Neurons With Object-Centered Spatial Selectivity in Macaque SEF: Do They Represent Locations or Rules?

LÉON TREMBLAY, SONYA N. GETTNER, AND CARL R. OLSON

Center for the Neural Basis of Cognition, Mellon Institute, Pittsburgh, Pennsylvania 15213-2683

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Tremblay, Léon, Sonya N. Gettner, and Carl R. Olson. Neurons with object-centered spatial selectivity in macaque SEF: do they represent locations or rules? J Neurophysiol 87: 333–350, 2002; 10.1152/jn.00356.2001. In macaque monkeys performing a task that requires eye movements to the lefthemost or rightmost of two dots in a horizontal array, some neurons in the supplementary eye field (SEF) fire differentially according to which side of the array is the target regardless of the array’s location on the screen. We refer to these neurons as exhibiting selectivity for object-centered location. This form of selectivity might arise from involvement of the neurons in either of two processes: representing the locations of targets or representing the rules by which targets are selected. To distinguish between these possibilities, we monitored neuronal activity in the SEF of two monkeys performing a task that required the selection of targets by either an object-centered spatial rule or a color rule. On each trial, a sample array consisting of two side-by-side dots appeared; then a cue flashed on one dot; then the display vanished and a delay ensued. Next a target array consisting of two side-by-side dots appeared at an unpredictable location and another delay ensued; finally the monkey had to make an eye movement to one of the target dots. On some trials, the monkey had to select the dot on the same side as the cue (right or left). On other trials, he had to select the target of the same color as the cue (red or green). Neuronal activity robustly encoded the object-centered locations first of the cue and then of the target regardless of the whether the monkey was following a rule based on object-centered location or color. Neuronal activity was at most weakly affected by the type of rule the monkey was following (object-centered-location or color) or by the color of the cue and target (red or green). On trials involving a color rule, neuronal activity was moderately enhanced when the cue and target appeared on opposite sides of their respective arrays. We conclude that the general function of SEF neurons selective for object-centered location is to represent where the cue and target are in their respective arrays rather than to represent the rule for target selection.

INTRODUCTION

The supplementary eye field (SEF), an area of the dorsomedial frontal lobe discovered by Schlag and Schlag-Rey (1985, 1987), is widely thought to contribute to eye-movement control. This view has arisen from studies demonstrating that electrical stimulation of the SEF at low currents (<50 μA) evokes saccadic eye movements (Chen and Wise 1995b; Fujii et al. 1995; Lee and Tehovnik 1995; Mann et al. 1988; Mitz and Goldschalk 1989; Russo and Bruce 1993; Tehovnik and Lee 1993; Tehovnik and Sommer 1997; Tehovnik et al. 1994; Tian and Lynch 1995) and that neurons in the SEF fire in conjunction with saccadic eye movements, exhibiting selectivity for particular saccade directions (Bon and Lucechetti 1992; Chen and Wise 1995a,b, 1996, 1997; Hanes et al. 1995; Mann et al. 1988; Mushiake et al. 1996; Russo and Bruce 1996; Schall 1991a,b; Schlag and Schlag-Rey 1985, 1987; Schlag-Rey et al. 1997).

That the functions of the SEF are not simply motoric has been suggested by several findings indicating that neuronal activity accompanying the planning and execution of eye movements is sensitive to the task context. Eye-movement-related activity in the SEF: varies across the course of learning as monkeys acquire arbitrary associations between visual patterns and eye-movement directions (Chen and Wise 1995a,b, 1996, 1997); varies as a function of whether monkeys are performing a prosaccade or antisaccade task (Schlag-Rey et al. 1997); varies according to whether the target of the saccade has been guided by a cue marking the location or by a foveal pattern associated with the location (Olson et al. 2000); is affected by the level of conflict under which the monkey is performing (Gettner and Olson 1996; Stuphorn et al. 2000); is affected by the anticipation and delivery of reward (Amador et al. 2000; Stuphorn et al. 2000); and varies according to whether arm movements do or do not accompany eye movements (Mushiake et al. 1996).

Further evidence that SEF neurons serve diverse and not solely motoric functions has arisen from studies assessing spatial selectivity in the context of oculomotor performance. On one hand, there have been indications that neuronal activity is yoked to saccade direction. Electrical stimulation elicits fixed vector saccades from certain sites in the SEF (Bon and Lucechetti 1992; Mitz and Godschalk 1989; Russo and Bruce 1993; Schlag and Schlag-Rey 1987). Furthermore some SEF neurons fire in conjunction with saccades in preferred directions regardless of the eyes’ starting point (Mitz and Godschalk 1989; Russo and Bruce 1996; Schlag and Schlag-Rey 1987).

On the other hand, there is considerable evidence that neuronal activity in the SEF can be decoupled from saccade direction. Electrical stimulation at some sites in the SEF drives the eyes to a certain angle in the orbit regardless of initial direction (Russo and Bruce 1993; Tehovnik 1995; Tehovnik and Lee 1993; Tehovnik et al. 1994). Furthermore some SEF neurons fire as a function of the angle of the eyes in the head during fixation (Bon and Lucechetti 1990, 1992; Lee and Tehovnik 1995; Schlag et al. 1992). Finally, in studies from our laboratory, it has emerged that some SEF neurons exhibit selectivity for the object-centered locations of saccade targets. In mon-
keys planning and executing eye movements to the left or right end of a horizontal bar (Olson and Gettner 1995, 1999) or to the leftmost or rightmost of two dots in a horizontal array (Olson and Tremblay 2000), around half of task-related SEF neurons fire differentially on trials when the target is at the left or right end of the reference object even when the location of the object on the screen is manipulated so as to keep the screen-centered location of the target constant and the physical directions of the eye movements equivalent.

Object-centered spatial selectivity in the SEF is not likely to play a role in purely motor processes because a target’s object-centered location, unlike its retina-centered or head-centered location, need not be taken into account in programming an eye movement to it. However, there are at least two premotor functions in which object-centered spatial selectivity might play a role. First, the general function of SEF neurons with object-centered spatial selectivity might be to represent the rule for selection of the target. We will term this the rule hypothesis. Second, the general function of these neurons might be to represent the location of the target however it was chosen. We will term this the location hypothesis. To choose between these hypotheses on the basis of results from previous studies is not possible because, in these studies, monkeys were instructed to select a target by its object-centered location with the consequence that rule and location were confounded (Olson and Gettner 1995, 1999; Olson and Tremblay 2000). The aim of the present experiment was to generate data that would allow choosing between them. The approach was to monitor neuronal activity in the SEF under conditions in which the monkey selected targets on the basis either of their object-centered location.

![Diagram of experimental conditions](http://jn.physiology.org/)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Spatial Conditions</th>
<th>Color Conditions</th>
<th>Color Conditions</th>
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<tbody>
<tr>
<td>Sample array: location on screen</td>
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<td>R R R R L L L L</td>
<td>R R R R L L L L</td>
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<tr>
<td>Cue: location in array</td>
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<tr>
<td>Cue: color</td>
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</tr>
<tr>
<td>Target array: location on screen</td>
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<td>R L L L R L L L</td>
<td>R L L L R L L L</td>
</tr>
<tr>
<td>Target: location in array</td>
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<td>R A R A R A R A R A R A</td>
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</tr>
<tr>
<td>Target: location on screen</td>
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<td>a b c a b c a b c a b c</td>
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<td>x x x x x x x x</td>
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locations or their color. According to the rule hypothesis, SEF neurons should signal the target’s object-centered location on trials in which the basis for selection is an object-centered rule and should signal its color on trials when the basis for selection is color. According to the location hypothesis, SEF neurons should signal a target’s object-centered location regardless of the rule by which it has been selected and should not signal the target’s color.

**METHODS**

**Subjects**

Two adult male rhesus monkeys were used (*Macaca mulatta*; laboratory designations *Ju* and *Po*). Experimental procedures were approved by the Carnegie Mellon University Animal Care and Use Committee and were in compliance with the guidelines set forth in the United States Public Health Service Guide for the Care and Use of Laboratory Animals.

**Preparatory surgery**

At the outset of the training period, each monkey underwent sterile surgery under general anesthesia maintained with isoflurane inhalation. The top of the skull was exposed, bone screws were inserted around the perimeter of the exposed area, a continuous cap of rapidly hardening acrylic was laid down so as to cover the skull and embed the heads of the screws, a head restraint bar was embedded in the cap, and scleral search coils were implanted on the eyes with the leads directed subcutaneously to plugs on the acrylic cap (Remmel 1984; Robinson 1963). Following initial training, a 2-cm-diam disk of acrylic and skull, centered on the midline of the brain approximately at anterior 21 mm (Horsley-Clarke coordinates), was removed and a cylindrical recording chamber was cemented into the hole with its base just above the exposed dural membrane.

**Color-location task**

This task required monkeys to make eye movements to one or the other of two dots in a horizontal array. On randomly interleaved trials, they had to select the dot on the basis of either its color or its location in the array. Essential features of the task are summarized in Fig. 1A. At the beginning of each trial, while the monkey was fixating a central spot (panels 1 and 1'), a sample array was presented, consisting of two white dots (panels 2 and 2'). The ensuing events differed according to whether the trial required use of an object-centered-location rule or a color rule. On trials requiring the monkey to choose by an object-centered-location rule, a white cue was presented in superimposition on one of the dots in the sample array (panel 3). After a delay, a target array appeared, consisting of two white dots (panel 5). After a second delay, extinction of the central fixation spot (panel 6) signaled the monkey to make an eye movement to one of the dots in the target array (panel 7). Reward was delivered only if the monkey made a saccade directly to the dot in the target array having the same object-centered location as the cue presented earlier in the trial. To perform this task successfully, the monkey had to remember whether the cue had been presented on the left or right side of the sample array. Remembering the location of the cue on the screen would not suffice because the target array did not necessarily appear at the same location on the screen as the sample array. On trials requiring the monkey to choose by a color rule, a cue colored red or green was presented in superimposition on one of the white dots in the sample array (panel 3'). After a delay, a target array appeared, consisting of one red and one green dot (panel 5'). After a second delay, extinction of the central fixation spot (panel 6') signaled the monkey to make an eye movement to the selected dot in the target array (panel 7'). Reward was delivered only if the monkey made a saccade directly to the dot in the target array matching the cue in color. To perform this task successfully, the monkey had to remember the color of the cue. Remembering the location of the cue in the sample array would not suffice because the dot in the target array that matched the cue in color might or might not be at the cue’s object-centered location.

**Interleaving of conditions**

Several factors other than type of rule varied across trials. These included the location of the sample array (Fig. 1B: L or R), the location of the target array (Fig. 1B: L or R), the location of the cue (Fig. 1B: a, b, or c), and the location of the target dot (Fig. 1B: a, b, or c). Within the color category, the color of the cue (red or green) also varied across trials. Systematic variation of these factors gave rise to 8 spatial conditions and 16 color conditions (Fig. 1C). Trials corresponding to these 24 conditions were interleaved pseudorandomly according to the rule that one trial of each type had to be completed successfully before initiation of the next block. An essential feature of this design was the dissociation of object-centered location (the right...
or left side of the array) from other factors that might influence neuronal activity in the SEF, notably the location of the cue on the screen (and thus the location of its image on the retina) and the location of the target on the screen (and thus the physical direction of the eye movement). A cue at one screen location (Fig. 1B: b) could mark either the right dot of a left-displaced sample array (Fig. 1B: L) or the left dot of a right-displaced sample array (Fig. 1B: R). Similarly, an eye movement in one physical direction (Fig. 1B: 2) might be directed to either the right dot of a left-displaced target array (Fig. 1B: L) or the left dot of a right-displaced target array (Fig. 1B: R).

Stimuli

The fixation spot was a 0.38° white square presented at the center of the screen. The sample array consisted of two 0.38° white squares presented 5.8° above fixation with a horizontal center-to-center distance of 4.6°. The cue was a 0.96° white, red or green square. The target array consisted of two 0.58° white squares presented 5.8° above fixation with a horizontal center-to-center distance of 4.6°. The background of the display had a luminance of 6.9 cd/m², and CIE x and y chromaticity coefficients of 0.27 and 0.31. White stimuli had a luminance of 193 cd/m², and CIE x and y chromaticity coefficients of 0.31 and 0.34. Red stimuli had a luminance of 79 cd/m², and CIE x and y chromaticity coefficients of 0.56 and 0.38. Green stimuli had a luminance of 181 cd/m², and CIE x and y chromaticity coefficients of 0.28 and 0.61.

Single-neuron recording

At the beginning of each day’s session, a varnish-coated tungsten microelectrode with an initial impedance of several megohms at 1 kHz (Frederick Haer, Bowdoinham, ME) was advanced vertically through the dura into the immediately underlying cortex. The electrode could be placed reproducibly at points forming a square grid with 1-mm spacing (Crist et al. 1988). The action potentials of a single neuron were isolated from the multineuronal trace by means of an on-line spike-sorting system using a template matching algorithm (Signal Processing Systems, Prospect, Australia). The spike-sorting system, on detection of an action potential, generated a pulse that was stored with 1-ms resolution.

Experimental control and data collection

All aspects of the behavioral experiment, including presentation of stimuli, monitoring of eye movements, monitoring of neuronal activity, and delivery of reward, were under the control of a 486- or Pentium-based computer running Cortex software provided by R. Desimone, Laboratory of Neuropsychology, National Institute of Mental Health. Eye position was monitored by means of a scleral search coil system (Remmel Labs, Ashland, MA, or Riverbend Instruments, Birmingham, AL) and the x and y coordinates of eye position were stored with 4-ms resolution. Stimuli generated by an active matrix LCD projector were rear-projected on a frontoparallel screen 25 cm from the monkey’s eyes. Reward in the form of ~0.1 ml of water or juice was delivered through a spigot under control of a solenoid valve on successful completion of each trial.

Statistical analysis of the dependence of firing rate on task factors

We employed independent ANOVAs to analyze the impact on the firing rates of individual neurons of several factors of interest, notably object-centered location, color, rule, and cue-target match status. Some procedures were tailored to the needs of the individual analyses; those are described in the text. Other procedures, consistent across analyses, are noted here. We analyzed, independently, data from three trial epochs: delay 1 (from cue-onset until target onset), delay 2 (from target-onset until fix-spot offset), and the movement period (from the initiation of the saccade until 100 ms after its completion). These epochs, while arbitrary, serve to block out periods of time when the location of the target array could not yet exert any impact on neuronal activity (delay 1), when the imperative signal could not yet exert any activity on neuronal activity (delay 2), and when the neuronal machinery for eye-movement generation was fully committed to a response (movement period). They correspond to epochs used in previous studies (Olson and Gettner 1999; Olson and Tremblay 2000). In the analysis of data from delay 1, we restricted consideration to a subset of conditions in which the location of the cue on the screen was directly above fixation (location b in Fig. 1B). In the analysis of data from delay 2 and the movement period, we restricted consideration to conditions in which both cue and target were directly above fixation. Thus the retinal location of the cue and target were held constant while other factors varied. Except in analyzing the impact of cue-target mismatch, we excluded from consideration all color-rule trials in which the cue and target were at opposite sides of their respective arrays. We employed a criterion for statistical significance of $P < 0.05$.

The fact that data were collected during twice as many trials involving a color rule as involving an object-centered-location rule could potentially have affected the conclusions of this study, either through an effect of sample size on the sensitivity of the t-test or through an effect of unequal sample sizes on the reliability of the F test underlying the ANOVA. Most comparisons actually carried out in this study circumvented the problem. However, there was one exception: an ANOVA analyzing the dependence of firing rate on the factors of rule-type (color vs. object-centered location) and location (left vs. right). This ANOVA, described under Neuronal selectivity for object-centered vs. color-based rule, involved a data matrix in which the numbers of counts differed by a factor of two across some cells. Differences in counts can reduce the reliability of the F test. Accordingly, rather than rely exclusively on the ANOVA, we carried out an additional test immune to the influence by the unequal numbers of trials involving the two types of rule (Fig. 8). This test independently confirmed the conclusion of the ANOVA that neuronal signals reflecting object-centered location were more robust than neuronal signals reflecting the type of rule.

Localization of recording sites

In each monkey, recording was carried out in a pair of regions, each a few mm in extent, disposed approximately symmetrically across the interhemispheric midline. One of the monkeys (Po) is still under study in behavioral experiments. In the other monkey (Ju), the brain was photographed following death by an overdose of pentobarbital sodium and transcardiac perfusion with 10% formalin. Marks indicating the location of the recording chamber were compared with gross anatomical landmarks including the hemispheric midline and the arcuate and principal sulci. On the basis of the grid coordinates at which the electrode had been placed, recording sites were then projected onto the image of the cortical surface.

RESULTS

Behavior

We analyzed behavioral data to determine whether there were variations in performance across condition. Our measures were the percent correct score (the average computed across all neuronal data collection sessions, with consideration restricted to trials in which the monkey made an eye movement to one end or the other of the array) and reaction time (the average computed across all neuronal data collection sessions; consideration restricted to successfully completed trials). Note that
reaction time probably did not reflect decision time because a delay was imposed between presentation of the target array (after which the target could be selected) and permission to move.

**COLOR.** Across trials in which the target had to be selected on the basis of its color, we asked whether performance varied as a function of whether the target was red or green.

**Percent correct.** In *monkey Ju*, the percent-correct score was the same on red and green trials (96%). In *monkey Po*, the percent-correct scores on red and green trials were 91 and 87%, respectively. This difference was significant (2-tailed paired *t*-test, *P* = 0.04).

**Reaction time.** In *monkey Ju*, the behavioral reaction times on red and green trials were 141 and 131 ms, respectively. This difference was highly significant (2-tailed paired *t*-test, *P* = 0.0001). In *monkey Po*, the behavioral reaction times on red and green trials (149 and 146 ms, respectively) were not significantly different. Thus *Ju* responded more slowly (by 10 ms) when the target was red while *Po* made more correct choices (by 4%) when the target was red.

**RULE.** We analyzed data collected under all trial conditions to determine how performance varied as a function of whether target-selection was determined by an object-centered-location rule or a color rule.

**Percent correct.** In *monkey Ju*, the percent-correct scores on object-centered-location and color trials were 94 and 96%, respectively. The difference was significant (2-tailed paired *t*-test, *P* = 0.02). In *monkey Po*, the percent-correct scores for object-centered-location and color trials (89% in each case) were not significantly different.

**Reaction time.** In *monkey Ju*, the behavioral reaction times on object-centered-location and color trials were 138 and 136 ms, respectively. The difference between these times was highly significant (2-tailed paired *t*-test, *P* = 0.0007). In *monkey Po*, the behavioral reaction times on object-centered-location and color trials were 143 and 147 ms, respectively. This difference was significant (2-tailed paired *t*-test, *P* = 0.02). Thus *Ju* gave more correct responses (by 2%) and was faster (by 2 ms) on color trials, while *Po* was slower (by 4 ms) on color trials.

**MATCH.** Across color trials, we asked whether performance reflected the match or mismatch between the location of the cue in the sample array and the location of the target of corresponding color in the target array (match and mismatch occurred equally frequently).

**Percent correct.** In *monkey Ju*, the percent-correct scores on match and mismatch trials (97 and 96%, respectively) were not significantly different. In *monkey Po*, the percent correct scores were the same on match and mismatch trials (89%).

**Reaction time.** In *monkey Ju*, the behavioral reaction times on match and mismatch trials were 134 and 137 ms, respectively. This difference was significant (2-tailed paired *t*-test, *P* = 0.04). In *monkey Po*, the behavioral reaction times on match and mismatch trials were the same (147 ms).

**SUMMARY.** Percent-correct and reaction-time measures varied across conditions. However, the differences were extremely small (on the order of a few percent and a few milliseconds) and were inconsistent across monkeys. Thus they are unlikely to account for large and systematic condition-dependent variations in neuronal activity.

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**Overview of single-neuron data collection and analysis**

We recorded from the superficial cortex of the dorsomedial frontal lobe bilaterally in *monkey Ju* and in the right hemisphere of *monkey Po*. The sites were within a restricted zone in which many neurons showed task-related activity and exhibited direction selectivity in standard oculomotor tests requiring eye movements to small spots. Neurons were considered for study if they appeared to exhibit task-related activity during performance of a standard ocular delayed response task (Olson and Tremblay 2000). Data were collected, during full runs of the color-location task, in 74 neurons from *monkey Ju* (16 and 58 in the left and right hemispheres respectively) and 23 neurons from *monkey Po*. The distribution of recording sites in *monkey Ju* is shown in Fig. 2A, where each dot represents one site and the size of the dot indicates how many neurons at that site contributed data to the present paper. These sites are within the confines of the SEF as defined by previous studies based on mapping with electrical stimulation, as shown in Fig. 2B and summarized by Tehovnik (1995). Furthermore they coincide with the region in which task-related activity was observed during performance of memory-guided saccades by the same monkey (Olson and Tremblay 2000, Figs. 2 and 14).

To determine whether neuronal activity depended on the object-centered location of the cue and target (left or right), their color (red or green), the rule the monkey was following (object-centered-location or color), and the match status of the cue and target on color trials (on the same side or opposite sides of their respective arrays), we carried out a series of analyses described in the following sections. These analyses...

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FIG. 2. **A**: recording sites superimposed on a dorsal view of the cerebral hemispheres of *monkey Ju*. Each dot indicates a recording site, and the area of each dot is proportional to the number of neurons at that site contributing data to the present paper. The largest dot, in the left hemisphere, represents 24 neurons, and the smallest dot, also in the left hemisphere, represents 1 neuron. **B**: extent of the supplementary eye field (SEF) as defined by mapping with intracortical microstimulation in studies from ten laboratories listed in Table 1 of Tehovnik (1995). Tehovnik brought results from different laboratories into register by use of 2 landmarks: for mediolateral register, the hemispheric midline, and for anteroposterior register, the genu of the arcuate sulcus, as marked by the horizontal line spanning A and B in this figure. For each study listed by Tehovnik, we generated a rectangle encompassing, to the nearest mm, the anterior, posterior, lateral, and medial limits of the region in which electrical stimulation elicited eye movements. Then, on each point in a 1×1-mm grid spanning the cortex, we superimposed a dot the area of which was proportional to the number of studies including that point. The number of times a site was counted could range from zero (not marked on this figure: sites not implicated by any study) through one (smallest dots visible in this figure: sites implicated by just one study) to 10 (largest dots visible in this figure: sites implicated by all 10 studies). Note that sites in which recording was carried out in this study (dots in A) overlap the relatively anterior region in which electrical stimulation in previous studies most consistently elicited eye movements (largest dots in B). as, arcuate sulcus; cs, central sulcus; ps, principal sulcus.
were confined to data from trials in which the cue and target were directly above fixation so that, while factors of interest varied, the retinal location of the cue and the physical direction of the eye movement were held constant. When monkeys execute eye movements to a dot in a horizontal array, in the context of a delay paradigm, the landing position of the eye is virtually unaffected by whether the dot is the left or right element of the array; furthermore, such very small variations as do occur in the eye’s landing point cannot account for object-centered spatial selectivity (Olson and Tremblay 2000).
Neuronal selectivity for object-centered location

Many neurons in the sampled population fired at a rate determined by the location of the cue in the sample array and the location of the target in the target array. These neurons were selective for object-centered location regardless of the rule that the monkey was following. Figure 3 shows data from one such neuron collected during trials in which the object-centered location of cue and target (on the right or left end of the respective dot array) varied but their screen-centered location was always directly above fixation (location b in Fig. 1B). During delay 1, the period between presentation of the cue and onset of the target array, this neuron’s rate of firing was markedly higher if the cue had been presented on the left side of the sample array (Fig. 3, A, C, E, H, and J) than on the right side (Fig. 3, B, D, F, G, and I). During delay 2, following onset of the target array, the neuron fired more strongly on trials in which the left element of the array was the target. This was true regardless of whether the monkey had selected the target by an object-centered-location rule (Fig. 3, A and B) or by a color rule (Fig. 3, C–J). On color trials with spatial mismatch—trials in which the object-centered location of the cue and the object-centered location of the target dot were opposite—the firing rate shifted markedly between delays 1 and 2. When, in response to a cue appearing on the left side of the sample array, the monkey selected as target a dot on the right side of the target array, the neuron’s firing rate fell precipitously (Fig. 3, H and J). Conversely, if a cue on the right side of the sample array led to selection of a dot on the left side of the target array, firing rose steeply (Fig. 3, G and I). For example, under the conditions of Fig. 3J, the neuron fired strongly following presentation of a green cue on the left end of the sample array but its firing subsided following onset of a target array in which the dot that was green (and therefore was target) occupied the array’s right end. Thus the rate of activity of this neuron was determined primarily by the object-centered location of the cue (during delay 1) and the object-centered location of the target (during delay 2 and the movement period).

To determine the degree to which object-centered activity was consistent across the two rule conditions, we carried out a population analysis. In each monkey and for each task epoch (delay 1, delay 2, and the movement period), we analyzed the correlation across neurons between measures of object-centered selectivity obtained during trials in which the monkey was following an object-centered-location rule or a color rule.

FIG. 3. Data from a neuron selective for cues and targets at the left sides of their respective arrays. Each histogram represents firing rate versus time under 1 trial condition. Conditions were distinguished by the nature of the display at the time when the cue was presented (panel labeled “cue”) and at the time when the target array was visible (panel labeled “target”). For example, during trials on which histogram J is based, the sample array appeared on the right of the screen, a green cue flashed on the array’s leftmost element, the display was extinguished, a delay ensued, the target array (red dot on the left and green dot on the right) appeared on the left of the screen, remaining visible during a 2nd delay, and then the monkey made an upward-directed saccade to the green target element. Note that in all conditions on which this figure is based both the cue and the target were at the center of the screen, directly above fixation. Nevertheless, the neuron fired differentially as a function of the cue’s object-centered location (during delay 1) and the target’s object-centered location (during delay 2) and did so regardless of whether the monkey was following an object-centered location rule (top row: A and B) or a color rule with a red cue (2nd row: C and D) or a color rule with a green cue (3rd row: E and F). Finally, during color trials with spatial mismatch (bottom 2 rows: G–J), the neuron’s rate of firing 1st reflected the object-centered location of the cue and then, shortly after the appearance of the target array, shifted to reflect the object-centered location of the target. Conditions in this figure correspond to the following conditions as defined in Fig. 1C. A: C = 10, D = 15, E = 18, F = 23, G = 14, H = 11, I = 22, and J = 19. Each histogram was formed by aligning action potentials from successive successfully completed trials on target-onset and then computing the mean firing rate in each 10-ms bin. The times of cue onset and trigger onset are indicated as a range because delay 1 (from cue-onset to target-onset) and delay 2 (from target-onset to fixation-spot-offset) were variable (Fig. 1A). Ticks on the horizontal axis mark 500-ms intervals.

FIG. 4. Demonstration that selectivity for object-centered location was conserved across trials in which the monkey followed a rule based on object-centered location and trials in which he followed a rule based on color. Each dot represents measurements made on 1 neuron during 1 trial epoch (delay 1, delay 2, or movement period). Position with respect to the horizontal axis represents the dependence of firing rate on object-centered location during trials in which the monkey was following a rule based on object-centered location. Position with respect to the vertical axis represents the dependence of firing rate on object-centered location during trials in which the monkey was following a rule based on color, A: for monkey Ju, there are 222 points (74 neurons × 3 epochs), B: for monkey Po, there are 69 points (23 neurons × 3 epochs).

We considered only those color-rule trials in which the cue and target were on the same side of their respective arrays (match trials). We employed as an index of object-centered selectivity...
the mean firing rate on trials when the cue and target were on the left side of the array minus the mean firing rate when they were on the right side. In both monkeys and in every epoch, a highly significant \( P < 0.0001 \) positive correlation was present. Values of \( R^2 \) ranged from 0.51 to 0.88 without any obvious trend across monkeys or epochs. Data collapsed across all epochs (Fig. 4) make clear the very strong tendency for object-centered selectivity to generalize across rule conditions. To investigate the possibility that object-centered signals differed slightly in strength between the two rule conditions, we compared, for each monkey and for each epoch, the distribution across neurons of the absolute value of the index of object-centered selectivity. The difference was significant \( (0.51 \text{ spikes}^{-1}, P = 0.022) \) during delay 1 for monkey Ju and

**FIG. 5.** Both before and after target onset, this neuron fired significantly more strongly on green (3rd row) than on red (2nd row) trials. Indeed, it exhibited one of the strongest observed effects of color (its data are represented by the circled c in Fig. 6). Nevertheless, the effect was far from robust. Each histogram represents neuronal activity under 1 trial condition representing a unique combination of: rule for target selection (A and B: object-centered location; C–F: color), cue-color (C and D: red; E and F: green), and cue location relative to sample array (A, C, and E: left; B, D, and F: right). In all conditions shown here, cue and target were presented at the same screen-centered location directly above fixation. Conditions in this figure correspond to the following conditions as defined in Fig. 1D: \( A = 2, B = 7, C = 10, D = 15, E = 18, \) and \( F = 23 \). Other conventions as in Fig. 3.
approached significance (1.5 spikes⁻¹, P = 0.054) during delay 2 for monkey Po. In each case, the absolute value of the index was larger under conditions in which the monkey was following an object-centered rule. In monkey Ju, across all task epochs, the absolute value of the object-centered-selectivity index was reduced by 8% in color-rule trials as compared with trials requiring the monkey to follow an object-centered-location rule. The corresponding reduction in monkey Po was 11%. Thus while selectivity for object-centered location was present and of consistent sign in trials requiring the monkey to use object-centered-location and color rules, its strength was slightly greater when the monkey was selecting the target on the basis of its object-centered location.

**Neuronal selectivity for color**

We next asked whether SEF neurons displayed selectivity for color on trials requiring monkeys to remember the cue’s color and select a target matching in hue. In most neurons, including the one shown in Fig. 3, this was not the case. However, in a few neurons, the rate of firing during trials involving a color rule seemed to depend on whether the cue and target were red or green. An example is shown in Fig. 5. This neuron’s activity, during the first and second delay periods, appeared slightly greater on trials when the cue and target were green (Fig. 5, E and F) than when they were red (Fig. 5, C and D). However, the effect was far from robust. Indeed, it requires close scrutiny to confirm by eye that the rate of firing between cue onset (gray bar on left) and fixation offset (gray bar on right) was greater overall on green trials considered collectively (Fig. 5, E and F) than on red trials considered collectively (Fig. 5, C and D).

To assess systematically the influence of color on neuronal activity, we carried out analyses of variance on data collected from each neuron during color-rule trials. We considered independently data from three trial epochs as defined in METHODS (delay 1, delay 2 and the movement period). In each analysis, there was one dependent variable (firing rate) and there were two factors: object-centered direction (right or left) and color (red or green). The results are summarized in Table 1. Many neurons exhibited selectivity for object-centered location (48, 49, and 34% during delay 1, delay 2, and the movement period respectively). A few neurons exhibited a main effect of color (13, 8, and 8% during delay 1, delay 2, and the movement period, respectively). One of these was the neuron shown in Fig. 5, in which the level of significance of the dependence of firing rate on color during delay 2 was at the maximal observed level (P < 0.001). The observed frequency of these effects, although low, was greater than expected by chance, given the significance criterion (P < 0.05) applied to results from the ANOVA (P = 0.0001, χ² test). The number of neurons exhibiting color-by-location interaction effects (2, 9, and 5% during the 3 epochs) was no greater than expected by chance (P = 0.70, χ² test). From this analysis, we conclude that the impact of color on neuronal activity was markedly weaker than the impact of object-centered location. This result is particularly striking in light of the fact that the analysis concerned only color-rule trials—trials in which the monkey had to process color and was free to ignore object-centered location.

Counts of neurons exhibiting statistically significant effects must be interpreted with caution because statistical significance is dependent on adventitious circumstances including the duration of the measurement epoch and the number of trials per condition. To circumvent this problem, we also carried out an analysis based on mean firing rate without regard to significance. This analysis was based on data collected under the same conditions as used for the ANOVA described in the preceding text. We computed two indices of neuronal selectivity. 1) Object-centered-location signal. For each neuron in the recorded population and for each of three epochs (delay 1, delay 2, and the movement period), we computed the absolute value of the difference in firing rate between object-left and object-right targets (for each epoch). This analysis was carried out for each neuron in the recorded population and for each of three epochs (delay 1, delay 2, and the movement period). We considered independently data from three trial epochs as defined in METHODS.
object-right trials, averaging across the two colors. 2) Color signal. For each neuron in the recorded population and for each of three epochs (delay 1, delay 2, and the movement period), we computed the absolute value of the difference in firing rate between trials involving red and green cues, averaging across the two object-centered locations. On comparing the magnitudes of the object-centered location and color signals across the neuronal population studied in each monkey, we observed a marked tendency for object-centered location signals to be greater (Fig. 6). This tendency was highly significant (paired 2-tailed t-test, \( P < 0.0001 \)). Thus across the neuronal population as a whole, firing rates were much more strongly affected by object-centered location (left or right) than by color (red or green) even though the data were from trials in which the monkey followed a color rule.

Could selectivity for color, insofar as it was observed, be explained in terms of brightness? During the initial period of training, we adjusted the luminance of the red stimulus, making it dimmer than the green stimulus, so as to counteract one monkey’s color bias. Throughout the period of data collection, the luminance remained at this level. Thus we felt it necessary to ask whether neuronal activity was indeed governed by the hue of the stimulus or, alternatively, was controlled by its brightness. If neuronal activity was controlled by brightness, we reasoned, then firing rates on trials involving white \((193 \text{ cd/m}^2)\) cues and targets should approximate more closely to firing rates on trials involving green \((181 \text{ cd/m}^2)\) cues and targets. To test this prediction, we computed for each neuron and each of three epochs (delay 1, delay 2, and the movement period) an index of the degree to which firing rates on white and green trials were more similar to each other than to firing rates on red trials

\[
\left| \text{abs}(r - w) - \text{abs}(g - w) \right| / \left( \text{abs}(r - w) + \text{abs}(g - w) \right)
\]

where \( w, g, \) and \( r \) were the mean firing rates during trials involving white, green, and red cues and targets, respectively. If neuronal activity were governed by stimulus brightness, then there would be a tendency across the neuronal population for this index to assume positive values. In monkey \( Po \), the distribution of index values was not significantly different from zero in any epoch (1-group, 2-tailed \( t \)-test with criterion of \( P \leq 0.05 \)). In monkey \( Ju \), the distribution barely achieved significance (mean, 0.4 spikes \(^{-1}; \ P = 0.049 \)) during the movement epoch. We conclude that the weak chromatic sensitivity of SEF neurons probably depended on the hue and not just on the relative brightness of the stimuli.

**Neuronal selectivity for object-centered vs. color-based rule**

In some neurons, the rate of firing was obviously affected by the type of rule the monkey was following. An example is shown in Fig. 7. This neuron was selective for object-centered location, firing more strongly when the target was on the right side of the array (Fig. 7, right) than when it was on the left (Fig. 7, left). In addition, late in the second delay period, its firing varied according to the type of rule the monkey was following, appearing greater on trials when the monkey was following an object-centered rule (Fig. 7, A and B) than on trials when he was following a color rule (Fig. 7, C–F). While this effect was statistically significant, it was far from robust. It can best be seen by focusing on the portion of the histogram immediately to the left of the gray bar marking fixation offset. On trials when the cue and target were on the left of their respective arrays, there was a moderate buildup of activity during this period, greater when the rule was based on object-centered location (Fig. 7A) than when it was based on color (Fig. 7, C and E). On trials when the cue and target were on the right of their respective arrays, there was strong activity throughout the second delay period regardless of the rule. However, close to the time of fixation offset, this activity became especially strong if the rule was based on object-centered location (Fig. 7B) as opposed to color (Fig. 7, D and F). We will refer to such activity as rule-based with the proviso...
that it might have been dependent on the color or brightness of the stimuli, a point taken up in detail in the DISCUSSION.

To assess the influence on neuronal activity of the type of rule the monkey was following, we carried out analyses of variance on data collected from each neuron during each of the three trial epochs defined in METHODS (delay 1, delay 2, and the movement period). In the analysis of data from each epoch, there was one dependent variable (firing rate) and there were two factors: object-centered location (right or left) and type of rule (object-centered-location or color). Many neurons (48, 59, and 39% during delay 1, delay 2, and the movement period, respectively) exhibited a significant main effect of object-

![Diagram illustrating neuronal activity during rule-based selection](http://jn.physiology.org/)

**FIG. 7.** Data from a neuron firing at a significantly higher rate during trials when the target was selected by a rule based on object-centered location (row 1) vs. color (rows 2 and 3). Differential activity was apparent during the late part of delay 2. Note that selectivity, while significant, was not robust, although this neuron was among those exhibiting the strongest effects of rule (its data are represented by the circled b in Fig. 8). Note that in this, as in all cases of apparent selectivity for rule, an alternative interpretation is possible, namely, that the neuron was selective for the color of the cue or target (white as opposed to red or green). Conventions as in Fig. 5.
centered location (Table 2). Few neurons (7, 18, and 10%, respectively) exhibited a significant main effect of type of rule (Table 1). One of these was the neuron shown in Fig. 7, in which the level of significance of the dependence of firing rate on type of rule during delay 2 was at the maximal observed level ($P < 0.001$). Interaction effects between object-centered location and type of rule (4, 8, and 6% during the three measurement epochs) were no more common than expected by chance, given the significance criterion of $P < 0.05$ ($P = 0.35$, $\chi^2$ test). These results indicate that the type of rule the monkey was following exerted only a modest effect on the mean rate of neuronal activity.

We assessed the impact of rule on neuronal activity by means of an additional analysis based on nonstatistical indices of neuronal selectivity. This analysis was based on the same set of trials as used for the ANOVA described above. We computed two indices of neuronal selectivity. 1) Object-centered location signal. For each neuron in the recorded population and for each of three epochs (delay 1, delay 2, and the movement period), we computed the absolute value of the difference in firing rate between object-left and object-right trials. 2) Rule signal. For each neuron in the recorded population and for each of three epochs (delay 1, delay 2, and the movement period), we computed the absolute value of the difference in firing rate between trials in which selection of the target was based on object-centered location and on color. On comparing the magnitudes of the object-centered location signal and the rule signal across the neuronal population studied in each monkey, we discovered a marked tendency for the object-centered signal to be stronger (Fig. 8). This tendency was highly significant (paired 2-tailed $t$-test, $P < 0.0001$).

Neuronal selectivity for match vs. mismatch

Color-rule trials were divided evenly between those in which the cue and target were at the same side of their respective arrays (match trials) and those in which they were at opposite sides (mismatch trials). In some neurons, the rate of activity during delay 2, following onset of the target array, appeared to depend on the trial’s match-mismatch status. This was true of the neuron shown in Fig. 9. It fired a strong burst during delay 2, following onset of the target array, on all trials when the target was on the right side of the array (Fig. 9, right). However, the properties of the burst differed between mismatch conditions (when the cue was on the left and the target was on the right) and match conditions (when both were on the right). In the first place, the net rate of firing was moderately (5.0 spikes/s) higher under mismatch conditions (Fig. 9, D and H) than under match conditions (Fig. 9, B and F). This can be confirmed, on inspection of the figure, by noting the greater height of the burst in Fig. 9, D versus B and likewise in H versus F (pairs identical in the color and location of the target but differing with respect to match-mismatch status). In the second place, the onset of firing occurred around 250 ms later (half the distance between successive tick marks) under mismatch conditions (Fig. 9, D and H) than under match conditions (Fig. 9, B and F).

To determine how commonly neuronal activity depended on the trial’s match-mismatch status, we carried out analyses of variance on data from delay 2 and the movement period. In each analysis, firing rate was the dependent variable and match condition (match vs. mismatch) was the independently varying factor. The results, summarized in Table 3, indicate that, during delay 2, 20/97 neurons fired at significantly different levels on match and mismatch trials. This number was significantly greater than expected by chance given the probability criterion of $P < 0.05$ ($\chi^2$ test, $P < 0.0001$). The neuron shown in Fig. 9 was one of those exhibiting a significant effect of match versus mismatch ($P < 0.016$). Of the 20 neurons in which the firing rate was significantly affected by the trial’s match-mismatch status, 18 fired more strongly on mismatch than on match trials. This level of preponderance is greater than expected by chance ($P = 0.0003$, $\chi^2$ test). No comparable effect occurred during the movement period.

**Table 2. Neurons with significant dependence on object-centered location and type of rule**

<table>
<thead>
<tr>
<th></th>
<th>Object-Centered Location</th>
<th>Type of Rule</th>
<th>Location * Type of Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Con &gt; Ips</td>
<td>Ips &gt; Con</td>
<td>Loc &gt; Col</td>
</tr>
<tr>
<td>Delay 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ju (74)</td>
<td>30</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Po (23)</td>
<td>3</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Sum (97)</td>
<td>33</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Delay 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ju (74)</td>
<td>27</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Po (23)</td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Sum (97)</td>
<td>33</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Move</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ju (74)</td>
<td>16</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Po (23)</td>
<td>6</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Sum (97)</td>
<td>22</td>
<td>16</td>
<td>9</td>
</tr>
</tbody>
</table>

For each neuron, an analysis of variance was carried out for each of three trial epochs—defined in the legend to Table 1—with neuronal firing rate as the dependent variable and with object-centered location (contralateral vs. ipsilateral) and type of rule (object-centered-location vs. color) as factors. Object-centered location: If neuronal activity was significantly dependent on which end of the sample array the cue had appeared on (delay 1) or which end the target dot was located on (delay 2 and movement period), then the neuron was classified in one of two categories according to whether stronger firing occurred on trials in which the end contralateral (Con) or ipsilateral (Ips) to the recording hemisphere had been cued or was the target. Type of rule: If neuronal activity was significantly dependent on the type of rule (object-centered-location or color), then the neuron was classified in one of two categories according to whether the location signal (absolute difference between the rate of firing on object-right and object-left trials) was greater under object-centered-location rule (Loc) or the color rule (Col).
4 curves were constructed, representing the absolute difference in firing rate as a function of time for all neurons exhibiting significant object-centered location selectivity: the location of the symbol with respect to this axis represents the difference as reflected in the bifurcation between firing rate trajectories on trials in which, the cue having been on the same side, the target appeared on opposite sides (pref-pref vs. pref-anti and anti-pref vs. anti-anti). The horizontal spread of the symbols exceeds the vertical spread. The circled b represents measures made on neuron jul182c21 (Fig. 7) during delay 2.

To analyze the dynamics of neuronal activity was more influenced by the object-centered location of the cue (left or right) than by the rule being followed (object centered location or color). Each symbol represents 1 neuron during 1 trial epoch (delay 1, delay 2, or the movement period). The identity of the symbol indicates whether, during the epoch in question, the neuron was significantly selective for object-centered location only (o), rule (r), both (b), or neither (n), as indicated by an ANOVA described in the text. Object-centered location signal: the location of the symbol with respect to this axis represents the absolute difference in firing rate between trials in which the cue was on the right or left side of the sample array (delay 1) or the target was on the right or left side of the target array (delay 2 and movement period). Rule signal: the location of the symbol with respect to this axis represents the absolute difference in firing rate between trials in which target-selection was based on a spatial or color rule. In computing both values, consideration was restricted to trials in which the cue and target were at a single screen-location, directly above fixation. A: monkey Ju: 222 points (74 neurons × 3 epochs). B: monkey Po: 69 points (23 neurons × 3 epochs). Note that the horizontal spread of the symbols exceeds the vertical spread. The circled b represents measures made on neuron jul182c21 (Fig. 7) during delay 2.

DISCUSSION

Selectivity for object-centered location persists during color-based target selection

SEF neurons selective for object-centered location continued to exhibit this trait even on color-rule trials, although, on these trials, the monkey was free to ignore the location of the cue in the sample array and the target in the target array. We conclude from this result that the general function of these neurons must be to encode the object-centered locations of things to which the monkey is attending; not the rule guiding their selection. We say “things to which the monkey is attending” rather than “targets selected for an eye movement” because neuronal activity on color-rule trials robustly encoded not only the object-centered location of the target but also the object-centered location of the cue. This conclusion is subject to two qualifications. First, there was a small but significant reduction in object-centered spatial signals on trials in which the monkey was following a color rule rather than an object-centered-location rule. Thus the strength, if not the occurrence, of object-centered signals was sensitive to the rule being used. Second, monkeys trained to follow an object-centered rule on some trials might have covertly implemented that rule, only to countermand it, in other trials. This qualification applies with equal force to an earlier observation that some SEF neurons in monkeys trained on object-centered tasks exhibit object-centered spatial selectivity outside task context (Olson and Gettner 1995, Fig. 3). The most straightforward way in which to test this possibility would be to record from the SEF in monkeys trained on the color variant of the task used here without being trained on the object-centered-location variant.

It may seem unsurprising that SEF neurons represent the locations of targets in a task requiring that targets be selected on the basis of color. After all, neurons in the frontal eye field
(Bichot and Schall 1999; Ferrera et al. 1999; Schall et al. 1995), prefrontal cortex (Hasegawa et al. 2000; Rainer et al. 1998) and parietal area LIP (Gottlieb et al. 1998) are known to represent the locations of eye-movement targets selected from an array of stimuli on the basis of their pattern or color. However, in all of these cases, neuronal activity represents the
location of the target in oculocentric coordinates and thus is task-relevant, constituting a potential control signal for the required voluntary eye movements. For object-centered signals to crop up in the context of such tasks is more striking because one can imagine the tasks’ being carried out without the object-centered location of the target ever being represented. Given the fact that the locations of cue and target were mismatched on half of color-rule trials, together with the fact that some SEF neurons exhibited object-centered spatial selectivity on these trials, we were able to deal with an issue concerning object-centered spatial selectivity unresolved in previous studies (Olson and Gettner 1995, 1999; Olson and Tremblay 2000). These studies had shown that SEF neurons with object-centered spatial selectivity might exhibit this trait either during delay 1 (following presentation of the instructional cue) or during delay 2 (following onset of the target object) or during both epochs. However, because the object-centered location of the cue (during delay 1) and the object-centered location of the target (during delay 2) matched, the possibility existed that object-centered signals observed during delay 2 were a product of passive carryover from delay 1. From the fact that the object-centered location represented by the activity of neurons in this study switched at the outset of delay 2 on mismatch trials, we conclude that object-centered activity during delay 2 is not a product of passive persistence but can arise actively, in the presence of a visible object, as a result of the monkey’s selecting one end of the object as a target.

Few SEF neurons represent color

We have found that neuronal activity in the SEF is only moderately sensitive to color even in monkeys performing a task requiring them to remember the color of a cue and to select a target for a saccade a dot of that color. This finding fits, in general, with the absence, in the extensive literature on the SEF, of any mention of selectivity for color or pattern. It fits, in particular, with the finding that SEF neurons in monkeys cued by foveal patterns to make saccades in particular directions exhibit selectivity for direction but not pattern (Chen and Wise 1995a,b, 1996, 1997; Olson et al. 2000). The present results go beyond previous findings in demonstrating that SEF neurons fail to exhibit selectivity for a visual attribute (color) even when targets for eye movements are selected on the basis of possessing that attribute. In this respect, the SEF appears to differ from dorsolateral frontal cortex (Fuster et al. 2000) and to resemble the frontal eye field. Neurons of the frontal eye field are only weakly selective for color (Ferrera et al. 1999) except to the degree that they respond more quickly to stimuli of a color on which bottom-up salience has been conferred through overtraining (Bichot et al. 1996).

Our aim in training monkeys to use a color-based rule went beyond determining whether SEF neurons would exhibit selectivity for color. Our intention was to use color as a tool for choosing between two interpretations of object-centered spatial selectivity in the SEF. According to the rule hypothesis, SEF neurons with object-centered location selectivity possess as their general function to represent the rules for selection of targets, a function that they express, in object-centered tasks, by firing at different levels on trials when the rule is “select the right dot” or “select the left dot.” According to the location hypothesis, these neurons possess as their general function to represent the locations of targets, a function expressed, in object-centered tasks, by firing at different levels when the target, regardless of the basis for its choice, is the right or left dot. To choose between these interpretations required training monkeys to select targets by using rules based on object-centered location and some other discriminandum, which, in this case, was color. Object-centered location and color were used in closely similar ways: there were two object-centered rules (select the left or right dot) and two color-based rules (select the red or green dot). Furthermore color was favored in that there were twice as many trials involving guidance by color as by object-centered location. According to the rule hypothesis, SEF neurons should have exhibited equal degrees of selectivity for object-centered location and for color. From the fact that color was not represented nearly as robustly as object-centered location, we conclude provisionally against the rule hypothesis and in favor of the location hypothesis. This conclusion is subject to one qualification: both monkeys had been trained first on tasks involving object-centered location. However, if use of the object-centered location rule were more deeply ingrained, we would expect performance under that rule to be better. In fact, one monkey was significantly better on

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**Table 3.** Neurons with significant dependence on spatial match vs. mismatch during color-rule trials

<table>
<thead>
<tr>
<th></th>
<th>Match &gt; Mismatch</th>
<th>Mismatch &gt; Match</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delay 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ju (74)</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>Po (23)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sum (97)</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td><strong>Move</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ju (74)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Po (23)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sum (97)</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

For each neuron, an analysis of variance was carried out for each of two trial epochs (delay 2 and move: see legend to Table 1) with neuronal firing rate as the dependent variable and with match condition as factor (match: the cue and the target appeared on the same side of their respective arrays; mismatch: the cue and the target appeared on opposite sides of their respective arrays). Consideration was restricted to trials requiring that the target be selected by a color rule. Match > Mismatch: Neuronal activity was significantly greater on match trials. Mismatch > Match: Neuronal activity was significantly greater on mismatch trials.
trials involving a color rule while the other monkey was equally good under both conditions.

The tendency of a few SEF neurons to fire differentially on trials involving red and green cues could be accounted for in at least three ways: innate chromatic sensitivity, representation of the chromatic rule in force on a given trial, or sensitivity to luminance (green stimuli were brighter than red). To choose among these interpretations would require further study. Our current inability to choose among them does not in any way affect the basic observation that color selectivity was far less common and far less robust than selectivity for object-centered location even on trials when the monkey was following a color rule.

Few SEF neurons represent the type of rule by which the target is selected

In a few SEF neurons, the rate of activity was influenced by the type of rule (location or color based) that the monkey was...
following. The activity of these neurons could be accounted for either in terms of sensitivity to the type of rule in use or in terms of sensitivity to color (the cue and targets were white in location-based trials, whereas they were red and green in color-based trials). To resolve this issue would require keeping the properties of stimuli constant across changes in the type of rule being followed, as in studies demonstrating rule-based activity in prefrontal cortex (Asaad et al. 2000; White and Wise 1999). We did not adopt this approach because it makes training markedly more difficult. Our central conclusion—that neuronal signals correlated with the type of rule in use were weak by comparison to neuronal signals reflecting object-centered location—is not undercut by the existence of a confound between color and rule because the impact of the confound would have been to increase the count of neurons sensitive to rule.

**Cue-target mismatch induces enhanced activity among object-centered neurons**

In trials involving a color-based rule, the object-centered location of the target might match or differ from the object-centered location of the cue. Match and mismatch trials were equally frequent. Under mismatch conditions, we found that the activity of SEF neurons with object-centered location selectivity was moderately but significantly enhanced. This phenomenon underscores the fact that neuronal activity in the SEF was sensitive to object-centered location even when the monkey was selecting targets on the basis of a color rule. That mismatch conditions were accompanied by greater activity is consonant with the general observation that neuronal activity in the SEF rises under conditions of conflict and stimulus-response incompatibility. Population activity is higher when monkeys performing a color-conditional eye movement task look away from rather than toward the color cue (Gettner and Olson 1996). Population activity is higher by 10–20 spikes/s during antisaccade as compared with prosaccade performance (Schlag-Rey et al. 1997). The greater magnitude of this effect (as compared with the effect of a few spikes/s observed in our study) may reflect the fact that antisaccade trials differ from prosaccade trials both in the presence of conflict and in the complexity of the rule being followed. Finally, in a subclass of SEF neurons, bursts of activity immediately follow the successful resolution of conflict in the countermanding paradigm (Stuphorn et al. 2000). Conflict-correlated increases in the activity of SEF neurons might reflect the area’s playing an active role in monitoring of conflict (Stuphorn et al. 2000) but might alternatively reflect its being subject to modulation by other areas that monitor conflict or be simply an emergent property of the machinery that underlies selecting and switching among targets.

We thank K. Rearick for excellent technical assistance.

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Present address of L. Tremblay: INSERM U289, Pavillon Claude Bernard, Hôpital de la Salpêtrière, 47 Blvd. de l’Hôpital, 75651 Paris Cedex 13, France.

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