

Saccade-Related Activity in Monkey Superior Colliculus

II. Spread of Activity During Saccades

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SUMMARY AND CONCLUSIONS

1. In the companion paper we described two classes of cells in the monkey superior colliculus (SC) that were related to saccade generation, buildup cells and burst cells, which fell into two functional sublayers within the intermediate layers of the SC. Fixation cells in the rostral SC were deemed to be part of the buildup cell layer. The buildup cells had several characteristics in common with cells in the cat described as having a "hill of activity" moving across the SC, but the burst cells had no such characteristics. In this paper we further investigate whether there is evidence for such a moving hill of activity in the monkey by analyzing the spatial and temporal activity of cells across the SC during the generation of visually guided saccades.

2. We recorded the activity of single cells while the monkey made saccades of different amplitudes ($0.5\text{--}60^\circ$). We recorded cells from locations extending from the rostral to caudal SC in order to sample cells whose optimal amplitudes ranged from small to large saccades. This allowed us to see any shift of activity across the SC before, during, and after saccades. It also allowed us to determine the fraction of the SC that was active during the successive phases of saccade generation.

3. During active visual fixation, the fixation cells in the rostral pole of the buildup layer showed an increased discharge rate. From the population reconstruction, we estimate that the zone of active cells spanned the most rostral 0.72 mm in each SC. Assuming the SC is 5 mm in length, $\sim 15\%$ of the cells lying along the horizontal meridian in the buildup layer would be active during fixation.

4. At least 100 ms before the initiation of a saccade, long-lead activity began to appear in the buildup layer at the site on the SC motor map related to the next saccade. Fixation activity in the rostral poles simultaneously began to diminish, but the cells in the burst layer remained relatively silent.

5. Approximately 25 ms before saccade onset, the fixation cells ceased firing and both burst and buildup cells began to burst. The active zone in the burst layer was estimated to be ~ 1.4 mm diam, occupying roughly 28% of the SC along a line running from the rostral pole through the center of the initially active zone. The size of this active area among the burst cells was independent of saccade amplitude. The size of the initially active zone in the buildup layer was larger than in the burst layer and was dependent on saccade amplitude; it was larger for larger saccades.

6. During the saccade, all cells in the buildup layer lying rostral to the initially active zone became active, and their peak discharge occurred later in the saccade as the cells were located more rostrally. Cells lying caudal to the initially active buildup cells were not activated. During the saccade, activity in the burst cell layer collapsed, but there was no shift in the locus of this activity in the SC.

7. We interpret the sequential activation of the buildup cells during a saccade as a spread of activity rostrally across the buildup layer of the SC. We saw no evidence for a spread of activity in the burst layer.

8. These experiments allow us to propose the following sequence of activity among the SC cells during generation of a saccade. During fixation, activity is confined to the fixation cells in the rostral SC, and we hypothesize that these cells suppress saccades via inhibitory connections directly onto the saccade cells in the caudal SC and excitatory connections onto the omnipause neurons in the pons. The buildup cells show the earliest activity preceding a saccade, and we suggest that this activity is related to preparation to make a saccade, including selection of target amplitude and direction. The burst cells are active just before saccade onset and could provide input to the pons for the amplitude and direction of the saccade. The pause in activity of the fixation cells is critical for the timing of the saccade. We think that the rostral spread of activity in the buildup cells, and the sharp reduction in burst cell discharge, are consistent with a feedback signal to the SC from the pons. We conclude that these changes in the spatiotemporal distribution of activity in the monkey SC are critical for controlling when a saccade occurs, its amplitude and direction, and its trajectory.

INTRODUCTION

In the companion paper (Munoz and Wurtz 1995) we argue that neurons with saccade-related activity in the monkey superior colliculus (SC) could be divided into two classes: burst cells and buildup cells. Burst cells discharged high-frequency bursts of activity before the onset of saccades; these bursts were superimposed on an otherwise silent background rate. Buildup cells had a long-lead anticipatory buildup of low-frequency activity and then frequently a burst of activity beginning just before the onset of saccades. Because of their location within the SC, we suggested that the burst and buildup cells form two functional sublayers, the burst and buildup layers, within the intermediate layers of the SC. In previous experiments (Munoz and Wurtz 1992a, 1993a,b) we had found a third type of cell in the monkey SC, the fixation cell, that was tonically active during fixation and paused for all but small contraversive saccades and that we found to lie at the rostral edge of the buildup layer.

In this paper we describe the changes in activity in the population of these three types of neurons during the execution of saccades. We investigated population activity because of the recent observations made in the cat by Munoz et al. (1991), who found that saccade-related cells in the cat SC appeared to discharge as if a "hill" of activity were moving across the SC during a saccade. Munoz et al. argued that when this moving hill of activity reached the fixation cells in the rostral SC, the movement was terminated. Consistent with this moving hill of activity was the observation of Munoz et

al. that saccade-related neurons had open-ended movement fields; maximal activity preceded a given amplitude saccade and some activity preceded any larger saccade. Thus a cell in the SC became active with all saccades of its optimal amplitude or larger and participated in the moving hill of activity as it swept rostrally across the SC during a saccade. In contrast, several previous studies in the monkey had identified saccade-related burst neurons (BNs) with closed movement fields: activity only occurred in relation to saccades of a given amplitude and direction (Mohler and Wurtz 1976; Sparks et al. 1976; Sparks and Mays 1980; Wurtz and Goldberg 1972). The clear implication of these closed movement fields is that activity does not shift across the SC during a saccade. In addition, Waitzman et al. (1988, 1991) recently emphasized that many saccade-related BNs in the monkey have their discharges clipped during the saccade, which would also be inconsistent with any moving hill of activity.

In the present experiments we attempt to resolve these differences between the cat and monkey by looking at the spatial distribution of activity across the SC among the population of burst, buildup, and fixation cells during saccades. In order to fully describe the spatial distribution of activity and evaluate whether there is a shift during a saccade, we also determined the size of the active zones within the SC during fixation and saccade generation. We recorded the activity of each cell while the monkey made saccades of different amplitudes, and we sampled cells in different rostral-to-caudal positions in the SC whose maximal discharge was for saccades ranging from small ($<1^\circ$) to large ($\sim 50^\circ$). The consistency of the monkey's saccades allowed us to compare the activity of many cells at different rostrocaudal positions in the SC during the generation of saccades of the same amplitude, even though they were recorded at different times.

The characteristics of the burst, buildup, and fixation cells led us to predict different activity patterns across these populations of cells during saccades. The burst cells have closed movement fields. For example, a burst cell that had its peak discharge for a 10° saccade would discharge little for a 5° or a 20° saccade. We would therefore expect to see the activity of all burst cells limited to one region of the SC throughout the saccade. In contrast, almost all buildup cells had open-ended movement fields. For example, a buildup cell that had its peak discharge for a 10° saccade would also discharge with a 50° saccade. Furthermore, the time of maximum activity occurred later and later in the saccade as the preferred amplitude of a given cell was smaller and smaller, which is consistent with a spread of activity along the buildup cells from caudal to rostral within the SC. The present experiments show that the activity of the burst cells swells and then collapses during saccade generation, but does not shift on the SC motor map. In contrast, the activity of the buildup cells is consistent with a caudal-to-rostral spread of activity during a saccade. The analysis also reveals that large fractions of cells within the SC are active with each saccade. These observations allow us to reconstruct the sequence of events in the SC during the generation of saccades and to refine our conception of the contribution of the SC to saccade generation.

Brief reports of some of these findings have appeared previously (Munoz and Wurtz 1992b; Wurtz and Munoz 1994).

METHODS

The behavioral, physiological, and analysis methods used in these experiments are described in the companion paper (Munoz and Wurtz 1995). Here we provide the criteria for including cells in the sample analyzed and a few additional methods used in data analysis.

Cells included in the analysis were from the four monkeys studied in the companion paper that we could classify as burst, buildup, or fixation cells. Each cell had to be recorded while the monkey generated several saccades of different amplitudes. All burst cells ($N = 43$) had a silent background discharge rate, showed a characteristic reduction of activity between target onset and saccade onset, and had closed movement fields. We did not include some burst cells in the caudal SC related to large saccades because we could not determine the far edge of their movement fields and therefore could not classify their movement fields as closed. Buildup cells ($N = 34$) had activity that continued between target onset and saccade onset, and had open-ended movement fields. Within this pool we included cells with open-ended movement fields even if we could not determine whether they had buildup activity, and we included buildup cells in the caudal SC related to large saccades, even though we could not evaluate their movement fields beyond 60° , provided they had continued activity between target onset and saccade onset. Because we were interested in looking at cells related to saccades of different amplitudes along the rostral-to-caudal extent of the SC, we concentrated on those cells whose preferred saccadic amplitudes were close to the horizontal meridian line running from rostral to caudal along the center of the SC. For the burst and buildup cells, 57% had their preferred direction within $\pm 10^\circ$ of the horizontal meridian, and 89% of the cells had their preferred direction within $\pm 30^\circ$ of the horizontal meridian. All fixation cells ($N = 14$) had the characteristic increase in discharge rate during active visual fixation and paused during saccades, although many cells had increased activity with small contraversive saccades.

We studied these cells during visually guided saccades spanning a wide range of amplitudes ($0.5\text{--}60^\circ$). We concentrated on the amplitudes between 2 and 50° , but the number of cells studied at each amplitude varied somewhat, so that in our sample the number of burst cells for each amplitude ranged from 15 to 40, the number of buildup cells ranged from 19 to 32, and the number of fixation cells ranged from 7 to 14. After analyzing the data, we found that we lacked buildup cells with peak amplitudes between 5 and 10° and collected additional cells in this region of the SC in a fifth monkey.

In order to compare the activity of cells across the SC, we needed to not only categorize the cell types but to describe the location of the cell along the rostrocaudal extent of the SC. First we defined the optimal saccade vector for each cell on the basis of the amplitude and direction of the saccade that produced the most intense activity. We then used this optimal saccade vector to estimate the cell's location in millimeters from the rostral pole of the SC. This distance was derived by taking the optimal saccade amplitude in degrees of angle and computing the distance along the horizontal meridian of the SC in millimeters by using the equation of van Gisbergen and coworkers (Ottes et al. 1986; Van Gisbergen et al. 1987). This logarithmic mapping function, which is based on the SC motor map derived by electrical stimulation (Robinson 1972), is as follows

$$u = B \ln(\text{sqrt}(R^2 + A^2 + 2AR)/A) \quad (1)$$

which can be reduced to

$$u = B \ln(1 + R/A) \quad (2)$$

where u is the anatomic distance from SC foveal representation measured along the horizontal meridian representation (mm), B is a scaling constant determining the size of the SC map along its u axis (mm), A is another constant that determines the shape of the

mapping ($^{\circ}$), and R is the retinal eccentricity of the optimal saccade amplitude ($^{\circ}$). We fixed A at 3.0 and B at 1.4 and obtained a good fit to the horizontal meridian of the stimulation map produced by Robinson (1972). Electrical stimulation of the monkey SC at the site of a cell with a closed movement field elicits a saccade whose amplitude and direction closely match the optimum of the cell (Van Opstal et al. 1990). Because the burst and buildup cells we encountered on the same penetrations through the SC had their peak discharge for saccades of similar amplitudes, we used the above method for both burst and buildup cells. We plotted the locations of all cells along the rostral-to-caudal extent of the SC using this millimeter scale, but for easier reference to the text, which describes saccadic amplitude in degrees, we frequently labeled each scale in degrees of saccade amplitude.

To compare saccade-related activity across many cells in the SC, we normalized the responses of each cell to a peak response. We first computed the spike density waveforms ($\sigma = 10$ ms) aligned on the onset and end of saccades. The waveforms were aligned on both the onset and end of the saccade to allow for subsequent analysis that was time-locked to both of these events. For burst cells, we normalized the activity of each cell to the peak discharge obtained for the optimal amplitude and direction of saccades. For example, for the burst cell illustrated in Fig. 11A in Munoz and Wurtz (1995), we normalized the spike density waveforms relative to the peak of 410 spikes/s. For the population of 43 burst cells analyzed, the average peak value was 445 ± 188 (SD) spikes/s (range 150–800 spikes/s). For buildup cells, we did not use the peak of a burst for normalization both because such a burst was not present in all buildup cells and because we wanted to represent the activity across a much wider range of saccadic amplitudes, including saccades greater than the optimal amplitude. We therefore normalized activity of each buildup cell relative to its peak level of activity associated with these larger-amplitude movements (40–60 $^{\circ}$, depending on the largest saccades studied). For some buildup cells the peak activity associated with large-amplitude saccades was similar to the peak at the optimum, while for others activity was less than that recorded at the optimum. The result of this approach was that after normalization some buildup cells had peak values >1.0 for saccades of the optimal amplitude. For example, we normalized the activity of the buildup cell in Fig. 11B in Munoz and Wurtz (1995) relative to 100 spikes/s, which was the value of the peak of activity for both the large-amplitude saccades and the optimal-amplitude saccade ($\sim 10^{\circ}$), whereas we normalized the activity of the buildup cell in Fig. 7B in Munoz and Wurtz (1995) relative to 150 spikes/s, which was the value of the peak activity for large-amplitude saccades but less than that at the optimum. The average value used to normalize the discharge of 34 buildup cells was 184 ± 66 (SD) spikes/s (range 60–375 spikes/s). We normalized fixation cells to their maximal discharge during active visual fixation. For the pool of 14 fixation cells, the average value was 94 ± 37 (SD) spikes/s (range 40–150 spikes/s).

We used the normalized activity of each cell and the position of that cell on the SC motor map to plot the activity of the entire sample of cells at selected times before, during, and after the execution of saccades of different amplitudes. This produced a plot describing the distribution of neuronal activity across the entire SC at a specific moment in time. A cubic spline fitting function (de Boor 1978) was then applied to these data derived from a series of cells. We used these curves to compare activity in the burst, buildup, and fixation cells at various times before, during, and after saccade generation.

RESULTS

Spatiotemporal distribution of activity during saccades

We identified very different activity patterns across the rostrocaudal extent of the SC for cells in the burst and

buildup layers during saccade generation. Figure 1 highlights these differences by showing the individual spike density profiles of 10 typical burst and buildup cells that we selected for illustration because they were spread across the SC (indicated by the location of the filled circles on the SC map). The 10 cells had different optimal saccade amplitudes, ranging from 2 $^{\circ}$ at the *top* to 28 $^{\circ}$ at the *bottom* for the burst cells (Fig. 1, *left column*) and 0.3–45 $^{\circ}$ for the buildup cells (Fig. 1, *right column*). The records are aligned on the onset of 50 $^{\circ}$ contraversive saccades (*left vertical lines in each column*). The 50 $^{\circ}$ saccades lasted ~ 90 ms, and the *right vertical lines* indicate saccade termination.

For the cells in the burst layer (Fig. 1, *left column*), only the most caudal cells were active before onset of the 50 $^{\circ}$ saccade (Fig. 1, *bottom left panels*), and the peak discharge of these cells occurred around the time of saccade onset. The activity of these caudal burst cells diminished during the saccade, so that by the end of the movement they were virtually silent. The critical point is that cells lying rostral to the initially active zone in the caudal SC remained silent throughout the planning and execution of the 50 $^{\circ}$ saccade (Fig. 1, *top left spike density profiles*); there was no sequential activation of burst cells lying rostral to the initially active zone during the saccade.

Among the cells in the buildup layer (Fig. 1, *right column*), the most caudal cells were active before onset of the 50 $^{\circ}$ saccade, and the peak discharge of these cells also occurred around the time of saccade onset (Fig. 1, *bottom right panels*). The spatial and temporal distribution of activity of the buildup cells differed from that of the burst cells. The buildup cells at the initially active zone in the caudal SC began to discharge earlier than did the burst cells. This is best seen in the spike density profiles of the most caudal cells (Fig. 1, *bottom right panels*), where activity was present 200 ms before saccade onset. In addition, all buildup cells lying rostral to the initially active zone in the caudal SC increased their discharge rate at some time during the 50 $^{\circ}$ saccade. This can be seen by looking up the *right column* of Fig. 1. The peak discharge occurred immediately before or at the onset of the 50 $^{\circ}$ saccade for the most caudal cells (*bottom 4 spike density profiles*) but occurred after saccade onset for more rostrally located cells (*middle spike density profiles*). The fixation cells (*top 2 spike density profiles*) were silent at the start of the 50 $^{\circ}$ saccade and began to discharge before the end of the saccade. Thus there was a clear shift in the peak discharge of the buildup cells from before saccade onset (*bottom 4 profiles*) to during the saccade (*middle 4 profiles*) to after saccade end (*top 2 profiles*). Not only was there a rostral shift in the peak discharge during the 50 $^{\circ}$ saccade, there was also a rostral shift in both the onset and offset of activity during the saccade.

Figure 2 shows the spike density profiles for the same 10 burst and buildup cells shown in Fig. 1 after normalization to a peak response. Burst cells were normalized to the peak discharge obtained for the optimal amplitude and direction of saccades, and buildup cells were normalized to the peak activity associated with large saccadic amplitudes (40–60 $^{\circ}$; see METHODS for rationale of normalization). The normalization process modified the heights of the discharge profiles of some cells only modestly but did not alter the times at which peak discharge occurred. The same key points can be

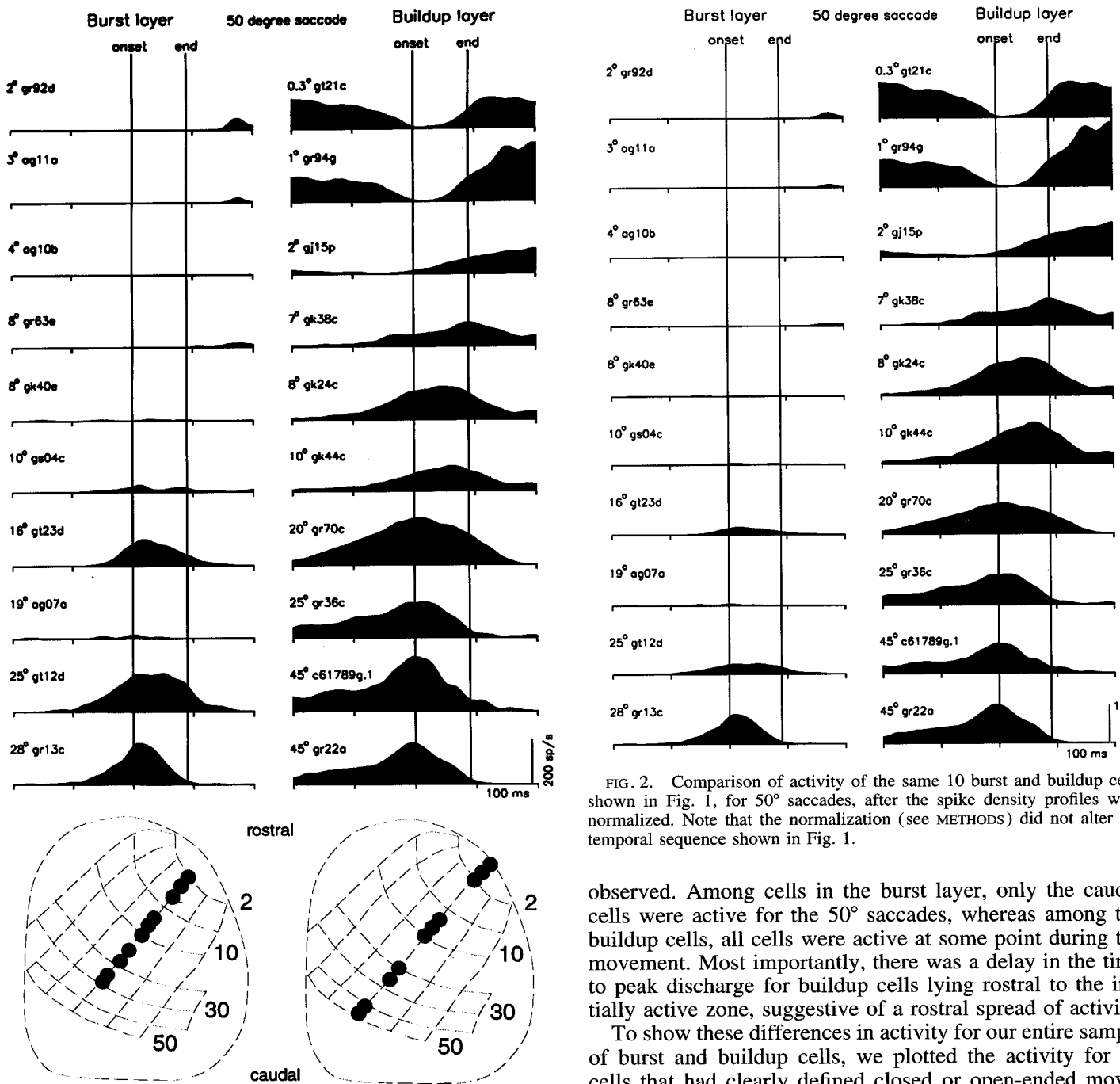


FIG. 1. Comparison of activity of 10 burst cells with closed movement fields and 10 buildup cells with open-ended movement fields for a 50° saccade. The cells were chosen to cover different rostrocaudal positions across the superior colliculus (SC) motor map. *Bottom*: SC map schematically shows the position of the 10 cells. Each filled circle corresponds to the optimal saccade amplitude for each cell. The optimum is also listed next to each spike density profile. The spike density profiles ($\sigma = 10$ ms) representing the discharge of each cell were computed from ≥ 8 saccades of identical amplitude. The profiles are aligned on saccade onset (*left vertical lines*). Abscissa: 200 ms before and after saccade onset. The 50° saccades were ~ 90 ms in duration. *Right vertical lines*: saccade termination. Activity in the burst layer is limited to the caudal cells. The movement fields of these cells included 50° saccades, with the exception of the cell with an optimal amplitude of 19°. The activity of the rostral burst layer cells after the end of the saccade is related to small corrective saccades. All cells in the buildup layer were active during the saccade; the 2 most rostral cells are fixation cells.

FIG. 2. Comparison of activity of the same 10 burst and buildup cells shown in Fig. 1, for 50° saccades, after the spike density profiles were normalized. Note that the normalization (see METHODS) did not alter the temporal sequence shown in Fig. 1.

observed. Among cells in the burst layer, only the caudal cells were active for the 50° saccades, whereas among the buildup cells, all cells were active at some point during the movement. Most importantly, there was a delay in the time to peak discharge for buildup cells lying rostral to the initially active zone, suggestive of a rostral spread of activity.

To show these differences in activity for our entire sample of burst and buildup cells, we plotted the activity for all cells that had clearly defined closed or open-ended movement fields. Figures 3 and 4 compare the distribution of activity at different times before (Fig. 3) and during (Fig. 4) the execution of a 50° saccade. Each plot shows activity at a given time across the entire SC for the sample of cells in the burst and buildup layers. Within each plot, each point represents the activity of a single cell at that time, and each cell is represented again on the following plots for succeeding times. The crosses in the buildup layer plots (*right columns*) represent the activity of fixation cells. The ordinate of each plot is the normalized level of activity for each cell for the 50° contraversive saccade. The abscissa is the rostrocaudal position of the cell in the SC. The caudal pole of the SC is on the *right side of the abscissa* and the more rostral points are to the *left*, with the vertical dotted line marking the rostral pole of the SC. Points to the *left of the*

vertical dotted line correspond to cells located in the SC ipsilateral to the direction of the saccade. The solid line in each plot is a spline fit through the separate group of data points for the burst and buildup cells. The dashed line is a spline fit through the population of fixation cells.

Beginning 200 ms before onset of the 50° saccade (Fig. 3, top), activity was confined to the fixation cells in the rostral poles of the buildup layer of both SCs. Then, in the time leading up to saccade onset (-150, -100, -50, and -20 ms), activity began to develop around the 50° locus on the map, first among the buildup cells and then later among the burst cells. Fixation-related activity in the rostral pole of the buildup cell layer simultaneously diminished. It is

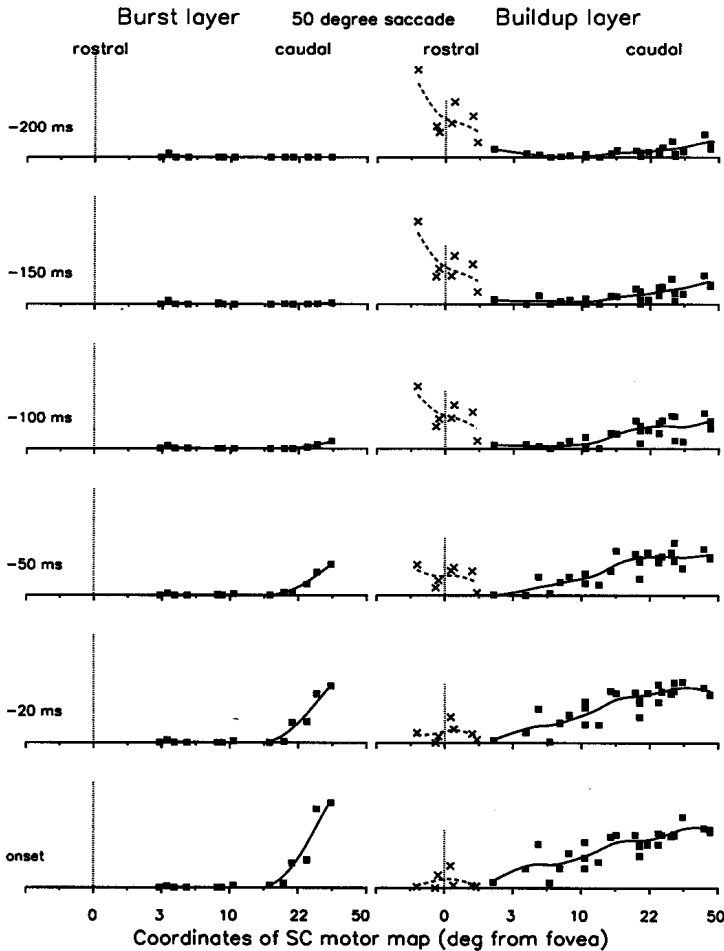


FIG. 3. Spatial distribution of activity in burst and buildup cell layers before a 50° saccade. Each buildup cell (right column) and each burst cell (left column) is represented by a filled square on each of the successive lines that show the magnitude of that cell's normalized response at successive times from 200 ms before saccade onset to saccade onset. Fixation cells are represented by the crosses in the rostral pole of the buildup layer. The position of a point on the abscissa corresponds to the cell's optimal saccade amplitude converted to mm from the rostral pole (see METHODS). The 0 point on the abscissa corresponds to the rostral border of the SC. Cells lying to the right of the 0 point were located in the SC contralateral to the direction of the saccade. Cells lying to the left of 0 were located in the ipsilateral SC. The solid lines were produced by a spline fitting function through the data points for each group of burst, buildup, and fixation cells. The largest tick marks on the abscissa indicate mm from the rostral pole of the SC (-1-4 mm full scale), but for ease of comparison to saccadic amplitude, the locations of 10° and 50° amplitudes are indicated. For reference, the buildup cell closest to the fixation cells is g15, shown in Figs. 8B and 16A in Munoz and Wurtz (1995).

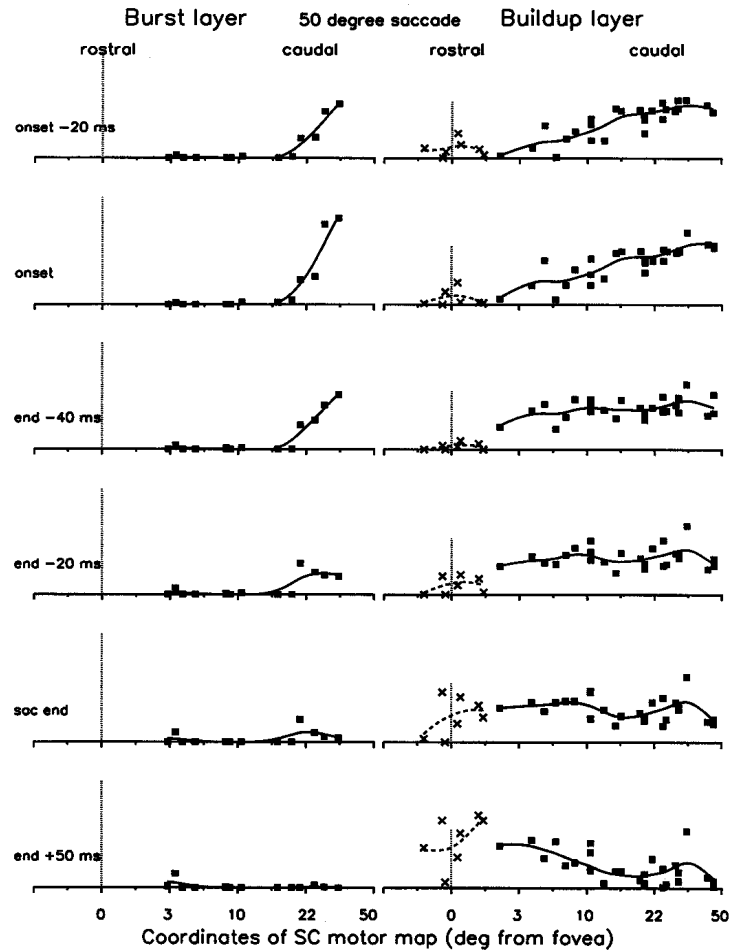


FIG. 4. Spatial distribution of activity in burst and buildup cell layers during and after a 50° saccade. Same organization as Fig. 3. Note that the buildup cells lying rostral to (to the left of) the cells active at saccade onset began to discharge during the 50° saccade, before activation of the fixation cells.

worth noting that at -20 ms, activity increased somewhat among the buildup cells lying rostral to the initially active cells. At saccade onset, fixation-related activity at the rostral pole of the buildup layer had ceased, and both burst and buildup cells in the caudal SC were maximally active.

The spatial distribution of activity in the two layers differed most dramatically as the saccade progressed (Fig. 4). In the burst cell layer, there was no change in the spatial distribution of activity during the movement; the level of discharge of cells in the initially active zone diminished from a peak at saccade onset to near zero at saccade termination. In contrast, the buildup cells lying rostral to the initially active zone all increased their discharge rate during the saccade. Their peak discharge occurred progressively later during the saccade as the cell was located more rostrally. By saccade termination, fixation cells in the rostral SC were reactivated. Looking down the column related to the buildup cell layer, an increase in activity is visible beginning in the caudal SC at saccade onset and moving to the rostral SC by saccade termination. Again, looking at the burst cell layer, no such widespread activity is evident.

Thus there were several key differences in both the temporal and spatial patterns of activity between the burst and

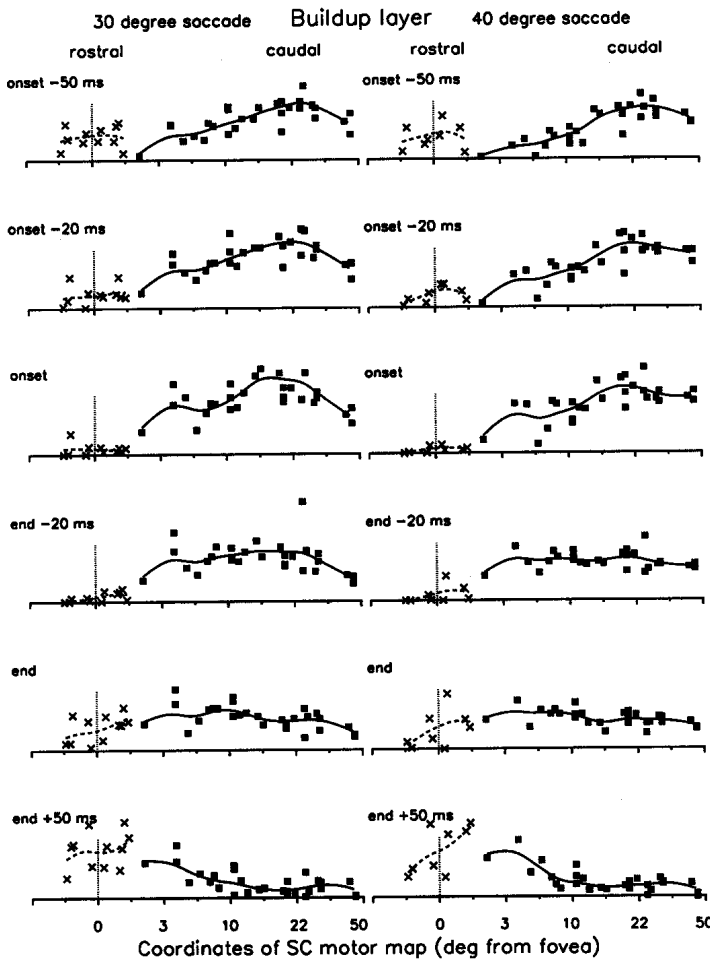


FIG. 5. Spatial distribution of activity in the buildup cell layer associated with 30 and 40° saccades. Same organization as Fig. 3.

buildup cell layers. 1) The buildup cells at the initially active zone in the caudal SC were activated before the burst cells before saccade onset. 2) All buildup cells lying rostral to the initially active zone were active during saccades, whereas many burst cells lying rostral to the initially active zone remained silent. 3) The more rostral buildup cells were activated later in time, as if activity spread forward across the SC from the initial active zone in the caudal SC to the rostral fixation cells.

The activity among the entire sample of buildup cells is illustrated again in Fig. 5 for two different amplitude saccades, 30° (left column) and 40° (right column). At the onset of these saccades there was an initially active zone in the caudal SC. For the 30° saccade, all buildup cells were active at saccade onset and the rostral spread of activity only occurred among the fixation cells. However, for the 40° saccade, some buildup cells lying rostral to the initially active zone and caudal to the fixation cells were essentially silent at saccade onset but became active during the saccade, before activation of the fixation cells. These observations also are consistent with a rostral spread of activity across the buildup layer during the generation of a saccade. Once again, it is worth noting that this rostral spread begins to appear ~20 ms before saccade onset (see Figs. 4 and 5).

Figures 4 and 5 do not reveal whether the activity among buildup cells actually extends in all directions, as does the

ripple of a pebble thrown into water, or only rostrally, because, for the large-amplitude saccades, activity always started in the caudal SC. Any caudal extension of the activity should be easily seen during smaller saccades, which have their initial activity located more rostral in the SC. Figure 6 shows the distribution of activity in the burst and buildup cell layers before, during, and after 2° saccades for the sample of cells. In the burst layer, activity peaked at the 2° site at saccade onset and then diminished at that same location during the saccade. In the buildup layer, activity also peaked at the 2° site, but most buildup cells in the caudal SC were not activated. Thus we see no evidence for a caudal spread of activity in the buildup layer during saccades.

We can characterize the differences in the activity in different rostral-caudal locations in the SC throughout the saccade by comparing the activity of the burst, buildup, and fixation cells for other saccadic amplitudes (Fig. 7). Population curves for four different amplitude saccades (· · ·, 1°; — — —, 5°; - - - -, 20°; ———, 40°; population curves derived as in Fig. 3) are superimposed for the times at 200 ms before saccade onset, saccade onset, saccade end, and 100 ms after saccade end. Activity was centered in the fixation cells in the rostral poles of the buildup layer >200 ms before saccade onset (Fig. 7B), and no activity was present in the burst layer (Fig. 7A). At the time of saccade onset,

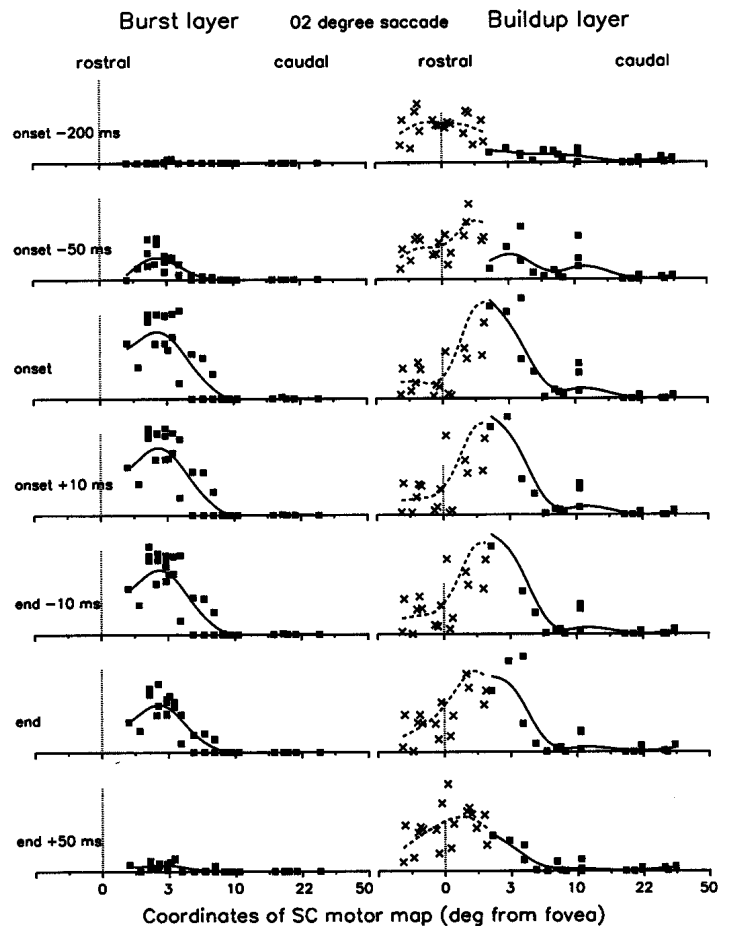


FIG. 6. Spatial distribution of activity in burst and buildup cell layers associated with a 2° saccade. Same organization as Fig. 3. Note the lack of any caudal (rightward) increase in activity in the buildup layer during the saccade.

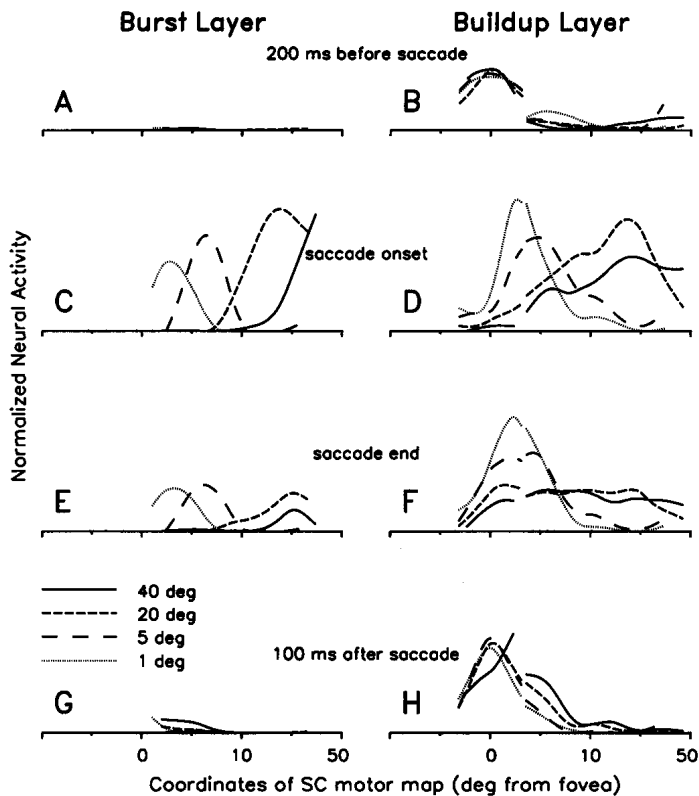


FIG. 7. Comparison of population spline curves for the burst cells (A, C, E, and G) and the buildup and fixation cells (B, D, F, and H) for saccades of 4 different amplitudes (1, 5, 20, and 40°). Curves: distribution of normalized neuronal activity across the SC 200 ms before saccade onset (A and B), at saccade onset (C and D), at saccade end (E and F), and 100 ms after the saccade (G and H). The center of activity remains constant in the burst cell layer during the saccade but changes in the buildup cell layer during the saccade.

fixation cell activity in the rostral poles had ceased (except for the 1° saccade, in which many fixation cells remained active, and the 5° saccade, in which some fixation cells remained active; Munoz and Wurtz 1993a), and the peak in each curve was then centered at the appropriate site within the SC in both the burst (Fig. 7C) and buildup (Fig. 7D) cell layers. At the end of the saccade, the population curves differed greatly between the burst and buildup layers. In the burst layer (Fig. 7E), the curves remained centered at the same location they were at saccade onset, but the peaks were dramatically reduced. In the buildup layer (Fig. 7F), residual activity was present at the initially active zone and all points rostral, including the fixation cells. Only after the end of the saccade did the caudal cells in the buildup layer stop firing; activity was again focused on the rostral fixation cells (Fig. 7H).

A center of gravity measure (Fig. 8) shows the shifts in activity between the beginning and end of the saccade. For each of the burst (Fig. 8A) and buildup (Fig. 8B) layers, we compared the center of neural activity at saccade onset to the center of neural activity at saccade end. The center of gravity was derived from the population curves like those shown in Fig. 7 for 10 different amplitude saccades. Note that the vertical lines drawn between the centers of gravity at saccade onset and end all run more or less vertically for the burst cell layer (Fig. 8A). In contrast, the lines for the

buildup cell layer (Fig. 8B) all slant toward the *bottom left*, indicating the shift in the center of gravity toward the rostral SC, even though the fixation cells were excluded from the analysis. The tilt of each line in Fig. 8B became greater as initial activity was situated more caudally on the SC map. Figure 8, C and D, plots this shift in the center of gravity (ordinate) against the distance of the initial peak from 0 (abscissa). Note that the slope of the linear regression line in the burst layer was only 0.05 (Fig. 8C), whereas the slope of the line for the buildup layer was 0.34 (Fig. 8D). This analysis reveals that the center of gravity in the buildup cell layer shifted during saccades and that the amount of the shift increased with larger saccades.

Reduction in activity at the initially active zone

Waitzman et al. (1991) recently found that many saccade-related cells in the monkey SC end their activity as the saccade ends, and hypothesized that this reduction resulted from feedback to the SC related to the progress of the saccade. We noticed that the reduction of activity in both the burst and buildup layers varied with the eccentricity of the initially active zone. To show this effect, we measured the

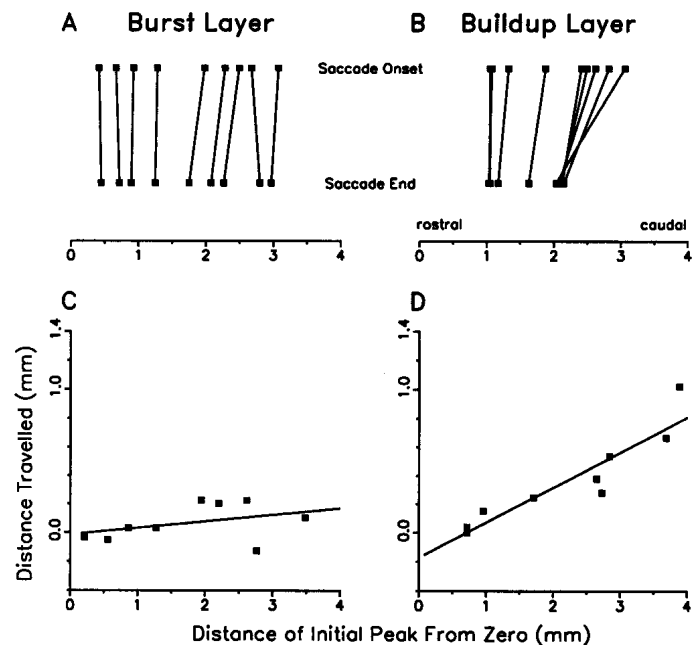


FIG. 8. The center of gravity shifts in the buildup cell layer (B and D) but not the burst cell layer (A and C) during saccades of different amplitudes (burst cells: 0.5, 1, 2, 5, 7, 10, 15, 20, and 30°; buildup cells: 0.5, 1, 2, 5, 10, 20, 30, 40, 50, 60°). A and B: start and end of each line represent the center of gravity at saccade onset and end, respectively. We computed the center of gravity by first calculating the area under each spline curve of the burst and buildup cells with different amplitude saccades, as shown by sample individual curves in Fig. 7. The collicular coordinate was the point having 50% of the activity on each side. This method underestimated the center of gravity for large saccades (>30° in amplitude) in which the peripheral border of the population spline curves was not available. The lines for burst cells are almost vertical, whereas those for buildup cells all veer toward the *bottom left*. C and D: plots of distance of shift in center of gravity vs. location of the initial peak on the SC map (distance of initial peak from 0). Solid lines produced by regression analysis. Slope, Y-intercept, and correlation values for the line in C were 0.05, -0.02, and 0.39, respectively, whereas these values in D were 0.25, -0.17, and 0.93, respectively.

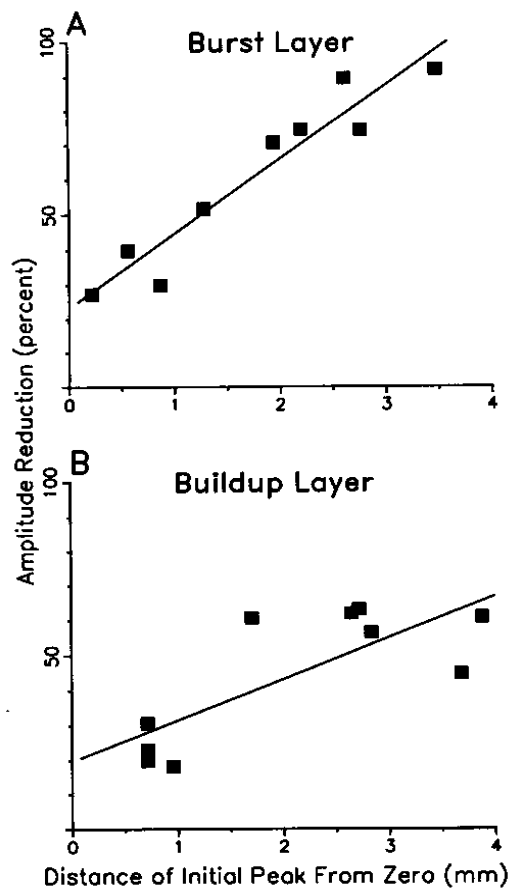


FIG. 9. Reduction of activity at the initially active zone as a function of the location of this zone on the SC map. Graphs show reduction of activity between saccade onset and saccade termination (ordinate) vs. the location of the initial peak (abscissa). Each point is the drop in height of the spline curve at the initial peak for a different amplitude saccade. (A—burst cells: 0.5, 1, 2, 5, 7, 10, 15, 20, and 30°; B—buildup cells: 0.5, 1, 2, 5, 10, 20, 30, 40, 50, and 60°). Solid lines produced by linear regression analysis. The slope, Y -intercept, and correlation values for the line in A were 21.3, 23.4, and 0.96, respectively, whereas in B they were 11.8, 19.7, and 0.77, respectively.

percent reduction of activity at the initially active zone at the end of the saccade and plotted this against the eccentricity of the initial peak of activity (Fig. 9). The regression line for the burst cells showed a strong correlation between eccentricity of the initially active zone and the percent reduction (Fig. 9A: slope = 21.3, $r = 0.96$); the greater the eccentricity, the greater the reduction. Thus, although there was a “clipping” of activity in the initially active zone, the amount of reduction in activity during the saccade was dependent on saccade amplitude or eccentricity of the peak on the SC motor map. The greater the amplitude of the saccade, the greater the amount of clipping. We found a somewhat weaker correlation in the buildup layer (Fig. 9B: slope = 13.7, $r = 0.80$).

Size of active regions for burst, buildup, and fixation cells

In order to understand how the ensemble of saccade-related neurons within the SC controls saccades, it is essential to know what fraction of the cells in the burst and buildup layers are active at any one time. We were able to estimate

the size of the region within the SC that was active before, during, and after saccades of different amplitudes because we had a sample of activity taken from cells spread across the SC. We made these estimates for burst, buildup, and fixation cells.

BURST CELLS. We first estimated the size of the active zone in the burst cell layer by measuring the diameter of individual closed movement fields. Figure 10A shows the move-

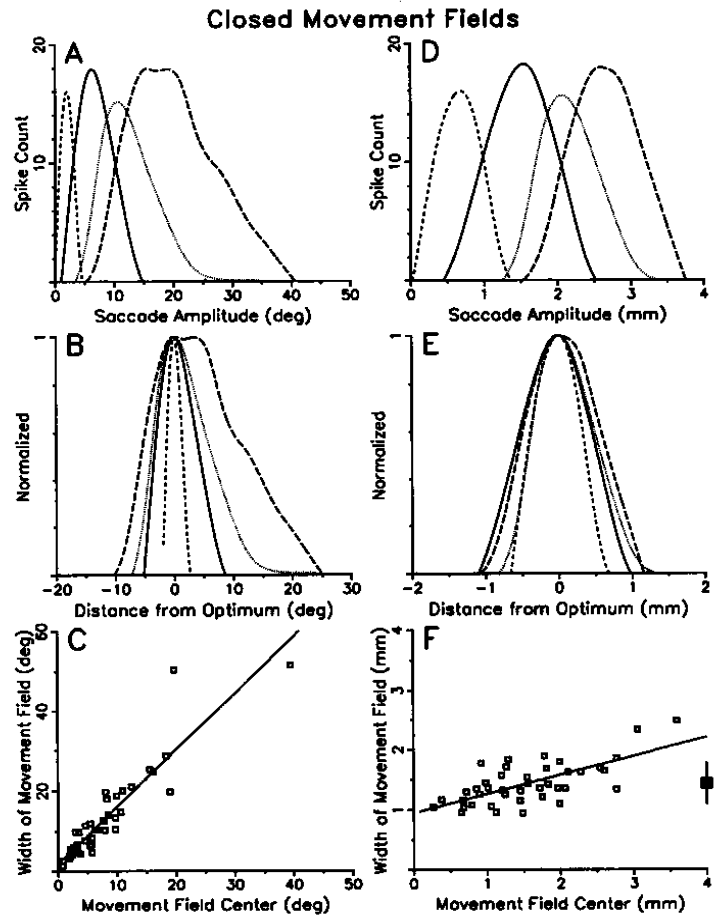


FIG. 10. Size of the active zone in the burst cell layer estimated by analysis of movement fields of single burst cells. A: spline curves representing the movement fields of 4 representative cells with closed movement fields. The optimal saccade amplitude for each cell was 2° (---), 5° (solid line), 9° (· · ·), and 16° (— — —). B: same curves as in A after normalization on the peak of each curve and alignment of the peaks. C: plot of movement field width vs. eccentricity for cells with closed movement fields. Width was defined as spanning from 25% of the peak on ascending side to 25% of the peak on the descending side for curves like those shown in A. Only 41 of the 43 cells with closed movement fields were included because the optimal amplitudes for 2 cells were <1° and we could not assess the ascending side of the field (i.e., <0.25°). Solid line: least-squares regression through the data points; it had a slope of 1.42, Y -intercept at 1.78, and a correlation value of 0.92. D: curves from the same cells as shown in A but with saccade amplitudes converted to mm from the foveal representation of the SC using the equation given in METHODS. E: same curves as in D after normalization along ordinate and alignment of the peaks. Notice that curves now have a very similar shape. F: plot of movement field width vs. eccentricity for 41 cells with closed movement fields. Width was defined as spanning from 25% of the peak on ascending side to 25% of the peak on the descending side for curves like those shown in D. Slope of the regression line is 0.32, Y -intercept is 0.95, and correlation value is 0.68. Solid square with error bars: mean movement field width for the 41 cells plotted, which was 1.4 ± 0.3 (SD) mm.

ment fields of four burst cells whose optimal saccadic amplitudes were 2, 5, 9, and 16°. The continuous functions were generated by fitting a spline curve to the plot of saccade amplitude versus number of spikes as in the companion paper (see Fig. 8 in Munoz and Wurtz 1995). Direct comparisons between cells were made by normalizing the curves relative to their peaks and then aligning the peaks (Fig. 10B). All burst cells had movement fields that were asymmetrical; they were skewed toward larger saccades. We defined the width of the curves shown in Fig. 10B as the distance from 25% of the peak value on the ascending (*left*) side to 25% of the peak on the descending (*right*) side, and Fig. 10C shows the strong dependency of movement field width on movement field eccentricity for 41 cells with closed fields for which we had adequate samples of saccade amplitudes. Movement field size increased as the field became more eccentric, as has been reported previously (Ottes et al. 1986; Sparks et al. 1976). The linear regression line has a slope of 1.42 and a correlation value of 0.92.

To determine whether the skewed shape of the movement field and the relationship between the width of the movement field and its eccentricity was due to the nonhomogeneous mapping within the SC where small amplitudes have an expanded representation (e.g., see Fig. 4B in Robinson 1972), we replotted the movement fields in Fig. 10A onto the collicular coordinate system. We converted saccade amplitude in degrees of arc (Fig. 10A) to millimeters across the SC (Fig. 10D) using the equation in METHODS. The four curves in Fig. 10D (same cells as in Fig. 10A) now assume a similar shape: they lack any significant skewing. Shifting to SC map coordinates also reduced the dependency of movement field width on movement field eccentricity, as can be seen by comparing the spline curves of the four cells in Fig. 10, B and E.

The decreased dependency of movement field size on eccentricity was evident when we replotted the data for the 41 burst cells on SC map coordinates (Fig. 10F). Only a weak correlation remained between movement field eccentricity and width. The regression line through the data points now had a slope of only 0.32 and a correlation value of 0.68. The asymmetry in the shape of the closed movement fields was therefore due to the nonhomogeneous mapping within the SC.

Because the movement field width plotted in SC coordinates (mm) varied so little with eccentricity, we took the mean of the field widths of all 41 cells and plotted that value as the solid square at the *right side* in Fig. 10F. The mean movement field width was 1.4 ± 0.3 (SD) mm. The boundaries of this average movement field define the locus of all cells in the burst cell layer active for a saccade.

We also used a second method to calculate the average width of the active zone within the burst cell layer that was based on the width of the population spline curves fit to the activity of the population of burst cells at saccade onset for several saccades of different amplitudes (as in Fig. 7C), rather than the curves fit to the movement fields of the individual cells (as in Fig. 10, A and D). Figure 11A shows the curves obtained from between 15 and 40 cells for 10 different saccade amplitudes plotted in collicular coordinates, and Fig. 11B shows the seven curves having both ascending and descending portions after they were normalized to the peak

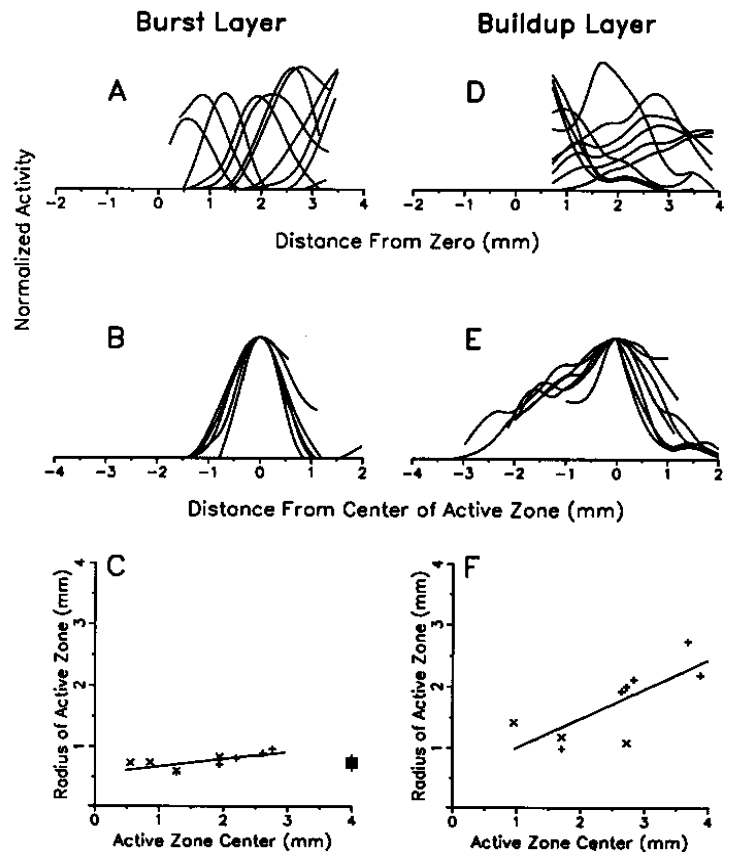


FIG. 11. Comparison of active zone size for the burst (A–C) and buildup (D–F) cell layers. A: population spline curves obtained from burst cells for 10 different saccadic amplitudes at onset of movement. B: normalization along ordinate and alignment of the peaks for the 7 curves in A that had both an ascending and descending phase. C: plot of active zone radius vs. eccentricity for the 7 saccadic amplitudes shown in B. We measured the width of the ascending phase (25% of the peak to the peak: +) and the descending phase (peak to 25% of the peak: ×). These widths provide a measure of the radius of the active zone, and the solid regression line was nearly flat, indicating that the radius of the active area was nearly the same at any point on the SC (slope = 0.12, Y-intercept = 0.56, correlation = 0.71). Solid square: radius of the mean active zone computed from the 7 saccade amplitudes, which was 0.7 ± 0.1 (SD) mm. D: population spline curves for buildup cells for 10 saccades of different amplitudes at movement onset. E: same curves as in D after normalization along ordinate and alignment of the peaks. F: plot of active zone radius in the buildup cell layer vs. eccentricity on the SC motor map. Same symbols as in C. We only include data from saccades where either the ascending or descending phases were clearly delineated. Slope, Y-intercept, and correlation values of the regression line were 0.47, 0.54, and 0.75, respectively. Note the strong dependency of active zone size on eccentricity, which is predominantly due to an increase in the size of the ascending phase (+).

and aligned on their peaks. These population curves (Fig. 11B) revealed similar shapes and widths as had the movement fields for individual cells (Fig. 10E). We plotted the distance from 25% of the peak value on the ascending (*left side*) phase to the peak (+) and the distance from the peak to 25% on the descending (*right side*) phase (×) against eccentricity of the active zone (Fig. 11C). We fit a regression line through this measurement of the radius and found a slope of 0.12 ($r = 0.71$). To compute the average radius of the active zone we computed the mean radius, which was 0.7 ± 0.1 (SD) mm, as shown by the solid square at the *right side* of Fig. 11C.

Thus these two different methods yielded the same value

of 1.4 mm for the diameter of the active zone on the SC map in the burst layer for a saccade. If we assume that the SC spans 5 mm along the horizontal meridian (Robinson 1972), then an active region of 1.4 mm would make up ~28% of the horizontal meridian. Therefore, regardless of the amplitude of a horizontal saccade, more than one fourth of the burst cells in the SC lying along the horizontal meridian would be active with each saccade.

BUILDUP CELLS. We can make the same estimate of the size of the active zone in the buildup cell layer (Fig. 11, *D–F*). We did not use the movement fields of individual buildup cells because they were open-ended and revealed no similar shape (e.g., see Fig. 8, *B, D, and F*, in Munoz and Wurtz 1995). Instead we used the curves representing activity across our entire sample of buildup cells at saccade onset for 10 different saccade amplitudes (Fig. 11*D*). Figure 11*E* shows the same curves after they had been normalized and aligned on their peaks and shows that the curves from the buildup layer were wider than those in the burst layer. Furthermore note that, although the curves fit to the burst layer (Fig. 11*B*) form symmetrical bell-shaped profiles, those from the buildup layer (Fig. 11*E*) were skewed to the left (i.e., toward the rostral pole, where the fixation cells are located). We measured the ascending phase and the descending phase and plotted them against eccentricity of the peak (Fig. 11*F*). The solid line was generated by a linear regression analysis through these radius measurements (+, ×). From the data in Fig. 11*F* it is obvious that the active zones in the buildup layer at saccade onset are much larger than those in the burst layer, and that the size of the initially active zone increased with eccentricity of the peak on the SC motor map. The slope of the line in Fig. 11*F* was 0.47 ($r = 0.75$). We therefore did not estimate an average active zone size for the buildup layer because it depended so strongly on saccade amplitude. However, we estimated that the active zone had a diameter of 2 mm for a 5° saccade and >3 mm for saccades $\geq 20^\circ$ in amplitude. Once again, if we assume that the SC spans 5 mm along the horizontal meridian, then ~40% of the buildup cells would be active at the start of a 5° saccade and >60% of the cells would be active at the start of saccades $\geq 20^\circ$.

FIXATION CELLS. We used spline curves through our sample of both fixation cells and buildup cells to visualize the size of the active zone within the SC during fixation. Figure 12 shows spline curves obtained 200 ms before eight saccades of different amplitudes. This shows the distribution of activity during active fixation and emphasizes the gradual transition from fixation to buildup cells described in the companion paper (see Fig. 16 in Munoz and Wurtz 1995). The edge of the fixation zone, however, is best estimated by the location of the first buildup cell (Fig. 12, short vertical dotted line). The distance from the 0 point on the SC map (long vertical dotted line) to this buildup cell is 0.72 mm, and we take this as a reasonable estimate of the size of the fixation zone. This translates into activation of 15% of the cells along a 5-mm horizontal meridian in each buildup layer during active visual fixation.

DISCUSSION

We found that the sequence of activity across the SC differed for burst and buildup cells during the generation of

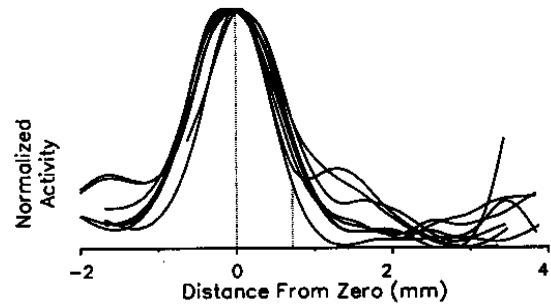


FIG. 12. Size of the active zone of fixation cells. The spline curve fit through both the fixation and buildup cells shows the extent of fixation-related activity 200 ms before the onset of saccades of 8 different amplitudes. The shape of the curves emphasizes the gradual transition between the fixation cells and the adjacent buildup cells as reported previously (Munoz and Wurtz 1995). The distance between the center of activity at the rostral end of the SC (middle vertical line) and the location of the 1st buildup cell (short vertical line) is 0.72 mm, which is the best estimate of the functional size of the fixation cell region of the SC.

saccades. Buildup cells began to discharge long before saccade onset, and during the saccade, all buildup cells lying rostral to the initial zone of activity increased their discharge rate. This spread of activity included the fixation cells in the rostral pole. For burst cells, the activity began shortly before the onset of the saccade and usually ended close to the time of saccade termination. Only burst cells within the region of the SC active at saccade onset remained active during the saccade: there was no rostral spread of activity.

A population reconstruction revealed that large fractions of the neurons were active at different times during the generation of saccades. During fixation ~15% of the cells along the horizontal meridian of the buildup layer of each SC were active. This region in the rostral pole corresponded to the zone of the SC containing the fixation cells. At the start of a horizontal saccade, ~28% of the burst cells along the horizontal meridian were active, regardless of the size of the movement, whereas in the buildup layer the size of the active zone was even larger. We estimated that ~40% of the buildup cells lying along the horizontal meridian were active at the start of a 5° saccade and >60% of the cells were active at the start of saccades $\geq 20^\circ$. We will discuss the evidence for interpreting these observations as indicating a spread of activity among the buildup cells and our conception of the sequence of neuronal events in the SC during saccade generation.

Spread of activity in buildup cells

We infer that there is a rostral spread of activity across the buildup cells during a saccade, and this is based on two observations. The first observation is that all buildup cells rostral to the initially active cells increased their discharge during a saccade, in contrast to burst cells, which did not. This is consistent with the previous observation that buildup cells had open-ended movement fields and discharged with all saccades larger than their optimal amplitude (Munoz and Wurtz 1995). The second observation is that the time at which the more rostral buildup cells became active with respect to saccade onset was later and later as they were located farther away from the site of initial activity. That is, the peak discharge of a buildup cell occurred later in the

movement for saccades larger than the cell's optimum (Munoz and Wurtz 1995). This implies that the buildup cells at the initially active zone achieved peak discharge before the more rostral buildup cells, which in turn were activated before the fixation cells at the rostral pole. This indication of rostral spread of activity was most evident during large saccades. For example, during the execution of a saccade of 50° the sample of buildup cells at the 30–50° site reached peak activity around saccade onset (see Figs. 1–4). The buildup cells around the 10° site reached peak discharge before the buildup cells at the 2–5° site, and these cells were activated before fixation cells.

We also found that activity in the buildup cell layer spread rostrally but not caudally during saccades. This absence of any caudal spread of activity was most evident for small saccades (e.g., see Fig. 6 for 2° saccades). Buildup cells preferring large-amplitude saccades were not active during smaller saccades, as they would have to be if activity also spread caudally across the SC. Thus the spread of activity appears to be in one direction rather than both rostrally and caudally, as would be the case of a disturbance spreading out from a central point like the ripples formed by tossing a pebble into a pond.

Although we believe that the rostral spread of activity in the buildup cells is related to execution of the saccade, there are other possible interpretations that must be considered. This rostral spread of activity was not due to the sequential activation of the visual receptive fields of buildup cells lying closer and closer to the foveal representation, as previously debated for the cat SC (Guitton et al. 1993; Sparks 1993). This visual stimulation cannot explain the sequential activation of buildup cells in the monkey, because the spread of activity in these cells occurred even when the monkey made saccades to remembered targets while in complete darkness (see Fig. 13 in Munoz and Wurtz 1995). During such saccades no visual target was present, and no visual receptive field stimulation could have occurred.

Another issue considered for the cat SC was that the sequential activation of buildup cells in the rostral SC might be related to the occurrence of small corrective saccades (Guitton et al. 1993; Sparks 1993). This seems unlikely, because we have shown in the companion paper that the discharge of buildup cells for large saccades was the same whether a subsequent corrective saccade occurred or not (see Fig. 14 in Munoz and Wurtz 1995). We cannot, however, rule out the possibility that the rostral spread of activity was related to the preparation to make such corrective movements. We have argued in the companion paper (Munoz and Wurtz 1995) that the activity of the buildup cells preceding the saccade is not obligately tied to the generation of a saccade. We therefore cannot exclude the possibility that it is the preparatory activity of the buildup cells for a possible corrective saccade that produces the activity in the more rostral cells. Although we cannot rule out this possibility, we think it is unlikely because the rostral spread of activity is synchronized with the first saccade. If the spread of activity were related to the planning of a subsequent corrective movement, why would its timing be tied to the onset of the first saccade? Furthermore, the buildup cells lying rostral to the initial active zone were activated sequentially rather than simultaneously. That is, for a 50° saccade, buildup cells

around the 10° site on the motor map increased their discharge before cells at the 2–5° site, which increase their discharge before the fixation cells. If this spread of activity were related only to the planning of a corrective movement, the reason for a sequential pattern of activation is not obvious. Finally, our trained monkeys never made corrective saccades as large as 10° for 50° target offsets, so that the region related to 10° saccades should not have been activated as it was during a 50° saccade.

One interpretation of the increased activity of the buildup cells in the rostral SC at the end of a saccade is that such activity results from the increased activity of the adjacent fixation cells. That is, as activity in the buildup cells in the caudal SC falls and activity of the fixation cells in the rostral SC rises, what we have interpreted as a spread of activity is simply the change in level of activity between these two hills of asynchronous activity. Although our observations are not extensive enough to reject this view, one observation is not consistent with it: ~20 ms before the saccade, when activity in the fixation cells was falling, we observed activity increasing somewhat in the rostral buildup cells (Figs. 3–5). Furthermore, during a large saccade, the rostral buildup cells were activated before the fixation cells (see Fig. 16 in Munoz and Wurtz 1995). This change of activity of the fixation and buildup cells is consistent with the rostral spread of activity, not the simultaneous but independent decrease of a stationary caudal hill of activity and increase of a stationary rostral hill.

The rostral spread of activity in the buildup layer in the monkey has substantial similarities to the original observations in the cat, which were interpreted as indicating a hill of activity moving across the SC motor map during a movement (Munoz et al. 1991). The key features of this moving hill of activity in the cat were 1) that activation of cells was sequential, from the caudal, initially active zone rostrally toward the fixation cells; 2) that individual cells had open-ended movement fields (i.e., no distal border); and 3) that the peak in the cell's discharge occurred later in the movement for larger-amplitude movements. Buildup cells in the monkey also had all these characteristics, as we have described both here and in the companion paper (Munoz and Wurtz 1995).

One important difference between buildup cells in the monkey and the moving hill cells in the cat is the level of activity spreading across the SC. A given buildup cell in the monkey frequently had a peak discharge at its optimal saccade amplitude that was greater than that recorded during larger-amplitude movements (e.g., see Figs. 7B and 13B in Munoz and Wurtz 1995), whereas for cells in the cat the discharge for larger movements was usually as intense as that for the optimal saccade (e.g., see Figs. 7 and 8 in Munoz et al. 1991). The burst of activity of some buildup cells in the monkey had peaks in the spike density profiles >500 spikes/s, and such a level of activity was never attained in the cat cells. In both the cat and the monkey, however, it is the lower-frequency activity shifting across the SC that constitutes the rostral spread of activity.

Another difference between the monkey buildup cells and the moving hill cells in the cat was the difference in the shape of the activity moving across the SC during a saccade. With the exception of the rostral fixation cells, most of the

moving hill cells in the cat ceased to discharge by the end of the movement (e.g., see Fig. 14 in Munoz et al. 1991). The consequence of this pattern of activity was that during the movement, activity shifted across the SC map as a hill with both an ascending and a descending component. The population spline curves we derived from our monkey data revealed a different shape of shifting activity, that of a moving front. At the time of saccade termination, all buildup cells from the initial active zone forward to the rostral pole were active (e.g., see Figs. 4, 5, and 7). It remains to be determined whether this difference in the shape of the shifting active zone was due to a difference in the species or the experimental conditions. Our experiments were performed in monkeys whose heads were immobilized during cell recording, whereas the cat experiments were performed with the head unrestrained (Munoz et al. 1991).

Sequence of events in SC during saccade generation

By systematically recording in different areas of the monkey SC during the same size saccades, we were able to reconstruct the size of the population active zones and the changes in activity across the population of burst, buildup, and fixation cells before, during, and after a saccade. Several studies have previously identified the importance of ensemble coding of saccade amplitude and direction in the SC (Lee et al. 1988; McIlwain 1991; Munoz and Guitton 1991; Sparks et al. 1976; Sparks and Mays 1980; Van Gisbergen et al. 1987). Because the saccade cells in the SC frequently had large, broadly tuned movement fields, these studies concluded that many cells are active for any one saccade. Deactivation of a small region of the monkey SC produced saccadic dysmetrias verifying that the entire population of active cells contributed to the coding of saccade amplitude and direction (Lee et al. 1988). Our observations on the fractions of the SC active not only during saccade generation but also during fixation and saccade preparation further support this interpretation.

From the observations presented here and in the companion paper (Munoz and Wurtz 1995), we can refine the conceptual framework that describes how the monkey SC may contribute to the control of saccades. Figure 13 summarizes schematically the spatiotemporal sequence in saccade-related activity within the SC and shows how we think these collicular events may shape the activity of saccadic premotor neurons residing in the contralateral paramedian pontine reticular formation (PPRF).

FIXATION. During periods of active visual fixation (Fig. 13A), neuronal activity was confined to the rostral poles of the buildup layer where we found fixation cells. We have previously described the activity of SC fixation cells in the monkey and the consequences of the alteration of this activity (Munoz and Wurtz 1993a,b). We show the cells lying in the buildup layer because we suggest that fixation cells form part of that layer (Munoz and Wurtz 1995), and this interpretation is similar to that proposed earlier for the cat (Munoz and Guitton 1991). From the population reconstructions, we estimated the active zone during fixation to span ~ 0.72 mm of the buildup layer in each rostral pole (see Fig. 12). If we assume that each SC is 5 mm long, then $\sim 15\%$

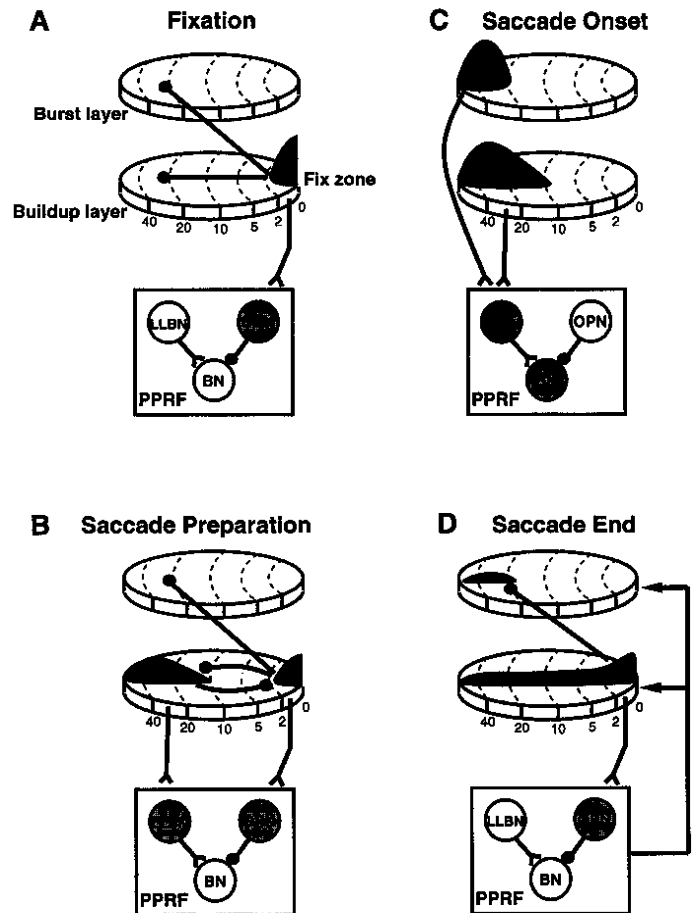


FIG. 13. Schematic representation of sequence of activity in the SC during generation of a saccadic eye movement. Lines ending in open angles: excitatory connections. Lines ending in filled circles: inhibitory connections. BN, burst neurons; LLBN, long-lead burst neurons; OPN, omnipause neurons; PPRF, paramedian pontine reticular formation. Shaded areas in the PPRF indicate cell activity. See text of DISCUSSION for details.

of the cells lying along the horizontal meridian of the buildup layer are active during fixation.

We assume that the activation of the fixation cells is dependent on inputs to the SC from other sources such as cerebral cortex. We can only speculate that the input is from cortical areas where similar fixation activity is also observed, such as posterior parietal cortex (Lynch et al. 1977; Mountcastle et al. 1975; Sakata et al. 1980) and frontal cortex (Bon and Lucchetti 1992; Schlag et al. 1992; Suzuki and Azuma 1977).

Activation of fixation cells leads to direct suppression of the saccade-generating system (Munoz and Wurtz 1993b). There are at least two possible ways in which fixation cells could produce this suppression, as indicated by the projections in Fig. 13A. First, at least some fixation cells may directly inhibit the saccade-related cells in the caudal SC, because electrical stimulation of the rostral SC leads to inhibition of both burst and buildup cells at monosynaptic latencies (Munoz and Wurtz 1993c). Second, at least some fixation cells project to the region of the omnipause neurons (OPNs) in the contralateral PPRF in both monkey (Istvan et al. 1994) and cat (Guitton and Munoz 1991; Munoz and Guitton 1991). Furthermore, electrical stimulation of the SC

in both monkey (Raybourn and Keller 1977) and cat (Pare and Guitton 1994) led to monosynaptic activation of OPNs. These OPNs are tonically active during fixation and pause for saccades (Keller 1974; Luschei and Fuchs 1972), a discharge pattern very similar to collicular fixation cells. The OPNs directly inhibit burst neurons (BNs) in the PPRF that provide the saccadic burst signal to the extraocular muscle motoneurons (Scudder et al. 1988; Strassman et al. 1986a,b, 1987).

SACCADE PREPARATION. The earliest change of activity in the SC leading to the generation of a saccade was an increase of activity in the caudal region of the buildup layer at a site related to the amplitude and direction of the impending saccade and a simultaneous reduction in fixation activity (Fig. 13B). Before initiation of a saccade, attention must be disengaged from the current point of fixation and shifted to a newly selected target (Fischer and Weber 1993). We found that the timing of initial changes in the discharge of fixation cells in the monkey was closely related to the long-lead anticipatory activity of buildup cells: as the buildup cells began to discharge, the activity of fixation cells began to decline (Fig. 3 in this paper; Fig. 17 in Munoz and Wurtz 1995). The fall of activity of fixation cells might be regarded as underlying the disengagement from the current point of attention and the rise of activity in the buildup cells as the engagement of a newly selected target, because these changes often occurred ≥ 100 ms before saccade onset.

There are several possible sources of input to the SC that could produce the switch in activity from the fixation cells to the buildup cells. Excitatory inputs from cortical sources such as the frontal eye fields (Segraves and Goldberg 1987; Stanton et al. 1988), supplementary eye fields (Shook et al. 1990), and posterior parietal cortex (Lynch et al. 1985), and disinhibition from the substantia nigra (Hikosaka and Wurtz 1983) could alter the distribution of activity in the buildup cell layer. Because these areas also reveal changes in neuronal discharge ≥ 100 ms before saccade onset, the processes of selection of a target for the next saccade and the disengaging of active fixation that precedes that saccade may be distributed among these areas and the buildup and fixation cells in the SC.

Inhibitory connections intrinsic to the SC may also mediate the simultaneous increase in buildup cell discharge and reduction in fixation cell discharge. We suggest that a subset of the fixation and buildup cells may interact locally within the SC (Fig. 13B, buildup layer) as part of a target selection mechanism, as was previously hypothesized (Munoz and Guitton 1991; Munoz and Wurtz 1993a). Electrical stimulation of the caudal monkey SC leads to inhibition of fixation cells at monosynaptic latencies, and stimulation of the rostral SC leads to monosynaptic inhibition of burst and buildup cells (Munoz and Wurtz 1993c). Long-duration, low-frequency stimulation of the rostral SC during saccade preparation not only delayed saccade initiation (Munoz and Wurtz 1993b) but also prevented the activation of burst cells (Munoz and Wurtz 1993c). Buildup cells were also inhibited by stimulation of the rostral SC, but during the long-duration, low-frequency train of stimulation, buildup cells were activated at their typical low-frequency buildup discharge. Thus buildup cells and fixation cells can be active simultaneously,

whereas burst cells can only be activated after cessation of fixation cell discharge.

Some cells in the PPRF of the monkey also have long-lead activity preceding saccades. Long-lead BNs (LLBNs) discharge a burst of action potentials before all ipsiversive saccades but are activated well in advance of a saccade with a sporadic low-frequency rate of discharge (Keller 1974; Luschei and Fuchs 1972). LLBNs receive powerful monosynaptic excitatory input from the SC (Raybourn and Keller 1977), and this input could be mediated by the buildup and burst cells within the SC, because they both project to the contralateral PPRF (Istvan et al. 1994), but only the buildup cells have the long-lead anticipatory activity preceding the saccade.

SACCADE GENERATION. Once a new target has been selected (i.e., almost no fixation cell activity remains in the rostral poles but buildup cell activity has increased), then the burst cells become active (Fig. 13C). This later onset of burst cell activity suggests that it might be either 1) the input from the buildup cells lying below that activates the burst cells in a bottom-up flow of information, as has been suggested previously (Mohler and Wurtz 1976; Wurtz and Albano 1980); 2) a disinhibition produced by cessation of fixation cell activity; or 3) a combination of these events. As in the case of these previous suggestions, we cannot rule out the possibility that the burst cells themselves also get a direct input at a time later than do the buildup cells. Regardless of the source of input to the burst cells, they only begin to burst ~ 20 ms before saccade onset (Sparks 1978; see Fig. 18 in Munoz and Wurtz 1995), which is immediately after the onset of the pause in fixation cells. We suggest that the burst cells may receive the same input as the buildup cells, but they are unable to respond because they are strongly inhibited by activity in the fixation zone of the SC (Munoz and Wurtz 1993c). Thus the critical step in onset of the high-frequency activity of the burst cells may be the disinhibition after onset of the pause in fixation cells.

Our data demonstrate that the size of the active zone in the burst layer remained remarkably constant, regardless of saccade size (see Figs. 10 and 11, A-C), which is consistent with previous observations (Ottes et al. 1986). Using two methods, we estimated that the diameter of the active zone within the burst layer was ~ 1.4 mm, corresponding to activation of roughly 28% of the burst cells lying along the horizontal meridian of the SC during a horizontal saccade. That both methods yielded the same value of active zone diameter strengthens our conclusion that this diameter is ~ 1.4 mm, regardless of saccade direction or amplitude. This constant size of the active region in the burst layer has important implications regarding the organization of connections within the SC that may lead to generation of activity within this layer. It may be that an excitatory input to the burst layer produces a constant size active zone because of invariance in the density and weight of excitatory and inhibitory afferent connections and the intrinsic connections across this layer.

The size of the active zone in the buildup layer at saccade onset was larger than in the burst layer and was dependent on saccadic amplitude (Fig. 11, D-F). We estimated that 40% of the buildup cells lying along the horizontal meridian

were active for 5° horizontal saccades and >60% of the buildup cells were active for saccades of $\geq 20^\circ$. That the fractions of cells active at saccade onset is so different between the burst and buildup layers implies that inputs to or intrinsic connectivity within these layers is organized very differently.

SACCADE TERMINATION. Figure 13D shows schematically the rostral spread of activity in the buildup layer toward the fixation zone, whereas the locus of activity in the burst layer remains stationary and diminishes in intensity. The rostral spread of activity across the buildup layer during the saccade may have important implications in the spatiotemporal transformation that must occur between the SC and the PPRF, where the LLBNs and BNs are located. It was originally hypothesized that this rostral shift in activity that occurred during the movement represented a spatially coded gaze motor error signal (Munoz et al. 1991). The reduction of activity within the burst layer is consistent with previous reports for saccade-related burst cells in the monkey, where the burst peaked around saccade onset and diminished during the saccade, and the movement fields of individual cells were closed (Sparks and Mays 1980; Waitzman et al. 1991). This clear lack of spread of activity among the burst cells probably accounts for some of the hesitation to believe that such a spread occurs in the saccade-related cells in the cat SC (Guitton et al. 1993; Sparks 1993).

Our interpretation of the activity of the buildup cells in the monkey as indicative of a rostral spread of activity raises several questions that are experimentally testable. If the spread of activity in the buildup cells is involved in controlling saccade trajectory, then modification of the activity of the buildup cells lying rostral to the initially active site should perturb the saccade. Initial evidence indicates that such a perturbation does alter at least the trajectory of the saccade (Aizawa and Wurtz 1994). Another question raised by the idea of a spread of activity is the direction of the spread on the two-dimensional map within the SC. Although our current experiments indicate that the spread is rostrally rather than caudally directed, we do not know the extent to which the spread is orthogonal to this axis. Finally, our interpretation of a spread of activity in the buildup layers suggests that a given buildup cell's activity may be the same when the motor error is the same during saccades of different amplitude, and this also can be experimentally determined.

A number of proposals have been made that the SC lies within the internal feedback loop controlling the amplitude of the saccade (Arai et al. 1994; Droulez and Berthoz 1991; Keller 1979; Lefèvre and Galiana 1992; Munoz et al. 1991; Optican 1994; Van Opstal and Kappen 1993; Waitzman et al. 1988, 1991). One recent hypothesis interpreted the clipping of the response of SC burst cells at the end of the saccade as an indication that the monkey SC received feedback during the saccade (Waitzman et al. 1991). Our finding that the reduction in the size of the hill in the burst layer varies with saccade amplitude (Fig. 9) implies that the amount of clipping that occurs during the saccade is dependent on a cell's location on the motor map. This is not consistent with the notion of only the burst cells providing the motor error signal (i.e., the difference between current and desired positions of the visual axis) in a feedback control

model (Waitzman et al. 1991). An alternative hypothesis proposed that feedback to the SC was necessary to shift activity across the motor map in the form of a moving hill (Munoz et al. 1991). According to this hypothesis, the saccade continued until the shifting activity reached the rostral SC, where the fixation cells are located. Activation of the fixation cells would lead to reactivation of the OPNs and the termination of the movement. Larger-amplitude saccades resulted from having the initially active zone placed farther away from the fixation cells, so that more SC surface had to be traversed by the moving hill. We suggest that feedback to the SC is necessary for both the sharp reduction of activity in the burst layer and the shift of activity in the buildup layer, because these events only occur in relation to the saccade. This feedback has been represented in Fig. 13D by the arrows projecting from the PPRF to the burst and buildup layers of the SC. The source and nature of this feedback is unknown and may involve structures other than the PPRF. The nature of this feedback is a central tenet of a new model that has been proposed for the control of saccades (Optican 1994).

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