Evidence Against a Moving Hill in the Superior Colliculus During Saccadic Eye Movements in the Monkey

ROBIJANTO SOETEDJO,1 CHRIS R. S. KANEKO,2,3 AND ALBERT F. FUCHS2,3

Departments of 1Bioengineering and Physiology and 2Biophysics and 3Regional Primate Research Center, University of Washington, Seattle, Washington 98195

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Soetedo, Robijanto, Chris R. S. Kaneko, and Albert F. Fuchs. Evidence against a moving hill in the superior colliculus during saccadic eye movements in the monkey. J Neurophysiol 87: 2778–2789, 2002; 10.1152/jn.00974.2001. Saccadic eye movements of different sizes and directions are represented in an orderly topographic map across the intermediate and deep layers of the superior colliculus (SC), where large saccades are encoded caudally and small saccades rostrally. Based on experiments in the cat, it has been suggested that saccades are initiated by a hill of activity at the caudal site appropriate for a particular saccade. As the saccade evolves and the remaining distance to the target, the motor error, decreases, the hill moves rostrally across successive SC sites responsible for saccades of increasingly smaller amplitudes. When the hill reaches the “fixation zone” in the rostral SC, the saccade is terminated. A moving hill of activity has also been posited for the monkey, in which it is supposed to be transported via so-called build-up neurons (BUNs), which have a prelude of activity that culminates in a burst for saccades. However, several studies using a variety of approaches have yet to provide conclusive evidence for or against a moving hill. The moving hill scenario predicts that during a large saccade the burst of a BUN in the rostral SC will be delayed until the motor error remaining in the evolving saccade is equal to the saccadic amplitude for which that BUN discharges best, i.e., its optimal amplitude. Therefore a plot of the burst lead preceding the “optimal” motor error against the time of occurrence of the optimal motor error should have a slope of zero. A slope of −1 indicates no moving hill. For our 20 BUNs, we used three measures of burst timing: the leads to the onset, peak, and center of the burst. The average slopes of these relations were −1.09, −0.79, and −0.58, respectively. For individual BUNs, the slopes of all three relations always differed significantly from zero. Although the peak and center leads fall between −1 and 0, a hill of activity moving rostrally at a rate indicated by either of these slopes would arrive at the fixation zone much too late to terminate the saccade at the appropriate time. Calculating our same three timing measures from averaged data leads us to the same conclusion. Thus our data do not support the moving hill model. However, we argue in the DISCUSSION that the constant lead of the burst onset relative to saccade onset (~27 ms) suggests that the BUNs may help to trigger the saccade.

INTRODUCTION

Saccades serve to shift the direction of gaze rapidly from one interesting target to another. An intense burst of action potentials is required to innervate the extraocular muscles to bring the eyes to the target quickly. This burst of action potentials is generated in the burst neurons of the pontine, medullary, and mesencephalic reticular formations, which are part of a saccadic burst generator (for review, see Fuchs et al. 1985).

Not only are saccades fast, they are also accurate. To produce an accurate saccade, the burst neurons (BNs) must emit specific numbers of action potentials proportional to the desired saccade amplitude (Scudder et al. 1988; Strassman et al. 1986). To describe how this is accomplished, several investigators have proposed local feedback models of the saccadic burst generator (e.g., Jürgens et al. 1981; Robinson 1975; Scudder 1988). In all of them, the burst generator is driven by a dynamic motor error signal, which is the difference between the desired target (and hence gaze) displacement and an estimate of current eye displacement (E∗) (Fig. 1A). At the onset of a saccade, the dynamic motor error is equal to the desired gaze displacement and gradually decreases to zero as the saccade moves closer to its goal.

The desired gaze displacement signal originates in the intermediate and deep layers of the superior colliculus (SC), which project both mono- (Chimoto et al. 1996) and disynaptically (Keller et al. 2000; Raybourn and Keller 1977) to BNs. A neuron in the intermediate and deep layers of the SC discharges most vigorously and with the longest lead for saccades of a particular amplitude and direction (its optimal vector). As the vector deviates from optimal, the discharge decreases in both intensity and lead time until saccades with nonoptimal vectors are accompanied by no discharge at all. The range of response vectors associated with a burst constitutes a neuron’s movement field. Neurons across the SC are organized topographically according to their optimal saccade vector: caudal neurons discharge best for larger saccades, rostral neurons for smaller saccades. Consequently, before a 50° saccade, for example, the population of neurons at the 50° vector site are the most active. Nearby neurons with slightly different optimal vectors also are active but at lower rates so that the entire active population can be pictured as a hill with its peak at the 50° vector site (Fig. 1A). The desired gaze displacement is extracted by population averaging of the discharge of all active neurons (Lee et al. 1988). Thus the desired gaze displacement signal is represented as the spatial location of the active SC site. Because burst neurons in the local feedback circuit encode saccade amplitude in the number of action potentials in their
burst, the desired gaze displacement signal from the SC must be transformed to a temporal discharge pattern (e.g., Moschovakis et al. 1998). Once the 50° saccade starts, the feedback circuit calculates the dynamic motor error, which continues to decrease to zero as the saccade progresses.

Initially, the feedback circuit was proposed to lie solely in the brain stem (Robinson 1975). More recently, it has been suggested that the SC itself may be part of the feedback loop (Guitton et al. 1990; Keller 1981; Waitzman et al. 1988). Waitzman et al. (1988, 1991) suggested that the declining phase of the burst of saccade-related neurons in the SC is related to dynamic motor error. However, several other studies have shown that the firing rate profile of the burst is poorly related to the dynamic motor error (Frens and van Opstal 1998; Goossens and van Opstal 2000; Keller and Edelman 1994; Soetedjo et al. 2002). Furthermore, our earlier study, in which saccades were slowed by injection of muscimol in the region of the omnidirectional pause neurons (OPNs), involved in a different type of feedback scheme to maintain the burst of SC saccade-related neurons until the end of the saccade (Soetedjo et al. 2002).

Guitton et al. (1990) proposed that the dynamic motor error may actually be coded in the spatial pattern of population activity in the SC. Because the SC systematically represents saccade amplitude along its rostrocaudal axis, a saccade would be accompanied by a sequential rostralward shift of active neuronal populations starting from the caudal population (Fig. 1B, gray arrow in the SC). From this moving hill of activity, a signal proportional to dynamic motor error could be extracted. Consequently, if a neuron that discharges best for a small saccade, say 10° (Fig. 1C, heavy trace), is recorded while the subject makes a 50° saccade (Fig. 1C, gray trace), the discharge of this neuron would be delayed to occur at the time that the motor error reached 10° as the activity initiated at the caudal 50° site was passing through. In this scenario, the lead of the burst to a 10° motor error, which occurs at both the onset of a 10° saccade (heavy trace) and the time when a 50° saccade trajectory (gray trace) reaches 40° in amplitude (vertical line), would be equal. Thus the plot of the lead of the burst to a unit’s optimal motor error (10° in this example) as a function of the latency of optimal motor error to saccade onset ($L_{\text{me}}$) would yield a relation with a slope of zero (Fig. 1C, inset).

The hypothesis of a moving hill in the SC was first proposed after experiments with cats showed that a class of saccade-related burst neurons, the tecto-reticulo and tecto-reticulo-spinal neurons, indeed seemed to time their burst in relation to motor error (Munoz et al. 1991). In addition, a population of fixation neurons, which ceased their tonic discharge for saccades in all directions, was discovered in the rostral SC. Several lines of evidence suggested that they were active at the end of the saccade (Munoz and Guitton 1991; Munoz and Wurtz 1993). Therefore when the moving hill reached and activated the rostral fixation neurons, the saccade stopped.

A similar rostral movement of activity has been suggested for homologous neurons in the monkey that exhibit a prelude of increasing activity (a build-up) before discharging a burst of spikes for saccades (Munoz and Wurtz 1995a). The timing evidence in favor of a rostrally moving hill, however, is less clear in the monkey than in the cat SC, and four different experiments have provided conflicting evidence for its existence. First, Munoz and Wurtz (1995b) suggested that the activity in the SC spreads rostrally instead of moving rostrally. They based their conclusion on the observation that the center of gravity of active build-up neurons (BUNs) had moved rostrally at the end of a saccade. However, they normalized the level of activity of each BUN and included the fixation neurons of the rostral SC. Both these strategies cause activity at rostral sites to be artificially high, giving the appearance that activity has spread to the rostral sites at the end of the saccade (see discussion). Second, Aizawa and Wurtz (1998) claimed to support the rostral spread by showing that pharmacological inactivation of a specific site in the SC caused saccadic trajectories to curve. They opined that the curvature was the result of a diversion of the rostral spread of activity around the inactivated site. However, data from only a single injection, which

![Conceptual diagrams of a saccade generator with feedback](http://jn.physiology.org/)

**FIG. 1.** Conceptual diagrams of a saccade generator with feedback within the brain stem (A) or routed through the superior colliculus (SC) (B). See text for descriptions. $E^*$, an internal estimate of current eye amplitude. C: hypothesized shift in burst firing associated with the moving hill hypothesis. $A_1$ and $A_2$ indicate the latencies of a 10° optimal motor error ($L_{\text{me}}$) for a 50° (gray trace) and a 10° (black trace) saccade. $B_1$ and $B_2$ indicate the lead of a build-up neuron (BUN) burst relative to optimal motor error for the same saccades. If the SC is in the feedback loop, the inset shows the expected relation (slope = 0) of burst lead vs. $L_{\text{me}}$. 

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influenced oblique saccades, were presented to support their claim (see DISCUSSION). Third, a one-dimensional analysis of 42 BUNs by Anderson et al. (1998) did not show a systematic rostral spread of activity. However, these negative results also might be suspect because the investigators used saccade amplitudes of $\pm 20^\circ$, which might not have allowed enough intrasaccadic time resolution to detect a spread (see DISCUSSION).

Fourth, Port et al. (2000) recorded from a pair of rostral and caudal SC neurons simultaneously and found that during large saccades the activity of the rostral neuron was slightly delayed compared with that of the caudal neuron. However, they did not indicate whether the optimal directions of both neurons were aligned. This is an important consideration because the bursts associated with saccades that are not optimal for an SC neuron are delayed relative to those that are (see DISCUSSION).

With their various limitations, we believe that these four experiments have not resolved whether there is a moving hill of activity across the monkey SC. We tried to address this issue directly by recording from a population of BUNs that had $6-15^\circ$ optimal amplitudes and therefore lay in the putative path of neural activity moving forward from the caudal sites of initiation of much larger saccades. If sequential activation on the topographic map of the SC is related to the remaining motor error, one would expect to observe systematic shifts in the timing of BUN discharges as saccade amplitude increases (Fig. 1C). Part of this report has been published in abstract form (Soetedjo et al. 1998).

**METHODS**

**Animal preparation**

Two juvenile rhesus macaques (Macaca mulatta; monkeys A and B) underwent aseptic surgeries to implant three acrylic head stabilization lugs, a stainless steel chamber for introducing the recording electrode, and a search coil on the left eye for measuring eye movement with an electromagnetic technique (Soetedjo et al. 2002). In monkey A, the SC was accessed through a chamber that was tilted backwards by $38^\circ$ and aimed at a point 15 mm dorsal and 1 mm posterior to stereotaxic zero. In monkey B, the chamber was tilted to the left by $15^\circ$ and aimed at a point 2 mm dorsal and 1 mm posterior to stereotaxic zero. The chamber was secured to the skull with stainless steel screws and dental acrylic. The animals were given 7 days to recover from the surgery.

**Behavioral training**

We used two behavioral paradigms. First, to elicit visually guided saccades, we trained the monkeys to follow with their eyes a red laser spot that jumped on a tangent screen in the dark. The tangent screen was 68 cm from the monkey. The monkeys were required to make a targeting saccade within 500 ms of the target jump and to land within a reward window. Normally the window was set at $\pm 2^\circ$, but for large saccades, it was increased to $\pm 5^\circ$. When the monkey’s saccades satisfied both the time and detection-window criteria and the eyes stayed on target for $\approx 700$ ms, the monkey was rewarded with a drop of fortified apple sauce. Second, to elicit memory-guided saccades, we trained the monkeys to fixate a central red dot. During fixation, a white peripheral target was flashed for 500 ms and after an additional 1.5 s of fixation, the fixation spot went out as a signal for the monkey to make a saccade to the memorized location of the white peripheral target. If the monkey’s saccade reached a point within the detection windows within 500 ms after the fixation spot was extinguished and

![Image](http://jn.physiology.org/)

**FIG. 2.** Peak firing rate as a function of saccade direction (A) and amplitude (B) for an exemplar BUN (BU82.1). A: fit curve: [peak firing rate] = $a + b\times\sin(c\times|\text{saccade direction}|) + d$. $\uparrow$, peak of the fit; $\downarrow$, estimated optimal target direction determined during the experiment. B: $\bullet$, the 5 optimal amplitude saccades (see text).

if the eyes stayed on target for $\approx 400$ ms, the monkey received the apple sauce reward.

The behavioral paradigm was controlled by a Macintosh computer (Apple) equipped with analog interface boards (National Instruments). The red and white spots were generated by a laser tube and a slide projector, respectively, whose beams were deflected by mirror galvanometers and then back-projected onto the screen. The diameters of the red and white spots subtended 0.4 and 0.6$^\circ$, respectively.

All surgical and experimental protocols were conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and in compliance with the recommendations from the Institute of Laboratory Animal Resources and the Association for Assessment and Accreditation of Laboratory Animal Care International.

**Unit recording and data analysis**

Extracellular action potentials were recorded with tungsten microelectrodes. A hydraulic drive advanced the electrode into the brain through the chamber via a 22-gauge hypodermic needle, which served as a guide tube. The action potentials of single neurons were amplified, filtered (300–10 kHz), displayed on an oscilloscope, and played over an audio monitor. Both eye- and target-position signals were captured (300 kHz), displayed on an oscilloscope, and played over an audio monitor. Both eye- and target-position signals were low-pass filtered at 500 Hz. All analog signals and the associated unit action potentials were recorded on a PCM video tape recorder (Vetter 4000A) for off-line digitizing.

Horizontal and vertical eye and target position signals were digitized off-line at 1 kHz. Action potentials were represented as time stamps with a temporal resolution of 10 $\mu$s. After the data were digitized, they were analyzed with an interactive program that marked the onset and end of saccades (10$^\circ$/s velocity criterion) and the associated spikes automatically. If necessary, these markings were adjusted by the first author. The program also calculated the peak firing rate of the neuron as the average rate of the shortest five consecutive spikes in the burst.
Further data analyses, i.e., calculation of the vector of a saccade’s trajectory, generation of the spike density function, timing measurements, spline fits, and linear regressions, were done in Matlab (Mathworks). We used 1 SD to describe the variability of a mean. The two-tailed Student’s t-test was used to quantify the significance of means and regression slopes. The significance level was 0.05 unless otherwise stated in the text.

DETERMINATION OF OPTIMAL DIRECTION AND AMPLITUDE. The superficial layers of the SC were identified by the presence of neurons with a visual response and the deeper layers by the presence of neurons that discharged a burst of spikes in relation to saccades. Once we isolated any saccade-related neuron, we established its optimal vector by requiring the monkey to make saccades of at least five different amplitudes and five directions around the apparent center of the movement field as assessed by responses heard on the audio monitor. We also tested each neuron for saccades larger than the optimal vector by presenting target jumps of 40–60° in the neuron’s preferred direction. At least four different large target jumps were used.

The accurate determination of optimal direction is crucial to our analysis because a shift in burst timing that might be considered to be diagnostic of a moving hill also occurs if saccades are not made along an SC neuron’s optimal direction (Freedman and Sparks 1997). To confirm that the estimated optimal direction used during the experiment corresponded to the actual optimal direction of the neuron, after the experiment we fit a half sine wave to the relation between peak burst firing and saccade direction for data obtained when the monkey had made optimal-amplitude saccades in different directions. The peak of the sine wave was the actual optimal direction of the neuron. Figure 2A shows a typical fit. The difference between the peak sine fit (1) and the estimated direction used during the experiment (2) was 2.2°. For all 20 units identified as BUNs (see RESULTS), the saccade direction estimated during each experiment was within 10° of the actual direction determined after the experiment (absolute mean: 4.65 ± 3.24°).

The optimal amplitude for each BUN was determined as the peak of a spline fit of peak firing rate against saccade amplitude in the optimal direction (Fig. 2B). All saccade amplitudes within the optimal amplitude ± 15% (Fig. 2B, ■) were considered to have optimal amplitudes (n = 5–22; Fig. 2B). Vector eye-movement amplitudes were calculated from individual horizontal and vertical eye positions by the Pythagorean theorem.

Testing the shift in burst occurrence with saccade size along the optimal direction

We used two different analyses to measure the timing relation between BUN discharges and the optimal motor error. In the first, we used data from individual saccade trials (Fig. 3), and in the second, we used averaged data from similar-amplitude saccades (Fig. 4) as other studies have done (Munoz and Wurtz 1995b; Munoz et al. 1991).

TIMING OF MOTOR ERROR SHIFT. After determining the optimal amplitude for a BUN, we calculated when the remaining motor error for larger saccades along the BUN’s optimal direction reached that optimal amplitude (recall Fig. 1). The latency of this optimal motor error (Lme) was measured from saccade onset. For example, the BUN
illustrated in Fig. 3 had an optimal amplitude of 9°, which, for a 9° saccade, occurred at saccade onset, i.e., when $L_{me}$ was 0 (Fig. 3A). For the 28 and 50° saccades shown in Fig. 3, B and C, respectively, a 9° motor error (note that all traces are aligned on the time that motor error equals 9°) occurred later as saccade size increased, i.e., $L_{me}$ increased with amplitude.

TIMING OF BURST SHIFT. To measure the timing of the burst, we first converted the discharge associated with each saccade to a continuous spike density function (SDF) by replacing each spike with a Gaussian function ($\sigma = 10$ ms) (Munoz and Wurtz 1995a, b; Richmond et al. 1990). For the BUN shown in Fig. 3, for example, the burst onset and offset were determined when the SDF rose above and fell below, respectively, 50% of the peak SDF (Fig. 3, upward arrows on SDF curves). The search to find the 50% threshold was started from the peak of the burst. Every saccade was checked to ensure that the burst did not include the visual response related to the target jump (asterisks in Fig. 3, A and B); this would have distorted the determination of burst onset. When saccadic reaction times were so short that a separate visual response could not be distinguished, those trials were not used (55 of 1,674 trials).

To ensure that the variability in the SDF peak that occurred with large, nonoptimal saccades did not obscure significant timing relations, we used three different measures to document the timing of the burst. These included the time of the peak of each SDF, the time of burst onset, and the time halfway between burst onset and burst offset. Each of these times was measured relative to the time of occurrence of the remaining motor error appropriate for the unit considered (9° for the BUN of Fig. 3) as intervals a–c, respectively. Negative leads indicate that the particular timing measure precedes the optimal motor error and vice versa.

The trend of the three measures of burst lead as a function of $L_{me}$ was documented by linear regression. The moving hill hypothesis requires that the slope of the burst lead versus $L_{me}$ relation be close to 0, thus indicating that the BUN burst always is timed to occur at the appropriate motor error. On the other hand, a slope of –1 would show that the lead determined by that burst measure increases by as much as the latency of the optimal motor error. In other words, the burst does not shift at all as saccade amplitude increases.

In earlier studies, Munoz and colleagues used the peak of the averaged SDFs as the timing marker of the burst (Munoz and Wurtz 1995b; Munoz et al. 1991). Therefore we also performed an analysis that was similar to theirs as illustrated in Fig. 4 for the BUN of Fig. 3. The top panel shows the optimal-amplitude saccades (9°) and the next three panels show saccades that were generated by three different target sizes (28, 42, and 60°). In each panel, the saccades are displayed with their associated neuronal responses (SDF, gray traces) together with the mean saccade trajectory and mean SDF (black traces). In Fig. 4, both motor error latency ($L_{me}$) and the burst lead measures a (time to peak average rate), b, and c are identical to those illustrated in Fig. 3, but here they are determined from the mean saccade trajectory and SDF. Again, the trend of the three measures of burst lead as a function of $L_{me}$ was documented by linear regression. Because both mean saccade trajectory and SDF were calculated from the magnitudes of individual eye positions and SDFs, respectively, the measurements of timings from average saccade trajectory and SDF do not indicate the variability of those four timing measures. In addition, because we used only four data points, an $|r| \geq 0.95$ is required to reach a significance level of 0.05 (Rosner 1995). Therefore the goodness of fit for the linear regression on these averaged data cannot be determined reliably.

For all BUNs, in addition to the optimal saccades (Fig. 4, top), we chose three additional target steps to obtain four different mean SDFs.
One of these target steps elicited the largest saccade that the head-fixed monkey would make on that particular recording day (Fig. 4, bottom). The remaining two saccadic amplitudes were chosen to lie between the optimal and largest saccades so that the time from the onset of the saccade to the time that the saccadic motor error reached the BUN's optimal amplitude was roughly equally spaced for the four saccadic amplitudes. There were at least five saccades in each group, except for neurons AU6.1 and AU70.1, for which we were able to gather only three and four saccades, respectively, in the largest amplitude group.

RESULTS

Identification of buns

We isolated 94 saccade-related neurons (including fixation neurons) from the SC of two monkeys. Of these, 20 were identified off-line as BUNs according to the two criteria of Munoz and Wurtz (1995a). First, the mean SDF firing frequency at 100 ms before optimal saccade onset had to be ≥30 spikes/s during memory-guided saccades. Figure 5 shows a representative BUN with a mean rate of 94 spikes/s at 100 ms before saccade onset (†). The average rate at 100 ms before the saccade for our 20 BUNs was 72.3 ± 37 spikes/s. Second, the BUN had to have an open movement field. To confirm that it did, we plotted the peak firing rate against saccade amplitude for saccades in the optimum direction. The BUN illustrated in Figs. 3 and 4 continued to discharge a burst for saccades as large as 60° (Fig. 6A). To illustrate the relation of peak firing with saccade amplitude in this BUN’s optimal direction, we fit its data with a cubic spline curve. The other 19 BUNs also discharged a burst for the largest saccades (range from 35 to 58°) that the monkey made on the day of the experiment. Data for all 20 BUNs are represented by the spline fits of their peak firing rate versus saccade amplitude relations (Fig. 6B). The average peak firing rates during optimal vector and large-amplitude saccades were 637.2 ± 299.3 and 111.3 ± 83 spikes/s, respectively.

The 20 BUNs had a variety of preferred amplitudes and directions. Preferred amplitudes ranged from 6 to 15° and preferred directions ranged from nearly horizontal to nearly vertical (Fig. 7).

Burst lead and saccade size

As saccade amplitude increases beyond the optimal amplitude for a BUN, the moving hill model predicts that the timing of the burst will be delayed. We tracked the timing of saccadic bursts in each of our 20 BUNs using three measures: the lead of the peak of the SDF, of the center of the burst and of the onset of the burst (recall Fig. 3 and 4, intervals a, c, and b, respectively).

Figure 8 shows an example of the regressions of the three measures of burst timing as a function of $L_{me}$ for our example neuron BU82.1 (raw data in Figs. 3 and 4). Recall that if the burst changed its timing to always occur at the same time relative to optimal motor error, as would be expected of a moving hill, all the data would lie around 0 slope, i.e., at a constant lead (horizontal dashed line). In contrast, if the timing of the burst did not change at all with the timing of the optimal motor error, all the data would lie around the line with a slope of −1 (diagonal dashed line).

These regressions for the analysis using individual SDFs and saccades (analysis of Fig. 3) are shown in Fig. 8, A–C. The lead of the peak of the burst increases with $L_{me}$ with a slope of $-0.45$ ($r = -0.54, P < 0.01$). The leads of the center of the
burst and burst onset show similar trends with slopes of $-0.28$ ($r = -0.52, P < 0.01$) and $-1.05$ ($r = -0.82, P < 0.01$), respectively. Similar regressions are obtained when averaged data like those in Fig. 4 are considered (Fig. 8, D–F). The slopes of the peak, center and onset timing relations are $-0.88$ ($r = -0.99, P = 0.002$), $-0.31$ ($r = -0.57, P = 0.43$), and $-1.10$ ($r = -0.90, P = 0.1$).

For all 20 BUNs, the slopes of all linear regressions of each of the three measures of burst lead with $L_{me}$ using analyses of individual trials as illustrated in Fig. 3 were negative and significantly different from zero ($n = 42–130; P < 0.01$; Fig. 9, A–C). The average slope and correlation coefficient of the peak burst lead regression are $-0.79 \pm 0.32$ (range $-1.43$ to $-0.31$) and $-0.74 \pm 0.18$ (range $-0.98$ to $-0.30$), respectively (Fig. 9, A, D, and G). The average slope and correlation coefficient of the lead of the center of the burst regression are $-0.58 \pm 0.25$ (range $-0.96$ to $-0.22$) and $-0.73 \pm 0.18$ (range $-0.94$ to $-0.32$), respectively (Fig. 9, B, E, and H). The average slope and correlation coefficient of the lead of burst onset regression are $-1.09 \pm 0.21$ (range $-1.66$ to $-0.74$) and $-0.86 \pm 0.10$ (range $-0.97$ to $-0.62$), respectively. Fifteen neurons have regression slopes of burst onset lead with $L_{me}$ between $-0.8$ and $-1.2$, and the mean slope of all 20 regressions is not significantly different from $-1$ ($P > 0.05$). Therefore the onset of the burst is almost constant for saccades of any amplitude. The average onset of the burst as determined by the average of the regression intercept occurs $27.64 \pm 9.27$ ms before saccade onset.

For all 20 BUNs, we also analyzed the slopes of all the linear regressions of each of the three measures of burst lead with $L_{me}$ obtained using averaged SDFs and saccade trajectories as illustrated in Fig. 4. The regressions of the lead of the peak mean SDF regression (Fig. 10, A, D, and G) have an average slope and correlation coefficient of $-0.93 \pm 0.18$ (range $-1.23$ to $-0.56$) and $-0.97 \pm 0.07$ (range $-0.99$ to $-0.69$), respectively. However, 3 of the 20 slopes are not significantly different from 0. The center of the burst lead regression (Fig. 10, B, E, and H) has an average slope and correlation coefficient of $-0.70 \pm 0.34$ (range $-1.39$ to $-0.23$) and $-0.94 \pm 0.10$ (range $-0.99$ to $-0.57$), respectively. However, 8 of the 20 slopes are not significantly different from 0. Finally, the onset of the burst lead regression (Fig. 10, C, F, and I) has an average slope and correlation coefficient of $-1.22 \pm 0.27$ (range $-1.80$ to $-0.81$) and $-0.98 \pm 0.03$ (range $-0.99$ to $-0.90$), respectively. However, 2 of the 20 slopes are not significantly different from 0.

More than 75% (47/60) but not all of the regressions obtained from the mean SDF analysis are significantly different from 0, in contrast with those obtained from the individual SDF analysis where all (60/60) are. However, the average slopes of the three lead measures from both analyses show similar trends and are very significantly different from 0 ($P < 0.0001$).

A recent study of fixation neurons in the cat suggested that the resumption of the discharge of each fixation neuron was related to a specific motor error (Bergeron and Guitton 2000). Because fixation neurons have been shown to inhibit the BUNs (Munoz and Istvan 1998), we tested whether the offset of the burst of our BUNs was time-locked with the BUN’s optimal motor error as saccade amplitude increased. If the offset of the
burst is time-locked with the optimal motor error, one would expect to see that burst offset leads optimal motor error by a constant amount so that the regression of burst offset lead with saccade amplitude has a 0 slope. In our plots, a positive lead means that the burst ends after the end of the optimal motor error and vice versa.

For our exemplar BUN (BU82.1), the saccadic burst ended after the time of optimal motor error (positive offset lead) and increasingly later as saccade amplitude grew (Fig. 11A, positive slope). For all 20 BUNs, the offset lead is >0 for all saccades less than ~23° (Fig. 11B). The regressions of 7 of 20 BUNs have positive slopes (range = 0.26 to 0.87) and the regressions of 11 have negative slopes (range = −0.83 to −0.27; Fig. 11, B and C). The absolute correlation coefficient ranges from 0.09 to 0.68. For large saccades, 6 of the 11 neurons whose regression slopes are negative ended their burst...
well before the saccade trajectory reached the optimal motor error (Fig. 11B, *). Only two neurons have slopes that do not differ significantly from 0 (Fig. 11C, ■) and therefore have burst offset times locked to the optimal motor error.

**DISCUSSION**

**Our timing evidence against the moving hill in the monkey**

We tested whether BUNs in the SC of the monkey supported the moving hill hypothesis, which posits that during a saccade, the population of active neurons in the SC moves or spreads rostrally and produces dynamic motor error. This hypothesis requires that the bursts of BUNs at rostral SC sites (our units had optimal amplitudes between 6 and 15°) should have a predictable delay as the hill of activity, initiated at a more caudal site to generate a large saccade, passes through. In particular, the burst lead to the BUN’s optimal motor error should be constant (recall Fig. 1C).

In our 20 BUNs identified by the criteria of Munoz and Wurtz (1995a), none of the three measures of burst timing consistently showed a constant lead to the time of occurrence of optimal motor error. For the three burst timing measures evaluated by two different regression analyses, the average slopes of the relations of burst timing to the time of optimal motor error were −0.79 and −0.93 for the peak of the SDF, −0.58 and −0.70 for the center of the burst, and −1.09 and −1.22 for the onset of the burst (Figs. 9 and 10). All of the slopes of the regressions from individual trials, and 78% of those from averaged trials are significantly different from 0. The offset of the burst also did not show a constant relation with the time of optimal motor error. Therefore all four measures do not support the moving hill hypothesis, which requires slopes of 0 in all these relations.

We conclude that our data are inconsistent with the existence of a moving hill or a rostral spread that produces dynamic motor error. This conclusion is based on several reasonable assumptions. First, that the timing of the burst in our 20 BUNs is representative of the whole population of BUNs with intermediate optimal vectors. Second, that the moving hill must reach the fixation zone in the rostral SC at the end of the saccade to terminate it. For the hill to reach the rostral SC at the appropriate time, it must pass each of the intervening neurons when the motor error is appropriate for that BUN’s optimal saccade amplitude. A consequence of this assumption is that the lead of the burst in BUNs to the motor error should be constant. However, our data show that the slope of this relation is much less than 0. For example, the onset of the burst has a slope of roughly −1 as a function of optimal motor error time. During a 58° saccade, a 9° motor error is actually reached ~80 ms after saccade onset. However, because the onset of the burst regression has a slope of −1, the 9° site in the SC would start its burst before the 58° saccade starts, not 80 ms after. Similarly, although the peak and center lead regressions do decrease with the time of optimal motor error occurrence, a hill of activity moving rostrally at a rate indicated by either of these slopes would arrive at the fixation zone much too late to terminate the saccade at the appropriate time.

The regression analysis of the onset of BUN bursts suggests that BUNs along the rostrocaudal axis of the SC do not produce saccadic bursts sequentially during a saccade. Instead, they consistently start bursting ~27 ms, on average, before all saccades whether they are large or small. This suggests that a large area of the SC starts bursting almost simultaneously before a saccade. What is the significance of starting the burst of smaller optimal amplitude sites simultaneously during larger saccades? Anatomic and electrophysiological studies have shown that the density of direct projections from the SC to the OPNs is highest from the most rostral sites and decreases gradually for more caudal sites (Büttner-Ennever and Horn 1994; Gandhi and Keller 1997; Parez and Guitton 1994). To start the saccade, the OPNs must be inhibited. Perhaps, during large saccades, simultaneous bursting of more rostral sites and the optimal caudal site is needed to inhibit the OPNs more effectively and trigger the saccade. Indeed, pharmacological inactivation of small optimal amplitude sites increases not only the latency of small saccades but that of large saccades as well (Hikosaka and Wurtz 1985).

To be able to participate in the moving hill or rostral spread, the BUNs must still be active until the saccade trajectory reaches the optimal motor error. However, the regressions of the lead of burst offset to optimal motor error versus saccade amplitude (Fig. 11) show that six of 20 BUNs ended their saccadic burst before reaching the appropriate motor error (Fig. 11B, *). Thus these six BUNs cannot participate in producing the dynamic motor error.

In addition to the inappropriate timing of their bursts, BUNs seem to be unlikely candidates to provide a consistent dynamic motor error signal to drive the brain stem saccade generator because their firing rates during large saccades are much lower than during optimal-vector saccades (Figs. 3 and 4) (Sparks and Mays 1980). Furthermore, the synaptic strength of rostral SC neurons is weaker (Moschovakis et al. 1998) than that of caudal ones so that the magnitude of the hypothetical spatial motor error signal would decrease as it moved rostrally, further diminishing the output. These two facts suggest that once the putative spatial dynamic motor error signal reaches the rostral
SC, the resultant activity of the rostral BUNs might be too weak to excite brain stem burst neurons.

As with the previous studies, which we will discuss in detail in the following section, our study also has certain caveats. First, we believe that we correctly identified the BUNs because we used the same selection criteria as their discoverers (Munoz and Wurtz 1995a). Second, the interpretation of our timing data requires that the tested saccades be well aligned with the optimal vector of the recorded BUN. We determined that for our 20 neurons the absolute difference in the directions estimated during the data collection and those analyzed later based on the actual data averaged only 4.6° with a range of 0.24–10°. Therefore we believe that our data cannot be explained by misalignment of the optimal and tested saccades. Third, the choice of a timing measure to document the shift in burst lead presents a major problem. As the motor error optimal for a rostral BUN occurs later during larger saccades, the saccadic burst becomes longer in duration and decreases in frequency (Figs. 3 and 4). These two factors often conspire to make it difficult to identify a peak firing rate for large saccades because the SDF is flatter. Consequently, we tried to examine timing measures that captured various aspects of the burst behavior objectively. We chose the peak burst, the onset and offset of the burst, and the center of the burst. We considered the center of gravity of the whole discharge as used by others [e.g., the median activation time analysis by Port et al. (2000)], but we believe this measure is biased in favor of the moving hill. Because a visual discharge is biggest for targets eliciting the optimal saccade, timing measures would be biased forward in time for optimal amplitude saccades but would be little affected for larger saccades where the visual discharge is small if present at all. As an alternative, we decided instead to use the center of the saccadic burst between the burst onset and offset (Figs. 3 and 4, open downward arrows).

These caveats show that an unequivocal demonstration for or against the moving hill is a difficult proposition. As mentioned in the introduction, several studies have addressed this issue with different approaches, and we conclude the discussion by evaluating their results in the context of our data.

Previous studies to test the moving hill hypothesis

Observations on a rostrally moving hill in the cat. Guitton et al. (1990) proposed a feedback model of gaze control that utilized a rostrally moving active population (moving hill) in the SC to produce the motor error. Munoz et al. (1991) showed that the tecto-reticulo and tecto-reticulo-spinal neurons [TR(S)Ns] in the cat SC produced delayed bursts as the amplitude of head-free gaze shifts increased. To support the hypothesis that the moving hill in the SC signals gaze motor error, they showed that the peak of TR(S)N bursts occurred when the gaze motor error reached the optimal vector for those neurons. More recently, however, Kang and Lee (2000) reported that during head-fixed saccades in cats, the time of peak activity of saccade-related neurons in the SC did not occur at the time of the appropriate motor errors.

Observations on a rostrally moving hill in the monkey. Two studies in the monkey support the existence of a phenomenon similar to the moving hill in the cat. In the first, Munoz and Wurtz (1995b) suggested that a rostral spread of activity occurs in the monkey SC but only in the active population of BUNs. To show that the behavior of BUNs is analogous to that of cat TR(S)Ns, they compared the centers of gravity of the population activity along the rostrocaudal axis at the beginning and end of the saccade. Indeed, the center of gravity of their active BUN population calculated at the end of a large saccade did deviate more rostrally than the one calculated at the beginning, but there are two concerns regarding their data. First, in calculating the center of gravity they included BUNs that respond best for small-amplitude saccades in the rostral SC (Munoz and Wurtz 1995a). However, such rostral BUNs not only burst for small contralateral saccades, they also pause during large saccades and then exhibit a rebound in activity before the saccade ends (top 2 neurons in Figs. 1 and 2 of Munoz and Wurtz 1995b). Consequently, the rebound in activity pulls the center of gravity of all active BUNs rostrally at the end of saccades. Second, they exaggerated the contribution of these rostral BUNs by normalizing the neural activity of each neuron.

We are unable to test Munoz and Wurtz’s evidence directly as we did not sample BUNs along the rostrocaudal axis of the SC. However, consideration of our data does not support the rostral movement of the center of gravity of the BUN population activity. First, for the center of gravity to shift rostrally, one would expect that the peak of the saccadic burst would shift toward the end of increasingly larger saccades as the appropriate motor error occurs later and later. On the contrary, our data show that the peak of saccadic burst occurred closer to the beginning of the saccade as saccade amplitude increased (slopes: −0.79 and −0.97 for both types of regression). Second, 11 of our 20 BUNs increased their burst onset lead relative to the optimal motor error as saccade amplitude increased (Fig. 11, negative slopes) and for 6 of those, their saccadic bursts ended well before the saccade trajectory reached the appropriate motor error (Fig. 11B, *). Therefore these neurons contribute nothing to reestablishing the rostral activity at saccade end. Thus our various lead measures are not consistent with a rostral spread of the center of gravity of active BUNs.

In the second study, Aizawa and Wurtz (1998) tested the spatial integrator model of the SC (Optican 1995), which utilizes a moving hill of activity, by pharmacologically inactivating a “small portion” of the SC and asking the monkey to make saccades much larger than the optimal vector of the inactive site. The spatial integrator model predicts that after focal inactivation of a rostral site in the SC, large saccades would be hypermetric because the dynamic motor error stops decreasing when the hill reaches the inactivated site. They observed that large oblique saccades still landed on target, but their trajectories became curved and slower; these data were interpreted as evidence that the rostral spread of activity in the SC controls saccade trajectories. The rostral spread of activity detours around the inactive area, thereby causing the saccade trajectories to become curved. Unfortunately, they showed the trajectories of only a single injection site, which had an oblique optimal direction. Because the firing rate of saccade-related neurons in the SC is related to saccade velocity (Berthoz et al. 1986; Munoz et al. 1991; Rohrer et al. 1987), a possible alternative explanation of their curved saccadic trajectories is that the injection caused an imbalanced innervation of the vertical and horizontal burst generators. In this scenario, one orthogonal component of the saccade might become slower...
than the other, thereby producing curved and slower trajectories. It would be more definitive if they had shown that a curved trajectory also occurred after inactivating a site with a pure horizontal optimal direction.

LIMITED OR ABSENT SPREAD OF ACTIVITY. Port et al. (2000) tested the spread of activity over the monkey SC by recording from a rostral and caudal neuron simultaneously while the monkey made saccades of different sizes. They reported that the average timing difference of the discharges of caudal and rostral neurons was \(-23\) ms. In our data, the peak burst lead falls as a function of motor error latency \(L_{me}\) with a mean slope of \(-0.79\) and a mean intercept of \(-1.45\) ms (Fig. 9A). Because the average largest motor error lead from our 20 BUNs is 88 ms, the peak burst occurs, on average, 71 ms before the saccade trajectory reaches the optimal motor error. Therefore the peak burst is delayed by only \(-17\) ms from saccade onset. If a similar calculation is performed on the delay of the center of the burst, whose regression has mean slope of \(-0.58\) and mean intercept of \(-5.26\) ms (Fig. 9B), the center of the burst is delayed 32 ms from the onset of the saccade. Therefore the average burst lead reported by Port et al. (2000) falls right between our two estimates of burst lead based on peak firing and the center of the burst. However, our data also indicate that the burst of BUNs starts at a relatively constant \(27\) ms before the onset of all saccades that are larger than or equal to the optimal amplitude; consequently, the entire BUN population starts bursting almost simultaneously, instead of sequentially from caudal to rostral. Therefore the slight delay in our data and in those of Port et al. (2000) may actually indicate a slight rostralward movement of the peak activity of the active BUN population rather than a rostral spreading of activity. It should be emphasized that in neither our study nor theirs is the estimated peak delay anywhere near the amount of the delay in optimal motor error. The slight rostralward movement of peak activity during large saccades is too little to keep up with the motor error and therefore cannot be used to terminate the saccade.

Two other labs have studied the population activity of the SC during a saccade. Moschovakis et al. (2001) used functional imaging to measure local glucose utilization in the SC during saccades. They found that SC activity was very localized, rather than “smeared” caudorosally as predicted by the moving hill or rostral spread model. Anderson et al. (1998) used an indirect method to reconstruct the two-dimensional population activity across the SC during a saccade. By combining data from single-unit recordings obtained over different experiment sessions and different animals, they concluded that the activity of the BUN population did not spread rostrally during a saccade.

Has it been impossible to demonstrate a moving hill in the monkey because most studies, unlike those in the cat, have been performed with restrained head gaze shifts? During head-unrestrained gaze shifts, Freedman and Sparks (1997) found that the lead time of the burst was greatest during optimal vector gaze shifts and less for gaze shifts that were larger, smaller, or in nonoptimal directions. However, during the largest gaze shift, the burst lead time decreased by only \(-25\) ms (their Fig. 10B), which, as we argue in the preceding text, is too small to support the moving hill model. Furthermore, they measured the onset of the burst using a fixed 50 spikes/s threshold rather than a threshold that was proportional to the peak firing rate. Because saccade-related burst neurons discharge less vigorously during the largest saccades, the decrease in burst lead time may have been even less than reported by Freedman and Sparks (1997).

Overall, we think our data refute the moving hill hypothesis of saccade control, so it should be abandoned in favor of more fruitful models such as those that include cerebellar involvement (e.g., Scudder et al. 2002).

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