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Sequential Activity of Simultaneously Recorded Neurons in the Superior Colliculus During Curved Saccades

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Port, Nicholas L. and Robert H. Wurtz. Sequential activity of simultaneously recorded neurons in the superior colliculus during curved saccades. *J Neurophysiol* 90: 1887–1903, 2003; 10.1152/jn.01151.2002. The visual world presents multiple potential targets that can be brought to the fovea by saccadic eye movements. These targets produce activity at multiple sites on a movement map in the superior colliculus (SC), an area of the brain related to saccade generation. The saccade made must result from competition between the populations of neurons representing these many saccadic goals, and in the present experiments we used multiple moveable microelectrodes to follow this competition. We recorded simultaneously from two sites on the SC map where each site was related to a different saccade target. The two targets appeared in rapid sequence, and the monkey was rewarded for making a saccade toward the one appearing first. Our study concentrated on trials in which the monkey made strongly curved saccades that were directed first toward one target and then toward the other. These curved saccades activated both sites on the SC map as they veered from one target to the other. The major finding was that the strongly curved saccades were preceded by sequential activity in the two neurons as indicated by three observations: the firing rate for the neuron related to the first target reached its peak earlier than did the rate of the neuron for the second target; the timing of the peak activity of the two neurons was related to the beginning and end of the saccade curvature; a weighted vector-average model based on the activity of the two neurons predicted the timing of saccade curvature. Straight averaging saccades ended between the targets so that they did not go to either target, and they were accompanied by simultaneous rather than sequential activation of the two neurons. Thus when multiple populations of neurons are active on the SC movement map, the resulting saccade is determined by the relative timing of the activity in the populations as well as their magnitude. In contrast, SC activity at the two sites did not predict the final direction of the saccade, and several control experiments found insufficient activity at other sites on the SC map to account for that final direction. We conclude that the SC neuronal activity predicts the timing of the saccade curvature, but not the final direction of the trajectory. These observations are consistent with SC activity being critical in selecting the goal of the saccade, but not in determining the exact trajectory.

INTRODUCTION

Control of behavior depends on populations of neurons in which each neuron is active in the generation of many behaviors and each behavior results from the activity of many neurons (Hinton et al. 1986). Nowhere is the evidence for such a distributed representation clearer than in the areas of the brain related to the generation of rapid or saccadic eye movements. Individual neurons in the frontal cortex, parietal cortex, basal ganglia, and superior colliculus (SC) change their activity before the onset of saccades. The control of movement by a population of neurons is most compelling in the monkey superior colliculus (see review by Sparks and Hartwich-Young 1989). Each SC neuron has a movement field that encompasses a range of saccadic vector directions and amplitudes for which the SC neuron is active (Wurtz and Goldberg 1972), and these vectors are spread out across the SC in an orderly map (Robinson 1972).

Although much is known about the control of saccadic eye movements by the SC, studies have focused almost exclusively on how the SC responds to the presentation of one target at a time. Yet the visual world presents multiple potential targets that can be brought to the fovea by saccadic eye movements. In recognition of this, more recent experiments have used multiple target tasks (Basso and Wurtz 1997, 1998; Dorris and Munoz 1998; Edelman and Keller 1998; Glimcher and Sparks 1992, 1993; McPeek and Keller 2002; Munoz and Wurtz 1995; Ottes et al. 1987; van Opstal and van Gisbergen 1990). The multiple targets should activate multiple populations of neurons on the SC movement map both with the onset of the targets and during the evolution of the activity that precedes the generation of the saccade. Because there are multiple saccadic targets available, but only one saccade can be made, the activity for this one saccade should become concentrated in one population of neurons on the map that is related to the vector of the saccade to be made, and the evolution of this concentration should occur over space and time on the SC map.

So far it is the change in the spatial distribution of activity on the SC map that has been investigated during selection between multiple targets. In one type of experiment, in which one of a set of multiple targets was selected for the saccade on a given trial, the activity of SC saccade related neurons was shown to increase at the site on the SC map related to the selected target, whereas it decreased at other sites (Basso and Wurtz 1997, 1998; Dorris and Munoz 1998; Munoz and Wurtz 1995). In a second type of experiment, the activity of these SC neurons was investigated when the monkey made straight averaging saccades between the two visual targets (Edelman and Keller 1998; Glimcher and Sparks 1993; van Opstal and van Gisbergen 1990) and SC neurons were active when such averaging saccades were made. In these previous multiple target experiments, the spatial changes were inferred from recordings of

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one neuron at a time, and little could be inferred about the temporal interactions between the active sites on the SC map.

In the present experiments, we studied these temporal interactions between different sites on the SC map while the monkey selected one of two stimuli as the target for the next saccade. We used a behavioral task that emphasized temporal factors by presenting two targets in rapid succession, and we required the monkey to discriminate which target was first by making a saccade immediately to it. In these initial experiments, we recorded from neurons whose visual and movement fields had little overlap to see the activity of each neuron independently of the other when saccades were made to one target or the other. We placed the targets near the center of the movement field of each of the two neurons (Fig. 1*A*). We concentrated on the interactions between the two neurons during that fraction of saccades that began by going toward one target and then veered toward the other target. We reasoned that these strongly curved saccades should activate neurons at both target sites on the SC map and provide one of the first studies of the interaction between SC neuronal populations recorded simultaneously.

We found that the occurrence and timing of the saccade curvature was predicted by the sequence of activity in the two SC neurons. In contrast, we found that the final direction of the trajectory of the curved saccades could not be predicted by the vectors represented by the two neurons, and a subsidiary set of experiments found insufficient activity in other regions of the SC to account for the curvature. We think these experiments reveal the importance of timing of activity on the SC map in determining the saccade to be made. Further, they emphasize the close relation between the activity of SC saccade related neurons and the selection of the saccadic goal, which is in

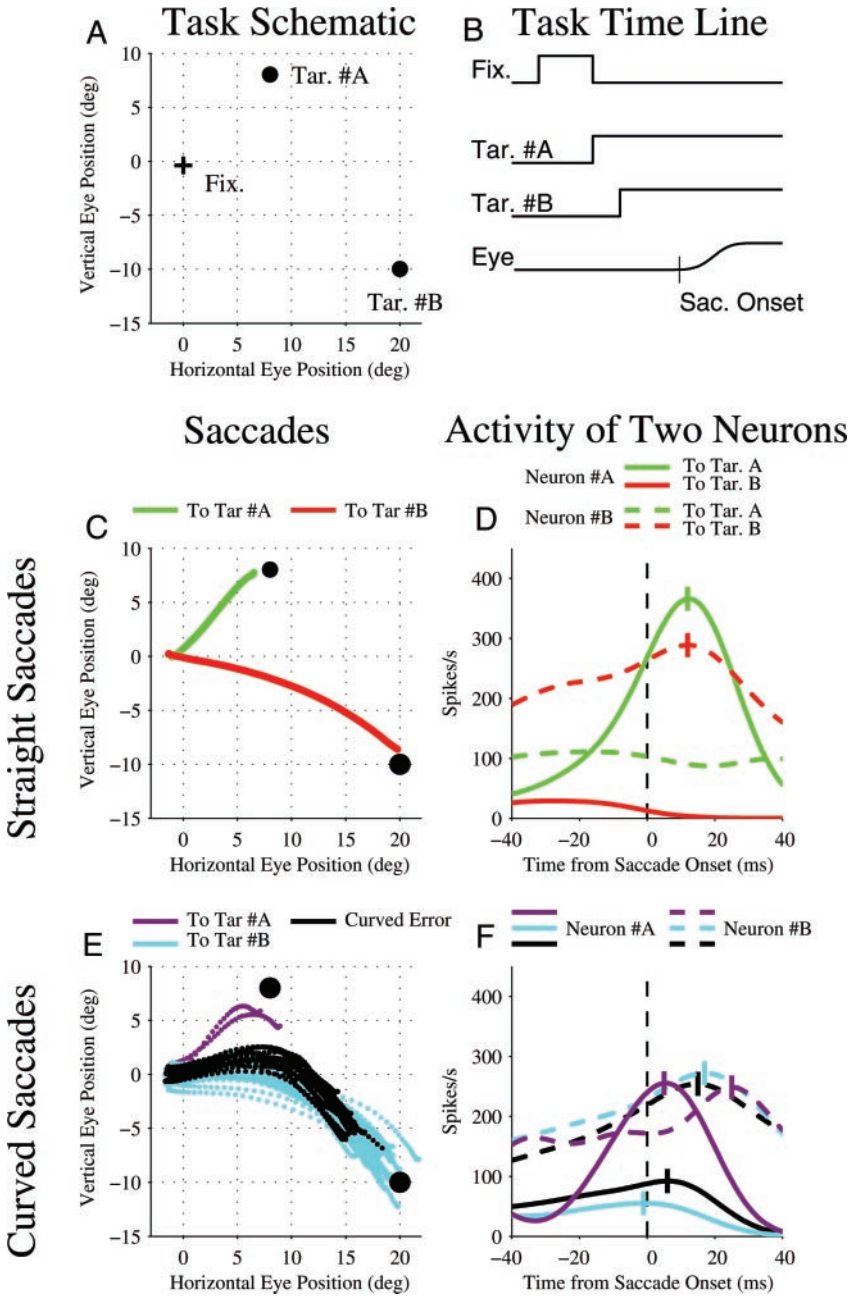

FIG. 1. Sequence of SC neuronal activity during two-target task. *A*: *target A* was placed in center of movement field of *neuron A* and *target B* was placed in center of movement field for *neuron B*. *B*: in two-target task monkey was required to make saccades to target that came on first; order of appearance and interval between their onset was randomized on successive trials. *C*: mean trajectory of straight saccades made to *target A* (green) and to *target B* (red) when both targets were presented. *D*: mean activity of two neurons recorded simultaneously, color-coded to eye movements shown in *C*. Solid line always represents *neuron A* and dashed line represents *neuron B*. Line color always represents type of saccade made, i.e., in *C* to *target A* or to *target B*. Tick marks indicate time at which mean peak firing rate occurred. Note *neuron B* had passive visual activity and is a "build-up" neuron with a greater amount of early activity. *E*: three groups of strongly curved individual saccades. For all three groups of curved saccades, the eye initially pointed more toward *target A* (or at points in between *A* and *B*) and then curved to point toward *target B*. Average circular SD for purple, black, and cyan saccade groups is 22.6, 23.5, and 25.7°, respectively (see METHODS). *F*: mean activity of two neurons recorded during curved saccades shown in *E* and indicating sequence of peak activity, first in *neuron A* and then in *neuron B*.

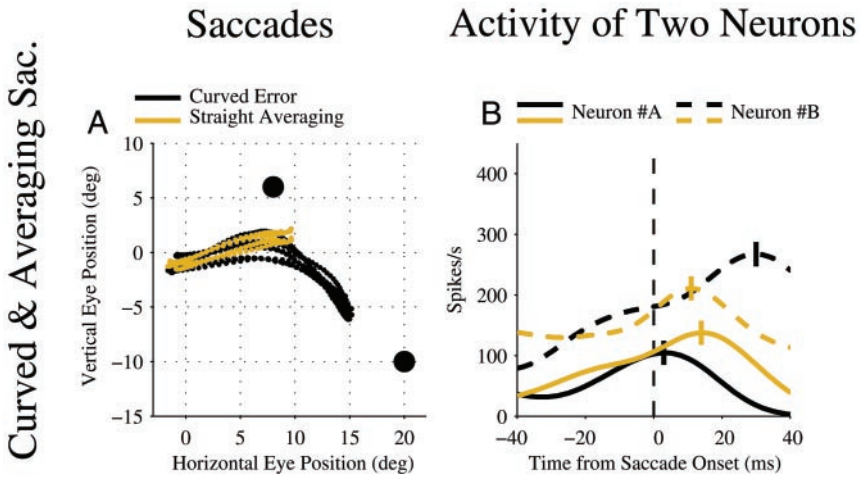

FIG. 2. Comparison of sequence of neuronal activity during curved saccades and straight averaging saccades. *A*: averaging saccades (yellow) and strongly curved saccades (black) for same target configuration as shown in Fig. 1 but for different neuron pair. Average circular SD for averaging (yellow) and curved saccade group (black) is 7.6 and 23.8°, respectively. *B*: mean activity for the two neurons, again color-coded to saccades in *A*. Peak activity of *neuron A* precedes that of *neuron B* during curved saccades but not during straight averaging saccades.

contrast to their more limited contribution to the determination of final saccadic trajectory.

METHODS

The procedures for behavioral control, recording eye position, and recording from several SC neurons simultaneously are identical to those described previously (Port et al. 2000). All animal care and experimental procedures were approved by the Institute Animal Care and Use Committee and complied with Public Health Service Policy on the humane care and use of laboratory animals.

Behavioral tasks and measures

DELAYED SACCADE TASK. The activity of each neuron was first examined using a delayed saccade task that allowed us to estimate the location and center of the movement field of each neuron. The task began when a fixation point came on in the center of the tangent screen 57 cm in front of the monkey. The monkey was required to fixate this point for 400 to 800 ms (randomized in 5 equal periods of equal probability) and then to continue fixating after a peripheral target spot came on. Between 500 to 1000 ms (5 equally probable periods) after the peripheral target spot came on, the fixation point went off, and the monkey was rewarded for making a saccade to the peripheral target within 500 ms.

TWO-TARGET TASK. In this task the monkey again began by fixating on a spot in the center of the screen, and it was rewarded for making a saccade immediately toward the first of two targets that came on in rapid succession. The reward was given if the end of the saccade fell into a relatively large reward window around the target; the size of the window varied with the eccentricity of the target but the mean window was size was 6 × 6°. A benefit of this task was that it produced strongly curved saccades. After a fixation period of 400 to 800 ms, the first of the two targets came on in one region of the visual field and then, after a variable time, the second target came on in a different part of the field. Note there was no enforced delay between target presentation and the monkey's saccade initiation. The time between onset of the first and second target was one of four times that were multiples of X ms, so that for X = 5, the four times were 5, 10, 15, and 20 ms. On the first day of recording, X was 50 ms so that the monkey could easily learn the task. Within 2 to 3 days, X was 10 to 20 ms according to the eccentricity of targets on that recording day. To avoid overtraining, the monkeys did not perform the two-target task until the first day of recording, although they had previously been trained on the delayed saccade task. There were 11 trial types in each block: four in which *target A* was the first asynchronous target, four in which *target B* was the first asynchronous target, one simultaneous presentation, and two control types in which *target A* and *target B* were presented alone. The 11 trial types were presented in random order in each block with no replacement for error trials. We rerandomized the order of the trials for each of the 50 repetitions for a total of 550 trials per recording session. In the simultaneous condition the monkeys were randomly rewarded 50% of the time. In all trials types, after the monkey made a saccade into the reward window, it was required to fixate the target for an additional 500 ms to receive a liquid reward. There was no enforced delay between target presentation and target selection as there was in the delayed saccade task. The advantage of the two-target task over a visual search task with multiple distracters was that in the two target task the regions activated by the targets on the SC map were centered on two identifiable locations on the SC map (in addition to any activity related to fixation in the rostral SC). Our electrodes were placed at those two locations.

Saccade measures

The start and end of all saccades was taken as the point at which the eye speed exceeded or dropped below 50°/s; this ensured that the eye did not stop and then resume the movement in the middle of the curved saccade. Eye movements were low-passed filtered with a zero lag 10 coefficient FIR filter with a −3-dB cutoff of 166 Hz.

DEFINITION OF STRONGLY CURVED SACCADES. The curved saccades we studied are most similar to those referred to by Minken et al. (1993) as strongly curved. The saccades observed fell along a continuum from slightly to strongly curved but, to extract the variation of neuronal activity with saccade curvature, we concentrated on those saccades with large curvature. We measured the curvature using standard circular statistics and specifically regarded a saccade as strongly curved if the angular SD of the trajectory was >20°. Intuitively, the circular SD was derived by first determining the instantaneous direction of the eye each millisecond for a given trial while the eye was in motion, plotting these directions on a 360° unit circle to produce a histogram of directions, and measuring the circular SD of the distribution of directions in this histogram (for computation see Batschelet 1981). If the eye traveled in a fairly straight path, the distribution of directions was narrow, and the angular SD was small. However, if the eye did not follow a straight path, the distribution was large, and the angular SD was large. We chose 20° as our minimum angular SD because it was these trials that we agreed were qualitatively strongly curved when we visually inspected all of the trials.

This amount of curvature in our strongly curved saccades was substantially greater than the smaller deviations seen during many saccades that have been studied extensively (Becker 1989) and whose magnitude and significance has recently been analyzed (Quaia et al. 2000). For comparison with the metric of Quaia et al. (2000), for which we can make a quantitative comparison, their curved saccades

had an angular SD of the trajectory closer to 10°. For comparison with another method of measuring such curved saccades, that of Smit and van Gisbergen (1990), their curvature measure for the purple, black, and cyan saccade groups in Fig. 1*E* would have been 0.17, 0.17, and 0.19, respectively, whereas the average circular SD for these groups was 22.6, 23.5, and 25.7°, respectively.

GROUPING OF CURVED SACCADES. For each saccade we first determined whether it was strongly curved using the criteria of a minimum angular SD of 20° as described above. In further analyses we did not include saccades that fell in the zone between clearly straight and strongly curved saccades (angular SD of 10 to 20°). We next grouped these strongly curved saccades according to their shapes to have at least a sample of similar saccades that allowed us to see the consistency of the timing of the two neurons across multiple saccades. The saccades in a group had to meet the following criteria: similar endpoints (within approximately 3°), duration (within approximately 13 ms), range of directions during the first few and the last few ms of travel (within approximately 10°), and a qualitatively similar shape. We did not include the oddball curved saccades with a trajectory shape that occurred only once.

BEGINNING AND END OF CURVATURE. For these groups of curved saccades, we adopted a standard criterion for designating the time at which the curve began and ended, and although this criterion was arbitrary, it allowed us to apply the same method to all of the saccades. Because we found that the first and the last few points of the curved saccades fell roughly along a straight line, we took the deviation from this line as the start or end of the curved part of the saccade using the following procedure. For the beginning of each group of curved saccades, a straight line was fitted through the points from the earliest indication of movement (>50°/s) up to an eye speed of around 33% of peak speed (see the *inset* at the lower right of Fig. 3 for an example of these points on a group of curved saccades). Next, we calculated the size of an error zone of 10° on each side of this straight segment. The time when the eye left this zone was taken as the beginning of the curve. To determine when the curve ended, a straight line was calculated through the last few points of the movement from the time the eye speed fell below ≈33% of the peak until the end of the saccade (<50°/s), again a 10° zone was calculated around this line, and the time at which the eye entered the error zone was deemed to be the end of the curve.

STRAIGHT SACCADES. Saccades were classified as straight if the angular SD of the trajectory was <10°. Saccades that fell between 10 and 20° of curvature were omitted from the analysis. Many straight saccades occurred when *target A* and *target B* were presented asynchronously and, of course, when either *target A* or *target B* was presented alone. In addition, we found straight saccades that ended midway between the targets, which we refer to as straight averaging saccades.

Neuron recording and analysis

DUAL RECORDING. The requirements for successfully recording from two neurons simultaneously in our experiment were three-fold. First, it was necessary to record from two neurons in different regions of the SC. We did this by directing our guide tubes to different regions of the SC, typically placing one in the upper visual field near the fovea and placing the second in the lower visual field away from the fovea. Second, we had to isolate and characterize neurons that increased their activity before saccade onset. This required moving both electrodes to successive neurons in the intermediate SC layers without losing the neuron on the other electrode. Third, two well-isolated neurons had to

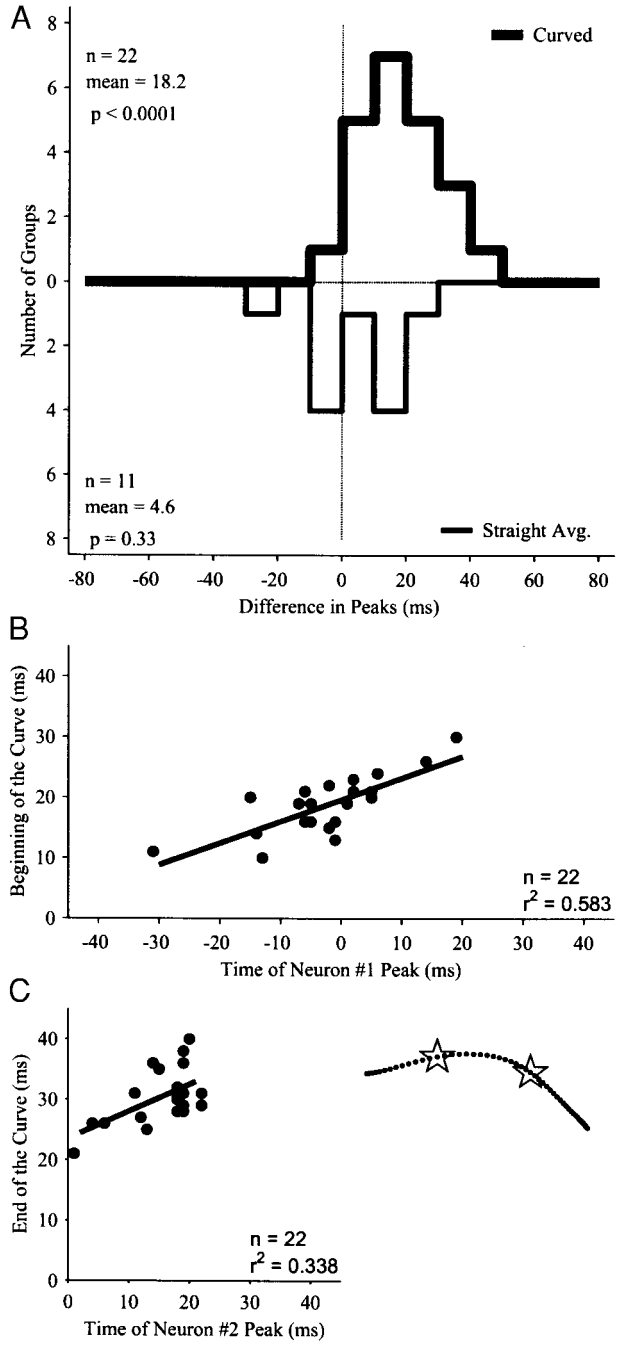

FIG. 3. Difference in time of peak activity in two neurons across sample of neurons (*A*) and relation of peaks to time of beginning and end of curvature (*B* and *C*). In comparing across sample of neurons, we always defined target for final direction of curved saccade as *target 2*. Other target became *target 1* by default. *A*: *top histogram*: difference in time of peak activity of *neuron1* and *neuron 2* for 22 groups of saccades recorded in 13 neuron pairs (in some cases more than one group of curved saccades was obtained from a neuron pair, as in Fig. 1*E*). Values to right of zero on abscissa indicate that time to peak of *neuron 1* preceded that of *neuron 2*, and values to left of zero show time difference when *neuron 2* preceded *neuron 1*. In inverted histogram, same time differences are given for 11 groups of straight averaging saccades (in 11 neuron pairs). Across sample of neurons there tended to be a sequence of activity for curved saccades but not for straight saccades. *B*: relation of peak activity of *neuron 1* to beginning of saccade curvature (see METHODS for curvature determination). Zero on both abscissa and ordinate in *B* and *C* is time of saccade onset. Intercept of regression equation is 19.6 and slope is 0.36. *C*: relation of peak of *neuron 2* to end of the curve. Intercept of regression equation is 23.5 and slope is 0.45. *Inset* (*lower right corner*): example of curved saccade with beginning and end of curvature determined using procedure described in METHODS indicated by stars. Across sample, time of curvature change was related to peak activity of *neuron 1* and *neuron 2*.

be obtained to increase the probability that both neurons remained identifiable during the lengthy time required to first estimate the movement field of each neuron using the delayed saccade task and then to record a sufficient number of trials during the two-target task.

The method we found successful for isolating and holding two neurons was the following. We lowered each electrode separately to the uppermost superficial visual layers of the SC and then waited 10 to 15 min. Next, we separately lowered each electrode until we encountered background multiunit activity before saccade onset and then again waited 10–15 min. Finally, we slowly moved each electrode, switching back and forth between electrodes, until two cells were well isolated and again waited 5–10 min, because in our experience, if we lost a neuron, it tended to be early in the recording period. Finally if both cells remained well isolated, we proceeded with the experiment.

We studied only those neurons that increased their activity before saccades. Of the 70 neurons in the 35 neuron pairs studied in 2 monkeys, 47 showed increased activity just before the saccade with no delay activity (burst neurons), and 23 neurons had increased activity during the delay period (buildup neurons), as indicated by a discharge rate of ≥50 spikes/s at the end of the delay period (Munoz and Wurtz 1995). In the perisaccadic period considered in this report, there was no difference in activity between burst and buildup neurons and so the results for the two groups were combined.

MOVEMENT FIELDS OF NEURONS. In the dual recording experiments we carefully estimated the center of the movement field, although we did not use the monkey's limited working time to determine the extent of the movement field more than qualitatively because by this time much of the monkey's working time had already been used just to isolate the appropriate neuron pair. For most of the neuron pairs yielding curved saccades, the targets were configured similar to that for the pair illustrated in Fig. 1. In our sample of 35 neuron pairs, 19 had multiple trials with similar curved saccades. For most of these (16 of 35), the target closest to the fixation point was in the upper visual field and a more distant target was in the lower part of the same visual hemifield. The targets for these 16 neuron pairs varied in target eccentricity and elevation according to the exact position of their movement field. A few more (3 of 35), had substantially different configurations but both targets were still in the same visual field. For the remaining pairs (16 of 35) there was no repetition of similar curved saccades across trials according to our saccade grouping algorithm (see above), so we did not study these neuron pairs further: 5 were recorded in the same hemisphere and 11 in opposite hemispheres.

In a subsequent set of experiments (related to Figs. 5 to 7), performed several months after the dual recording experiment, we reversed this priority by extensively determining the movement field of a neuron but then only recording from one neuron. In these experiments (see Figs. 5 to 7), we made quantitative maps of the movement field by interpolating between the recorded activity accompanying saccades made to each of 96 targets distributed in the contralateral and ipsilateral visual fields. Single targets were spaced every 15° at 4 different eccentricities (6, 10, 18, 32°) and each target was repeated 5 times in random order. To do this interpolation, the location of each saccadic endpoint was replaced with a 2D Gaussian function with SD of 4° and with a height set to the peak firing rate on that trial. For one neuron (included in the analyses of Fig. 7*C*), the variability of neuronal discharge was sufficiently large that a triangle linear estimate of

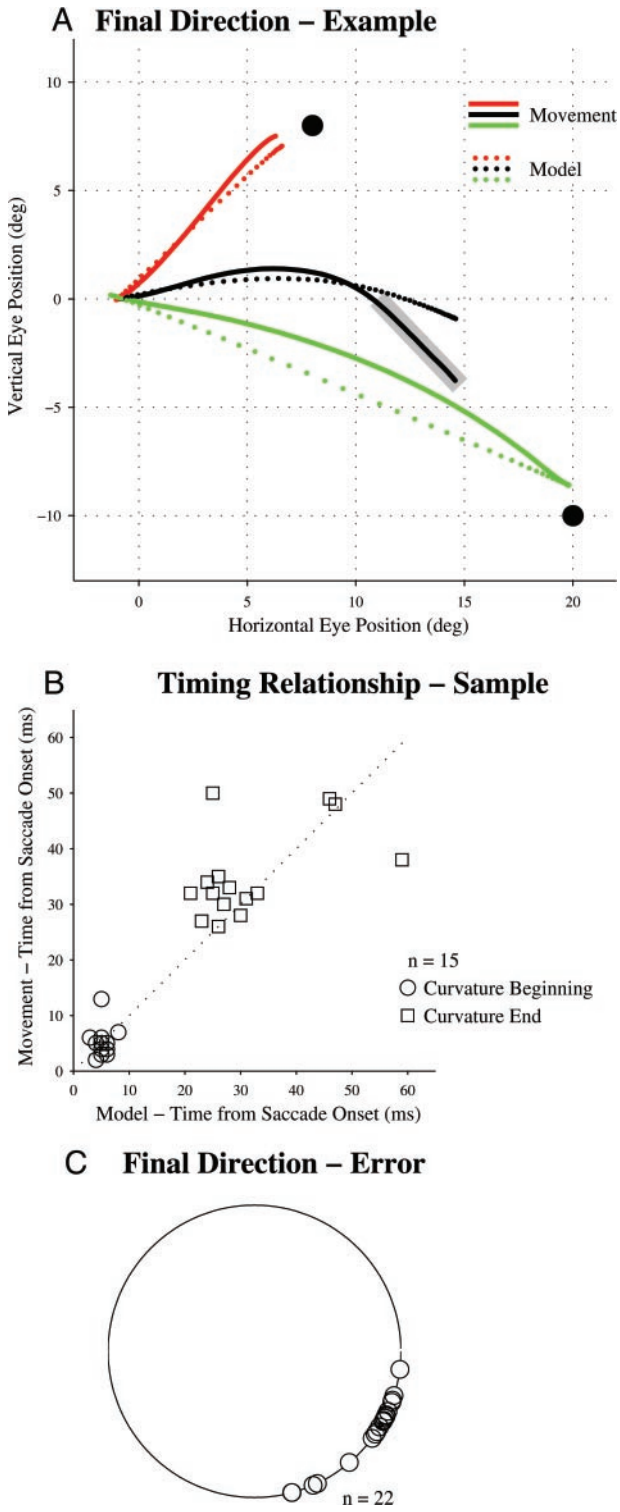

FIG. 4. Comparison between observed saccades and those simulated by vector-average model. *A*: illustration of observed (solid lines) and simulated (dotted lines) mean trajectory for curved saccades (black lines, same black saccade group as in Fig. 1, *E* and *F*) and for straight saccades made to either target. *B*: comparison of timing of beginning and end of saccade curvature in observed curved saccades and those simulated by vector-average model. In determining time of curvature change (see METHODS), a 5°, rather than 10°, window was used in the analysis because the model produced simulated saccades that never contained as much curvature as observed in real movements. *C*: greater downward final direction of saccade than predicted by model across sample of 22 groups of curved saccades. Each symbol on circle represents simulated final direction from model minus observed final direction for each of 22 groups of curved saccades. All points fall in quadrant between 0 and −90° with mean difference of −35°. Symbols represent difference between model prediction and actual saccade so that minus values indicate greater downward vector of real saccade than that predicted by model. Configuration of targets across sample was largely as in *A* so that the downward direction across sample is not surprising. Model predicted time of curvature change but not exact final direction of saccade.

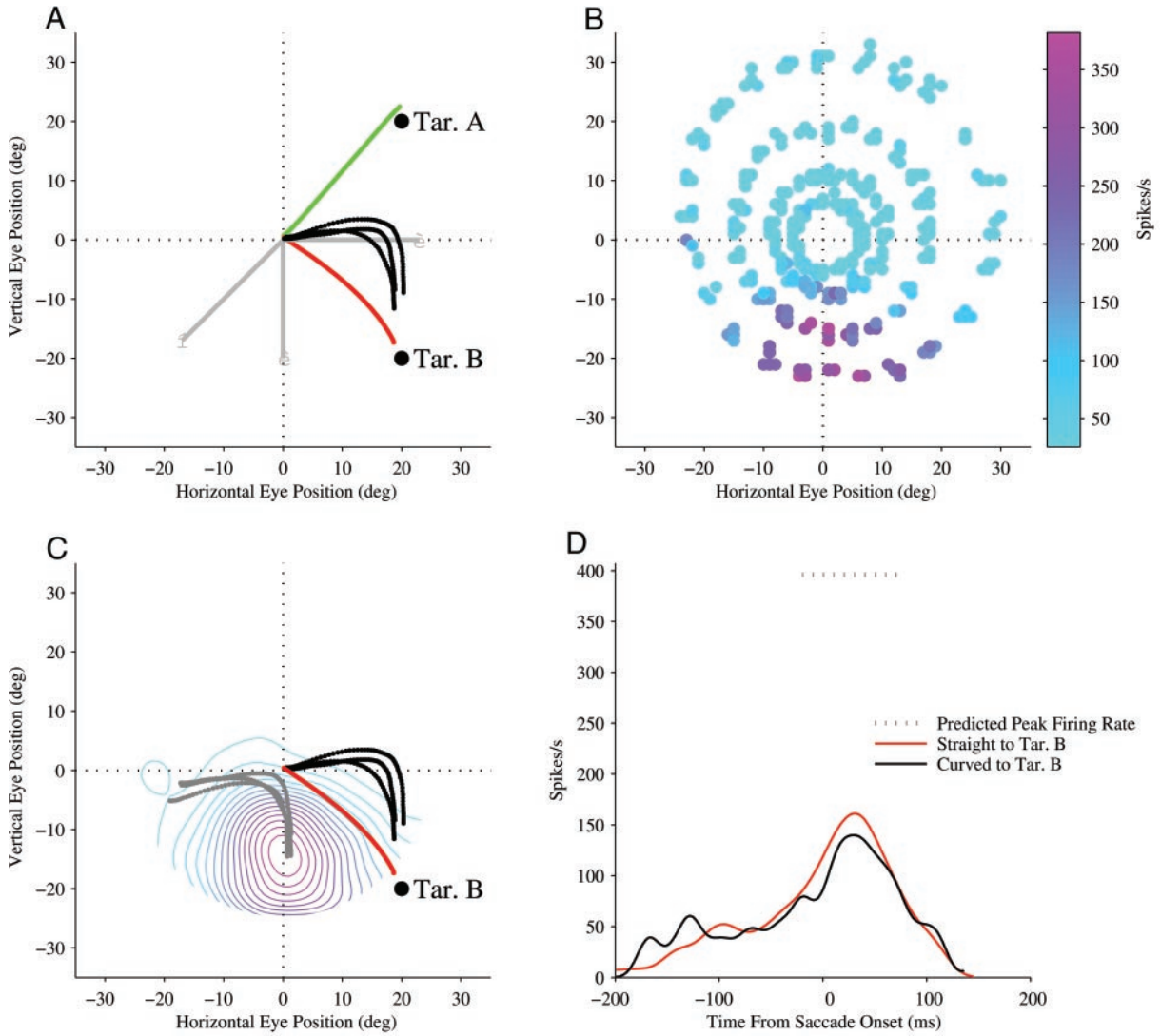

FIG. 5. Example of activity at locations on SC map other than those representing two saccade targets. *A*: saccades made in two-target task with *target A* 20° right and 20° up, and *target B* 20° right and 20° down. *Black traces*: individual "right-angle" curved saccades. *Green trace*: mean of straight saccades made to *target A*. *Red trace*: mean of those made to *target B*. Downward gray arrows indicate sample downward and ipsilateral downward vectors that could contribute to downward direction at end of curved saccades; horizontal gray arrow indicates vector that could contribute to horizontal phase of curved saccades. *B*: endpoints of saccades (solid circles) made while plotting the movement field of a neuron made to single targets presented every 15° at 4 different eccentricities (6, 10, 18, 32°) during delayed-saccade task. The 96 targets were repeated 5 times for total of 480 trials. Color coding of circles indicate peak firing rate within ±20 ms of saccadic onset. *C*: contour lines for activity indicate interpolated estimate of movement field with each of successive 15 lines, with each indicating a 6.7% decrease in activity from peak rate; color code is same as in *B*. Peak rate was 407 spikes/s and center of this movement field is 17° eccentric downward on vertical meridian. *Gray traces*: curved saccades of *A* transposed so that origin of downward phase is at center of movement map (see RESULTS). *Black traces*: nontransposed curved saccades from *A*. *D*: mean of neuronal activity for curved and straight saccades to *target B*, aligned to saccade onset. Difference between peak of curved (*black trace*) and straight saccades (*red trace*) was 21 spikes/s and between curved saccades and that predicted from movement field (gray dotted line) was 256 spikes/s.

the movement field yielded a more appropriate fit than did the Gaussian algorithm.

NEURONAL FIRING RATES. We used the peak firing rate of each of the neurons of a pair to compare neuronal activity to saccade curvature. To determine their peak, we first searched for the time of the peak mean firing for a group of curved saccades within a ±20 ms window centered on saccade onset. We then determined whether this peak rate was significantly different from activity in a delay epoch between the visual and motor burst of activity. (We did not use the background activity during fixation because many of our SC neurons were silent during fixation.) Specifically, we did the following. On each trial we measured the mean activity during the delay epoch (60 to 40 ms before saccade onset). Then on that same trial we measured the discharge rate at the time of the peak mean firing rate around saccade onset. These value pairs were collected for each trial within a group of curved saccades, and a comparison was made using a Student's pairwise *t*-test. If there was a significant increase ($P < 0.05$) then this group of trials with curved saccades was studied. For 3 neuron pairs, the number of trials was fewer than 4, which made the *t*-test unreliable, and for these pairs saccadic activity was considered significant if the peak was >50 spikes/s and was 1.5 times the firing rate of the preceding delay epoch.

We used the time of the peak activity related to saccade onset rather than the time of initial rise of activity before the saccade. Because the

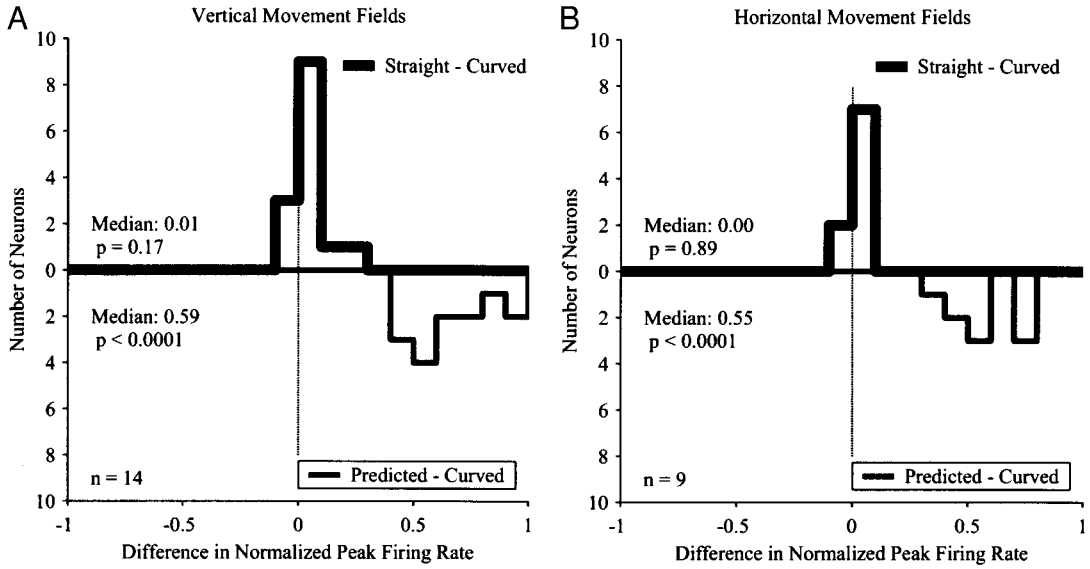

FIG. 6. Activity of sample of neurons for locations on SC map other than those representing two saccade targets. *A*: comparison of activity of 14 neurons with movement fields along vertical meridian (eccentricity, 12–20°) during right-angle saccades. Abscissa for upper, thick-lined histogram shows index of firing rate that was derived by first normalizing firing rate of each cell to its peak firing rate and then subtracting firing rate of curved saccades from straight saccades made to *target B*. The index in the inverted, thin-lined histogram shows difference when normalized firing rate on curved trials was subtracted from value expected if downward portion of saccade had been made to center of movement field. *B*: comparison of activity of 9 neurons during right-angle saccades whose movement fields were along horizontal meridian. Same conventions as in *A*. Neurons with vertical and horizontal vectors were not as active as expected if they provided those vectors for curved saccades.

neurons had visual as well as saccade related activity and our task was a reaction time task, the visual response blended into the saccade related burst. If we took a point on the initial rise of activity, we would frequently have a measure only of the onset of the visual response rather than the onset of the presaccadic activity. It is worth noting that in comparing the neuronal activity to that predicted by a model, we used the entire waveform of the perisaccadic activity, not just the peak activity.

We analyzed the neuronal data as a function of time using spike density functions (MacPherson and Aldridge 1979) in which the spikes sampled every millisecond were represented by a Gaussian function with SD of 10 ms. We calculated the spike density functions on a trial-by-trial basis and this allowed us to convert the discrete single spike events into a continuous function.

Vector-average model

The weighted vector-average model we used was fundamentally similar to those used to model the saccadic (Lefèvre and Galiana 1992; Quaia et al. 1999; Tweed and Vilis 1985; Van Gisbergen et al. 1985) and reaching systems (Georgopoulos et al. 1988), and was based on the optimal vector of each neuron and the ratio of activity between them

$$\vec{V}^{t}_{model} = \frac{\frac{(f^{t}_{a} - b_a)\vec{V}_a}{P_a} k_a + \frac{(f^{t}_{b} - b_b)\vec{V}_b}{P_b} k_b}{2}$$

where $\vec{V}^{t}_{model}$ is the predicted direction of the saccade each ms during the saccade; $\vec{V}_a$ and $\vec{V}_b$ are the fixed optimal vectors for *neuron A* and *neuron B*, which were determined from the mean saccade endpoint during the control trials to *target A* and *target B*, respectively; f^{t}_{a} and f^{t}_{b} are the average discharge rates across 2–34 trials (mean = 11) during each ms of the saccade made with two targets present; P_a and P_b are the peak mean saccade related discharge rates of each neuron during their corresponding control trials; b_a and b_b are the background firing rate (if any) for *neuron A* and *neuron B*, respectively; k_a and k_b are constants;. Thus the activity of each neuron is represented each ms by the product of its optimal vector ($\vec{V}_a$) and its firing rate (f^{t}_{a}) minus any background activity (b_a), divided by its peak firing rate (P_a) to normalize its discharge to its peak rate. The contributions of *neuron A* and *neuron B* were then added and divided by 2 to obtain the vector average. The recorded neuronal activity was shifted forward 10 ms in time to account for delays between SC activity and the movement (Miyashita and Hikosaka 1996). This 10-ms shift was made in the model but not in the other analyses.

There was no reason to believe that the contributions of the two neurons to the saccade generation would be exactly equal, especially because they always had movement fields optimally related to different saccadic amplitudes. To allow for this difference in amplitude, the term for each neuron was multiplied by a constant (k_a, k_b). Note that this constant only alters the relative contribution of the two neurons to the average, but does not alter the temporal sequence of each neuron's contributions. The value used for any given pair of neurons ($k = 0.01$ to 2.00) was the one that gave the smallest difference between the observed and simulated saccades across all movements. Once determined, a single value of (k_a, k_b) was used for all time bins throughout the saccade and for all saccade types (straight, curved, and averaging) within a given neuron pair. The mean value of k_a across the simulated neuron pairs was 1.01 and the mean value of k_a was 0.43. The larger value for k_a than for k_b results from the tendency in our sample of neuron pairs for *neuron B* to have a greater eccentricity for its optimal target than did *neuron A* by about 50%. For neuron pairs in which *neuron B* was of a greater eccentricity, the k_b term effectively allowed for the unbalanced eccentricity to be normalized.

RESULTS

Sequential SC activity and saccade curvature

STRAIGHT AND CURVED SACCADES IN A SAMPLE NEURON PAIR. In 35 recording sessions, we recorded simultaneously from two well-isolated SC neurons whose discharge increased before saccade onset. We first determined the location of the centers

of the movement fields of each neuron by requiring the monkey to make visually guided saccades to targets in the relevant region of the visual field. For our two-target task, the targets were positioned at the centers of these movement fields (Fig. 1*A*, *target A* for *neuron A* and *target B* for *neuron B*). On each trial of the two-target task, the monkey began fixating at a spot in the center of the screen and was rewarded for making a saccade toward the first target that appeared after the fixation point disappeared (Fig. 1B).

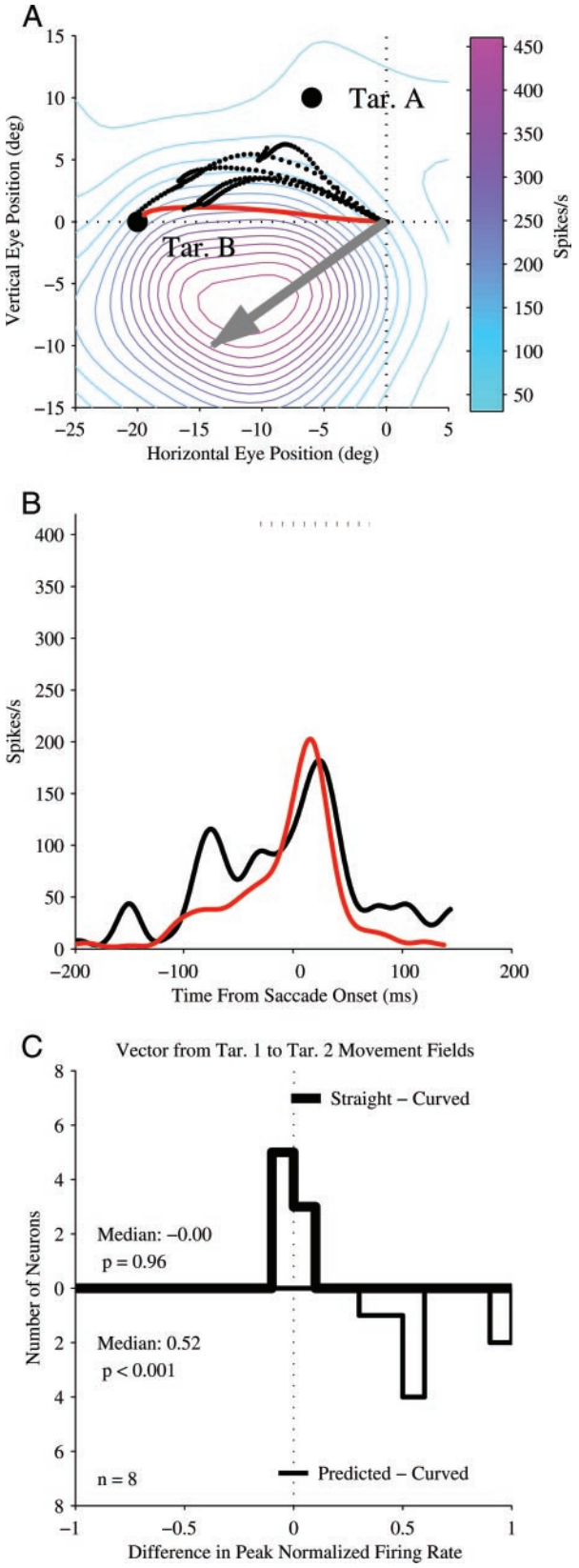

Figure 1, *C–F* shows the results for one of the 35 neuron pairs studied. Even when two targets were present, the vast majority of saccades were straight to one target or the other: 94.6% of the 13,574 saccades in 35 neuron pairs in two monkeys. Figure 1*C* shows the average trajectories for the straight saccades made to one target or the other with saccades to *target A* in green and those to *target B* in red. Figure 1*D* shows the activity of a pair of SC neurons during these saccades. In this and subsequent illustrations, solid lines always represent the activity of *neuron A* and dashed lines represent *neuron B*. The color of the line indicates to which target the accompanying saccade was directed. As expected, the activity of the neuron whose movement field overlapped the location of *target A* increased for saccades to *target A* (solid green line) but not for saccades to *target B* (solid red lines), and vice versa for *neuron B* (dashed lines). The activity of both neurons peaked at approximately 10 ms after the onset of saccades into their respective movement fields (see tick marks on the mean spike density functions, Fig. 1*D*). Thus the activity of the two neurons during straight saccades to the targets did not reveal any unexpected characteristics (Sparks and Hartwich-Young 1989).

About 4.8% of the saccades, however, were strongly curved and veered from one target to the other (the remaining 0.6% were straight averaging saccades). Saccades tended to *1*) initially point more toward *target A* and veer toward *target B* without obtaining it (Fig. 1*E*, *purple traces*), *2*) initially contain an intermediate direction and then veer toward *target B* without obtaining it (*black traces*), or *3*) initially contain an intermediate direction and successfully veer toward *target B* (*cyan traces*). The mean latency of the curved saccades was slightly longer (10 ms) than that for straight saccades (*t*-test and Kolmogorov–Smirnov test, $P < 0.00001$). Curved saccades occurred more frequently when short target onset asynchronies increased task difficulty: the frequency of curved saccades increased as the percentage of correct trials decreased (Pearson $r = 0.295$, $P < 0.001$). When the targets were asymmetric, as in Fig. 1, the monkeys tended to have a bias for curved saccades going from the closer target to the farther target. When the targets were symmetrical, we observed bowed saccades toward either target.

The shape of the curved saccades was related to the *timing* of the peak activity of the SC neurons. Figure 1*F* illustrates this timing difference for the same sample neuron pair, using the 3 groups of similarly shaped curved saccades illustrated in Fig. 1*E* (*purple*, *black*, and *cyan traces*; see METHODS for basis of

FIG. 7. Activity of neurons in which movement field covers vector from *target A* to *target B*. *A*: contour lines indicate movement field of neuron; conventions as in Fig. 5*C* (peak discharge = 491 spikes/s). *Black traces*: individual curved saccades. *Red trace*: mean trace of straight saccades to *target B*. Gray arrow is vector from *target A* to *target B* transposed to the origin. *B*: neuronal activity of group of curved saccades (black), straight saccades to *target B* (red), and predicted peak activity from transposed vector of *target A* to *target B* (gray dashed lines). *C*: difference in normalized firing rate (conventions as in Fig. 5) across our sample of neurons showing that neurons were not as active as expected if they provided vector for *target A* to *target B*.

grouping). For the curved saccades that landed near target A (Fig. 1*E*, *purple traces*), the saccades initially were directed more toward *target A*, but then turned and ended pointing toward *target B*. The activity of the two neurons (as gauged by their peak activity indicated by the tick mark in Fig. 1*F*) was also separated in time: the discharge of *neuron A* (purple solid line) peaked near saccade onset, but that for *neuron B* peaked about 20 ms later (purple dashed line). Both the curved saccade groups that ended near *target B* (Fig. 1*E*, *cyan traces*) and the saccades that landed between *target A* and *target B* (Fig. 1*E*, *black traces*) also showed a separation in their neuronal peak activities (Fig. 1*F*). The salient point is that in all 3 groups of curved saccades the peak activity of *neuron A* preceded the peak of *neuron B*, and this paralleled the tendency of these saccades to go initially more toward *target A* and terminate pointing more toward *target B*.

AVERAGING SACCADES IN A SAMPLE NEURON PAIR. An important test of this relation of peak activity timing to saccade curvature would be to compare the sequence of activity of the same neurons when the saccades were not made to either target but were also not curved, as is the case with averaging saccades. Averaging saccades are those that end roughly halfway between the two targets, and they were investigated in previous studies of the SC (Edelman and Keller 1998; Glimcher and Sparks 1993; van Opstal and van Gisbergen 1990). Unfortunately, straight averaging saccades occurred very infrequently in our behavioral paradigm (0.6% of the saccades in our sample). However, in the second sample neuron pair shown in Fig. 2, the monkey made both straight averaging saccades and curved saccades. For the curved saccades (*black traces* in Fig. 2*A*), the peak activity of *neuron A* again preceded that of *neuron B* by more than 20 ms (Fig. 2*B*); this difference was not observed during averaging saccades (*yellow traces* in Fig. 2*A*). Thus for these sample pairs of neurons, the sequence of their peak activity appeared to be critical: if the timing was sequential from *neuron A* to *neuron B* the saccade was curved, but if it was nearly simultaneous the saccade was straight.

SEQUENTIAL ACTIVITY ACROSS THE SAMPLE OF NEURON PAIRS. To determine the consistency of this sequence of activity across neuron pairs, we examined this timing of the peak activity across all of the neuron pairs that met the following criteria. To have a uniform description of the saccades across the sample of neurons, we adopted the following designations. The final direction of the curved saccade always pointed toward a target and we always defined this as *target 2*. The other target became *target 1* by default. The neuron whose movement field included *target 2* became *neuron 2* and the other neuron whose movement field overlapped *target 1* became *neuron 1*. Thus for the analysis across the sample of neurons, we switched from a *target/neuron A–B* nomenclature to a *target/neuron 1–2* nomenclature. It is important to note that these definitions have no relationship to which target appeared first or whether the targets were presented simultaneously.

First, from the experiments on each neuron pair we had to obtain groups of strongly curved saccades that had similar shapes. Of the 35 neuron pairs, 19 met these criteria for saccade curvature. Having groups of similar shapes was necessary so that we could look for the consistency of neuronal response across similar curved saccades; activity during saccades with unique curvatures was not analyzed. Those pairs that had no strongly curved saccades included 5 pairs with targets in the same visual field and 11 pairs recorded in the two opposite SCs with targets placed symmetrically across the vertical meridian. Of the 19 pairs that had groups of curved saccades, we studied only those neurons in which a peak firing rate could be identified in both neurons (see METHODS, NEURONAL FIRING RATES), which reduced the number of pairs to 13. Those neurons with no statistically significant peak were buildup neurons that did not have a statistically significant increase in activity before saccade onset (Munoz and Wurtz 1995). Within these 13 pairs, however, there were sometimes more than one group of saccades with similar curvature. This yielded 22 groups of curved saccades, which is the sample we now analyze.

The histogram in Fig. 3*A* shows the timing difference of the first and second neuron for the 22 groups of curved saccades, with those pairs in which the peak of *neuron 1* preceded the peak of *neuron 2* shown as positive values on the abscissa. For all but one case, the peak of *neuron 1* preceded the peak of *neuron 2*. The mean difference in peak times was 18 ms and the probability that this was different from zero was highly significant (*t*-test, $P < 0.00001$). For the 11 groups of averaging saccades in 11 neuron pairs, the inverted histogram in Fig. 3*A* shows that the differences in peaks were distributed about zero, with the mean of 4.6 ms not significantly different from zero (*t*-test, $P = 0.33$). For the averaging saccades, neurons were designated as *1* and *2* based on their assignment during the accompanying curved saccade trials. If we now go back to examine the difference in the timing of the neuronal activity during saccades made directly to *target 1* or *target 2* across our sample of neurons (as in Fig. 1*C*), we would not expect to see any difference in the timing of the peaks of activity (as was the case in Fig. 1*D*), and we did not (*t*-test, $P = 0.64$). We conclude that across our sample of strongly curved saccades there was a sequence in the timing of the peak activity of SC neurons that we did not observe during straight saccades, either direct or averaging.

Sequential SC activity and timing of saccade curvature

If this pattern of neuronal activity is causally related to the change in direction during a strongly curved saccade, the timing of each neuron's activity should be related to the time of the beginning and end of curvature. Specifically, the point at which the activity of *neuron 1* reaches its peak and begins to decline should correspond to the beginning of the curve. We therefore plotted, for all of the groups of curved saccades (Fig. 3*B*), the time of peak discharge for *neuron 1* against the time at which saccade curvature began (METHODS). The regression line on the plot shows a moderate ($r^2 = 0.583$) but highly significant correlation (f-test, $P < 0.0001$). For *neuron 2* one would expect the peak and decline to be related to the end of the curve, assuming that *neuron 2* is involved in directing the saccade toward *target 2*. This was the case (Fig. 3*C*, $r^2 = 0.338$. $P < 0.005$). There is therefore a tendency for earlier neuron activity to be associated with earlier saccade curvature, either for the beginning of the curve (*neuron 1*) or the end (*neuron 2*). In contrast, the opposite correlations, time of peak discharge of *neuron 1* to the *end* of the curve and time of peak of *neuron 2* to the *beginning* of the curve, were not significant (f-test, $P = 0.149$ and $P = 0.461$, respectively). Note that for

both the beginning (Fig. 3*B*) and the end of the curvature (Fig. 3*C*), the neuronal activity always preceded the onset of the change in curvature, as indicated by the positive values for curvature onset and ending on the ordinate of the figure. On average, the peak firing rate of *neuron 1* was 2.5 ms before saccade onset, whereas the peak firing rate of *neuron 2* on average was 15.7 ms after saccade onset and was always before the end of saccade curvature.

To further test the relationship of neuronal firing and saccadic curvature, we compared the timing of the curvature of the saccade actually made with that simulated by a model that relates neuronal activity to movement. We used a simple weighted vector-average saccadic model (METHODS) that has been experimentally tested in the SC (Lee et al. 1988). The model produced a simulated vector direction for each ms during the saccade based on the optimal vector of each neuron and the ratio of activity between them. Figure 4*A* illustrates the simulated trajectory produced by the model (*dotted traces*) and the observed saccade (solid line) for the same neuron pair as in Fig. 1. To produce this 2D plot of the simulated trajectory, the direction of the saccade in each ms is given by the vector produced by the model, but the length of the vector is taken from the actual position of the eye movement. For this neuron pair, in which the difference in neuronal peak firing was 18 ms, the model produced a curved saccade (black dotted line in Fig. 4*A*) and, at a qualitative level, there is a modest relationship between the model and saccade curvature.

To compare the curvature of the model and the movement quantitatively, we compared the timing of both the beginning and the end of the saccade curvature using the same type of analysis of the beginning and end used in Fig. 3, *B* and *C*. Figure 4*B* compares the times of saccade beginning and end for the actual and simulated saccades. Most values lie near the equality line (Pearson correlation $r = 0.90$, $P < 0.00001$), indicating a substantial relationship between simulated and actual curved saccades. The neuron pairs represented in Fig. 4*B* are those 15 of 22 in which the difference in peak-firing rate was >12 ms. For the remaining 7 neurons the model produced simulated saccades with very little curvature, a point considered in the next section.

We conclude that across our sample of neurons the timing of activity of the two populations of neurons predicts both the occurrence of the curved saccades and the timing of the phases of that curvature, and that this timing relationship is also present in the simulation of the curved saccades.

SC activity and the final saccadic direction

Unlike the timing of the curvature, the final direction of the curved saccades seems less likely to be accounted for by the sequential activity of the neuronal populations represented by target-related neurons. For the example in Fig. 4*A*, the final downward phase of curvature would seem to require a downward vector that is poorly represented by either of the two neurons, whose optimal vectors are indicated by the straight saccades to the centers of their movement fields. This can be assessed by using the same vector-average model described above. Figure 4*A* compares an actual curved saccade (black solid line) with that simulated by the model (black dotted line). Whereas the model predicted the terminal directions of the straight saccades to either target, although not the slight curvature of the saccades to the lower target, it did not predict the end direction for the curved saccade; the final phase of the actual movement had a greater downward component than did the model. Across our sample of 22 curved saccade groups, the mean terminal direction of the movement (during the last 5 ms) was 35° more downward than predicted by the model (Fig. 4*C*). The shift was downward because the targets usually had configurations generally similar to those shown in Fig. 1.

One obvious question is whether the downward vector in the observed curved saccades but not in the model is represented by neurons in other areas of the SC map whose contribution has not been included in the model and whose activity we did not record. Because we presented only two visual targets for saccades, it seemed unlikely to us that neurons at locations on the SC map remote from the representation of these targets would be active. However, given that the curved saccades themselves were unusual, they may have been accompanied by activity in other parts of the SC that was also unusual. To explore this possibility, we conducted a subsequent series of control experiments on one monkey.

In these control experiments, we used the same two-target task, but the targets were positioned in the same place in the upper and lower visual fields (Fig. 5*A*) over a series of experimental sessions extending over a number of months. This produced, in addition to curved saccades similar to those seen in the first experiment (Fig. 1*E*), saccades that were highly reproducible from one recording session to the next and that had a horizontal and vertical component with a nearly right angle turn halfway through the movement, saccades we call "right-angle" saccades (Fig. 5*A*, *black traces*). Although these saccades curved abruptly, the instantaneous velocity never dropped below 50 deg/s, which precluded them from being two saccades. This target configuration allowed us to record from neurons at different locations on the SC map and to determine whether these neurons, which represented vectors quite different from those of the two targets, became active during these almost stereotyped right-angle curved saccades. In this experiment, we recorded from one neuron at a time to be able to quantitatively map the movement fields.

VERTICAL VECTORS. There are several combinations of vectors that could produce the final downward movement observed in the curved saccades that is not accounted for by our model. The curved saccades illustrated in Fig. 5*A* have a clear rightward and downward component, and it is the downward component we analyzed first. To do so, we recorded from a neuron at the site on the SC movement map that should be making the largest contribution to the downward vector of the saccades: those neurons on the vertical meridian with an amplitude of about 15° downward (Fig. 5*A*, gray downward arrow). Figure 5*B* shows the movement field for one of these neurons mapped using a total of 96 randomly presented targets. By interpolation, we then generated a contour map of the movement field (Fig. 5*C*; see METHODS) so that we could predict what the discharge rate of this neuron should be for a saccade anyplace in its movement field.

For comparing firing rates observed during curved saccades and those predicted by the movement field of the recorded neurons, we transposed the downward phase of the curved saccade to the center of the movement map (the fixation point for the monkey; Fig. 5*C*). To do this transposition, we first

determined the straight portion at the beginning and end of the movement (as in Fig. 3, *B* and *C*), then found the intersection of two least-squares-fit lines through these portions, and took this as the *origin* of the downward phase of the curved saccade. The end of this downward component was then superimposed on the interpolated movement field of the neuron (Fig. 5*C*). We could then ask whether the activity of this neuron during the curved saccades, which ended at the edge of this neuron's movement field (*black traces* in Fig. 5*C*), was like that of a saccade directly to *target B*, which would be at the edge of its movement field (*red trace* in Fig. 5*C*), or was like that of the downward phase of the curved saccades made to the center of the movement field (*gray curves* in Fig. 5C). If the neuronal activity was like a saccade directly to *target B*, the discharge would be like the *red trace* in Fig. 5D with a peak firing of 161 spikes/s. If the activity was like the downward phase of the curved saccade, the discharge would be like the dashed gray line in Fig. 5*D* with a peak firing rate of 396 spikes/s. The discharge rate we *actually* observed with the curved saccades was the *black curve* in Fig. 5*D* with a peak rate of 140 spikes/s, which is very close to that expected with saccades to the edge of this movement field. Thus this downward coding neuron was not as active as expected to produce the downward phase of the observed saccade, but instead was only as active as expected with a saccade that ended at the edge of its movement field.

We tested 14 neurons with movement fields along the downward vertical meridian and found highly consistent results (Fig. 6*A*). The abscissa for the *top histogram* shows an index derived by subtracting the peak normalized activity of a neuron during the downward phase of the curved saccade from that of the straight saccades made to *target B* (as in Fig. 5*D*). The normalization value was the peak firing rate of the neuron at the center of the movement field. No difference between the firing rate of the right-angle and straight saccades would give a value of zero. Across the sample of neurons, the index value was not statistically different from zero (*t*-test, $P = 0.17$; Fig. 6A, *top histogram*). The abscissa for the inverted histogram shows an index derived by subtracting the normalized firing rate during the right-angle saccades from that expected if the downward portion of the saccade had been made near the center of the movement field. This difference was large (*t*-test, $P < 0.00001$). We conclude that there is no evidence that the neurons along the vertical meridian contribute substantially to the downward phase of curved saccades.

IPSILATERAL VECTORS. If ipsilateral SC activity was involved, a vector directed toward the lower ipsilateral field might provide the necessary downward vector; an appropriately weighted average of vectors to *target 1*, *target B*, and an ipsilateral vector could produce a downward saccade. To test this we recorded from 8 neurons at a site in the SC representing a vector equal and opposite to that of *target 1* (Fig. 5*A*, gray ipsilateral leftward-downward arrow). For these ipsilateral neurons, there was no activity at all during curved or straight saccades to either *target A* or *target B*. There is no evidence for a contribution of this region of the ipsilateral SC to these curved saccades.

HORIZONTAL VECTORS. As an additional control, we also recorded 9 neurons with movement fields along the horizontal meridian (Fig. 5*A*, gray rightward arrow) and analyzed the results in the same manner as the vertical meridian cells. We now took the intersection of the least-squares-fit lines (as explained for Fig. 5*C*) as the end of the rightward phase of the right-angle saccades. The difference in neuronal activity between the right-angle saccades and the straight saccades to *target B* was not significantly different from zero (*t*-test, $P = 0.89$; Fig. 6*B*, *top histogram*), whereas the difference in activity during the right-angle saccades and that predicted by a contribution of these neurons with horizontal movement fields was very large (*t*-test, $P < 0.00001$; Fig. 6*B*, *inverted histogram*). Thus there is no evidence that these neurons along the horizontal meridian contribute to the horizontal phase of right-angle curved saccades.

In conclusion, after examining neurons representing vertical, ipsilateral, and horizontal directions, we find no indication that neuronal activity in these selected regions of the SC remote from areas representing the targets is sufficient to account for the curvature of strongly curved saccades.

Concurrent saccade processing

A somewhat different possibility is that curved saccades result from the programming of two sequential saccades. If that were the case, we might see some indication in the velocity profile of the saccades indicating a shift from one saccade to the next, such as changes in instantaneous saccadic speed. We therefore examined the 22 groups of curved saccades to determine whether there was more than one peak in the velocity profile. For 65% of the curved saccades, there was only a single peak in the instantaneous eye speed, but for 35% of the curved saccades there was a double peak with a mean interval between peaks of 30.5 ms. For these neurons with a double peak, we then checked to see whether there also might be a time difference between the peak activity of the two neurons recorded simultaneously. However, we found no significant correlation for the interval between the peaks in speed and the interval between the peaks in neuronal discharge (Pearson $r = 0.216$, $P = 0.094$).

The multiple changes in the speed in the curved saccades raise the possibility that the curved saccades represent two separate saccades occurring in rapid sequence. If they are two sequential saccades, however, we would expect to see activity in the SC related to the vector of the second saccade. For example, the curved saccades shown in Fig. 7*A*, which initially have intermediate trajectories between *target A* and *target B* and then curve toward *target B*, could result from a series of two programmed saccades: a saccade to *target A* followed by a saccade from *target A* to *target B*. If this were the case, we should see activity among neurons that represent the vector from *target 1* to *target B* (gray arrow in Fig. 7*A* with the origin transposed to the fixation point.

To test whether there is any evidence of two sequential saccades, we recorded from neurons whose movement fields included that vector by recording just the neurons representing that vector while plotting the movement field in detail as in Fig. 5. Figure 7*A* plots the contours of a movement field of an example neuron. The *target A* to *target B* vector clearly lies within the movement field of the neuron and the predicted firing rate for a saccade with this vector is 402 spikes/s. The curved saccades (*black traces* in Fig. 7*A*) and the straight saccades to *target B* (red line in Fig. 7*A*) terminate on the edge

of the movement field. In Fig. 7*B*, the neuronal activity for the curved (black) and straight (red) trials are similar, but the predicted peak firing rate of a saccade made along the *target A* to *target B* vector is much higher (dotted gray line). In this example then, the activity of the neuron is similar to that expected for saccades ending at the edge of the movement field and not at the center as would be expected if the *target A* to *target B* vector were making a significant contribution.

We did experiments on 11 cells, 8 of which had both curved saccades and had the vector from *target A* to *target B* within the movement field of the recorded neuron. Using the same analysis for the sample as in Fig. 6, we plotted firing rates for straight minus curved saccades (Fig. 7*C*, *top histogram*) and predicted minus curved saccades (Fig. 7*C*, *inverted histogram*). Across our sample, there was no difference between straight and curved saccades (*t*-test, $P = 0.96$), whereas a large difference existed between predicted and curved saccades (*t*-test, $P < 0.00001$). Thus there is little evidence that the neurons that would be responsible for generating a vector from *target A* to *target B* contribute to the strongly curved saccades.

DISCUSSION

By simultaneously recording from two sites on the SC movement map, each related to a saccade target, we directly investigated the interactions between populations of neurons in the SC. We concentrated on the timing of the activity by using a task in which two competing targets were presented in rapid succession, and the monkey made saccades toward them with no enforced delay. Our analyses concentrated on the activity of these two neurons during strongly curved saccades, those saccades that initially headed more toward one target and then veered to head instead toward the other target.

Our major finding is that when the saccade was strongly curved, the activity of the two SC neurons was sequential. Three analyses supported this finding. First, the timing of the peak activity of each neuron occurred sequentially: the neuron for the first target reached its peak earlier than did the neuron for the second target (Fig. 3*A*). The simultaneous neuronal activity underlying straight averaging saccades acted as a fortuitous control for this analysis. Thus SC activity occurring simultaneously predicted straight saccades, whereas that occurring sequentially predicted strongly curved saccades. Second, the timing of the peak activity was related to the beginning and end of saccade curvature. The time at which *neuron 1* reached its peak and had already maximally influenced the saccade toward *target 1* was correlated with the time the eye began to curve from the first target to the second (beginning of the curve in the saccade, Fig. 3*B*). The time at which *neuron 2* reached its peak, and presumably already had its maximal effect in directing the saccade to *target 2*, was correlated with the saccade going toward *target 2* (end of the curvature, Fig. 3*C*). Third, a weighted vector-average model based on the activity of the two neurons simulated the time of rotation of the vectors from one target to the other (Fig. 4*B*). However, we also found that the activity of the SC neurons alone was insufficient to predict the final direction of the strongly curved saccades. This observation was supported by the failure of the same vector-average model to predict the final direction of the curved saccade and by the failure in our subsequent experiments to find activity in other parts of the SC (or in the opposite SC) that could have contributed to the saccade curvature.

We now discuss the relation of the SC populations of neurons to the type of saccade made, the lack of a close correspondence between this neuronal activity and the final direction of the saccade trajectory, the close relation of the SC activity to the selection of the saccadic goal, and concurrent processing for saccade generation.

Timing across the population of SC neurons

In the presence of multiple targets, multiple sites would be expected to be activated on the SC movement map, presumably one site for each available target. The competition between sites leading up to saccade generation could be resolved by a number of mechanisms. If a winner-take-all mechanism were operating, when the activity at one site became greater than at any other, the neuronal activity at the other sites would decline (possibly attributed to lateral inhibition), and the movement would be made to that one target. If there were a vector-average mechanism, the average or weighted average of the activity at several sites would lead to a saccade to the location represented by the averaged activity. Both mechanisms have been found to operate in primate neuronal populations. For example, in neurons related to visual motion processing in the primate (Ferrera and Lisberger 1997; Groh et al. 1997; Recanzone and Wurtz 1999), the mechanism that prevails depends on stimulus conditions, including the temporal and the spatial positioning of the stimuli. Both mechanisms probably operate in the SC during saccade generation, again depending on the conditions under which the saccades were made.

In our two target experiments, when the stimuli were presented with relatively large temporal intervals, a relatively straight saccade was made to one target or the other, and the SC activity was largely related only to the target selected. This winner-take-all condition is not surprising given both the temporal and the spatial separation of the targets (and the consequent separation of the related activity on the SC map), and given that the activity recorded is just before the saccade (long after the activity related to the two targets).

When we shortened the temporal interval between our target presentations (while maintaining the spatial positioning), we think the rare curved saccades on some trials can best be regarded as resulting from a vector-averaging mechanism. If the curved saccades went directly to one target and then were redirected and to the next, the curved saccades could be regarded as two successive winner-take-all decisions that occurred late in the saccade: the first neuron was the initial winner, and then the second neuron became the winner. However, we did not see such saccades pointing to one target and then to the next. Instead we saw saccades whose initial direction was in the direction of an averaging saccade between the two targets (*black* and *cyan traces* in Fig. 1*E*). Even saccades that were largely directed toward one target (*purple trace*, Fig. 1*E*) showed a turn toward the location of the second saccade but did not come close to it. Because even the initial trajectory reflects the presence of the two targets and the level of the activity of two neuronal populations, the most parsimonious description is one of averaging between the two populations. The average, however, is shifting during the course of the saccade: instead of this competition being resolved before the

onset of the saccade, which would produce a straight averaging saccade, it is resolved after the saccade onset. The continuing shift in the average is then visible as a change of direction in the midst of the saccade. If these two neurons are representative of two populations of neurons, the first direction of the saccade is predicted by the population whose activity peaks first *with respect to* the activity of the second population. Therefore as the multiple neuron recording technique demonstrates, it is not only the relative magnitude of the activity in the competing populations of neurons that is critical in determining which population controls the goal of the saccade, but the *relative timing* of the activity in the two populations as well. Of course, by closely spacing the stimuli temporally while spacing them widely spatially, we maximized the temporal interactions of the populations of SC neurons.

That there were interactions between the two SC neuronal populations was not surprising because previous experiments had shown neuronal activity at one site on the SC map varies depending on the presence of other target stimuli (Basso and Wurtz 1997, 1998; Dorris and Munoz 1998; Glimcher and Sparks 1992; Munoz and Wurtz 1995). The averaging occurring during the curved saccades, which must indicate two sites of simultaneous activity, probably also indicates that the lateral inhibition between different active sites is not as complete as might have been expected. Previous physiological experiments in the SC have shown that activity at one site alters activity at other sites by excitation (McIlwain 1982; Pettit et al. 1999) and inhibition (Meredith and Ramoa 1998; Munoz and Istvan 1998), with inhibition likely to predominate at the distances employed in the present experiments (Munoz and Istvan 1998). Certainly if the inhibition is as strong as implied by the physiology, the curved saccades indicative of activity at two SC sites simultaneously would seem improbable. However, recent evidence indicates that because the inhibition in the physiological experiments was demonstrated by electrical stimulation, some of its effect could have resulted from the activation of inhibitory fibers from the substantia nigra pars reticulata rather than from local inhibitory interneurons (Hall et al. 2001). We suggest that the curved saccades in our experiments provide additional evidence that inhibitory interactions between adjacent populations of SC saccade related neurons may not be as powerful as previously assumed.

A vector-averaging mechanism was clearly demonstrated on those saccades that went to a point between the two targets. Thus under the conditions of our experiments, the averaging saccades could have resulted simply from the vector average of the two populations of SC neurons without requiring any activity of the neurons specifically representing the vector of the actual averaging saccade. This interpretation is consistent with the conclusion reached by Edelman and Keller (1998) with single neuron recordings during express saccades. They found that averaging saccades did not activate an SC neuron nearly as much as did a single saccade made to the same point as the averaging saccade. They further found that the movement field of neurons often expanded dramatically during averaging saccade between two targets. Thus both the experiments of Keller and Edelman and ours are consistent with the hypothesis that single saccades and averaging saccades with similar metrics are generated by different activity within the SC, as had been suggested previously by van Opstal and van Gisbergen (1990). Glimcher and Sparks (1993), however, found that the movement field of SC neurons did *not* change in size when averaging saccades were made between two targets. Unfortunately, in our experiment in which we observed averaging saccades, we did not quantify the movement field of the neuron and thus cannot quantitatively address this discrepancy in the literature.

Curved saccades and the SC control of saccadic trajectory

The simplest explanation of the saccadic trajectory of a strongly curved saccade would be that it results from an averaging of the vectors represented by the SC populations of neurons activated by the two targets. However, simply looking at one of these strongly curved saccades (e.g., *black solid curve* in Fig. 4*A*) it seems unlikely that the vector needed to determine the endpoint of the saccade is represented in the two populations of neurons. The weighted vector-average model confirmed this, given that it was unable to predict the final direction of the observed saccade either in this neuron pair (*black dotted curve* in Fig. 4*A*) or across the sample of pairs (Fig. 4*C*).

Given this, we explored the possibility that other populations of SC neurons contributed the vector necessary to produce the observed curvature, or what we might refer to as the "missing vector." On the one hand, it seemed unlikely that other regions of the SC would be active because there were only two targets present in the visual field, each of which fell on the visual and movement fields of the two neurons studied. On the other hand, the strongly curved saccades are unusual, and this raised the possibility that they might be accompanied by unusual activity in other regions of the SC map. We sampled from areas we felt were optimal candidates for providing the missing vector (Figs. 5 and 6), but we did not find activity sufficient to account for the curvature. Although from our limited experiments we cannot exclude the possibility that SC activity at different sites could account for the final direction of the saccade, the evidence we do have indicates that it is not determined by SC activity alone. This conjecture is consistent with other observations showing that SC activity alone does not predict the actual saccade, including studies of the upward bias in memory-guided saccades (Stanford and Sparks 1994), the metrics of catch-up saccades during smooth pursuit (Keller et al. 1996), perturbed saccades during blinks (Goossens and Opstal 2000), and the change in saccade amplitude with adaptation (Frens and Van Opstal 1997; Melis and van Gisbergen 1996).

Our results on the final phase of the trajectory are therefore consistent with a shift in thinking about the SC in which, rather than the SC controlling the trajectory and metrics of a saccade (e.g., Wurtz 1996; Wurtz and Optican 1994), the SC does so in conjunction with other oculomotor areas (as for example, Quaia et al. 1999), including structures parallel to SC (e.g., the cerebellum and FEF) and structures downstream from these three. Assuming this is true, the weighted vector-average model we used probably is appropriate for modeling interactions of SC activity related to selection of the goal of a saccade but inappropriate for predicting the trajectory of the saccade because it does not take into account the contribution of downstream and parallel structures and the probability of oculomotor feedback to the SC (Soetedjo et al. 2002; Waitzman et al. 1991).

Assuming that the SC does not alone control the trajectory of

a saccadic movement, it is interesting to relate this to what is known about the control of movement in another area of the brain: the primary motor cortex (area 4). The activity of neurons in primary motor cortex is adequate to predict the instantaneous speed and direction of the arm during curved drawing arm movements (Moran and Schwartz 1999; Schwartz and Moran 1999, 2000), and their activity therefore can predict the trajectory of a curved arm movement. Thus there appears to be a striking difference between SC and area 4. Activity of the saccade-related SC neurons may not predict the movement metrics, even though it is frequently regarded as a brain stem region for saccade execution, whereas neurons in area 4 may predict the details of the reaching movement (and have monosynaptic connections to spinal motor neurons) even though cerebral cortex is frequently believed to be responsible for higher more abstract levels of processing.

Curved saccades and the selection of the saccadic goal

Taken together, our findings regarding the neuronal activity underlying strongly curved saccades provide additional insight into where SC neurons lie in the sequence of processing between target selection and movement execution. If it is correct that these saccade related neurons lie above the level at which the metrics of the saccade are specified, then the curvature is not just an issue of movement execution. Instead, the shift in the direction of the saccade first more toward one target and then curving toward the other reflects a change in the selection of one saccadic goal and then another, where the term goal selection includes target selection through preparation to move. The key evidence for a shift in saccadic goal is the relatively close relation of the timing of the change in direction (the curvature) to the change in activity of the saccade related neurons. If the curve reflects the change in saccadic goal selection and these neurons contribute to that change, the two should be correlated, as we have shown.

By the logic of this interpretation, the curved saccades indicate either a lack of decision at the beginning of the movement followed by a decision of the selected target or two successive decisions. The curved saccades occur rarely probably because such a late change in goal selection occurs only rarely. Consistent with this interpretation is our observation that the frequencies of the curved saccades increased as the frequency of correct trials decreased, that is, the curved saccades were more frequent in situations where the task of deciding between the targets was more difficult. Also consistent with this interpretation are the significantly longer latencies of the curved saccades (about 10 ms), indicating a later decision for goal selection. In the vast majority of the trials in our experiments that did not produce curved saccades, the latencies were shorter and the saccade was made directly to one target or the other. In most cases then, target selection is made early and nothing about the process is revealed other than the goal eventually selected. In other studies using multiple targets, a change in goal was sometimes made, but it occurred after the first saccade was nearly completed. Such a "redirected saccade" has been demonstrated in a visual search task by McPeek and Keller (2000, 2002). In net, our interpretation is that the saccade made reflects the time of the goal selection: early decision results in a single saccade to one target; delayed decision results in a curved saccade; and a late decision results in a second or redirected saccade. An advantage of trials with curved saccades is that in their very shape they appear to be providing a visual representation of a change in decision.

Although the possibility that the type of saccade made is related to the time of target selection is speculative, the fact that SC activity reflects decisions related to target selection is not. The early activity of SC neurons, referred to as buildup activity (Wurtz and Munoz 1994) or prelude activity (Glimcher and Sparks 1992), appears to be closely related to selection between two targets because activity at SC sites representing these targets increases as the selection of one or the other is being made (Dorris and Munoz 1995; Munoz and Wurtz 1995). Selection of one target is accompanied by development of a burst of activity in the related population of neurons and a decline in the population related to the other target. Neurons with early activity are also likely to be those that show activity related to direction of motion in a motion-discrimination task (Horwitz and Newsome 1999), which is also consistent with early target selection. In our experiments, we saw no difference in the activity of the buildup and burst neurons in relation to the curved saccades, but it should be emphasized that the changes we examined here are in the final burst before the saccade, not in the earlier prelude or buildup activity.

At a behavioral level, changes in saccade trajectory related to target selection have been seen repeatedly. The trajectory of saccades in humans (Sheliga et al. 1995) was skewed by attentional biases, and electrical stimulation in monkeys during attention and decision tasks led to endpoint shifts (Gold and Shadlen 2000; Kustov and Robinson 1996). Changes in saccades and the visual fixations between saccades revealed strategies used during visual search (Hooge and Erkelens 1998; McPeek et al. 2000; Zelinsky 1996) and during tasks requiring sequential movement of objects (Hayhoe et al. 1997). Saccades of monkeys during visual search showed a curvature on incorrect trials in the direction of the subsequent correct trials (McPeek and Keller 2001). Furthermore, strongly curved saccades were observed primarily in difficult decision tasks such as visual search tasks and our two-target task. In our study, the frequency of strongly curved saccades increased as the task became more difficult, as indicated by the decrease in the number of correct trials.

Curved saccades and concurrent processing

A possibility that we have not yet discussed is that the saccade-related activity during curved saccades is related to the programming of two saccades to the two potential saccade targets, that is, the concurrent generation of two saccades. Experiments by Becker and Jurgens (1979) elicited two saccades with very short intersaccadic intervals by flashing an initial target and then flashing a second target in a new location before the onset of any saccadic movement. Because the onset of the second saccade was fixed to the time of the second target flash rather than to the time of the first saccade, they argued that the two saccades were being processed concurrently.

When we look at the underlying neuronal activity related to saccade generation rather than just the observed saccades, we must define more clearly, not only whether there is concurrent processing, but the nature of that processing. We suggest that the issue is appropriately regarded as one of determining whether there is concurrent processing for one saccade that is

in some way perturbed (as in curved or redirected saccades) or whether there is concurrent processing for two successive saccades. These alternatives make quite different predictions about the sites on the SC map that should be active before a curved saccade, and Fig. 8 illustrates these alternatives. If there were just one saccade that curved between the two targets, the sites on the SC map active before the saccade should be those for the two vectors from the fixation point to *target A* and from the fixation point to *target B* (Fig. 8*A*). If the curved saccades were two successive saccades chained together, then the activity for the vector to *target B* would be different because it is a new saccade made after the first saccade, and its vector would be more downward from *target B*. However, because this second saccade is being programmed concurrently with the first saccade, the appropriate SC site of activity would be the downward vector from the fixation point (downward vector in Fig. 8*B*).

In our experiments, about a third of our sample of 22 groups of curved saccades did show two peaks in their velocity profile, but this would be consistent with either a single curved saccade or a change from the first to the second saccade if there were two sequential saccades. In all of our recordings from the two sites, whether the curved saccades had inflections, there was activity at both of the SC sites representing the vectors to the two saccade targets (Fig. 7). Furthermore in a small sample of neurons, we tested whether there was activity at the site of the vector to be made after the first saccade as in Fig. 8*B*, and we found no such activity. Both observations are consistent with the view that the programming is for a single saccade, although a curved saccade with multiple phases (Fig. 8*A*).

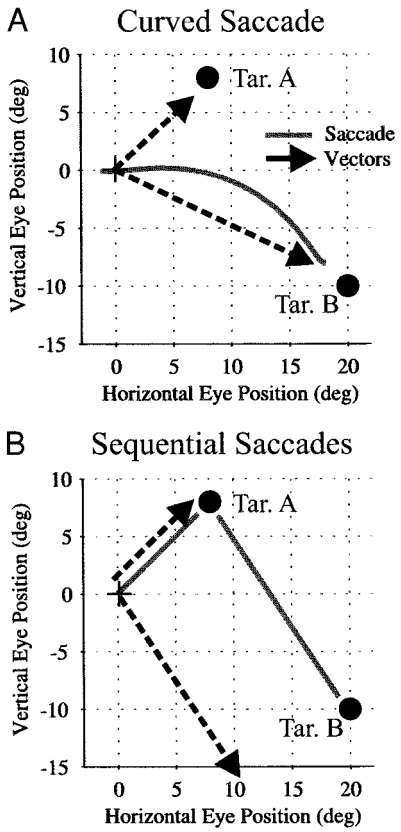

FIG. 8. Types of concurrent processing. *A*: concurrent processing related to two goals of curved saccade. Vectors represented in SC for saccades to *target A* and *target B* are indicated by gray arrows. *B*: concurrent processing of two sequential saccades. Vector for saccade to *target A* is as in *A*. Vector of saccade from *target A* to *target B* is placed at fixation point because processing for this saccade should start before saccade to first target is made to be regarded as concurrent.

We think that similar observations have been made for curved saccades in two related experiments. McPeek and Keller (2002) recorded from one point on the SC map using a visual search task with multiple targets that allowed them to also address the issue of concurrent saccade processing. They found that the monkey sometimes made saccades toward one of the search targets and then veered toward the other target, and in these cases there was activity at the SC site representing the second vector before the first saccade was made but not after the first saccade was made. This is consistent with the active sites in the SC representing the vectors needed for the upcoming saccades as one saccade (Fig. 8*A*) rather than two sequential saccades (Fig. 8*B*). A second related observation was made previously by Goossens and Van Opstal (2000), who looked at SC activity during a saccade perturbed by a blink. The perturbation produced a curved saccade but one that ended near the target, and after a pause in activity, the SC neuron continued to discharge so that the total number of spikes was nearly the same as if the saccade had been directly to the target. The relevant point is that the activity resumed after pause at the site related to the original target, which is again consistent with the programming of one saccade.

We conclude that the curved saccades that we see in our experiments represent the perturbations of single saccades rather than the chaining together of two successive saccades. The term *concurrent processing* was originally formulated to indicate that two successive saccades could be simultaneously programmed, and although this undoubtedly occurs under the appropriate experimental conditions, it was not the case in our experiments. Nonetheless, the curved saccades that we studied did incorporate activity related to two targets on the SC map and the resulting saccade did incorporate movement directed toward both targets. In this sense we are looking at concurrent processing of saccades, but concurrent processing related to two goals of one saccade not two saccades. This is in contrast to the concurrent processing for sequential saccades described by Becker and Jurgens (1979), which we would expect to have a different configuration of activity on the SC map.

To summarize, the curved saccades that we have studied are limited in number but have produced consistent results, and offer insights not available when the saccade travels simply from one target to another. Both the neuronal activity and the vector-average model predict the *timing* of the saccade curvature, but neither predicts the end *trajectory*. We think that close coupling of the SC activity to the timing of the saccade curvature is consistent with the idea that these neurons are closely linked to the selection of the saccadic goal. In contrast, the failure to predict the trajectory is consistent with the view that the SC contributes to, but does not determine, the metrics of the saccade. Both goal selection and saccade generation are of course not the result of SC activity alone but probably are the result of activity in a widespread circuit that includes cortex, basal ganglia, thalamus, midbrain, pons, and cerebellum. In light of this then, another way of expressing our conclusion is that the SC is near the end of the sequence of areas related to the selection of the saccadic goal as indicated

by the good predictions of the goal chosen by the SC activity. On the other hand, the SC is near the beginning of the sequence of activity in the brain stem and cerebellum that controls the trajectory of the saccade, as indicated by the less than complete ability of SC activity to predict the saccade metrics.

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