Target Selection for Saccadic Eye Movements: Direction-Selective Visual Responses in the Superior Colliculus

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Horwitz, Gregory D. and William T. Newsome. Target selection for saccadic eye movements: direction-selective visual responses in the superior colliculus. *J Neurophysiol* 86: 2527–2542, 2001. We investigated the role of the superior colliculus (SC) in saccade target selection in rhesus monkeys who were trained to perform a direction-discrimination task. In this task, the monkey discriminated between opposed directions of visual motion and indicated its judgment by making a saccadic eye movement to one of two visual targets that were spatially aligned with the two possible directions of motion in the display. Thus the neural circuits that implement target selection in this task are likely to receive directionally selective visual inputs and be closely linked to the saccadic system. We therefore studied prelude neurons in the intermediate and deep layers of the SC that can discharge up to several seconds before an impending saccade, indicating a relatively high-level role in saccade planning. We used the direction-discrimination task to identify neurons whose prelude activity "predicted" the impending perceptual report several seconds before the animal actually executed the operant eye movement; these "choice predicting" cells comprised ~30% of the neurons we encountered in the intermediate and deep layers of the SC. Surprisingly, about half of these prelude cells yielded direction-selective responses to our motion stimulus during a passive fixation task. In general, these neurons responded to motion stimuli in many locations around the visual field including the center of gaze where the visual discriminanda were positioned during the direction-discrimination task. Preferred directions generally pointed toward the location of the movement field of the SC neuron in accordance with the sensorimotor demands of the discrimination task. Control experiments indicate that the directional responses do not simply reflect covertly planned saccades. Our results indicate that a small population of SC prelude neurons exhibits properties appropriate for linking stimulus cues to saccade target selection in the context of a visual discrimination task.

INTRODUCTION

At any given instant, potentially interesting features may be present at many locations in the visual scene. Because visual acuity outside of the fovea is poor, many of these features cannot be analyzed adequately during a single fixation. In general, this problem is solved by bringing each feature onto the fovea by means of a sequence of saccadic eye movements. This strategy implies the existence of a "selection process" within the brain that, after each period of fixation, determines the target of the next saccade. To study the target selection process, several groups have recorded neural signals in eye-movement-related structures while monkeys made saccades to cued targets embedded within an array of distractor targets (Basso and Wurtz 1997, 1998; Bichot and Schall 1999; Bichot et al. 1996; Glimcher and Sparks 1992; Platt and Glimcher 1999; Schall and Hanes 1993; Schall et al. 1995; Thompson et al. 1996, 1997). In some cases, the animals were required to refrain from making a saccade to the selected target for several seconds (during an "instructed delay period") until receipt of a "go" signal. This procedure allowed investigators to analyze neural activity that follows the selection event, absent confounding bursts of activity that are time-locked to saccade execution.

When studied in this manner, subpopulations of cells in the frontal lobes, the lateral intraparietal area (LIP), and the superior colliculus (SC) exhibit target-specific preludes of activity well in advance of saccade execution (Schall and Thompson 1999). Such activity is consistent with a role for these neurons in the process of target selection but does not provide strong evidence in favor of this interpretation. For example, prelude activity might simply reflect preparation for a saccade to a target selected by processes elsewhere in the brain.

We have demonstrated previously that prelude activity of some SC neurons "predicts" choices made in a direction-discrimination task (Horwitz and Newsome 1999, 2001). Monkeys discriminated the direction of motion in a visual stimulus and reported their perceptual judgment by making a saccade to a target lying in the perceived direction of motion (Fig. 1). One target was positioned within the movement field of the neuron under study while the other target was positioned well outside the movement field. Choice-predicting neurons began discharging during the stimulus presentation and continued to fire during a delay period if the judgment resulted in a saccade into the movement field. The logic of this task dictates that neurons participating in target selection receive input, directly or indirectly, from other neurons that encode the direction of stimulus motion. Neurons that respond to motion with a leftward component, for example, should excite other neurons responsible for selecting a saccade target to the left of fixation. We thus propose that neurons responsible for selecting a target in a given region of space should be excited by visual motion flowing toward that region. On the other hand, neurons involved only in saccade preparation subsequent to the selection

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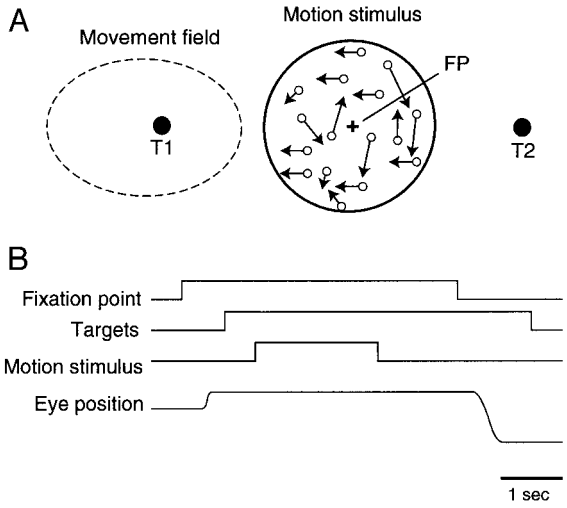

FIG. 1. The geometry of the display (*A*) and timing of events (*B*) in a 2-alternative, forced-choice direction-discrimination task. Three hundred milliseconds after the monkey foveated a fixation point, 2 saccade targets were illuminated. Five hundred to 900 ms later, a stochastic motion stimulus was shown at the center of gaze for 2 s and was followed by a delay period lasting from 1 to 1.5 s. After the delay period, the fixation point was extinguished, whereupon the monkey had 500 ms to shift its gaze to the target in the direction of stimulus motion. For each cell studied, 1 of the saccade targets (T1) was positioned inside the movement field and the other (T2) was positioned outside.

process should not respond this way; rather, their discharge should be more closely related to the metrics of the planned saccade.

Here we report the existence of two populations of SC neurons, one with response properties suggestive of a role in target selection and another with properties better suited for a role in postselectional saccade preparation. We established this classification initially by measuring responses to motion stimuli in blocks of passive fixation trials. As we have reported previously, one group of cells exhibited direction-selective responses to visual stimuli, whereas the remaining cells were unresponsive (Horwitz and Newsome 1999). In this paper, we briefly recapitulate the basic observation, then we describe several additional experiments that collectively make a strong case that the direction-selective responses do not result from covert saccade planning. Additionally, we present several novel analyses of responses recorded during performance of our direction-discrimination task. The two populations of cells may lie at opposite ends of a continuum along which sensory signals relating to a learned association evolve into, or guide, the generation of a command appropriate for driving a saccade.

METHODS

Surgical procedures

Three rhesus monkeys (*Macaca mulatta*, 2 female and 1 male) served as subjects in these experiments. Prior to data collection, each monkey underwent a pair of surgical procedures that were performed under aseptic conditions and general anesthesia. Details of the surgical procedures have been described elsewhere (Newsome and Stein-Aviles 1999). In an initial surgery, the animal was implanted with a head-restraint device and scleral search coil (Judge et al. 1980). After behavioral training, a second surgery was performed in which a craniotomy was centered on the midsaggital plane, a few millimeters posterior to the interaural line. A stainless steel cylinder was then implanted over the craniotomy through which electrodes could be inserted into the brain. For one monkey, this cylinder was tilted backward 19° from vertical, for the other two, it was tilted 28°. The anterior/posterior position of the craniotomy and the angle of the cylinder were selected so that the axis of the cylinder passed near the stereotaxic coordinates of the SC. All experimental procedures conformed to the standards established by the National Institutes of Health.

Data collection

We initially confirmed that our electrode was in the SC by establishing that visually responsive neurons in the superficial layers were retinotopically organized in accordance with the map of Cynader and Berman (1972) and by eliciting saccades using electrical microstimulation (10- to 20-μA current pulses) of the deep layers. All cells in our database were located in the intermediate or deep layers of the SC ($>$1 mm below the first point at which visual responses could be detected).

We employed electrical stimulation to estimate the movement field locations of recorded neurons and to document sites at which direction-selective neurons were isolated. Across the colliculus, the direction and amplitude of saccades elicited by electrical stimulation agreed closely with the location of the movement field at the stimulation site (Schiller and Stryker 1972) and was predictable from the known topography of the SC (Robinson 1972). Our stimulation trains consisted of repeated biphasic pulses of 500 μs, cathodal phase leading. Currents ranged from 10 to 50 μA and frequencies ranged from 300 to 500 Hz. Train durations were adjusted so that stimulation reliably evoked single saccades and rarely evoked multiple ("staircase") saccades. Three to 15 saccades were elicited per site (median: 10).

Electrophysiological signals were amplified and filtered using conventional electronic instruments. Individual action potentials were discriminated on-line on the basis of time and amplitude criteria. Times of action potential occurrence were stored by computer at a resolution of 1 ms.

Horizontal and vertical eye position was measured by the scleral search coil technique (Fuchs and Robinson 1966; Robinson 1963); eye-position signals were digitized and stored with a sampling rate of 250 Hz. Data acquisition and behavioral contingencies were controlled by the PC-based REX software system (Hays et al. 1982).

Behavioral paradigms and stimuli

Neurons were selected for study using the two-alternative, forced-choice, direction-discrimination task illustrated in Fig. 1. We trained monkeys to discriminate between opposed directions of motion in a stochastic random-dot display. On each trial, the monkey expressed its direction judgment by making a saccade to a visual target lying in the perceived direction of motion. A special-purpose graphics board (Number Nine Computer or Cambridge Research Systems), running in an IBM-compatible personal computer, controlled the visual stimuli and saccade targets, presenting them on a CRT monitor.

The visual stimulus was a random-dot motion display that has been used extensively in this laboratory (Britten et al. 1992, 1993; Salzman et al. 1992; Shadlen and Newsome 1996). Random-dot patterns appeared within a circular aperture that subtended 7° of visual angle; each dot subtended 0.1° of visual angle. Dots were white ($\sim$60 cd/m^2) against a black background ($<$0.001 cd/m^2). Monkeys were trained to discriminate the direction of "coherent" motion in the display. Coherent motion was created by replotting, after a delay of 50 ms, a specified percentage of the dots with a displacement of 0.15°. Thus these "signal" dots appeared to move at a speed of 3°/s in a common direction. The remaining dots in the display ("noise" dots) were replotted in random locations, thereby making the direction of coherent motion more difficult to perceive. The screen was refreshed at 60 Hz. The density of dots within each frame was 0.25 dots/deg^2, but the

apparent density of dots in the stimulus was much higher because of persistence in the visual system.

Figure 1 shows the geometry of the visual display and the timing of events in each trial. Each trial began when the monkey fixated a small point of light near the center of the CRT screen. Three hundred milliseconds after visual fixation was achieved, two target disks appeared, flanking the fixation point and collinear with it. A 2-s-duration motion stimulus movie was then presented, usually at the center of gaze. Following an enforced delay period of randomized length (1–1.5 s), the fixation point was extinguished, cueing the monkey to make a saccade to one of the two visual targets. A saccade to the target in the direction of coherent stimulus motion counted as a correct response and was reinforced with a liquid reward. For each cell isolated, the geometry of the display was adjusted for each experiment so that one of the targets, hereafter referred to as "T1," lay inside the movement field and the other, "T2," lay outside. The eccentricity of T1 ranged from 4 to 25° (median 15).

As the monkey performed this task, we recorded from neurons in the intermediate and deep layers of the SC. Roughly one-third of these neurons began discharging in a target-specific manner early in the trial, usually within a few hundred milliseconds of the onset of random-dot motion (Horwitz and Newsome 1999, 2001). For the large majority of neurons, neural activity was more intense when the monkey decided to make a saccade into the movement field of the neuron under study. Listening to this activity during the trial, an experimenter could usually predict which direction the monkey would choose at the end of the trial. We called these "choice-predicting" neurons and selected them for further study based on our qualitative impression during the initial search procedure. The discrimination task is described in more detail in the companion paper (Horwitz and Newsome 2001).

Choice-predicting neurons exhibited a variety of response properties characteristic of neurons in the intermediate and deep layers of the SC. These properties included a transient visual response to the onset of a saccade target inside the movement field, sustained activity during an enforced delay period and a burst of activity on saccade initiation. We measured these responses quantitatively in the context of the direction-discrimination task as reported in RESULTS. To a first approximation, most of the neurons we studied appeared similar to the populations of "build-up" or "prelude burst" neurons described by other groups (Glimcher and Sparks 1992; Munoz and Wurtz 1995). Some of our choice-predicting neurons (including many of the direction-selective cells that are the focus of this paper) probably correspond to the "quasi-visual cells" (QV cells) described by Mays and Sparks (1980). Although we did not perform the double-saccade experiments that would identify QV cells definitively, these choice-predicting neurons were similar to QV cells in yielding sustained discharges during the delay period and lacking peri-saccadic bursts (see RESULTS).

The primary goal of the current study was to determine whether individual SC neurons receive direction-selective input appropriate for mediating target selection in the direction-discrimination task. We measured responses to the presentation of visual motion stimuli while the monkey performed behavioral tasks that (in contrast to the direction-discrimination task) were designed to dissociate the direction of stimulus motion from the direction of a planned saccade. In the first, a visual fixation task, the monkey was not required to plan saccades at all but was rewarded simply for fixating. While the monkey fixated, a motion stimulus (appearing 300–1,000 ms after the monkey achieved fixation) flowed in one of either two or eight equally spaced directions. Stimulus presentations lasted 500–2,500 ms. In most experiments, the motion stimuli were presented at the center of gaze. In others, several stimulus locations were randomly interleaved within a block of trials. High coherence stimuli (51.2% coherently moving dots) were used in all measurements unless otherwise specified.

Direction-selective responses observed during the fixation task can be interpreted as reflections of covertly planned saccades. To discourage covert planning of saccades in the direction of stimulus motion, we conducted a second control task in which saccade planning was directed explicitly to a target located well away from the movement field of the cell under study. In these delayed-saccade trials, the monkey was instructed to plan and execute saccades to the same remote target location on every trial. Irrelevant motion stimuli were presented during the delay period following the saccade instruction so that visual direction tuning curves could be assessed while the monkey planned a saccade to a known location. In these trials, a single saccade target appeared outside of the movement field 300 ms after the monkey acquired the fixation spot. The target remained visible during a 1- to 3-s delay period, during which the irrelevant random-dot motion stimulus was presented at the center of gaze for 0.5–2 s. At the end of the delay period, the fixation point disappeared, cueing the monkey to initiate a saccade to the target with a latency of $<500-800$ ms to obtain a reward. The fixation point was extinguished either 1,000–1,500 ms after stimulus offset (3 cells), simultaneous with stimulus offset (2 cells), or preceding stimulus offset (17 cells). Standard fixation trials as described above were randomly interleaved with the delayed-saccade trials for comparison.

During fixation, the monkey was required to maintain its eye position within a $3° \times 3°$ electronically defined window surrounding the fixation point. If fixation was broken while the fixation point was lit, the trial was aborted. On saccade or discrimination trials, the trial was also aborted if the monkey failed to make a saccade within 500–800 ms of fixation point offset. The monkey received liquid rewards for maintaining accurate fixation or for making accurate saccades. Electronic windows around the saccade targets varied in size depending on the eccentricity of the target. Saccades landing in these windows tended to be quite accurate.

Direction-tuning curves

Direction-tuning curves were fit with Gaussian functions using a least-squares algorithm. Prior to fitting, responses were rotated so that the greatest response was at 180°. The response to the opposite direction of motion was duplicated and associated with both 0 and 360°. The fitted function had the form

$$\text{response} = A \cdot e^{(x-\mu)2/(2\cdot\sigma 2)} + B \quad (1)$$

where response, the firing rate of the neuron, is the dependent variable and x, the direction of stimulus motion, is the independent variable. All other variables are fitted parameters: A is the amplitude of the tuning curve, μ is the neuron's preferred direction; σ is the tuning curve width, and B is the baseline of the tuning curve. After fitting, preferred directions (μ) were shifted by an amount equal and opposite to the initial rotation of the responses.

Direction indices

We calculated direction tuning indices from responses to motion flowing toward and away from the movement field. A distribution of responses (in spikes/s) was compiled for each motion direction, and a receiver operating characteristic (ROC) curve was derived from these two distributions (Britten et al. 1992; Green and Swets 1966). The direction-tuning index is defined as the integrated area beneath the ROC curve. A cell that is not directionally tuned yields a direction tuning index close to 0.5. A value near 1 indicates that motion toward the movement field consistently evoked a stronger response than motion in the opposite direction; a value of 0 indicates that the neuron consistently preferred motion away from the movement field.

Statistical significance of direction tuning indices was assessed by permutation tests. Responses on individual trials were randomly assigned to the two directions of motion 2,000 times to generate a distribution of direction tuning indices under the hypothesis of no directional tuning. The cited P value is the proportion of direction

indices equaling or exceeding the value obtained from the original (unpermuted) data.

Database

Data from 119 neurons are presented in this paper. Ninety-six of these neurons were studied quantitatively in the direction-discrimination task as described in detail in the companion paper (Horwitz and Newsome 2001). Of these 96 neurons, 44 yielded direction-selective responses in a passive visual fixation task. This direction-selective response is the focus of this study, and the responses from these cells are analyzed in detail. The remaining 52 cells that lacked such direction-selective responses are included only in the few analyses that explicitly contrast the responses of direction-selective and non-direction-selective neurons (see RESULTS). An additional 23 direction-selective neurons are included in this study that qualified as choice-predicting based on qualitative assessment during the search procedure but were lost before we obtained quantitative direction-discrimination data.

Subsets of direction-selective neurons were tested in various control conditions tabulated in Table 1. Complete direction tuning curves (8 directions of motion, ≥5 trials per direction) were obtained for 22 cells in interleaved passive-fixation and delayed-saccade trials. Direction tuning was measured in multiple stimulus locations for 23 neurons. Direction selectivity was measured for 15 neurons at the time of saccade initiation. Responses to interrupted motion were measured for seven neurons. These control conditions are described in detail in RESULTS.

RESULTS

Analysis of direction-selective response properties

Most of the SC neurons we studied did not respond to motion stimuli presented during the passive-fixation paradigm. Those that did, however, were invariably direction selective. Figure 2 illustrates a direction tuning curve obtained from a single choice-predicting SC neuron during passive fixation (recall that choice-predicting refers to activity measured during the discrimination task). Figure 2*A* shows the geometrical relationship between the stimulus aperture (gray disk) and the mean saccade vector elicited with electrical stimulation at the recording site. The aperture subtended 7° of visual angle and was presented at the center of gaze. Electrical stimulation evoked saccades of ~10° amplitude, directed down and to the right (arrow). Responses of this cell to eight directions of stimulus motion (Fig. 2*B*) reveal that the cell was strongly tuned for the direction of visual motion with a preferred direction down and to the right.

The neural activity documented in Fig. 2*B* meets a standard definition of a visual response: during a block of trials in which

TABLE 1. *Numbers of cells studied*

	Studied Quantitatively in Direction Discrimination	Not Studied Quantitatively in Direction Discrimination
Directional cells	44 (of 96)	23
Number of directional cells studied in particular control conditions		
Delayed saccades	8	14
Multiple stimulus locations	11	12
Persistent motion	6	9
Interrupted motion	3	4

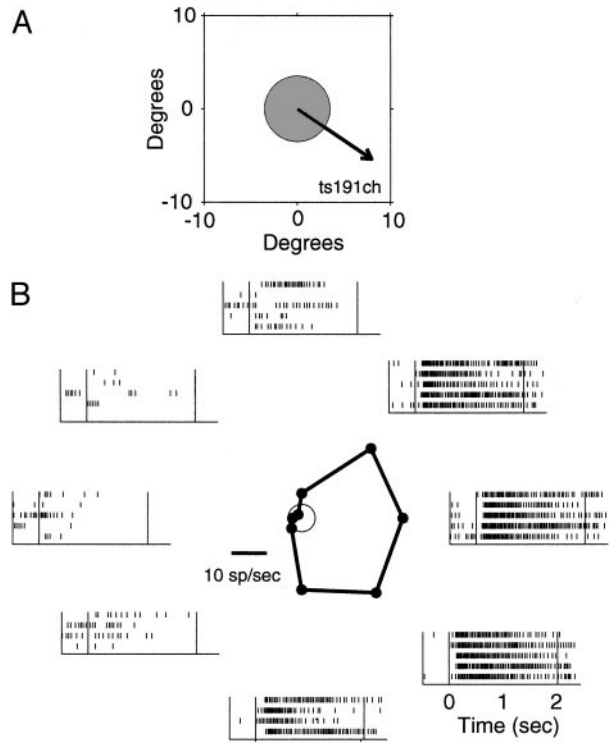

FIG. 2. Direction tuning measurement for visual responses of a single superior colliculus (SC) neuron. *A*: the motion stimulus (disk) subtended 7° of visual angle and was presented at the center of gaze. Electrical stimulation at the recording site (25 μA, 500 Hz for 130 ms) evoked 10° amplitude right-downward saccades (arrow). *B*: responses of an SC neuron at this stimulation site to 8 directions of visual motion. The positions of the spike rasters correspond to the 8 directions of motion. Vertical bars in the rasters delineate 2-s-long stimulus presentation intervals. The polar plot shows mean responses recorded during this interval. The small circle at the origin indicates baseline activity level.

the monkey is required to maintain visual fixation, the firing rate is consistently and closely time-locked to the presentation of the visual stimulus and not with any measurable aspect of behavior. The fact that the firing rate at the beginning of the stimulus presentation exceeds that at the end of the stimulus presentation is consistent with this interpretation. We will use the phrase "visual response" throughout this report to refer to the preceding definition (which, it should be noted, is agnostic concerning the functional significance of the discharge).

The directional visual response documented in Fig. 2*B* is surprising: although some SC neurons in the intermediate and deep layers exhibit visual responses, pronounced directional selectivity has not been previously reported in the primate SC. Importantly, the direction of motion preferred by this cell is very similar to the direction of the electrically evoked saccade vector (*A*), or equivalently, the preferred direction points toward the inferred location of the movement field. This is exactly the relationship expected from the sensorimotor demands of our direction-discrimination task. In the discrimination task, a motion stimulus at the center of gaze instructs a saccade to a target lying in the direction of motion. For example, motion flowing down and to the right would instruct a saccade into the movement field of saccade-related neurons in the neighborhood of the recorded cell. The cell in Fig. 2 carries the sensory signal appropriate for target selection into close registry with circuitry required for driving the operant saccade.

This pattern of results is suggestive of a role in implementing the sensorimotor link between motion direction and saccade vector.

Slightly fewer than one-half of the choice-predicting SC neurons we studied (~15% of the neurons we encountered in the intermediate and deep layers) exhibited direction-selective responses qualitatively similar to the one illustrated in Fig. 2. We measured direction tuning curves as well as electrically evoked saccades for 22 of these recordings. Tuning curves were fit with Gaussian functions to provide objective estimates of preferred directions (see METHODS). As shown in Fig. 3, visual preferred directions spanned a wide range and, in every case, agreed well with the direction of the electrically evoked saccade (circular-circular rank correlation coefficient = 0.76; $P < 0.0001$). For a small population of SC neurons, therefore, visual motion at the center of gaze generates directional visual responses that are systematically related to the location of the movement field.

Receptive field dimensions

To explore the area of the visual field over which the motion stimulus elicited a direction-selective response, we recorded from 23 cells while passively fixating monkeys viewed motion stimuli that appeared at 4–24 locations on the CRT screen. Figure 4 shows the results of this experiment for the same neuron illustrated in Fig. 2. In this experiment, we measured responses to eight different motion directions at each of five aperture locations; all aperture locations and motion directions were randomly interleaved. Each combination of location and direction was repeated five times.

The large axis grid in Fig. 4 is in retinal coordinates with the fovea at the origin. Gray disks, representing the stimulus aperture, are positioned at the five retinal locations tested. The thick arrow represents the average saccade vector evoked by electrical stimulation at the recording site. The position of each direction tuning curve corresponds to the aperture location at which it was measured.

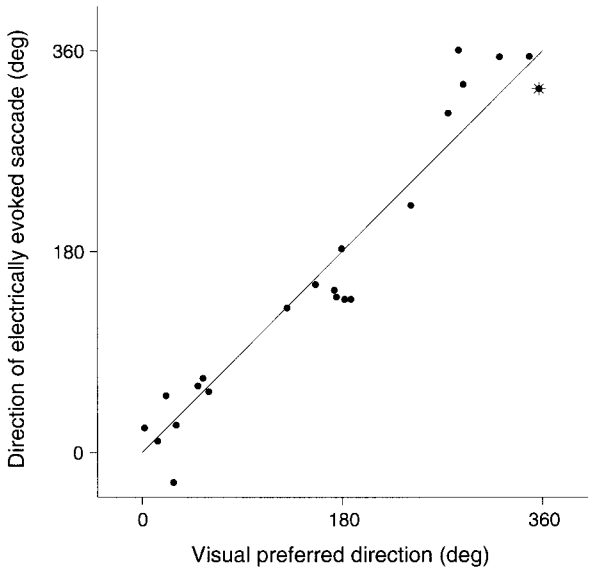

FIG. 3. Scatterplot of preferred visual direction against the direction of electrically evoked saccades. Data are shown for 22 direction-selective neurons; *, the data point for the cell in Fig. 2. In this coordinate system 0° is rightward (experiments in the left SC), 90° is upward, and 180° is leftward (experiments in the right SC).

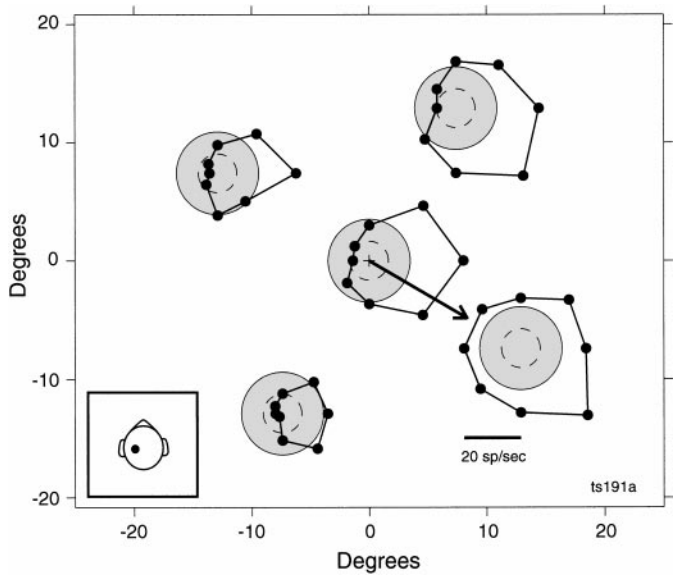

FIG. 4. Direction tuning of a single SC neuron for stimuli positioned at 5 locations in the visual field (gray disks). Direction tuning curves measured at each retinal location are displayed at corresponding locations in the figure. Dashed circles represent baseline responses and identify the origin of each tuning curve. Electrical stimulation at the site evoked stereotyped saccades (arrow). At the center of gaze, this cell preferred motion flowing toward the movement field; the preferred direction was roughly consistent at all locations tested.

This neuron responded to stimuli at a wide range of locations, including substantial portions of both hemifields. The strongest tuning occurred at the center of gaze where visual stimuli generally appeared during the direction-discrimination task, and the preferred direction of this cell was roughly constant across aperture locations. Surprisingly, strongly directional responses were obtained at one location that was contained entirely within the ipsilateral hemifield. This response is thus unlikely to be due to large, primarily contralateral receptive fields—the classical profile of visually responsive SC neurons.

Figure 5 illustrates the regions of visual space over which five representative direction-selective neurons responded. These regions were drawn by hand based on data sets like the one displayed in Fig. 4 and the statistical criteria described in the following text. For each aperture location tested, we determined the statistical significance of direction tuning by performing a one-way ANOVA on the responses. Solid contours indicate boundaries between retinal locations that yielded significant direction tuning ($P < 0.05$) and those that did not ($P \geq 0.05$). More often than not, however, neurons exhibited significant direction tuning at the most eccentric stimulus locations tested, so actual boundaries were frequently impossible to draw. In these cases, we drew dashed contours just outside these eccentric locations, indicating that directionally tuned responses extended at least this far eccentric. Notice that all of the cells depicted in Fig. 5 responded directionally to ipsilateral stimuli.

Preferred directions measured at different retinal locations differed only subtly for any individual cell. The largest difference in preferred direction observed between any pair of significantly tuned stimulus locations for the cells depicted in Fig. 5 was <90° (of 880 comparisons). No systematic relationship between aperture location and preferred direction was noticed.

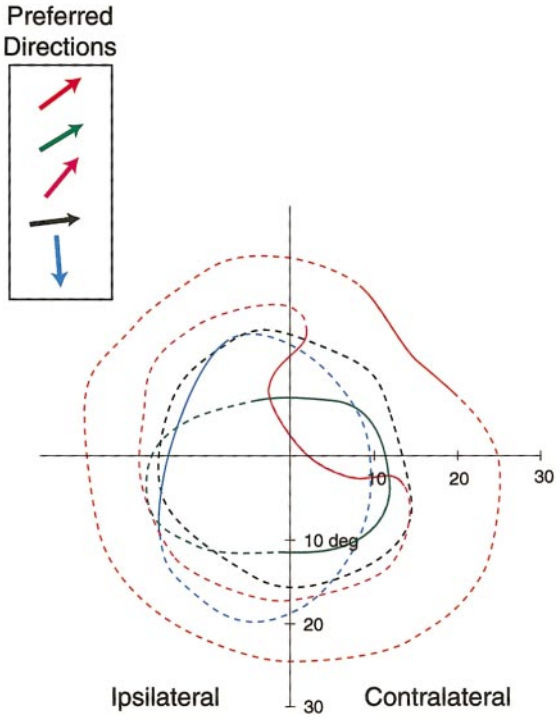

FIG. 5. Receptive field boundaries estimated from responses to the motion stimulus for 5 direction-selective SC neurons. Hand-drawn curves encompass all tested locations at which direction tuning attained statistical significance (ANOVA: $P < 0.05$). Solid curves indicate boundaries between direction-tuned and non-direction-tuned locations. Dashed curves encompass eccentric direction-tuned locations and indicate that more eccentric locations were not tested. Data from 3 cells recorded from the right SC have been flipped about the vertical axis so that, for all neurons shown here, the right side of the figure is contralateral and left is ipsilateral.

Testing the motor hypothesis

In principle, the direction-selective responses reported here could reflect motor intention. In this scenario, the monkey covertly plans saccades in the direction of stimulus motion. This hypothesis correctly predicts that direction-selective neurons should prefer motion flowing toward the movement field: motion flowing toward the movement field entices the monkey to plan a saccade into the movement field, and the cell responds as a consequence of this plan. Motion in the opposite direction would not cause the cell to respond because the planned saccade would be directed out of the movement field. By definition, our monkeys were never required to plan saccades during fixation trials, but extensive training on the direction-discrimination task may have caused our monkeys to plan saccades "reflexively" whenever a random-dot stimulus appeared, irrespective of whether they are rewarded for this behavior. In the next section, we describe three control experiments that address this issue directly. Together, these experiments argue that the direction-selective responses do not reflect covert saccade plans.

Manipulating saccade planning

In our first attempt to dissociate stimulus motion from saccade planning, we manipulated saccade planning directly by having the monkey perform a visually guided, delayed-saccade task. Figure 6 shows the event timing (*A*) and display geometry (*B*) employed in the delayed-saccade task. In this example, the saccade target (●) appeared above and to the left of the fixation point, far from the movement field location inferred from electrical stimulation (→). After the monkey acquired the fixation point at the beginning of the trial, the saccade target appeared. The monkey was required to make a saccade to this target on fixation point offset to obtain a reward. During the enforced delay period between the presentation of the target and disappearance of the fixation point, the motion stimulus was presented at the center of gaze. We measured responses to eight directions of motion presented during the enforced delay period. We assume that the monkey forms a plan to make a saccade to the target early in the trial and holds this plan throughout the enforced delay period. If the direction-selective responses we have studied result from covert saccade planning, we expect them to be eliminated or strongly reduced in the delayed-saccade trials. If the responses are truly a visual phenomenon, on the other hand, we expect them to be unaffected by the demand that the monkey prepare a saccade.

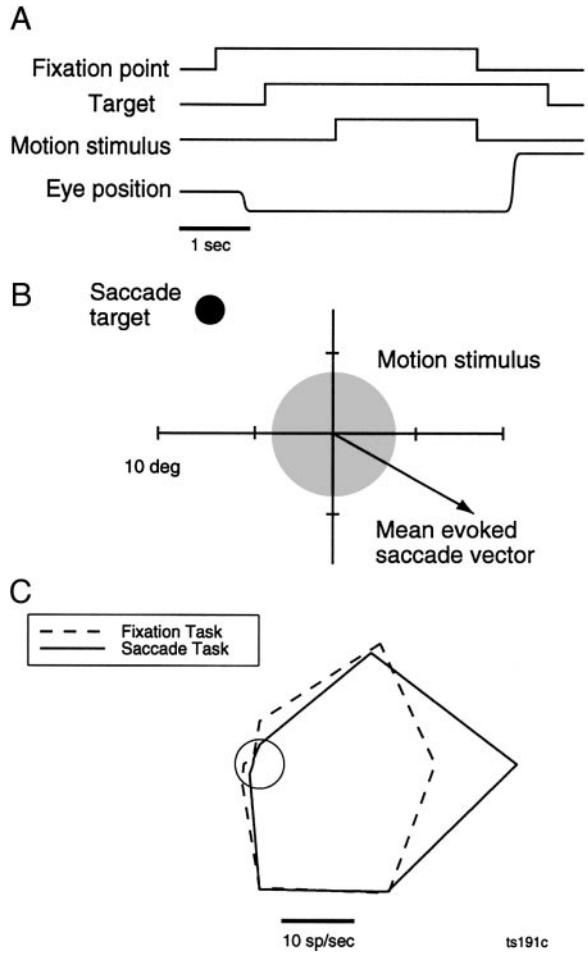

FIG. 6. Direction tuning of a single SC neuron during delayed saccades. *A*: 300 ms after the monkey achieved visual fixation, a single saccade target appeared. Eight hundred milliseconds later the motion stimulus was presented for 2,000 ms. The monkey received a liquid reward for making a saccade to this target within 500 ms of fixation point offset. *B*: the geometry of the display was adjusted so that the target (black disk) appeared at a location remote from the end points of electrically evoked saccades (arrow). *C*: direction tuning curves measured during passive-fixation (dashed) and delayed-saccade (solid) tasks were very similar. The circle at the origin of the tuning curves indicates the baseline firing rate.

Figure 6*C* shows data from a single SC neuron recorded during this task. The direction tuning curve obtained during passive fixation trials (- - -) appeared previously in Fig. 2. The direction tuning measured during the interleaved delayed-saccade trials (—) is essentially identical.

We studied 22 neurons in interleaved passive fixation and delayed-saccade trials and found consistently that direction tuning differed little between these conditions. We parameterized each direction tuning curve with fitted four-parameter Gaussian functions (see METHODS), and then compared the fitted parameter values between behavioral conditions as illustrated in Fig. 7. Across the population of cells, we found tight correlations in preferred direction (circular-circular rank correlation coefficient $r = 0.95$, $P < 0.0001$), tuning curve amplitude ($r = 0.81$, $P < 0.0001$), and tuning curve baseline ($r = 0.90$, $P < 0.0001$). Tuning widths varied little across experiments and were not significantly correlated between behavioral tasks ($r = 0.36$, $P > 0.1$). Additional statistical tests confirmed that preferred direction, amplitude, and tuning width did not differ between behavioral conditions (Wilcoxon tests: $P > 0.05$). These results suggest that the direction-tuned responses do not arise from covert saccade planning.

Persistent motion

It remains logically possible that the directional visual responses described in the preceding section could result from transient covert saccade plans in the direction of stimulus motion. In this scenario, the monkey must quickly change its plan near the end of the trial so as to make an appropriate saccade to the visual target located well away from the movement field. We tested this possibility in another set of experiments in which the random-dot motion stimulus was present ("persisted") until the monkey actually executed the saccadic

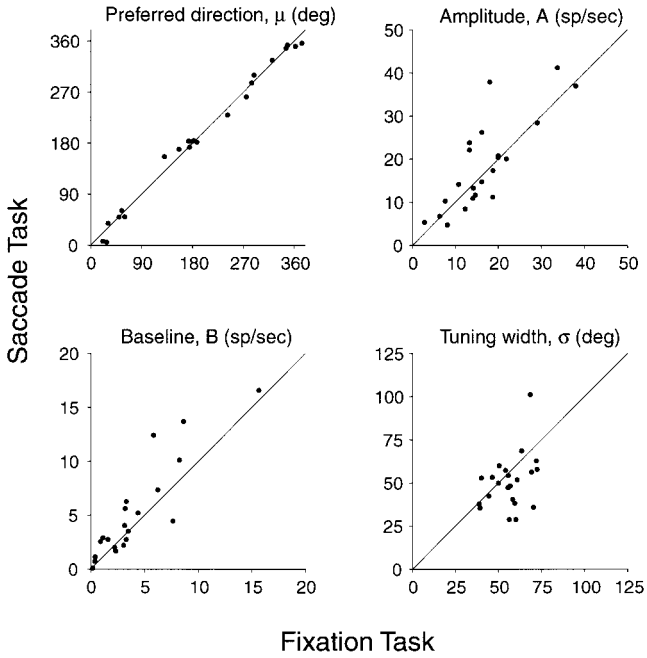

FIG. 7. Scatterplots of fitted parameters for direction tuning data measured during passive fixation (abscissa) and delayed-saccade (ordinate) trials. Corresponding symbols from *Eq. 1* are as follows: μ, preferred direction; *A*, tuning curve amplitude; *B*, baseline; σ, tuning width.

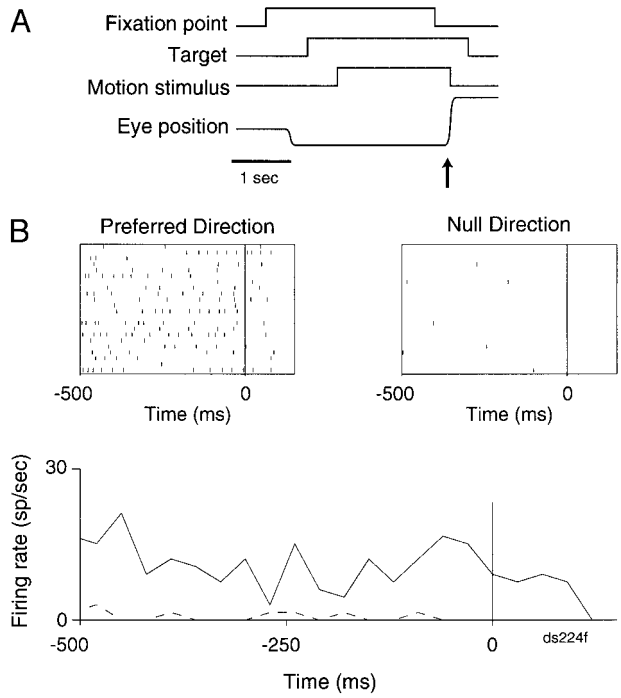

FIG. 8. Direction-selective response that persisted through saccade initiation. *A*: we measured direction tuning immediately prior to saccades directed to a visual target outside of the movement field (arrow). *B*: all trials are aligned to the time of saccade initiation (vertical bar). This cell responded to motion in 1 direction [left spike raster, solid peristimulus time histogram (PSTH)] but not the other (right spike raster, dashed PSTH) until, and slightly after, saccade initiation. Bin width = 30 ms.

eye movement to the remote visual target (Fig. 8*A*). If the neural response to random-dot motion reflects a covert saccade plan that is changed near the end of the trial, the response should cease prior to execution of the rewarded saccade. If, on the other hand, the neural activity indeed reflects a directional visual response to the random-dot stimulus, neural activity should continue until the saccade actually removes the stimulus from the receptive field. In these experiments, we measured responses to only two directions of motion: toward and away from the movement field. This allowed us to average across large numbers of trials and thus derive an accurate estimate of the firing rate at the time of saccade initiation.

Most direction-selective SC neurons, like the one illustrated in Fig. 8*B*, maintained their directional response up until the saccade and occasionally through and after it. This cell fired an average of 11 spikes/s when motion flowed toward the movement field and 1 spike/s when motion flowed in the opposite direction, and this difference persisted even at the instant of saccade initiation. Plainly, the direction-selective activity of this cell cannot reflect covert saccade planning; this cell responds specifically to visual motion flowing toward the movement field despite the fact that the monkey plans and executes a saccade to the same remote location on every trial.

A small number of the cells, however, stopped responding shortly before saccade initiation. Figure 9 illustrates the responses of one such neuron. This cell was strongly direction selective during most of the trial, discharging at an average rate of 18 spikes/s in response to motion toward its movement field and 3 spikes/s for motion in the opposite direction. Less than 100 ms before saccade initiation, however, the cell ceased

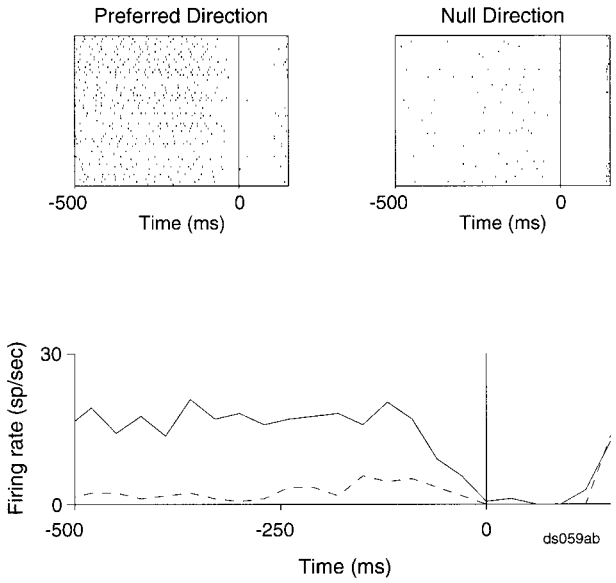

FIG. 9. A direction-selective response that ceased shortly before saccade initiation. Conventions as in Fig. 8*B*.

responding irrespective of the motion direction. In the absence of data like those in Fig. 8*B*, the activity of this neuron could support the hypothesis of an abruptly changing saccade plan.

We measured the responses of 15 neurons in this delayed-saccade task with "persistent motion." Figure 10 shows firing rate averaged across cells near the time of saccade initiation. Responses to motion directed toward and away from the movement field are drawn in thick and thin lines, respectively. The dashed lines indicate 1 SE above and below the mean responses. Across this population of cells, the firing rates induced by the two directions of stimulus motion differ significantly up to and including the time of the saccade. Analyzed individually, 11 of the 15 cells were significantly directional during the perisaccadic interval, defined as 50 ms preceding saccade initiation to 25 ms afterward (Mann-Whitney *U* tests, $P < 0.01$). We thus conclude that a majority of direction-selective cells exhibit a persistent directional response that is inconsistent with an abruptly changing saccade plan.

We considered the possibility that slight variation in saccade parameters might account for the direction-selective responses of the SC neurons we recorded. For each of the 11 neurons with persistent, direction-selective activity, we regressed perisaccadic firing rate onto the *x* and *y* components of the saccade endpoints, the peak velocity of the saccade, and the latency from fixation point offset to saccade initiation. After fitting this model, we asked whether the addition of motion direction as a predictor accounted for a significant fraction of the remaining variance in firing rate. This was the case for all 11 cells (partial *F* tests: $P < 0.01$, for each cell), indicating that firing rate and motion direction are related significantly, even after taking into account the potential influence of saccade parameters.

Interrupted motion

As a third test of the motor hypothesis, we measured the ability of direction-selective SC neurons to entrain their responses to a random-dot stimulus that alternated at 5 Hz between moving and stationary conditions ("interrupted" motion: Fig. 11*A*). If the direction-selective responses of SC neurons are of visual origin, we would expect the response to modulate with the onset and offset of stimulus motion. We do not, however, expect saccade plans to alternate at 5 Hz. Motion stimuli were presented as the monkey performed the passive fixation task described earlier. For comparison, we collected a separate block of fixation trials in which motion was not interrupted ("smooth" motion). All motion stimuli were 100% coherent and were presented in an aperture at the center of gaze. The dots flowed in the cell's preferred direction (toward the movement field). The smooth motion stimulus drifted at a constant speed of 3°/s. whereas the speed of the interrupted stimulus alternated between 3°/s and 0°/s. Importantly, the luminance did not modulate in either stimulus.

Figure 11, *B* and *C*, shows the responses of a single SC neuron to these two stimuli. Interrupted motion generated clear stimulus-locked modulations of the neural activity, although these modulations were less obvious in the second half of the trial. In contrast, smooth motion generated a single transient peak followed by a relatively steady firing rate for the duration of the trial. To determine the magnitude of the 5-Hz signal in the stimulus-locked neuronal response, we calculated the power spectrum of the PSTHs (Fig. 11*E*). The interrupted motion spectrum exhibited a small but pronounced peak at 5 Hz that was completely absent in the smooth motion spectrum.

To assess the statistical significance of the 5-Hz modulation, we first calculated for each spectrum the "relative 5 Hz power," defined as the power in the Fourier spectrum from 4 to 6 Hz divided by power from 2 to 200 Hz. The difference in relative 5-Hz power between the interrupted and smooth motion conditions was taken as a measure of how well the response entrained to the stimulus. We performed a permutation test (100,000 iterations), reassigning individual trials to the two stimulus conditions, to test the hypothesis that relative 5-Hz power was equivalent between conditions. For the responses shown in Fig. 11, the relative 5-Hz power was significantly

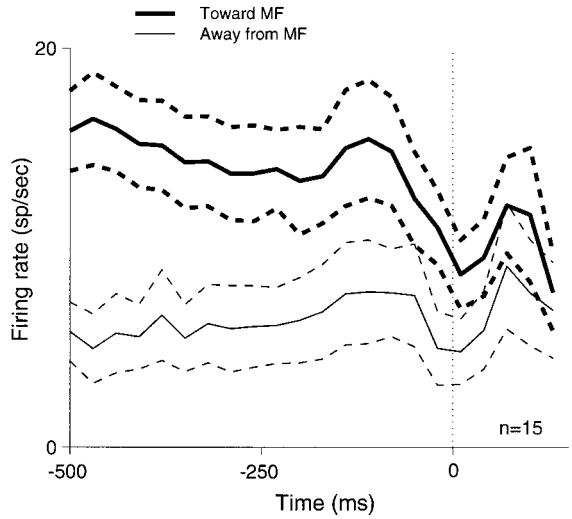

FIG. 10. Population responses to 2 opposed directions of stimulus motion. Responses were averaged over the 15 neurons tested in the persistent motion task. All trials were aligned to saccade initiation. Motion flowing toward the movement field (thick line) elicited greater responses than motion in the opposite direction (thin line) at all time points up to and including the time of the saccade. Dashed lines indicate ±1 SE of the mean.

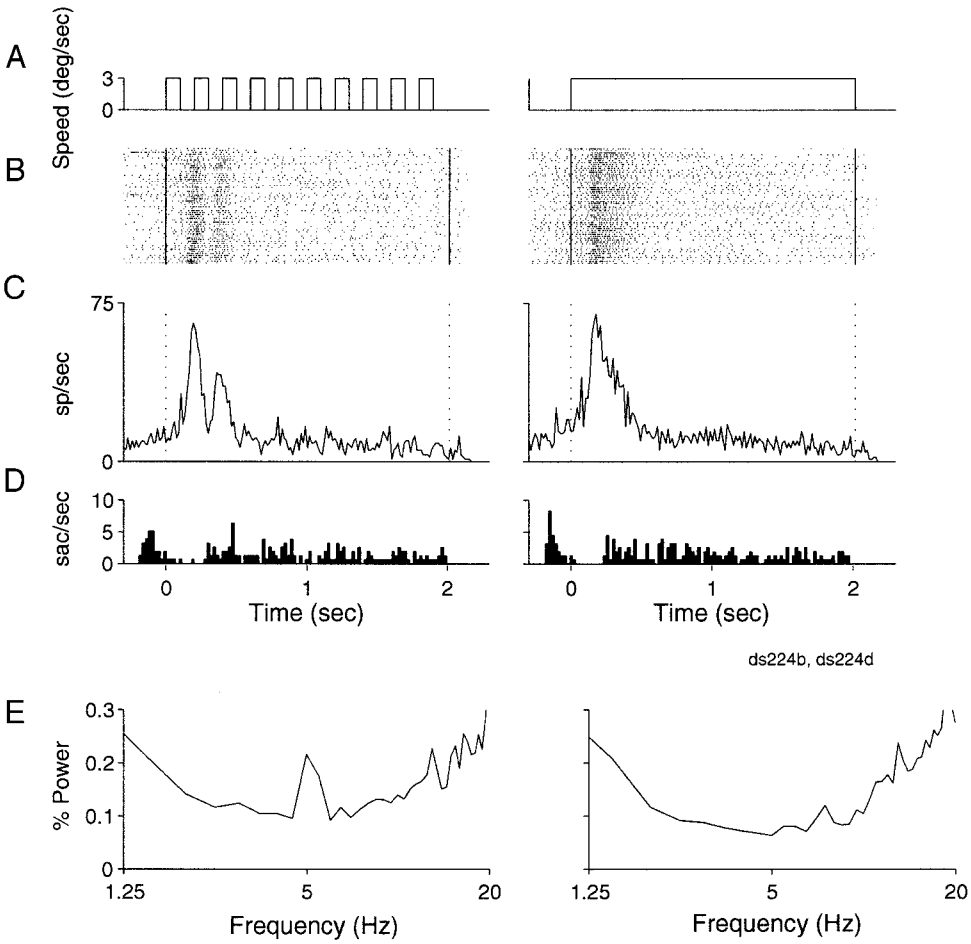

FIG. 11. Responses of a single SC neuron to interrupted and smooth motion stimuli. *A*: interrupted stimuli (*left*) alternated at 5 Hz between 3°/s motion in the preferred direction and stationary dots (0°/s). Smooth stimuli (*right*) moved constantly at 3°/s in the preferred direction. *B*: neural responses to interrupted (*left*) and smooth (*right*) motion stimuli. *C*: PSTHs of neural activity in *B*. *D*: histograms of the times of fixational saccades during interrupted and smooth motion. *E*: power spectra computed from the response PSTHs in *C*.

greater in the interrupted motion condition than in the smooth motion condition ($P < 0.001$). Figure 12 shows the outcome of this analysis for eight direction-selective cells. For seven of the eight cells, the interrupted motion stimulus generated significantly more 5-Hz power than did the smooth motion stimulus ($P < 0.001$).

The entrainment of neuronal responses to the interrupted motion stimulus is consistent with a fundamentally sensory basis for these signals (Groh and Sparks 1996). These data appear inconsistent with the covert saccade planning hypothesis; it seems highly unlikely that the monkey alternately plans and "unplans" saccades five times per second.

A possible objection to the result in Fig. 12 is that the interrupted motion stimulus may induce small, fixational eye movements entrained to the stimulus and that these eye movements were the basis of the modulated neuronal responses that we observed. The fact that our stimuli were always presented at the center of gaze adds credibility to this notion.

To address this objection, we analyzed the eye-position records measured during the interrupted motion experiments, identifying fixational saccades on the basis of velocity, duration, and frequency criteria. For a displacement in eye position to be classified as a saccade, its peak speed had to exceed 20°/s and its duration, defined as length of time that eye speed exceeded 10°/s, had to be ≥12 ms. Pairs of displacements that met these criteria, but were separated by <20 ms, were considered a single saccade. Measured by these criteria, the average amplitude of fixational saccades detected in these experiments was 0.75 ± 0.43° (mean ± SD).

To determine whether fixational saccades were linked to the 5-Hz stimulus modulation, we constructed PSTHs of saccade times, as shown in Fig. 11*D*. The difference in the relative 5-Hz power in these two saccade occurrence histograms was statistically significant as determined by a permutation test analogous to the test performed on the neuronal responses ($P < 0.05$). For this cell, therefore periodicity in the frequency of fixational saccades is a plausible explanation for the periodicity in firing rate. We detected significant 5-Hz modulation in the frequency of fixational saccades in only one other experiment, however, so fixational saccades cannot account for the bulk of the results in Fig. 12.

Some SC neurons, particularly those near the rostral pole, discharge in conjunction with smooth pursuit eye movements (Krauzlis et al. 1997; Schiller and Koerner 1971). Low-velocity smooth eye movements occurred frequently in our data because of the strong motion stimuli at the center of gaze, raising the possibility that smooth eye movements might account for the oscillatory neural activity. The neurons depicted in Fig. 12, however, were not located near the rostral pole. Electrical microstimulation at six of these recording sites evoked saccades that averaged 14 ± 8° in amplitude (range: 4.5–27°), placing them closer to the middle of the SC.

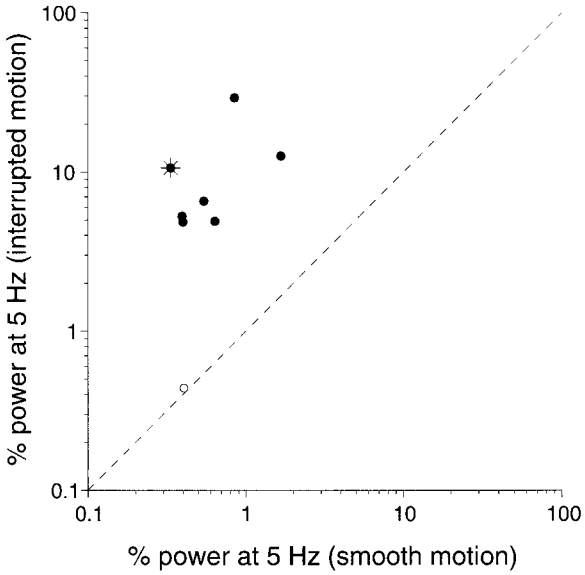

FIG. 12. Scatterplot of relative 5-Hz power in the neural responses to interrupted and smooth motion. Seven of 8 cells exhibited significantly more 5-Hz modulation in the response to interrupted motion (filled symbols, permutation test: $P < 0.001$). One cell did not show this effect ($P > 0.4$, open symbol). Asterisk indicates the cell whose responses are illustrated in Fig. 11. Note that the absolute percentages differ in Figs. 12 and 11*E* because "relative power" was used in Fig. 12 (see text).

Prelude and saccade-related discharge

As described in an earlier publication (Horwitz and Newsome 1999) and in the companion paper to this one (Horwitz and Newsome 2001), we gathered quantitative data during performance of the direction-discrimination task from 96 choice-predicting prelude neurons in the SC. Figure 13 documents the distribution of direction tuning indices obtained from these 96 neurons; ■ represents the 44 cells with statistically significant direction tuning (permutation test: $P < 0.05$), and □ represents the 52 cells without significant direction tuning. We hypothesized that the non-direction-selective cells might be closer to the motor output of the SC and thus less likely to play a role in target selection. This hypothesis is supported by

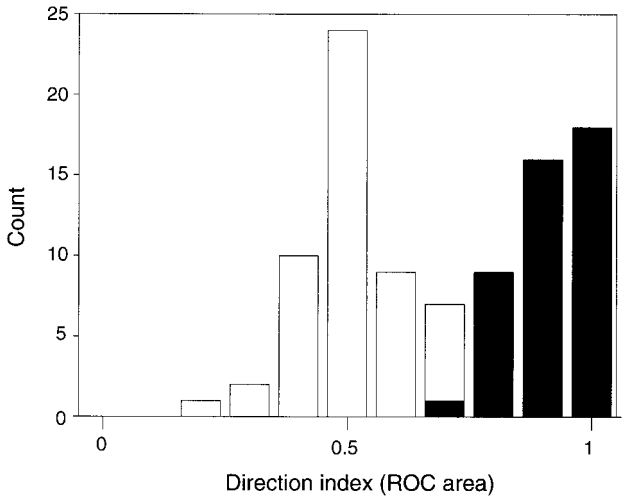

FIG. 13. Histogram of direction tuning indices from 96 choice-predicting neurons. A total of 44 significantly direction-selective neurons are represented by filled bars (permutation test: $P < 0.05$). The remaining 52 cells were not significantly direction selective (open bars).

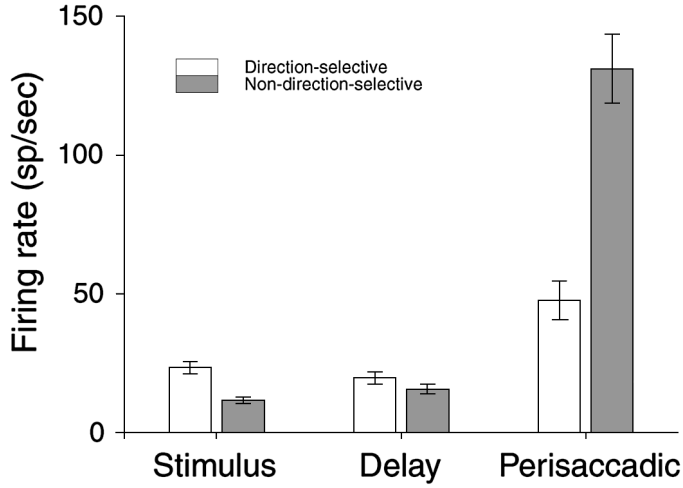

FIG. 14. Firing rate means and standard errors during the stimulus presentation, delay period, and perisaccadic interval for the population of direction-selective cells (open bars) and the population of non-direction-selective cells (filled bars).

analyses of saccade-related discharge, obtained while the monkeys performed the direction-discrimination task (Fig. 1), that reveal further differences between the groups of cells.

Figure 14 depicts average firing rates for the two types of prelude neurons (with and without directional visual responses) during three epochs of the trial: the stimulus presentation interval, the delay interval, and the perisaccadic interval that begins 50 ms before, and ends 25 ms after, saccade initiation. We analyzed trials with correct choices in which saccades were directed toward the target in the movement field. Direction-selective cells were significantly more active than non-direction-selective cells during the stimulus interval (Mann-Whitney U test: $P < 0.0001$), but not the delay interval (Mann-Whitney U test: $P = 0.23$). During the perisaccadic interval, when we would expect to see bursts of activity related to saccade execution, the non-direction-selective cells were substantially more active than the direction-selective cells (Mann-Whitney U test: $P < 0.0001$). The data suggest that the non-direction-selective cells may be more tightly linked to saccade execution.

We investigated this possibility further using a regression model to determine whether perisaccadic activity modulated in concert with subtle parametric variations in the saccadic eye movements. Recall that saccades on all of these trials were directed toward a salient target in the neuron's movement field. The saccades were thus quite stereotyped, with only minor trial-to-trial variations in parameters such as end point and peak velocity. For some neurons, however, the small variations in saccade parameters were systematically related to trial-to-trial fluctuations in firing rate. This was more often true for non-direction-selective cells than for direction-selective cells.

We employed an automatic model selection procedure (S+, Statistical Sciences) to customize the regression for each cell in an objective manner. Model selection was accomplished by "backward selection." To start, we fit the following model for each cell

$$\text{response} = \beta_0 + \beta_1 x + \beta_2 y + \beta_3 x^2 + \beta_4 y^2 + \beta_5 xy + \beta_6 \text{vel} + \beta_7 x\text{vel} + \beta_8 y\text{vel} + \beta_9 \text{lat}$$

where *x* and *y* are saccade endpoint coordinates (adjusted for differences in initial position), vel is the saccade peak velocity, and lat is saccadic latency. Coefficients were estimated by the method of least-squares. Individual predictors were dropped from the model in the order in which they accounted for firing rate variance [based on a C_p criterion (Linhart and Zucchini 1986)]. The procedure stopped when dropping additional variables did not serve to improve the model fit [based on an AIC criterion that penalizes models for incorporating too many variables (Linhart and Zucchini 1986)]. Final models included anywhere from one to eight predictor variables.

The proportion of cells with statistically significant ($P < 0.01$) regressions was higher for the non-direction-selective cells (44%) than for the direction-selective cells (30%), although this difference in proportion did not attain statistical significance (*z* test: $P > 0.1$). When we restricted our attention to the regressions that met a sterner criterion for significance ($P < 0.0001$), however, the distinction between the two groups became much more pronounced (2 and 23% for the direction-selective and non-direction-selective cells, respectively; *z* test: $P < 0.001$). Thus prelude neurons lacking directional visual responses appear to be more tightly linked to parametric specification of the saccadic eye movement, both in terms of the intensity of perisaccadic discharge and in terms of the quality of regressions of firing rate onto saccade parameters.

Classical visual responses

Many SC neurons that discharge saccade-related bursts also respond transiently to salient visual stimuli, particularly if the stimulus is to be the target of a saccadic eye movement. Classically, the visual receptive fields of intermediate and deep layer SC neurons are considered to be roughly co-extensive with their movement fields (Schiller and Koerner 1971; Wurtz and Goldberg 1972). We discovered serendipitously that the two populations of prelude neurons (with and without direction-selective visual responses) differ in the magnitude of this classical visual response. An initial clue to this difference was derived from an analysis of discharge associated with fixational eye movements during the direction-discrimination task. In the direction-discrimination task, one of the targets always appeared inside the movement field (Fig. 1), so fixational eye movements induced small motions of the target within the movement field. Some but not all neurons discharged after fixational saccades in a manner consistent with a visual response to saccade-induced target motion. We then asked whether the presentation of the target in the movement field elicited a visual response directly. Somewhat surprisingly, both analyses revealed that the non-direction-selective population yielded stronger classical visual responses than did the direction-selective population.

To assess the impact of fixational eye movements on neural activity, we calculated saccade-triggered average responses for the period of fixation when the targets were illuminated. Figure 15 illustrates saccade-triggered average responses across the population of direction-selective cells (*A*) and non-direction-selective cells (*B*). Both populations exhibited a transient increase in firing rate ~50 ms after the initiation of a fixational saccade, consistent with a short-latency visual response. The amplitude of this response was much larger in the population of

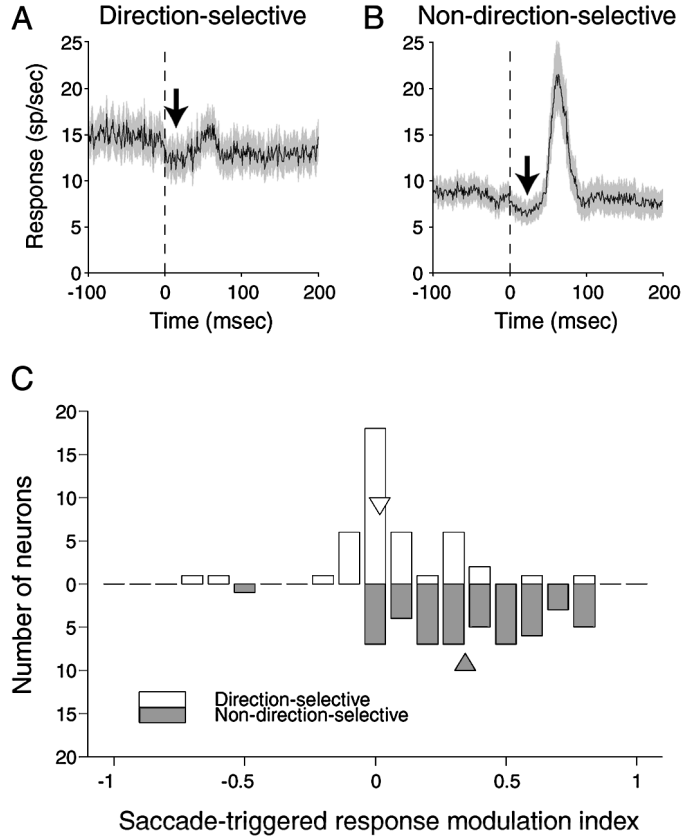

FIG. 15. Average fixational saccade-triggered responses across the population of direction-selective cells (*A*) and non-direction-selective cells (*B*). The gray band indicates ±1 SE. Fixational saccades were identified from the time of target onset until fixation point offset. Neuronal responses were aligned on the initiation of fixational saccades and averaged across trials and then across cells. Fixational saccades caused a transient, biphasic modulation of firing rate that was substantially larger in amplitude in the non-direction-selective population. The initial negative-going phase (arrows) is too rapid to have been a visual response and may reflect intracollicular inhibition that is time locked to saccade execution. *C*: histogram of saccade-triggered response modulation indices for direction-selective cells (open bars) and non-direction-selective cells (filled bars). Triangles indicate median index values.

non-direction-selective cells than in the population of direction-selective cells. Neither group of cells exhibited this response during the epoch preceding target illumination, suggesting that the presence of a target in the movement field is critical for the induction of this response (data not shown). The decrease in firing rate immediately preceding the presumed visual response (arrows), however, *was* observed in the absence of a target and is likely to reflect inhibition associated with saccade execution (Munoz and Istvan 1998; Walker et al. 1995).

For each cell, we calculated a saccade-triggered response index: (LATE − EARLY)/(LATE + EARLY), where early is the average firing rate 0–50 ms after a fixational saccade and late is the average firing rate over the subsequent 30 ms. This metric assumes positive values if late exceeds early, negative values if the reverse is true, and is constrained to lie between 1 and −1. A histogram of saccade-triggered response indices appears in Fig. 15*C*. Non-directional cells yielded significantly larger indices than direction-selective cells (Mann-Whitney *U* test: $P < 0.0001$), consistent with the idea that non-directional cells are more sensitive to motion of a visual target inside their movement fields.

We then asked to what degree the onset of the targets, one of which lay inside the movement field, excited the two populations of cells. Figure 16 shows PSTHs aligned on target onset and averaged across the populations of direction-selective (*A*) and non-direction-selective cells (*B*). As a population, non-direction-selective cells responded more strongly to the target presentation than did the direction-selective cells. Direction-selective cells exhibited a higher level of spontaneous discharge (before target onset) than did the non-directional cells.

For each cell we calculated a target onset response index: (TARG − BASELINE)/(TARG + BASELINE), where baseline is the average firing rate 0–50 ms after target onset (before onset of the visual response, see Fig. 16) and targ is the average firing rate over the subsequent 50 ms. Twenty-five cells (6 direction-selective and 19 non-direction-selective) that fired <1 spike/s during both epochs were excluded from this analysis. A histogram of target response indices for the 71 remaining cells appears in Fig. 16*C*. Non-directional cells yielded significantly larger indices than directional cells (Mann-Whitney *U* test: $P < 0.0001$), indicating that, as a population, non-directional cells are particularly sensitive to the abrupt onset of the visual targets. Many individual non-direction-selective neurons, however, lacked short-latency classical visual responses by both of our measures, indicative of substantial heterogeneity within this population.

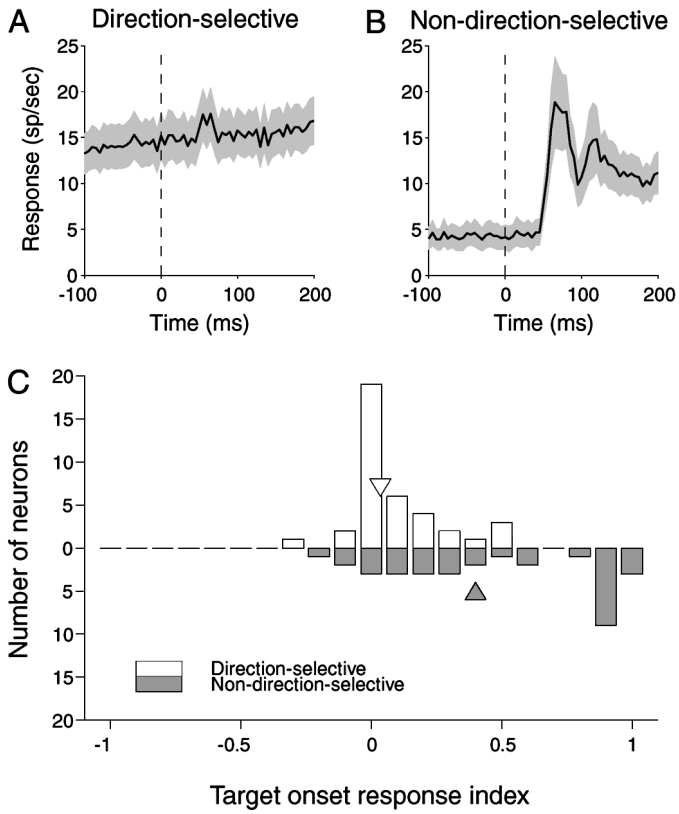

FIG. 16. Average response to target onset across the population of direction-selective cells (*A*) and non-direction-selective cells (*B*). Gray band indicates ±1 SE. *C*: histogram of target response indices for direction-selective cells (open bars) and non-direction-selective cells (filled bars). Triangles indicate median index values.

DISCUSSION

Roughly one-third of the neurons we encountered in the intermediate and deep layers of the SC exhibited target-specific preludes of activity while rhesus monkeys performed a direction-discrimination task. We subdivided these neurons into two populations based on their responses to a visual motion stimulus during passive fixation. A small population of SC neurons responded to the motion stimulus in a direction-selective manner. These neurons accounted for ~15% of all neurons isolated in the intermediate and deep layers or ~50% of the neurons that exhibited target-specific prelude activity during the direction-discrimination task. These cells responded to visual stimuli over an extensive region of visual space, and their preferred directions, measured with random dot stimuli positioned at the center of gaze, pointed consistently toward their movement fields.

In principle, direction-selective "visual" responses observed during the fixation task might reflect the intention to make a saccade in the direction of stimulus motion. Although saccade planning was not required in the fixation task, it was required in the direction-discrimination task that the monkeys had performed extensively. This training history may have caused the monkeys to plan saccades in the direction of stimulus motion, simply out of habit, whenever the motion stimulus appeared.

This "saccade-planning" explanation seems unlikely a priori for two reasons. First, the two trial types were presented in separate blocks of trials, and the monkeys received unambiguous information concerning the nature of the current block (saccade targets, for example, appeared at the beginning of each discrimination trial but never appeared during fixation trials). Second, half of the choice-predicting neurons identified during the direction-discrimination trials became completely inactive during the fixation trials. If the monkey was planning saccades identically in both conditions, identical cell populations should reflect the plan.

Three control experiments provided additional evidence that the direction-selective responses do not result from covert saccade planning. First, direction tuning was largely unaffected by an explicit requirement that the monkey make a delayed saccade to a visual target outside of the movement field. Second, the direction tuning of many cells persisted until the instant of saccade initiation to a target lying well outside the movement field, indicating that directional activity does not reflect a saccade plan that is changed late in the trial. Finally, the discharge of several direction-selective cells entrained subtly but significantly to a 5-Hz modulation in stimulus speed, which was presumably not accompanied by a similar modulation of saccade plan.

None of these control experiments are airtight, individually. The monkey need not plan saccades during the delay period of the delayed-saccade task because the target is illuminated throughout each trial. Not all of the neurons tested with persistent motion stimuli exhibited a persistent directional response. Response entrainment to the interrupted motion stimulus was subtle and accompanied, in a few experiments, by significant modulations in fixational eye movements. Collectively, however, the results of each of the three experiments point toward the same conclusion: the direction-selective responses are fundamentally visual in origin and do not reflect covert saccade planning. To conclude otherwise requires a

different ad hoc rationalization to explain away the results of each experiment (as in the preceding text). Thus the power of our conclusion lies not in any single result, but in its consistent and parsimonious ability to account for several experimental observations.

Hypothesized functional roles

Our working hypothesis is that the direction-selective cells described here play a role in saccade target selection. The fact that preferred directions pointed consistently toward movement fields agrees perfectly with the rules of target selection in our task: motion in a particular direction instructs the monkey to select the target lying in that direction. These cells thus carry sensory information required for selecting the correct target into close apposition with neurons in the SC that are involved in executing the appropriate operant saccade; the directional visual information is expressed at the topographic location occupied by the relevant saccade-related burst neurons.

The non-direction-selective prelude cells, on the other hand, appear to be more closely linked with specification of saccade parameters. These cells fire intense perisaccadic bursts that are related to precise saccade parameters as revealed by regression analyses. Both direction-selective and non-direction-selective neurons may also exist in the lateral intraparietal area (LIP) and the frontal lobes (the frontal eye fields and area 46) in monkeys trained on this direction-discrimination task, although the directional visual responses appear to be weaker and less commonly observed than in the SC (Kim and Shadlen 1998; Shadlen and Newsome 2001).

Origin of the direction selectivity

We suspect that the directional responses reported here are not computed de novo in the SC but rather are inherited from upstream areas of the visual cortex. Cortical areas MT, MST, and VIP are good candidates for supplying directional input to the SC, either directly or indirectly. Neurons in all three areas are strongly directional (Colby et al. 1993; Maunsell and Van Essen 1983; Mikami et al. 1986; Tanaka et al. 1986; Zeki 1974), and MT and MST are major sources of the sensory signals that underlie performance on our direction-discrimination task (Britten et al. 1992; Celebrini and Newsome 1994, 1995; Salzman et al. 1992; Shadlen et al. 1996). Anatomically, MT projects to the superficial layers of the SC (Fries 1984) and MST projects to the intermediate and deep layers (Maioli et al. 1992). Paré et al. (1999) recently employed antidromic activation techniques to identify a monosynaptic projection from direction-selective neurons in area VIP to the intermediate layers of the SC. We therefore hypothesize that training on our direction-discrimination task induces plastic changes in the wiring from cortical areas to the SC, giving rise to the precisely organized directional responses that we have observed in the SC.

While the directional responses in the SC appear to be of visual origin, the responses nevertheless differ substantially from those of MT neurons, for example. Latencies of directional responses in MT range from 35 to 60 ms and are fairly reliable, whereas latencies were more than doubled and considerably more variable in the SC. When tested with speed-modulated stimuli, MT neurons exhibit a strongly modulated response throughout the entire stimulus presentation (Bair and Koch 1996; Buracas et al. 1998). Our SC neurons, in contrast, were most strongly modulated during the first few cycles of the interrupted motion stimulus. Finally, most MT neurons respond briskly to both dot and bar stimuli. In a few qualitative tests, we were unable to elicit directional responses with bar stimuli in the SC. These differences suggest that nontrivial visual processing occurs between MT and the SC.

Importance of behavioral training

Direction-selective SC neurons are excited by motion stimuli at the center of gaze flowing toward the movement field. This relationship between preferred direction and movement field location has not been documented previously but agrees perfectly with the logic of our direction-discrimination task. We thus suspect that training on our task may be an important factor in establishing the directional responses documented in this report.

Previous studies have revealed a centrifugal organization of preferred directions in certain visual cortical areas of untrained cats and monkeys (e.g., Albright 1989; Rauschecker et al. 1987). Our results, while superficially similar to these, do not reflect the same phenomenon. First, the "receptive fields" that we measured in the SC occupied large portions of both hemifields, whereas those documented in the visual cortex were considerably smaller and confined to a single hemifield. Second, the direction-selective responses of SC neurons were neither consistently centrifugal nor centripetal. Rather the preferred direction consistently pointed toward the movement field of the neuron and could thus be centrifugal (with respect to the fovea) when measured in the contralateral hemifield or centripetal when measured in the ipsilateral hemifield.

In unpublished work in this laboratory, we have looked for direction-selective SC neurons in two monkeys who were trained only briefly to perform our standard direction-discrimination task. Preliminary observations indicate that direction tuning is much weaker in these animals than in those that experienced prolonged training (data will be presented in a later report). This strengthens the idea that task training is responsible for SC direction selectivity. To the extent that behavioral training is responsible for the direction selectivity we have documented, our results appear closely related to those of Bichot and colleagues, who demonstrated learning-related stimulus selectivity in FEF (Bichot et al. 1996) and may be related to a similar phenomenon in LIP (Sereno and Maunsell 1998).

Not a sensory vs. motor distinction

In general, the movement field and the visual receptive field of a typical SC visuomotor neuron are spatially superimposed (Schiller and Koerner 1971; Wurtz and Goldberg 1972). In our sample of prelude neurons, such "classical" visual responses were more common in the population of non-direction-selective cells. This difference was evident both in responses induced by small fixational eye movements (Fig. 15) and in responses to onset of the saccade targets (Fig. 16). In both cases, the visual response had a latency of ~50 ms, which was less than half the shortest latency we ever recorded for the direction-selective response. Thus the transient visual re-

sponses induced by fixational eye movements or by target onset appear to differ qualitatively from the direction-selective response. Although they are both "visual responses," they probably derive from different neural pathways. The fact that each population of prelude neurons carries a visual signal disallows a simple characterization of one group as "sensory" and the other as "motor." Only those few neurons that have neither direction-selective nor classical visual responses are reasonably classified as closer to the motor end of a sensorimotor continuum (Figs. 15 and 16).

The difference in visual response (direction-selective vs. classical) suggests different functional roles for the two groups of cells. Non-direction-selective cells carry signals relating to the retinal position of eccentric stimuli and the motor command to foveate them, whereas direction-selective cells respond in accordance with the learned association imposed by the logic of the direction-discrimination task. One functional scheme consistent with these observations is that non-direction-selective cells are components of a relatively simple neural circuit whose primary function is to guide the fovea to salient, eccentric stimuli (the so-called "foveal grasp reflex"). The ability of this circuit to produce a saccade, however, may be modulated by higher-level circuitry, represented by the direction-selective cells, that promotes saccades to some targets and inhibits saccades to others based on current behavioral context.

Neural mechanisms of target selection

Only in the laboratory is saccade target selection based on the direction of motion in a random-dot stimulus. Elsewhere, target selection may be driven and modulated by a variety of stimuli and contextual cues. We suggest that the cells that appear "direction-selective" in our experiment may integrate information from a variety of sources. The result of this integration, captured in the firing rate of the cells, reflects the likelihood of making a saccade into the movement field characteristic of their locations in the collicular map. That some SC neurons may integrate varied sources of sensory input relevant for saccade target selection has been demonstrated previously (Drager and Hubel 1975; Stein and Meredith 1994). For example, some SC neurons respond to both visual and auditory stimuli in the region of space corresponding to the movement field. Such neurons integrate across sensory modalities, but not position. We find that some SC neurons are capable of integrating information across many retinal locations; their receptive fields extend far beyond the movement field boundaries, which classically delimit the receptive field as well.

Our experimental paradigm is unusual in that the cue that governs target selection is spatially distinct from the targets themselves. Had the selection cue been a property of the target (e.g., color or luminance) we would not have been able to dissociate responses relating to the *instruction* to make a saccade of a particular direction from responses simply relating to the *presence* of a saccade target in the movement field (see also Glimcher and Sparks 1992). Indeed, in a simple delayed-saccade task, in which the illumination of a target in the movement field instructs a saccade to the same target, most direction-selective cells appeared to have a conventional tonic visual response to the target. Mays and Sparks described a small population of "quasi-visual" SC neurons that responded to the presence of a target in their receptive fields but also discharged when a saccade into the receptive field was cued by other means (Mays and Sparks 1980). There may be considerable overlap between our population of direction-selective cells and those examined by Mays and Sparks.

Basso and Wurtz (1998) studied a sample of SC neurons that, based on their screening criteria, are likely to overlap with both populations that we have studied (Basso and Wurtz 1998). Across the cells they investigated, activity modulated with the number of potential saccade targets presented in a visual display. As soon as a single correct target was cued, however, the influence of target number on firing rate disappeared. The authors interpreted their result as reflecting changes in the animal's confidence that a particular target in the array was the correct target. In light of the results reported here, it would be interesting to know if this effect was more pronounced in a subset of neurons that are the presumed counterparts to our direction-selective cells. These neurons could be classified on the basis of the magnitude of their classical visual response, prelude or perisaccadic responses, or a combination of these factors.

Schall and colleagues have described neurons in the frontal eye fields (FEF) that may also be involved in saccade target selection (Bichot et al. 1996; Schall and Hanes 1993; Thompson et al. 1997). In the context of a reaction-time visual search task, these cells predict target choices in a manner that is not obligatorily linked to saccade execution nor is well correlated with saccadic latencies. Heavy training on this task can systematically alter the visual response properties of some FEF neurons to reflect the learned sensorimotor association (Bichot et al. 1996). These results are remarkably consonant with the ones reported here despite significant differences in the experimental paradigms

Shadlen and colleagues recorded from neurons in LIP and FEF while monkeys performed the direction-discrimination task described in this paper (Kim and Shadlen 1998; Shadlen and Newsome 2001). Choice-predicting activity in these areas had qualitatively similar latency and time course to that observed in the SC. This crude comparison thus does not reveal where in the oculomotor system signals relating to target selection are first manifest. A more rigorous comparison is prevented, however, by methodological differences among the studies. Simultaneous recordings of pairs of neurons in different brain areas may reveal a stereotyped order of activation. Such a result would support a model in which target selection is accomplished by a series of processing steps that occur sequentially across different brain areas. On the other hand, SC, LIP, and FEF may comprise a distributed network that implements target selection in parallel fashion, in which case no single area would be expected to reflect the target choice more quickly than the other two.

The cognitive demands imposed by a behavioral task are likely to influence which neural circuits participate in saccade target selection. Tasks that involve complex associations between stimuli and operant responses lead to the emergence of cells in the frontal lobes with complex response properties (Hasegawa et al. 1998; Olson and Gettner 1999; Rao et al. 1997). These cells may be important for target selection in these tasks. In contrast, simpler sensorimotor associations, such as our direction-discrimination task, may invoke simpler neural circuits to accomplish target selection. Extensive behavioral training may further streamline the target selection pro-

cess. The fact that we used a simple task and trained our animals extensively may have contributed to the emergence of signals relating to target selection in the SC of our monkeys.

While the sensory responses we have analyzed in this paper suggest a role for a network of SC neurons in target selection, we have not yet considered how SC neurons actually respond during target selection, a topic that we now engage in the companion paper.

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REFERENCES

ALBRIGHT TD. Centrifugal directional bias in the middle temporal visual area (MT) of the macaque. *Vis Neurosci* 2: 177–188, 1989.

BAIR W AND KOCH C. Temporal precision of spike trains in extrastriate cortex of the behaving macaque monkey. *Neural Comput* 8: 1185–1202, 1996.

BASSO MA AND WURTZ RH. Modulation of neuronal activity by target uncertainty. *Nature* 389: 66–69, 1997.

BASSO MA AND WURTZ RH. Modulation of neuronal activity in superior colliculus by changes in target probability. *J Neurosci* 18: 7519–7519, 1998.

BICHOT NP AND SCHALL JD. Effects of similarity and history on neural mechanisms of visual selection. *Nat Neurosci* 2: 549–554, 1999.

BICHOT NP, SCHALL JD, AND THOMPSON KG. Visual feature selectivity in frontal eye fields induced by experience in mature macaques. *Nature* 381: 697–699, 1996.

BRITTEN KH, SHADLEN MN, NEWSOME WT, AND MOVSHON JA. The analysis of visual motion: a comparison of neuronal and psychophysical performance. *J Neurosci* 12: 4745–4765, 1992.

BRITTEN KH, SHADLEN MN, NEWSOME WT, AND MOVSHON JA. Responses of neurons in macaque MT to stochastic motion signals. *Vis Neurosci* 10: 1157–1169, 1993.

BURACAS GT, ZADOR AM, DEWEESE MR, AND ALBRIGHT TD. Efficient discrimination of temporal patterns by motion-sensitive neurons in primate visual cortex. *Neuron* 20: 959–969, 1998.

CELEBRINI S AND NEWSOME WT. Neuronal and psychophysical sensitivity to motion signals in extrastriate area MST of the macaque monkey. *J Neurosci* 14: 4109–4124, 1994.

CELEBRINI S AND NEWSOME WT. Microstimulation of extrastriate area MST influences performance on a direction discrimination task. *J Neurophysiol* 73: 437–448, 1995.

COLBY CL, DUHAMEL JR, AND GOLDBERG ME. Ventral intraparietal area of the macaque: anatomic location and visual response properties. *J Neurophysiol* 69: 902–914, 1993.

CYNADER M AND BERMAN N. Receptive-field organization of monkey superior colliculus. *J Neurophysiol* 35: 187–201, 1972.

DRAGER UC AND HUBEL DH. Responses to visual stimulation and relationship between visual, auditory, and somatosensory input in mouse superior colliculus. *J Neurophysiol* 38: 690–713, 1975.

FRIES W. Cortical projections to the superior colliculus in the macaque monkey: a retrograde study using horseradish peroxidase. *J Comp Neurol* 230: 55–76, 1984.

FUCHS AF AND ROBINSON DA. A method for measuring horizontal and vertical eye movement chronically in the monkey. *J Appl Physiol* 21: 1068–1070, 1966.

GLIMCHER PW AND SPARKS DL. Movement selection in advance of action in the superior colliculus. *Nature* 355: 542–545, 1992.

GREEN DM AND SWETS JA. *Signal Detection Theory and Psychophysics.* New York: Wiley, 1966.

GROH JM AND SPARKS DL. Saccades to somatosensory targets: eye-position-dependent somatosensory activity in primate superior colliculus. *J Neurophysiol* 75: 439–453, 1996.

HASEGAWA R, SAWAGUCHI T, AND KUBOTA K. Monkey prefrontal neuronal activity coding the forthcoming saccade in an oculomotor delayed matching-to-sample task. *J Neurophysiol* 79: 322–333, 1998.

HAYS AV, RICHMOND BJ, AND OPTICAN LM. A UNIX-based multiple process system for real-time data acquisition and control. *WESCON Conf Proc* 2: 1–10, 1982.

HORWITZ GD AND NEWSOME WT. Separate signals for target selection and movement specfication in the superior colliculus. *Science* 284: 1158–1161, 1999.

HORWITZ GD AND NEWSOME WT. Target selection for saccadic eye movements: prelude activity in the superior colliculus during a direction-discrimination task. *J Neurophysiol* 86: 2543–2558, 2001.

JUDGE SJ, RICHMOND BJ, AND CHU FC. Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res* 20: 535–538, 1980.

KIM JN AND SHADLEN MN. Neural correlates of a decision in the dorsolateral prefrontal cortex of the macaque. *Nat Neurosci* 2: 176–185, 1998.

KRAUZLIS RJ, BASSO MA, AND WURTZ RH. Shared motor error for multiple eye movements. *Science* 276: 1693–1695, 1997.

LINHART H AND ZUCCHINI W. *Model Selection.* New York: Wiley, 1986.

MAIOLI MG, DOMENICONI R, SQUATRITO S, AND RIVA SANSERVERINO E. Projections from cortical visual areas of the superior temporal sulcus to the superior colliculus, in macaque monkeys. *Arch Ital Biol* 130: 157–166, 1992.

MAUNSELL JHR AND VAN ESSEN DC. Functional properties of neurons in the middle temporal visual area (MT) of the macaque monkey. I. Selectivity for stimulus direction, speed and orientation. *J Neurophysiol* 49: 1127–1147, 1983.

MAYS LE AND SPARKS DL. Dissociation of visual and saccade-related responses in superior colliculus neurons. *J Neurophysiol* 43: 207–232, 1980.

MIKAMI A, NEWSOME WT, AND WURTZ RH. Motion selectivity in macaque visual cortex. I. Mechanisms of direction and speed selectivity in extrastriate area MT. *J Neurophysiol* 55: 1308–1327, 1986.

MUNOZ DP AND ISTVAN PJ. Lateral inhibitory interactions in the intermediate layers of the monkey superior colliculus. *J Neurophysiol* 79: 1193–1209, 1998.

MUNOZ DP AND WURTZ RH. Saccade-related activity in monkey superior colliculus. I. Characteristics of burst and buildup cells. *J Neurophysiol* 73: 2313–2333, 1995.

NEWSOME WT AND STEIN-AVILES JA. Nonhuman primate models of visually based cognition. *ILAR* 40: 78–91, 1999.

OLSON CR AND GETTNER SN. Macaque SEF neurons encode object-centered directions of eye movements regardless of the visual attributes of instructional cues. *J Neurophysiol* 81: 2340–2346, 1999.

PARÉ M, FERRAINA S, AND WURTZ RH. Visual motion signals from the ventral intraparietal area to the saccadic system. *Soc Neurosci Abstr* 25: 806, 1999.

PLATT ML AND GLIMCHER PW. Neural correlates of decision variables in parietal cortex. *Nature* 400: 233–238, 1999.

RAO SC, RAINER G, AND MILLER EK. Integration of what and where in the primate prefrontal cortex. *Science* 276: 821–824, 1997.

RAUSCHECKER JF, VON GRUNAU MW, AND POULIN C. Centrifugal organization of direction preferences in the cat's lateral suprasylvian visual cortex and its relation to flow field processing. *J Neurosci* 7: 943–958, 1987.

ROBINSON DA. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Biomed Eng* 10: 137–145, 1963.

ROBINSON DA. Eye movements evoked by collicular stimulation in the alert monkey. *Vision Res* 12: 1795–1807, 1972.

SALZMAN CD, MURASUGI CM, BRITTEN KH, AND NEWSOME WT. Microstimulation in visual area MT: effects on direction discrimination performance. *J Neurosci* 12: 2331–2355, 1992.

SCHALL JD AND HANES DP. Neural basis of saccade target selection in frontal eye field during visual search. *Nature* 366: 467–469, 1993.

SCHALL JD, HANES DP, THOMPSON KG, AND KING DJ. Saccade target selection in frontal eye field of macaque. I. Visual and premovement activation. *J Neurosci* 15: 6905–6918, 1995.

SCHALL JD AND THOMPSON KG. Neural selection and control of visually guided eye movements. *Annu Rev Neurosci* 22: 241–259, 1999.

SCHILLER PH AND KOERNER F. Discharge characteristics of single units in superior colliculus of the alert rhesus monkey. *J Neurophysiol* 34: 915–924, 1971.

SCHILLER PH AND STRYKER M. Single-unit recording and stimulation in superior colliculus of the alert rhesus monkey. *J Neurophysiol* 35: 915–924, 1972.

SERENO AB AND MAUNSELL JH. Shape selectivity in primate lateral intraparietal cortex. *Nature* 395: 500–503, 1998.

SHADLEN MN, BRITTEN KH, NEWSOME WT, AND MOVSHON JA. A computational analysis of the relationship between neuronal and behavioral responses to visual motion. *J Neurosci* 16: 1486–1510, 1996.

SHADLEN MN AND NEWSOME WT. Motion perception: seeing and deciding. *Proc Nat Acad Sci USA* 93: 628–633, 1996.

SHADLEN MN AND NEWSOME WT. Neural basis of a perceptual decision in the parietal cortex (area LIP) of the rhesus monkey. *J Neurophysiol* 86: 1916–1936, 2001.

STEIN BE AND MEREDITH MA. *The Merging of the Senses.* Cambridge, MA: The MIT Press, 1994.

TANAKA K, HIKOSAKA H, SAITO H, YUKIE Y, FUKADA Y, AND IWAI E. Analysis of local and wide-field movements in the superior temporal visual areas of the macaque monkey. *J Neurosci* 6: 134–144, 1986.

THOMPSON KG, BICHOT NP, AND SCHALL JD. Dissociation of visual discrimination from saccade planning in macaque frontal eye field. *J Neurophysiol* 77: 1046–1050, 1997.

THOMPSON KG, HANES DP, BICHOT NP, AND SCHALL JD. Perceptual and motor processing stages identified in the activity of macaque frontal eye field neurons during visual search. *J Neurophysiol* 76: 4040–4055, 1996.

WALKER MF, FITZGIBBON EJ, AND GOLDBERG ME. Neurons in the monkey superior colliculus predict the visual result of impending saccadic eye movements. *J Neurophysiol* 73: 1988–2003, 1995.

WURTZ RH AND GOLDBERG ME. Activity of superior colliculus in behaving monkeys. III. Cells discharging before eye movements. *J Neurophysiol* 35: 575–586, 1972.

ZEKI SM. Functional organization of a visual area in the posterior bank of the superior temporal sulcus of the rhesus monkey. *J Physiol (Lond)* 236: 549–573, 1974.