited the importance of lateral inhibitory interactions to produce target-distractor discriminative activity (Deco et al. 2002; Itti and Koch 2000; Koch and Ullman 1985; Usher and McClelland 2001). The lateral inhibition may be one of possible mechanisms underlying elevating and reducing modulations observed in this study. To illustrate that a simple network model with lateral inhibitory interactions can well reproduce our present results, we performed computer simulations using the competitive accumulator model proposed by Usher and McClelland (2001) (Fig. 11A). This model was recently used to explain the neural mechanisms underlying visuomotor transformation during visual search (e.g., Purcell et al. 2010, 2012; Schall et al. 2011). In this model, we consider only a simple neural network with two sets of input and accumulator neurons, but the simulation results would be essentially the same if the number of input and accumulator neurons were increased. Input units ($u_1$ and $u_2$) correspond to visual-area neurons with different receptive fields, and accumulator units ($x_1$ and $x_2$) correspond to visuomotor-area (e.g.,
LIP) neurons with the receptive fields co-centered with those of $u_1$ and $u_2$, respectively. Visual
signals from the input units propagate to the accumulator units, and the accumulator units are
mutually inhibited (synaptic strength, $\beta$). Although each accumulator unit is itself a perfect integrator,
it performs like a leaky integrator because of signal leakages via self-inhibition (synaptic strength, $k$).
Lateral inhibitions mutually inhibit the activity of the two accumulator units. Thus, these
connections can form a loop circuit in the network, suggesting that the accumulator units can receive
feedback influences via this loop.

Fig. 11B shows the visual signals from the input units ($u_1$ and $u_2$) to the accumulator units
($x_1$ and $x_2$). Under the TP condition, a singleton target was presented in the receptive field of one
input unit and a distractor was presented in the receptive field of the other input unit, whereas under
the TA condition, the same distractors were presented in the receptive fields of both units.
Visual-area neurons exhibit stronger activity when there is a feature contrast between the receptive
field stimulus and the surround stimuli than when there is no contrast (Allman et al. 1985; Kastner et
al. 1999; Knierim and van Essen 1992; Nothdurft et al. 1999; Li et al. 2000; Ogawa and Komatsu
2004; Schein and Desimone 1990). Such neuronal modulations increase after the response peak but
soon reach a steady-state plateau level (e.g., Burrows and Moore 2009; Knierim and van Essen
1992). To reproduce this response property, we set the model parameters so that the initial strength
of the visual signals was the same but the steady-state strength was stronger when a singleton target
appeared in the receptive field ($u_{\text{target}}$, solid curve in Fig. 11B) than when a non-singleton distractor
appeared in the receptive field ($u_{\text{distractor}}$, dashed curve). A decaying function was used to mimic
visual signals from visual-area neurons (Standage and Paré 2011; Trappenberg et al. 2001; Wong et
al. 2007).

Fig. 11C–D shows the output responses of the accumulator units ($x_1$ and $x_2$). If lateral
inhibitory interactions existed ($\beta = 0.12$, Fig. 11C), the response would be stronger when the target is
presented ($x_{\text{target}}$, solid black trace) but weaker when a distractor is presented ($x_{\text{distractor}}$, dashed black trace) relative to when only distractors are presented ($x_{\text{neutral}}$, solid gray trace) in the receptive field. The basic properties of the output responses were similar to our observations. First, although distractor-related reduction did occur, its occurrence was weaker and slower than that of target-related elevation (Figs. 6 and 7). This may be natural because suppressive influences on distractor-related activity via lateral inhibitory interactions would be initially evoked by increasing target-related activity but not vice versa. Second, the development of target-related elevation and distractor-related reduction was monotonic (Fig. 8). Importantly, if there were no lateral inhibitory interaction ($\beta = 0$, Fig. 11D), the model could produce neither distractor-related reduction nor the persistent development of target-related elevation, assuming the importance of lateral inhibitory interactions. Thus, the simple network model with lateral inhibitory interactions could reproduce the observed properties in elevating and reducing modulations in activity.

A simulation with this network model also provided important insights into the relationship between our findings and previous reports on lateral-inhibitory effects in LIP neurons. Falkner et al. (2010) have demonstrated that a saccade plan to locations outside the receptive field can suppress the response to the distractor stimulus flashed in the receptive field (e.g. Fig. 2A in Falkner et al. 2010), and this suppressive influence seems to start immediately after the onset of distractor responses, seemingly inconsistent with our observation (Figs. 4 and 5). However, an important point is that in their task, a saccade target was presented 500 ms before the appearance of a distractor stimulus. Under such a task sequence, the inhibitory influence from the target activation may substantially propagate to the distractor location at the timing of distractor onset, and this would produce the evident reduction in the initial distractor responses. To demonstrate this, we additionally performed the computer simulation using the same network model shown in Fig. 11A. Figure 11E illustrates the visual signals from the input units (correspond to visual area neurons) when the target
(black trace) and distractor (gray trace) stimuli were presented. This stimulus presentation sequence mimicked that of Falkner et al. (2010). Figure 11F illustrates the output signals from the accumulator units (corresponding to LIP neurons). The initial response to the distractor was suppressed when a target was presented in advance (solid gray trace) relative to when a target was not presented (dashed gray trace). Thus, our network model with lateral inhibitory interactions can reproduce not only the findings in this study but also the observation of Falkner et al. (2010). This suggests that the difference in the occurrence timing of reducing activity in our and Falkner's studies is due to the differences in the stimulus-presentation sequence and the task procedures.
DISCUSSION

By using the activity derived from target-absent trials as neutral activity, we successfully decomposed the target-distractor discriminative activity into target-related elevation and distractor-related reduction components. To our knowledge, this is the first study to separately investigate the response profiles of target-related elevation and distractor-related reduction components in neuronal activity during visual search. We found that most LIP neurons discriminated the target by the combination of target-related elevating and distractor-related reducing modulations or only by elevating modulations in their activity. However, very few neurons discriminated the target only by distractor-related reducing modulations (Fig. 4), suggesting that the elevating and reducing modulation processes are not independent but act cooperatively in networks that are responsible for the target-distractor discrimination in visual search. Furthermore, our results revealed the various response properties in the modulations of LIP neurons: the strengths of elevating and reducing modulations were highly correlated (Fig. 6), the occurrence of substantial target-related elevation was earlier than did distractor-related reduction (Fig. 7), and these modulations monotonically developed as saccade initiation time approached (Fig. 8). These properties could be reproduced by a neural network model with lateral inhibitory interactions (Fig. 10). In addition, the strengths of both elevating and reducing modulations were linked with the time of neuronal target discrimination (Fig. 9), suggesting that these modulations play a role in generating target-discriminative activity during visual search. Thus, our findings can provide insight into the target discrimination process during visual search.

Target-absent trial activity as neutral baseline reference

In the present study, TP trials were interleaved with TA trials. The behavioral requirements of the trials were quite different: monkeys had to make a saccade to the singleton target in TP trials but
maintain fixation until the trial ended in TA trials. Therefore, one might argue that the monkeys employed different task/cognitive sets between the two trial types. Indeed, the fixation-period activity of LIP neurons can vary with different task/cognitive sets (e.g., Herrington and Assad 2009, 2010; Stoet and Snyder 2004). If this were the case in this study, it would not have not been appropriate to regard TA trial activity as neutral activity. However, this possibility is unlikely for the following reasons. The monkeys were not able to anticipate whether the upcoming trial was a TP or TA trial because both types of trials were quasi-randomly interleaved with no cue stimulus. Nevertheless, it is still possible that the monkeys quickly altered their task/cognitive set after seeing a presented array stimulus. A previous study showed that it takes at least 160–230 ms for LIP neurons to alter the activity associated with a change in task set after cue stimulus presentation (Herrington and Assad 2009). However, the present results revealed that significant target-related elevation/distractor-related reduction at the population level started within 90–130 ms after stimulus presentation (Fig. 7A, Light–Easy or Dim–Easy TP trials). This timing is too early to be explained by the effects of a task-set change after a stimulus presentation. Together, we think that the TA trial activity was an appropriate neutral activity during visual search.

Possible neural mechanisms underlying elevating and reducing modulations

Previous model studies have emphasized that lateral inhibition plays a key role in producing target-discriminative activity during visual search (Deco et al. 2002; Koch and Ullman 1985; Itti and Koch 2000; Usher and McClelland 2001). Indeed, the currently observed properties of neuronal modulations could be simulated using the simple network model with lateral inhibitory interactions (Fig. 10). Furthermore, previous neurophysiological studies found lateral inhibitory effects in the activity of visuomotor-area neurons (LIP: Falkner et al. 2011; FEF: Cavanaugh et al. 2012; Schall et al. 1995a, 2004; SC: Dorris et al. 2007; Munoz and Istavan 1998). Falkner et al. (2010)
demonstrated that the LIP neuron response to a target inside the receptive field is strongly suppressed when a distractor stimulus flashes outside the receptive field. Suppression of LIP responses is spatially wide ranging (12–35°), raising the possibility that the currently observed distractor-related reduction is evoked by lateral inhibitory interactions even though the target appears at a location distant (17°) from the receptive field.

Alternatively, another hypothesis could explain the distractor-related reduction observed in this study. In the present task, because TP and TA trials were randomly interleaved with no explicit instruction, the monkeys had to search for the target even in TA trials. Under this experimental condition, the activity after exposure to an array stimulus in TA trials would be elevated as long as an array stimulus remains. Such facilitation in activity could be expected values of stimuli (Mirpour and Bisley 2012) or motor intention (Snyder et al. 1997). On the other hand, the activity in TP trials might drop to baseline levels once the monkey makes the decision to make a saccade away from the receptive field, positing that the reduction in response to a distractor stimulus could be explained as a consequence of a saccade being generated to a stimulus outside of the receptive field.

Although we have no direct evidence to determine which of the two hypothesizes is more plausible to explain the reduction of distractor-related activity, the present findings seemingly support the former hypothesis (lateral inhibitory interactions). If the latter hypothesis (activity drops to a baseline level after a decision making) were the case, the amount of the activity reduction should be invariant for stimulus conditions in visual search. However, the present results revealed that the strength of distractor-related reduction significantly varied across stimulus conditions (Fig. 5H).

Furthermore, if the latter hypothesis were the case, the strength of the distractor-related reduction should be independent of that of target-related elevation. But there was a significantly correlation between the strength of target-related elevation and that of distractor-related reduction (Fig. 6).

Taking together, the lateral inhibition mechanism seems to be more plausible to explain the present...
Under the assumption of the lateral inhibitory function, we could speculate on the neural architecture underlying visual target discrimination in the brain. The present study revealed that the majority of LIP neurons exhibited target-related elevation accompanied by distractor-related reduction or target-related elevation only, whereas a very small population exhibited distractor-related reduction only (Fig. 4C). The ratio of the last type of neuron was significantly smaller relative to the former two types of neurons, indicating that distractor-related reduction tends to emerge in the activity of those neurons that exhibit target-related elevation in their activity. This suggests that suppressive influences may particularly propagate to those neurons whose activity exhibits target-related elevating modulations. The observed cell-to-cell variability of elevating and reducing modulations of LIP neurons in a visual search paradigm may be consistent with the recent report that even though individual LIP neurons exhibit diverse response properties in a motion direction-discrimination paradigm, the aggregate response can reflect the temporal accumulation of sensory evidence (Meister et al. 2013).

Notably, the explanation based on lateral inhibition do not assume that distractor-related reducing modulations are mediated by direct inhibitory connections within LIP. Considering that visuomotor areas are tightly connected, i.e., LIP and FFE are reciprocally connected, both send descending inputs into the SC, and neural signals from the SC are fed back to the FEF via the thalamus (Andersen et al. 1990; Blatt et al. 1990; Ferraina et al. 2002; Lewis and Van Essen 2000; Paré and Wurtz 1997; Schall et al. 1995b; Sommer and Wurtz 1998, 2006), it is possible that lateral inhibitory effects are mediated by indirect pathways via other brain areas.

**Roles of distractor-related reduction in target discrimination**

A recent human neuroimaging study (Seidl, et al. 2012) measured BOLD signals in response to
natural scenes that could contain objects that were currently relevant (target), previously but not presently relevant (distracter), and never relevant (neutral). This experimental design was conceptually similar to that used in the present study. The authors demonstrated that information about the target objects at the level of high-order visual cortex was increased relative to the neutral objects, whereas information about the distracter objects was reduced relative to the neutral objects, and concluded that such active suppression may serve to prevent the erroneous selection of, or interference from, objects that are no longer relevant to ongoing behavior. The present findings also support this view and provided neuronal evidence at the level of spiking activity.

Our results demonstrated that the strength of distractor-related reduction was correlated with the time of neuronal target discrimination across neurons (Fig. 9B), suggesting that distractor-related reduction has a functional role in accelerating target discrimination processes during visual search. Nonetheless, one might argue that the occurrence time of distractor-related reduction, which we observed especially under the Hard conditions, is too late to functionally contribute to target discrimination: the occurrence time at the population level was 45–80 ms and 30–35 ms before saccade onset under the Easy and Hard conditions, respectively (Fig. 7B). Indeed, using a reaction-time motion discrimination paradigm, Shadlen and colleagues reported that once ramp-like activity in LIP has reached a fixed threshold level, the decision process is complete, and the monkey initiate saccades ~50 ms later (Churchland et al. 2009; Roitman and Shadlen 2002). Additionally, previous studies showed that electrical stimulation in LIP elicits saccadic eye movements, and latency ranged from 25 to 50 ms at the majority of stimulation sites (Constantin et al. 2007; Shibutani et al. 1984; Thier and Andersen 1998). One possible explanation for the late occurrence of distractor-related reduction under the Hard conditions is that such late suppressive effects in LIP may reflect the modulation derived from other cortical areas. A recent study showed that neurons in the dorsolateral prefrontal cortex (DLPFC) exhibited stronger suppression of
distractor-evoked responses compared with LIP neurons when goal-directed spatial attention was
directed toward a target location in advance, suggesting that DLPFC can produce suppressive effects
on distractor-related activity (Suzuki and Gottlieb 2012). We speculate that, in less efficient searches
(Hard conditions), distractor-related reduction may be dominantly produced in other brain areas
(such as DLPFC), and the influences from those areas may be propagated to LIP with a delay as
goal-directed attention, resulting in the late occurrence of distractor-related reducing modulations in
LIP activity (30–35 ms before saccade). In contrast, in efficient searches (Easy conditions),
distractor-related reduction may reflect stimulus-driven suppressive effects produced by neural
circuits involving LIP and other visuomotor areas, leading to the early occurrence of reduction
(45–80 ms before saccade).
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DISCLOSURES

The authors declare no competing financial interests.
REFERENCES


Dorris MC, Olivier E, Munoz DP. Competitive integration of visual and preparatory signals in the


Herrington TM, Assad JA. Temporal sequence of attentional modulation in the lateral intraparietal area and middle temporal area during rapid covert shifts of attention. J Neurosci 30: 3287–3296,


Li W, Thier P, Wehrhahn C. Contextual influence on orientation discrimination of humans and...


Nishida S, Tanaka T, Shibata T, Ikeda K, Aso T, Ogawa T. Discharge-rate persistence of baseline


Sato TR, Watanabe K, Thompson KG, Schall JD. Effect of target–distractor similarity on FEF visual

Schall JD, Hanes DP, Thompson KG, King DJ. Saccade target selection in frontal eye field of

Schall JD, Morel A, King DJ, Bullier J. Topography of visual cortex connections with frontal eye
field in macaque: convergence and segregation of processing streams. J Neurosci 15:
4464–4487, 1995b.

Schall JD, Purcell BA, Heitz RP, Logan GD, Palmeri TJ. Neural mechanisms of saccade target

Schall JD, Sato TR, Thompson KG, Vaughn AA, Juan C-H. Effects of search efficiency on surround

Schein SJ, Desimone R. Spectral properties of V4 neurons in the macaque. J Neurosci 10:

Seidl KN, Peelen M V., Kastner S. Neural evidence for distracter suppression during visual search in

Shadlen MN, Newsome WT. Neural basis of a perceptual decision in the parietal cortex (area LIP)

Shibutani H, Sakata H, Hyvärinen J. Saccade and blinking evoked by microstimulation of the

Snyder LH, Batista AP, Andersen RA. Coding of intention in the posterior parietal cortex. Nature

Sommer MA, Wurtz RH. Frontal eye field neurons orthodromically activated from the superior

Sommer MA, Wurtz RH. Influence of the thalamus on spatial visual processing in frontal cortex.


FIGURE CAPTIONS

Fig. 1. Behavioral task, visual stimuli, and predictions. A, B: Reaction-time visual search task. After a fixation of typically 1,000 ms, a search array consisting of six isoluminant elements was presented. A: In the target-present (TP) trials, an array consisted of a singleton uniquely colored element (target) and five identical elements (distractors), and the monkeys were required to make a saccade toward the target (arrow) after the array presentation. B: In the target-absent (TA) trials, an array consisted of six identical elements, and the monkeys had to maintain their fixation for 600–1,800 ms after array presentation. C: Visual stimuli. A search array was generated by manipulating target–distractor similarity (Easy vs. Hard) and stimulus luminance (Light vs. Dim). For illustration purposes, the stimulus colors were modified from the actual colors used in our experiments. D: Predicted neuronal activation. Four color surface plots depict the possible LIP neuron activation map during the present task. In each map, six activations are evoked by the six stimulus elements of a search array. In the TP trials, the visually evoked activation at the location of a singleton target (target-related activity, red outline in a) may be stronger than that at the distractor locations (distractor-related activity, blue outline in a). In the TA trials, six identical distractors may evoke activation of the same strength (neutral activity; black outline in c). By the effects of mutual lateral inhibitions, distractor-related activity in the TP trials would be more strongly suppressed by strong target-related activity (thick arrow in b), and target-related activity in the TP trials would be less strongly suppressed by weak distractor-related activity (dashed arrow in b) compared with neutral activities in the TA trials (thin arrows in d). As a result, neutral activity under the TA condition would be intermediate between target- and distractor-related activities under the TP condition and could be used to distinguish between the elevation of target-related activity and the reduction of distractor-related activity (e).
Fig. 2. Magnetic resonance images of recording sites from one monkey. A: Three-dimensional view of the brain. The five bright rods in the right hemisphere indicate tubes filled with a glycerin solution and embedded in a plastic base attached to the recording chamber. These tubes served as position reference markers. B: Penetration sites on the cortical surface. Large circles indicate the sites defined by extensions from the reference tubes. The penetration sites where neurons were recorded (small circles) were reconstructed with the coordinates determined by the reference tubes. C: Coronal slices representing the most anterior to the most posterior recording positions. The A–P levels are indicated in the upper center of each image. CS, central sulcus; IPS, intraparietal sulcus.

Fig. 3. Activity of an LIP neuron during a visual search task. A: Spike density functions (mean ± SEM), aligned on stimulus onset (left panel) and saccade onset (right panel). Red and blue traces indicate the activity observed when the target appeared in the receptive field (target-related activity) and activity when a distractor appeared in the receptive field (distractor-related activity) on the Light–Easy TP trials, respectively. Black trace indicates the activity observed during the Light TA trials (neutral activity). Saccade-aligned neutral activity (right panel) was virtually produced by assigning the saccadic reaction times of the TP trials using a bootstrap method. Solid and dashed black traces indicate the TA activity computed from the saccadic reaction times on the TP trials when the target appeared within and outside the receptive field, respectively. Vertical tick marks above the spike density functions indicate action potentials, and each row of rasters indicates one trial. Black ticks indicate saccadic reaction times, and red and blue arrowheads indicate the mean reaction times. B: Time courses of the AUCs reflecting the statistical discrimination of target-related and neutral activities (target AUC; red) and the discrimination of distractor-related and neutral activities (distractor AUC; blue). Asterisks indicate that target/distractor AUCs differ significantly from 0.5 (permutation test, P < 0.05).
Fig. 4. Target-related elevation and distractor-related reduction in population activity of LIP neurons.

A–B: Normalized spike density functions (A) and target/distractor AUCs (B) in the population averaged over the entire 122 neurons (± SEM) for the Light–Easy TP and Light TA trials. Asterisks indicate that AUCs significantly differed from 0.5 (t-test, \( P < 0.01 \)). C: The distribution of target and distractor AUCs measured in a 20-ms period prior to saccade onset for 122 neurons. Each data point indicates one neuron. Different symbols indicate whether target and distractor AUCs for each neuron are significantly greater or less than 0.5 (permutation test, \( P < 0.05 \)). The red rectangle indicates the mean value across neurons. D–F: The results when the same analyses were conducted for those neurons that exhibited sufficient target–distractor discrimination (AUC > 0.7) in their activity (\( n = 59 \)).

Fig. 5. Comparison of target-related elevation and distractor-related reduction in population across stimulus conditions. A–F: Normalized spike density functions and target/distractor AUCs for the Light–Hard TP and Light TA (A and B), Dim–Easy TP and Dim TA (C and D), and Dim–Hard TP and Dim TA (E and F) trials averaged over the 59 neurons. Conventions are the same as those in Fig. 4A and B. G–H: Comparison of target and distractor AUCs across stimulus conditions. I–L: Normalized spike density functions and target/distractor AUCs observed in the false-alarm errors in the Light (I and J) and Dim (K and L) TA trials.

Fig. 6. Constrained relationship between target-related elevation and distractor-related reduction in LIP activity. Pairs of target and distractor AUCs sampled from the population activity at different time epochs aligned to stimulus onset (A) and saccade onset (B) are superimposed across six stimulus conditions (successful trials under the Light–Easy, Light–Hard, Dim–Easy, and Dim–Hard

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TP conditions, false-alarm trials under the Light and Dim TA conditions). Solid black lines indicate
the least-squares fit to the data. Gray lines indicate equality of the absolute differences from 0.5. C:
Relationship between target and distractor AUCs for individual neurons recorded under six stimulus
conditions (n = 34). Six pairs of target and distractor AUCs for each neuron were calculated from the
activity measured in a 20-ms period prior to saccade onset (not shown), and they were fitted with a
regression line using a least-squares method. Each line segment indicates one neuron. D, E:
Distributions of the slopes of the regression lines (D) and Pearson's correlation coefficients (E)
computed from six pairs of target and distractor AUCs for each of 34 neurons. Arrowheads denote
the mean values across neurons for each distribution.

Fig. 7. Earlier occurrence of substantial target-related elevation relative to distractor-related
reduction in LIP activity during visual search. A, B: Comparison between the occurrence times of
target and distractor AUCs in the population activity (n = 59). The occurrence time in the population
for each stimulus condition is defined as the time point at which either the target or the distractor
AUC significantly differs from 0.5 (t-test, P < 0.01). Occurrence times are separately calculated
using neuronal activity aligned on stimulus onset (A) and saccade onset (B). Each data point
indicates one stimulus condition. C, D: The occurrence times of target/distractor AUCs for
individual neurons (left column, stimulus aligned; right column, saccade aligned). The occurrence
time for each cell is defined as the time point at which either the target AUC reaches 0.6 or the
distractor AUC reaches 0.4. These criteria were fulfilled for 29 (stimulus aligned) and 22 (saccade
aligned) neurons under the Light–Easy TP condition (C) and for 27 (stimulus aligned) and 22
(saccade aligned) neurons under the Dim–Easy condition (D). Each data point indicates one neuron.

Fig. 8. Persistently monotonic development of target-related elevation and distractor-related
A reduction in LIP activity during visual search. Time courses of target-related elevation are depicted as functions of the time from stimulus onset (left panel) or saccade onset (right panel). Thin gray and thick black traces indicate target AUCs for the individual neurons (n = 59) and their mean values, respectively. B, C: The distributions of Spearman’s correlation coefficients for individual neurons when monotonic increases/decreases in the time sequences of target AUCs were tested by moving a 10-ms window for analysis in 5-ms steps from stimulus onset (B) and saccade onset (C). Gray bars with positive and negative values indicate significant monotonic increases and decreases (Spearman’s correlation, P < 0.05), respectively. Triangles indicate the mean values in each distribution. D–F: Time courses of distractor-related reduction for individual neurons. Conventions are the same as those in A–C.

Fig. 9. Relationship between target discrimination time and each of target-related elevation and distractor-related reduction in activity. A, B: Correlation between target discrimination times and target (A)/distractor (B) AUCs across neurons. The target discrimination times (AUC > 0.7) were determined for 59, 24, 46, and 20 neurons (149 cases in total) under the Light–Easy, Light–Hard, Dim–Easy, and Dim–Hard conditions, respectively. To make a comparison across stimulus conditions with different cell populations, the values of target discrimination time and target/distractor AUCs (during 20-ms before saccade onset) were separately transformed into z scores under each condition and pooled across conditions (n = 149). Each data point corresponds to one condition for each neuron. Solid black lines indicate the least-squares fit to the data.

Fig. 10. Comparison of neuronal target discrimination between the reaction-time and delayed-response visual search tasks. A: Mean (± SEM) spike density functions across neurons (n = 42), aligned on stimulus array onset. Black and gray traces indicate the activity in the reaction-time
and delayed-response tasks, respectively. Solid and dashed traces indicate the target- and
distractor-related activity, respectively. The activity in the reaction-time task is illustrated in a
200-ms interval after stimulus onset. B: Distributions of target discrimination times for the
individual neurons (n = 35) in the two tasks. Dashed black and solid gray traces correspond to the
reaction-time and delayed-response tasks, respectively. Arrowheads denote the mean values across
neurons for each distribution.

Fig. 11. Computer simulations with a competitive accumulator model. A: Architecture of a network
model with lateral inhibitions in which the visual signals from two input units (μ₁ and μ₂) were
separately integrated by the two accumulator units (x₁ and x₂). The accumulator units are mutually
connected with lateral inhibitory interactions (synaptic strength, β) and receive the inhibitory
self-recursive connections (synaptic strength, k) that determine the leakage of temporal accumulation.
The activation level of each accumulator unit (xᵢ) is governed by the differential equation: \( \tau \frac{dx_i}{dt} = μᵢ - kxᵢ - βxᵢj \) (i, j = 1, 2), where μ₁ and μ₂ are the visual input signal to the accumulator units and τ = 10 ms is a time constant. B: Visual signals from the input units to the accumulator units when the
target appears in the receptive field (black trace) or when the distractor appears in it (gray trace).
These signals are modeled by a step-and-decay function with the differential equation \( \tau_μ \frac{dμᵢ}{dt} = μᵢ - μ_{plateau} + τ_μμ_{init}δ(t - t₀) \) (i = 1, 2), where μ_{init} = 40 Hz determines the strength of the initial visual
response, τ_μ = 25 ms determines the rate of response adaptation, δ(·) is the Dirac delta function, t₀ = 40 ms is the response onset delay (Bisley et al., 2004) prior to which \( μᵢ = 0 \), and μ_{plateau} determines
the plateau level, which was set to 20 or 16 Hz when the target or distractor is presented in the
receptive field, respectively. C, D: The output responses of the accumulator units when the lateral
inhibitory interactions exist (β = 0.12, k = 0.15) (C) or when they do not (β = 0, k = 0.15) (D). Solid
black and gray traces indicate the output responses when the target and distractor, respectively,
appear in the receptive fields. Dashed trace indicates the response when the target is absent. $E, F$:

The reproduction of the observation in Falkner et al. (2010). We attempt to simulate the LIP responses observed in Falkner et al. (2010) using the same network model ($A$), but replacing only visual signals from the input units to the accumulator units. $E$: The input-signal function mimicking visual signals that would be produced by the stimulus presentation sequence used in Falkner et al. (2010). The prolonged exposure to a target stimulus (horizontal black line) evokes persistent activation (black trace), whereas the transient exposure to a distractor stimulus (horizontal gray line) evokes a brief activation (gray trace). $F$: The accumulator outputs. By the preceding and prolonged input signal, the target activation is maintained (black trace) beyond the distractor appearance. This produces suppressive modulation in distractor activation even immediately after the distractor onset when the target is presented (solid gray trace) relative to when the target is not presented (dashed gray trace).
Table 1. Behavioral performance across stimulus conditions

<table>
<thead>
<tr>
<th>Stimulus condition</th>
<th>Light–Easy</th>
<th>Light–Hard</th>
<th>Dim–Easy</th>
<th>Dim–Hard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saccadic reaction time (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey Y</td>
<td>159.3 ± 5.2</td>
<td>199.4 ± 14.0</td>
<td>198.8 ± 10.0</td>
<td>242.3 ± 21.9</td>
</tr>
<tr>
<td>Monkey S</td>
<td>212.8 ± 16.5</td>
<td>277.0 ± 25.7</td>
<td>275.6 ± 19.6</td>
<td>365.7 ± 39.1</td>
</tr>
<tr>
<td>Correct rate (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey Y</td>
<td>91.2 ± 6.1</td>
<td>78.3 ± 6.9</td>
<td>91.8 ± 6.5</td>
<td>81.9 ± 7.2</td>
</tr>
<tr>
<td>Monkey S</td>
<td>78.2 ± 9.7</td>
<td>67.1 ± 10.1</td>
<td>76.6 ± 10.1</td>
<td>67.4 ± 10.8</td>
</tr>
</tbody>
</table>

Values are means ± SD across sessions. Monkey Y participated in 71 sessions, and monkey S participated in 51 sessions.

Table 2. Number of neurons that exhibited significant target-related elevation and/or distractor-related reduction

<table>
<thead>
<tr>
<th>Stimulus condition</th>
<th>Light–Easy</th>
<th>Light–Hard</th>
<th>Dim–Easy</th>
<th>Dim–Hard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of neurons</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target-related elevation</td>
<td>32 (54.2%)</td>
<td>37 (62.7%)</td>
<td>17 (28.8%)</td>
<td>37 (62.7%)</td>
</tr>
<tr>
<td>Distractor-related reduction</td>
<td>1 (1.7%)</td>
<td>4 (6.8%)</td>
<td>4 (6.8%)</td>
<td>3 (5.1%)</td>
</tr>
<tr>
<td>Both</td>
<td>25 (42.4%)</td>
<td>12 (20.3%)</td>
<td>36 (61%)</td>
<td>12 (20.3%)</td>
</tr>
<tr>
<td>Target-related reduction</td>
<td>0</td>
<td>0</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Distractor-related elevation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No modulation</td>
<td>1 (1.7%)</td>
<td>6 (10.2%)</td>
<td>1 (1.7%)</td>
<td>6 (10.2%)</td>
</tr>
</tbody>
</table>

The total number of neurons was 59. Statistical significance was examined using a t-test, with
significance set at $P < 0.05$.

Table 3. Presaccadic AUCs for subpopulations of neurons with and without saccade-burst activity

<table>
<thead>
<tr>
<th>Stimulus condition</th>
<th>Light–Easy</th>
<th>Light–Hard</th>
<th>Dim–Easy</th>
<th>Dim–Hard</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target AUC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saccade-burst neuron ($n = 20$)</td>
<td>0.81 ± 0.09</td>
<td>0.74 ± 0.11</td>
<td>0.78 ± 0.10</td>
<td>0.75 ± 0.11</td>
</tr>
<tr>
<td>Non-saccade-burst neuron ($n = 30$)</td>
<td>0.75 ± 0.10</td>
<td>0.69 ± 0.10</td>
<td>0.74 ± 0.11</td>
<td>0.71 ± 0.11</td>
</tr>
<tr>
<td><strong>Distractor AUC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saccade-burst neuron</td>
<td>0.40 ± 0.10</td>
<td>0.47 ± 0.08</td>
<td>0.32 ± 0.10</td>
<td>0.42 ± 0.09</td>
</tr>
<tr>
<td>Non-saccade-burst neuron</td>
<td>0.36 ± 0.09</td>
<td>0.43 ± 0.09</td>
<td>0.35 ± 0.12</td>
<td>0.44 ± 0.11</td>
</tr>
</tbody>
</table>

Values are means ± SD across neurons.
Figure 1

(A) Target-present (TP) trials
- Fixation: 1,000 ms
- Stimulus: 500 or 700 ms
- Response

(B) Target-absent (TA) trials
- Fixation: 1,000 ms
- Stimulus: 600–1,800 ms
- Hold

(C) Light vs. Dim
- Easy TP trials
- Hard TP trials

(D) TP trials vs. TA trials

(E) Target-related elevation
- Distractor-related reduction
Figure 7
Figure 11

A

Target-present trial
\[ \mu_1 \rightarrow \mu_{\text{target}} \quad X_1 \rightarrow X_{\text{target}} \]
\[ \mu_2 \rightarrow \mu_{\text{distractor}} \quad X_2 \rightarrow X_{\text{distractor}} \]

Target-absent trial
\[ \mu_1, \mu_2 \rightarrow \mu_{\text{distractor}} \quad X_1, X_2 \rightarrow X_{\text{neutral}} \]

B

Visual input

C

Lateral inhibition (\( \beta = 0.12 \))

D

No lateral inhibition (\( \beta = 0 \))

E

\[ \mu_{\text{target}} \quad \mu_{\text{distractor}} \]

F

\[ X_{\text{target}} \quad X_{\text{distractor (no target)}} \quad X_{\text{distractor (with target)}} \]