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# Motor cortical activity preceding a memorized movement trajectory with an orthogonal bend

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**Abstract.** Two monkeys were trained to make an arm movement with an orthogonal bend, first up and then to the left (↰), following a waiting period. They held a two-dimensional manipulandum over a spot of light at the center of a planar working surface. When this light went off, the animals were required to hold the manipulandum there for 600–700 ms and then move the handle up and to the left to receive a liquid reward. There were no external signals concerning the "go" time or the trajectory of the movement. It was hypothesized that during that period signs of directional processing relating to the upcoming movement would be identified in the motor cortex. Following 20 trials of the memorized movement trajectory, 40 trials of visually triggered movements in radially arranged directions were performed. The activity of 137 single cells in the motor cortex was recorded extracellularly during performance of the task. It was found that 62.8% of the cells changed activity during the memorized waiting period. During the waiting period, the population vector (Georgopoulos et al. 1983, 1984) began to grow approximately 130 ms after the center light was turned off; it pointed first in the direction of the second part of the memorized movement (←) and then rotated clockwise towards the direction of the initial part of the movement (↑). These findings indicate processing of directional information during the waiting period preceding the memorized movement. This conclusion was supported by the results of experiments in ten human subjects, who performed the same memorized movement (↰). In 10% of the trials a visual stimulus was shown in radially arranged directions in which the subjects had to move; this stimulus was shown at 0, 200, and 400 ms from the time the center light was turned off. We found that as the interval increased the reaction time shortened for the visual stimulus that was in the same direction as the upward component of the memorized movement.

**Key words:** Motor cortex – Direction of movement – Memorized trajectory – Monkey – Human

## Introduction

Cells in the motor cortex have well-established relations to motor output, muscles, and peripheral somatic input (see Phillips and Porter 1977; Asanuma 1981; Evarts 1981 for reviews). These relations are not rigid but can depend on the behavioral context of the motor task. This has been shown clearly in studies in which the relations of cells to motoneurons were established using spike-triggered averaging, and yet the cells were preferentially activated in some tasks but not in others even when the same muscles were used (Cheney and Fetz 1980; Muir and Lemon 1983).

In other studies it has been shown that the activity of cells in the motor cortex can show changes in the absence of any immediate motor output. Tanji and Evarts (1976) first demonstrated a change in the activity of cells in the motor cortex during an instructed or delay period prior to a movement. This change in activity occurred in the absence of electromyographic (EMG) activity. Since then, changes in motor cortical cell activity during a waiting period have been observed in many other studies (Kubota and Hamada 1979; Godschalk et al. 1981; Kubota and Funahashi 1982; Weinrich et al. 1984; Lecas et al. 1986; Wise et al. 1986; Georgopoulos et al. 1989; Riehle and Requin 1989; Alexander and Crutcher 1990; Hocherman and Wise 1991; Mushiake et al. 1991).

Another concern is the significance of cell activity in the absence of motor output. This has been addressed most extensively by recordings in the premotor cortex, in which the change in cell activity during a delay period has been related to motor intention or set (Weinrich and Wise 1982; Godschalk and Lemon 1983), the visual in-

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struction (Kubota and Hamada 1978; Godschalk et al. 1981; Rizzolatti et al. 1981; Weinrich and Wise 1982; Wise and Mauritz 1985; Mushiake et al. 1991), general anticipatory behavior prior to a predictable event (Mauritz and Wise 1986), or the internal triggering of the movement (Mushiake et al. 1991; Wise et al. 1992). In general, cells in the motor and premotor cortical areas which change activity in the delay period show similar relations to aspects of the upcoming movement, and differences, where they do exist, are quantitative rather than qualitative in nature (Lecas et al. 1986; Riehle and Requin 1989; Alexander and Crutcher 1990; Hocherman and Wise 1991; Mushiake et al. 1991). Finally, more complex processes can be reflected in the activity of motor cortical cells such as spatial trajectory operations (Hocherman and Wise 1991), precuing of directional information (Riehle and Requin 1989), memorized movements (Alexander and Crutcher 1990; Smyrnis et al. 1993), preparation for movement sequences (Clark et al. 1991; Kettner et al. 1991; Marciaro et al. 1991), and processing of directional information (Lurito et al. 1991).

In the present study we focused on the neural mechanisms underlying the generation of a bent trajectory from memory. It is possible that under these circumstances the upcoming trajectory is mentally rehearsed during the delay period. The mental rehearsal of motor acts is common in everyday life and is probably most frequent in certain sports in which the upcoming motor act is mentally rehearsed before performance (Suinn 1984). Moreover, mental rehearsal can improve actual performance (Phipps and Morehouse 1969; Minas 1978; Ryan and Simons 1983). We attempted to gain an insight into the neural mechanisms underlying this process by training monkeys to make a movement with an orthogonal directional bend and reproduce this movement from memory during an internally timed waiting period. We then recorded the activity of single cells in the motor cortex during the performance of this task. We complemented these experiments by measuring the performance of human subjects under similar conditions. We hypothesized that processing of the directional information in the human subjects during the memorized movement task might be reflected in the reaction times of the movements. A preliminary report of this work has been published (Ashe et al. 1992).

## Materials and methods

### *Animal studies*

*Animals.* Two rhesus monkeys (one male and one female, 3.5–4.5 kg body weight) were used.

*Apparatus.* A two-dimensional (2D) planar working surface and an articulated handle were used. The apparatus has been described previously (Georgopoulos et al. 1981; Georgopoulos and Massey 1987). The monkeys grasped the distal end of the handle with their right hand pronated, next to a 5-mm-radius Plexiglas circle. The working surface was a 25 × 25 cm Plexiglas square, tilted 15° from the horizontal towards the animal. For this experiment, the working surface was modified to restrict the motion of the handle along grooves, as shown in Fig. 1. In some cases the grooved surface was replaced by another one, in which the handle could move freely; in this case the animal had to perform the movement within computer-defined positional windows.

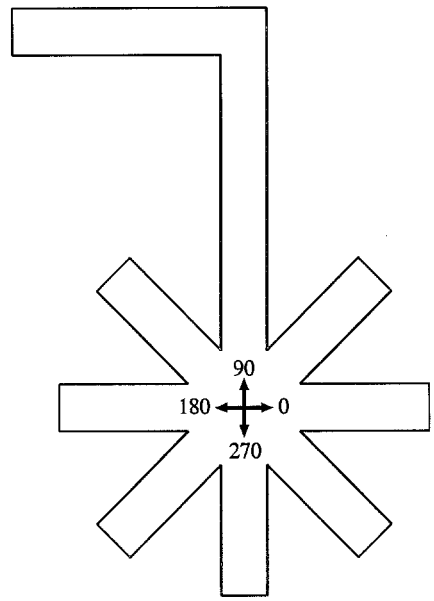


**Fig. 1.** Working surface used in the experiments. The *directional cross* and the *numbers* at the center indicate the convention used when referring to direction in degrees

*Behavioral task.* A trial started after a variable intertrial interval (1–3 s), during which all the lights were turned off. The center light was then turned on and the monkey was required to capture it within a 10-mm-radius, circular positional window ("center window"). After a variable period of time (500–1500 ms) the center light went off. The monkey had to hold the manipulandum at the center for 600–700 ms, then move it up (amplitude 8.3 cm), and then to the left (amplitude 4.7 cm). A liquid reward was given after 250 ms of holding the handle within a 20-mm-diameter window centered on the endpoint of the movement. Twenty trials were performed successively. Then, 40 trials of visually triggered, radially arranged movements were performed as follows. When the center light went off, a peripheral light was lit on a circle of 4 cm radius. The animal was required to move the handle from the center towards the peripheral target. When the animal reached the target window it received a liquid reward. Eight peripheral lights were arranged every 45°, and five trials of each movement were performed in a randomized block design.

*Neural recordings.* After an animal was trained in the task, we recorded the extracellular activity of cells in the motor cortex during the performance of the task. The electrophysiological techniques used to record the electrical signs of activity of single cells have been described in detail previously (Georgopoulos et al. 1982). A multielectrode recording system (Mountcastle et al. 1991) was used.

*Data collection.* A PDP11/34 laboratory minicomputer was used to control the lights on the plane, to monitor and record behavior, and to collect data. Neural data were collected as interspike intervals with a resolution of 0.1 ms. The position ($x$, $y$) of the manipulandum was sampled every 10 ms with a resolution of 0.125 mm.

*Data analysis.* Standard analysis (Sokal and Rohlf 1969; Winer 1971; Mardia 1972; Snedecor and Cochran 1980) and display (rasters, histograms, etc.) techniques were used to inspect, evaluate, and analyze the data. The BMDP/386 statistical package (Los Angeles, Calif.) was used in some of the analyses. For the purposes of analysis there were nine movement "classes": one was the memorized movement and the remaining were the eight movements to each of the eight visual targets.

*Behavioral epochs.* In the *memorized trajectory task*, the *control period* was from the time the animal captured the center light until this light was turned off. The *minimum waiting period* was 600–700 ms. Since there was not any target light in this task, there was no reaction time (RT). The time from the end of the minimum waiting period (600–700 ms) until the handle exited the center window was the *immediate premovement time*. The *movement time* was the time from exiting the center window until the endpoint window was entered. Finally, the *endpoint hold time* was the time during which the animal held the manipulandum within the endpoint window.

In the *visually triggered task*, the center hold and movement times were defined as above. The RT was from the time that the target light appeared until the handle exited the center window. The *target hold time* was the time during which the animal held the handle within the target window.

A paired *t*-test (Snedecor and Cochran 1980) was used to assess the statistical significance of the change in mean cell activity from the center hold period (control period) during the first three successive 200-ms epochs of the waiting period. In the visually triggered task, the change in cell activity was assessed during the RT.

*Directional analyses.* The *directional tuning* was analyzed from the frequency of discharge during the RT in the visually triggered task. The *preferred direction* was calculated using standard directional statistics (Mardia 1972). The value of the preferred direction thus calculated is identical to that calculated using multiple regression statistics (Georgopoulos et al. 1982). For the statistical significance of the directional tuning we used a nonparametric, statistical bootstrapping technique (Lurito et al. 1991) to determine whether the frequency of cell discharge during the RT was directionally tuned. This technique has an advantage over the multiple regression and other techniques used before (Georgopoulos et al. 1982) in that it does not depend on distributional assumptions for a test of statistical significance which, in this case, is generated from the data themselves.

The *neuronal population vector* is the weighted sum of vectorial contributions of individual cells (Georgopoulos et al. 1983, 1984, 1986, 1988). It provides information concerning the directional tendency of the neuronal ensemble and can be calculated from the average cell discharge in a particular epoch (Georgopoulos et al. 1983, 1986) or in an ongoing, time-varying fashion (Georgopoulos et al. 1984, 1988). For the calculation of the population vector, peristimulus time histograms (10 ms bin width) were centered on the time that the center light went off and computed using counts of fractional intervals as a measure of the intensity of cell discharge. For a given time bin, each cell made a vectorial contribution in the direction of its preferred direction and of a magnitude equal to the change in cell activity from that observed during 400 ms preceding the onset of the peripheral stimulus ("control rate," i.e., while the monkey was holding the handle at the center of the plane). For the visually triggered task and the memorized trajectory task the population vector $\mathbf{P}$ for the $j^{th}$ class and $k^{th}$ time bin is

$$\mathbf{P}_{j,k} = \sum_{i}^{N} w_{i,j,k}\, \mathbf{C}_i \qquad (1)$$

where $\mathbf{C}_i$ is the preferred direction of the $i^{th}$ cell and $w_{i,j,k}$ is a weighting function

$$w_{i,j,k} = (d_{i,j,k}) - a_{i,j} \qquad (2)$$

where $d_{i,j,k}$ is the square-root transformed discharge rate of the $i^{th}$ cell for the $j^{th}$ movement class (see above) and $k^{th}$ time bin, and $a_{i,j}$ is the similarly transformed control rate of the $i^{th}$ cell for the $j^{th}$ class. The square-root transformation was used as a variance stabilizing transformation for counts (Snedecor and Cochran 1980; Tukey 1977). The statistical significance of the population vector was assessed by using the modified Rayleigh test (Moore 1980). This test is sensitive to nonrandom concentration or scatter of vector angles.

### *Human studies*

*Subjects.* Ten healthy human volunteers (three women and seven men) participated in this experiment. They were naive to the purpose of the experiment. All subjects but one were right-handed and all performed with their preferred hand.

*Behavioral tasks.* A Silicon Graphics workstation (4D/210 GTX) was used to implement the tasks. The clock resolution was set at 1200 Hz. Subjects were seated 50 cm in front of the monitor. They moved the mouse in required directions on a horizontal working surface placed in the midsagittal plane. The mouse controlled the position of a red cursor (i.e., +) on the display. The subjects performed two tasks in the following sequence. (1) in the visually triggered task they moved the cursor in visually specified directions, from the center of the display to one of eight radially arranged visual targets. First, a black dot (0.3 cm radius) appeared at the center of the display and the subject had to capture it with the cursor. After a delay of 750–1000 ms the center dot disappeared while a peripheral, similar black dot appeared on an imaginary circle of 2.5 cm radius. The subject had to move the mouse quickly so that the cursor moved in the direction of the stimulus. They were not required to stop on the peripheral target. Ten trials for each direction were performed in a randomized block design. (2) The memorized plus visually triggered task consisted of two parts, the practice and the experiment itself. In the first part, used for practice, the subjects had to move the cursor up and to the left (⌜), within the limits shown on the display. Each segment of the trajectory was 5 cm long and 1.5 cm wide. First the subjects captured the black dot in the center of the display for 750–1000 ms. Then the black dot disappeared and the subjects had to wait during a period of at least 600 ms before initiating the movement. No indications were given when to move. It was never suggested to the subjects that they mentally rehearse the memorized trajectory in the delay period before the movement. The subjects had to move within the limits shown on the display, stop at the end of the trajectory, and hold there for at least 500 ms. At the end of each trial the subjects were informed whether the trial was correct or not. After 100 correct trials the practice finished and the second part of the task began, that is, the experiment itself. In this part, the up-and-to-the-left trials were randomly mixed with visually triggered trials (10% of total number of trials). In the visually triggered trials a peripheral stimulus appeared with a delay of 0, 200, or 400 ms after the center one disappeared. The same eight radially arranged positions of the peripheral stimulus used in the visually triggered task above were used in this task. Five trials for each direction and delay were performed, giving a total of 120 visually triggered trials which were randomly intermixed with 1080 up-and-to-the-left trials.

*Data analysis.* The experimental variable of interest was the RT of the visually triggered trials, which was measured from the presentation of the peripheral stimulus until when the cursor exited a central circle of 0.3 cm radius. The analyses were performed on the mean RT averaged over the repetitions of each condition for each subject. The mean RT of the visually triggered trials in the memorized plus visually triggered task was analyzed using an analysis of variance with the *delay* and the *direction* as within factors. The same analysis of variance was applied to the RT difference between the memorized plus visually triggered task and the visually triggered task. The immediate premovement time was computed for the up-and-to-the-left trials by subtracting the minimum delay of 600–700 ms from the time of movement onset.

## Results

### *Animal studies*

*Neuronal results: general.* The activity of 137 arm-related cells was recorded in the arm area of the motor cortex

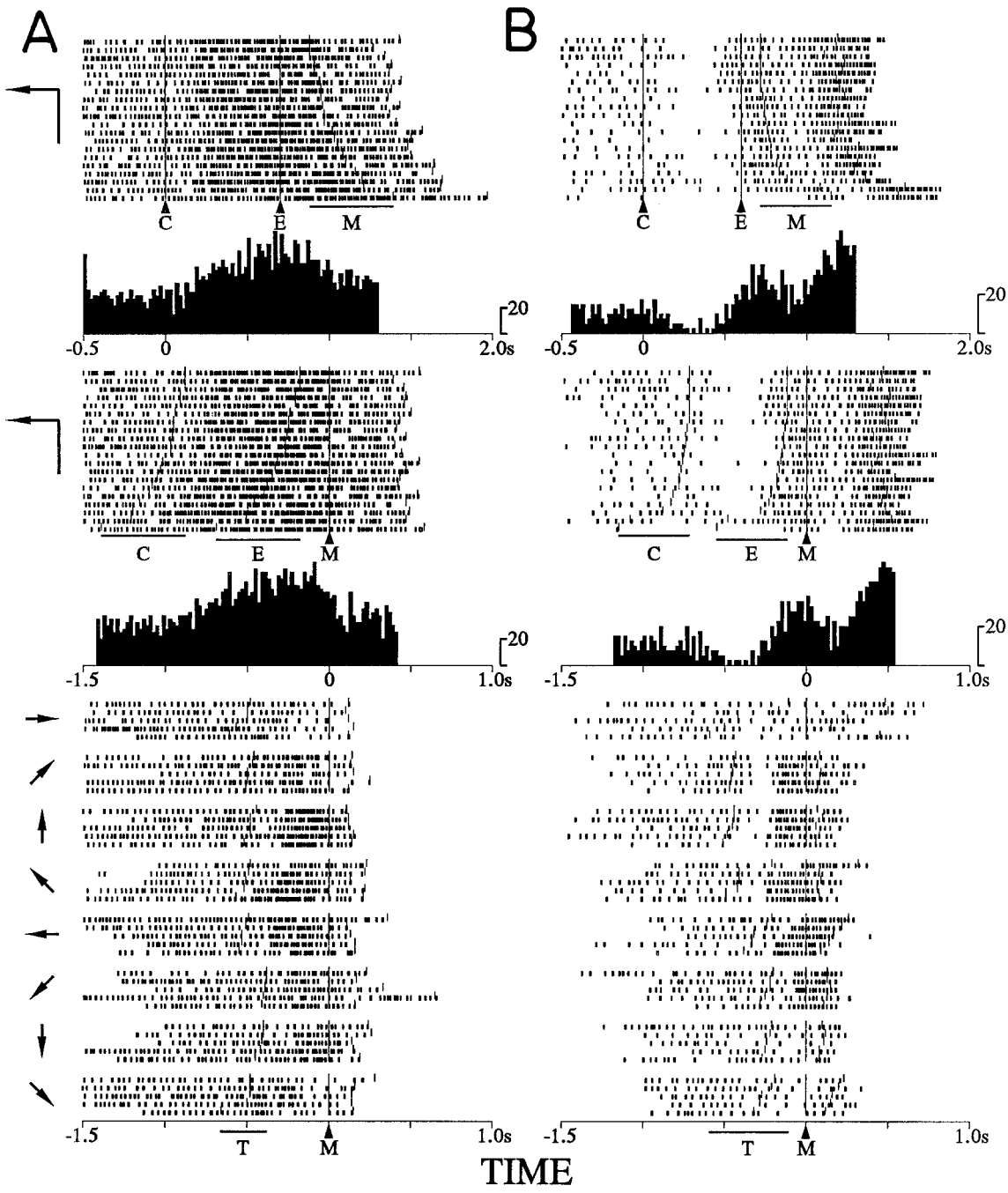


**Fig. 2A,B.** Changes in cell activity during the memorized period. Impulse activity (*short vertical bars*) of two cells (**A** cell Si032/5; **B** cell Pi066u/3) in the tasks used. For each cell, the following are plotted. At the *top*, 20 trials of impulse activity are shown aligned to the onset (*C*) of the delay (i.e., the time that the center light went off). Subsequent, *longer vertical bars* indicate the end (*E*) of the waiting period, the exit of the handle from the center (*M*), and the entrance into the endpoint window (not labeled). The *vertical scale* in the histogram is impulses per second. In the *middle*, the same data are plotted aligned to the exit of the handle from the center window. At the *bottom*, five trials of visually triggered movements in the direction shown to the *left* of the rasters are shown aligned to the exit (*M*) of the handle from the center window. The *longer vertical bar preceding M* indicates the onset of the visual target (*T*). *Filled triangles* indicate fixed events; *horizontal bars* are the range of the time for the event indicated below them

(two hemispheres, two animals). Many cells were recorded simultaneously (see Materials and methods). Each cell changed activity in relation to proximal movements of the contralateral arm, as judged by examination of the animal outside the behavioral task. Cells that changed activity in relation to distal movements (e.g., of the hand and/or fingers) were not studied because the movements of the manipulandum in the task were produced by motion about the proximal joints (shoulder and elbow). No obvious responses to visual stimuli (e.g., flashes of light) were observed.

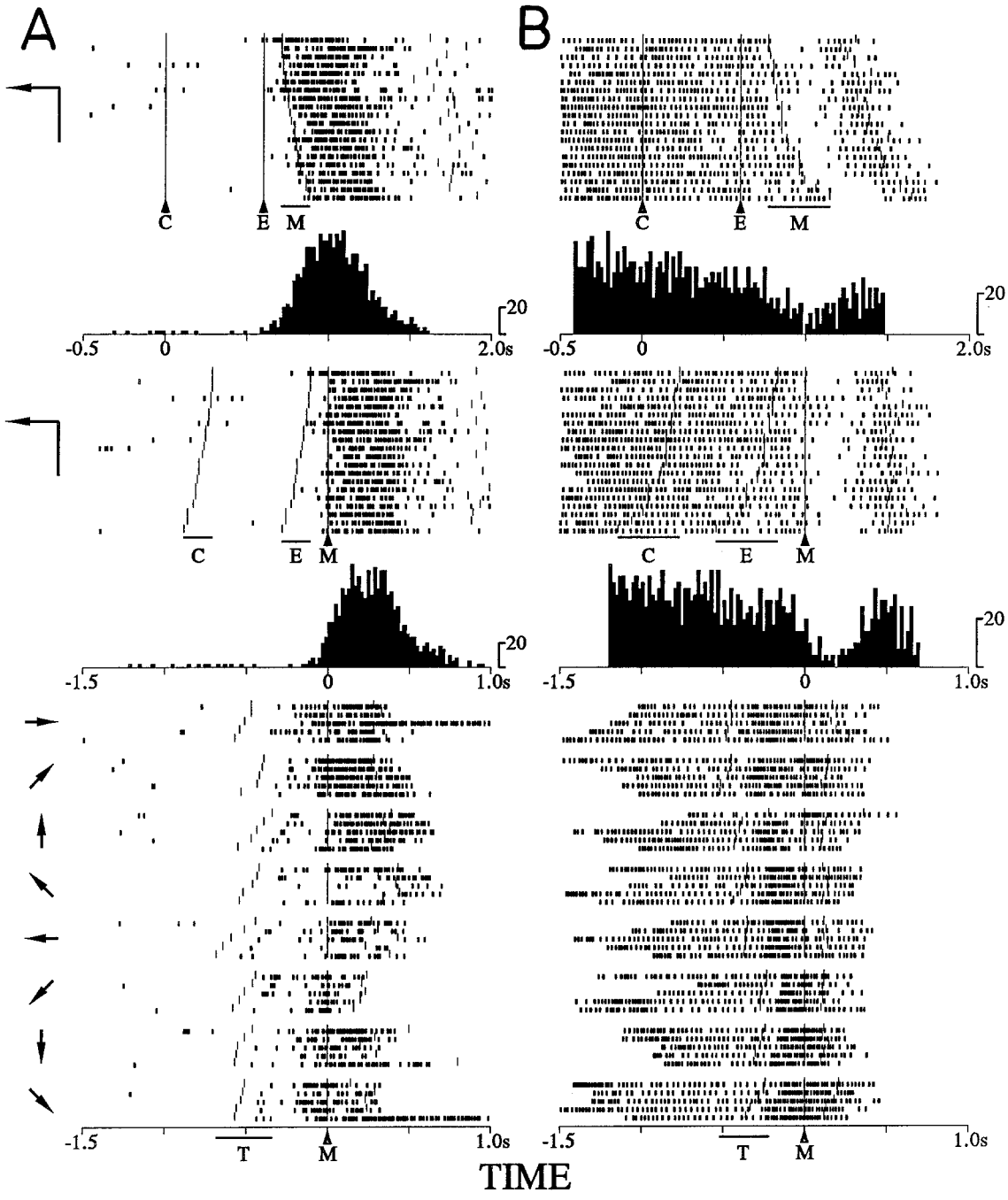


**Fig. 3A,B.** Changes in cell activity after the memorized period. **A** Cell Pi001/6; **B** cell Pi046u/1. Conventions as in Fig. 2

**Table 1.** Number of cells that changed activity (first increase or decrease) during the waiting period

| | Epochs during the waiting period (ms) | | | |
|---|---|---|---|---|
| | 0–200 | 200–400 | 400–600 | Total |
| Increase | 7 | 17 | 15 | 39 |
| Decrease | 18 | 14 | 15 | 47 |
| Total | 25 | 31 | 30 | 86 |

Each cell was entered only once in the table

*Behavioral performance.* The animals performed at 56% and 95% accuracy in the memorized and visually triggered task, respectively. The immediate premovement time (see Materials and methods) in the memorized trajectory task was $304 \pm 162$ ms (mean $\pm$ SD) and the movement time, $650 \pm 222$ ms ($n = 1850$ trials). The RT in the visually triggered task was $421 \pm 104$ ms ($n = 3708$ trials).

The animals moved along the bent trajectory equally well in the presence or absence of grooves. Apparently, the animals had memorized the trajectory, because they performed accurately on the first occasion that the grooves were removed.

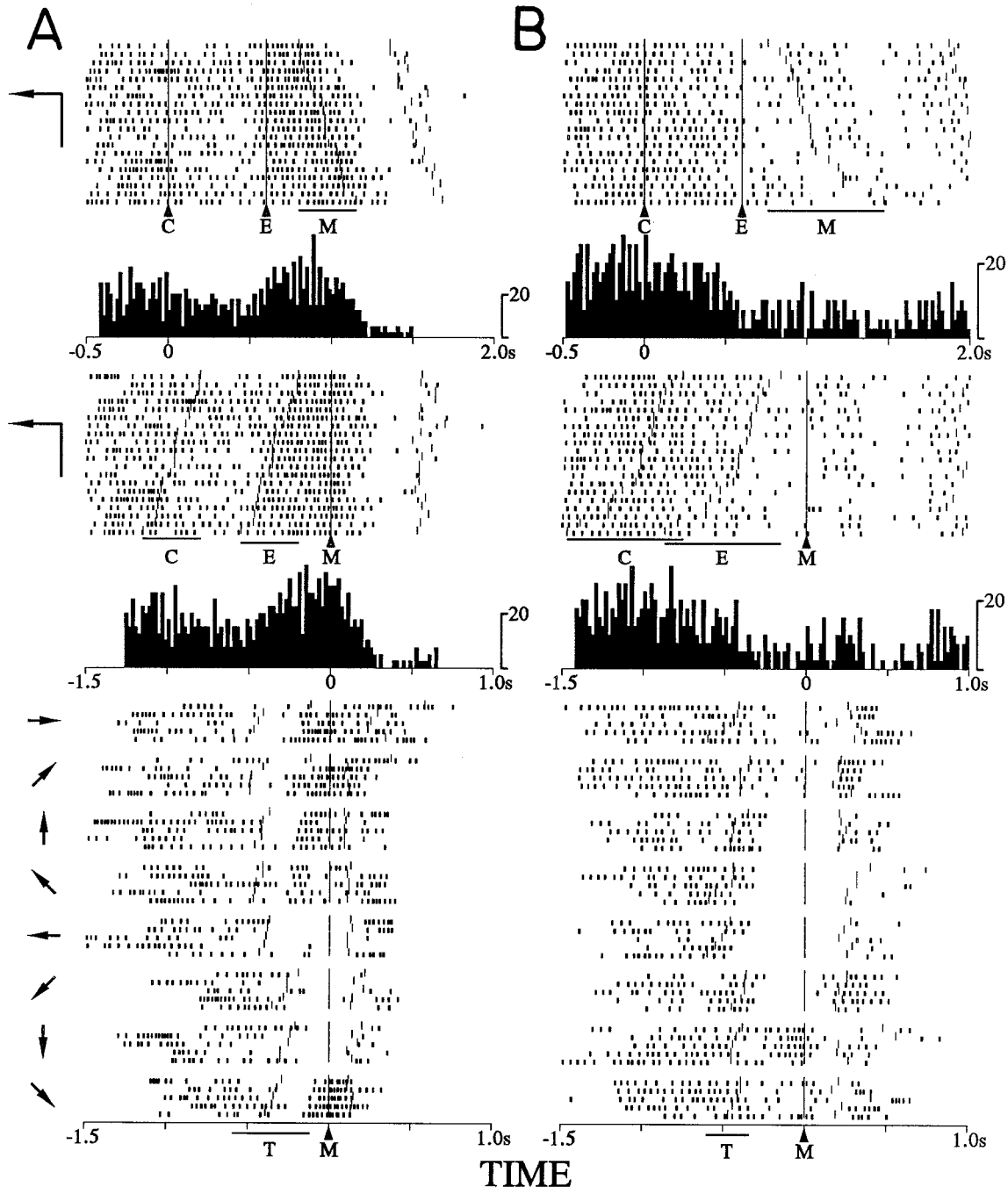


**Fig. 4A,B.** Changes in cell activity close to the end of the memorized waiting period. **A** Cell Pi041u/6; **B** cell Pi011/5. Conventions as in Fig. 2

*Kinematic data.* The average peak velocity in the upward movements in the visually triggered task was 159.8 ± 37.2 mm/s (mean ± SD; $n$ = 464 trials). The average peak velocity of the leftward movements in the same task was 141.8 ± 45.5 mm/s ($n$ = 463 trials). In the memorized task there were two velocity peaks: the first during the upward movement and the other during the movement to left. The average values of the velocity peaks were 289.0 ± 96.9 mm/s and 154.7 ± 28.1 mm/s ($n$ = 1850 trials), respectively. The peak velocities for the upward and leftward movements in the memorized task were significantly higher than the corresponding movements in the visually triggered task ($P < 0.001$, $t$-test).

*Single cell activity.* Cell activity in the *visually triggered movements* task was similar to that previously observed (Georgopoulos et al. 1982).

In the *memorized trajectory trials*, 86 of 137 (62.8%) cells changed activity during the waiting period ($P < 0.05$, paired $t$-test; Table 1). Examples are shown in Fig. 2. Other cells did not change activity until after the 600-ms minimum waiting time was over, as shown in Fig. 3. Oc-

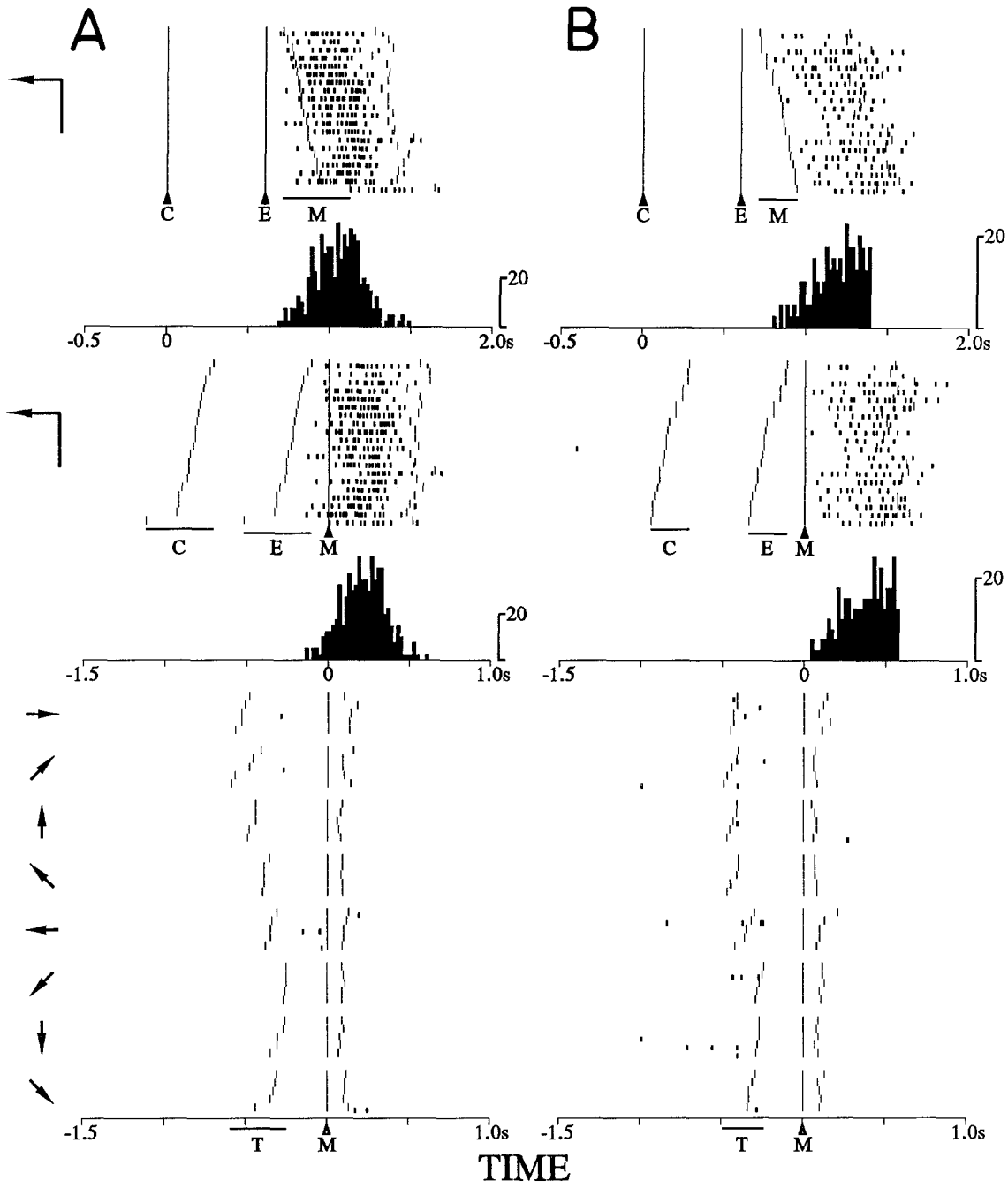


**Fig. 5A,B.** Changes in cell activity only during the memorized movement task. **A** Cell Pi054u/6; **B** cell Pi062u/4. Conventions as in Fig. 2

casionally, cell activity changed at almost exactly 600 ms after the center light was turned off (Fig. 4). A few cells were observed that changed activity exclusively during the memorized movement task. Interestingly, these changes occurred after the waiting period and during the movement; examples are shown in Fig. 5. The cell activation was confirmed in a second set of recordings. Finally, cells were found that changed activity only in the visually triggered movement task (Fig. 6).

*Directional analyses.* Of the 137 cells recorded, 101 (73.7%) were directionally tuned (see Materials and methods). Their preferred directions ranged throughout the directional continuum and were uniformly distributed (Rayleigh test). There was a highly significant association ($\chi^2$ (1) = 7.02, $P < 0.008$; Table 2) between the presence of directional tuning and the change in activity during the waiting period: the percentage of tuned cells was much higher in the group that changed activity during the waiting period than in the group that did not change their activity (81.4% vs 60.8%, respectively).

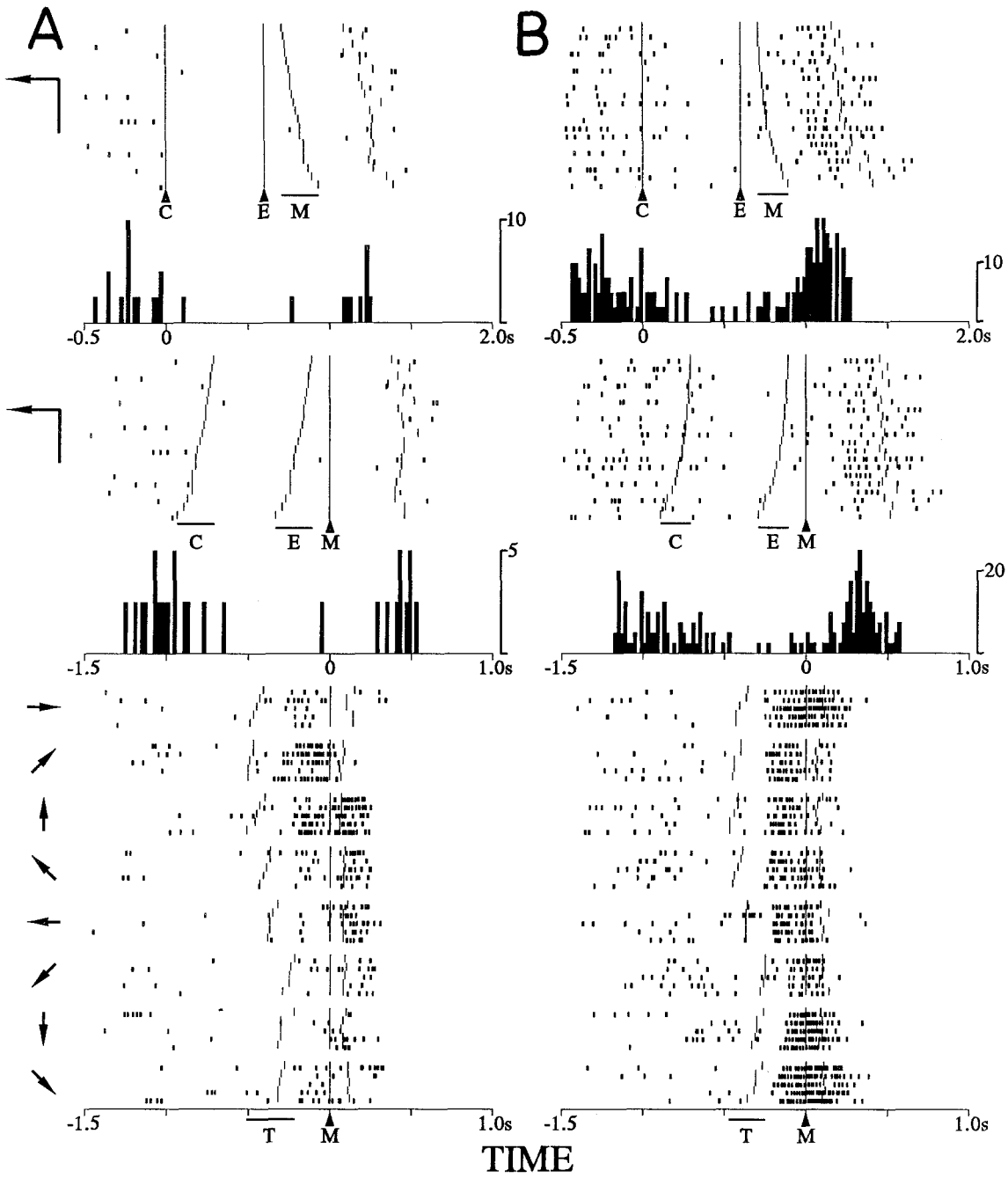


**Fig. 6A,B.** Changes in cell activity only during the visually triggered movement task. **A** Cell Pi055u/6; **B** cell Pi063u/4. Conventions as in Fig. 2

**Table 2.** Directional tuning of cells that changed activity during the waiting period

| | Change in activity during the waiting period | | | | |
|---|---|---|---|---|---|
| | Present | | Absent | | Total (*n*) |
| | *n* | % | *n* | % | |
| Tuned | 70 | 81.4 | 31 | 60.8 | 101 |
| Not tuned | 16 | 18.6 | 20 | 39.2 | 36 |
| Total | 86 | 100 | 51 | 100 | 137 |

*Population vector analysis.* During *visually triggered movements*, the population vector pointed in the direction of the radially arranged targets.

In the *memorized movement task*, the direction of the population vector changed systematically during the waiting period (Fig. 7). It pointed first near 180° and then rotated clockwise towards 90°, where it stabilized, preceding the initial part of the movement in that direction; later on, it rotated counterclockwise in the direction of the second part of the directionally bent trajectory. The length of the population vector is plotted against time in

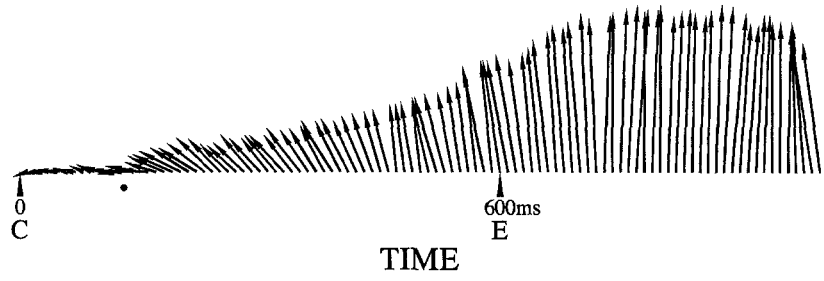


**Fig. 7.** Neuronal population vectors are plotted every 10 ms vs time. *C*, onset of the delay; *E*, end of the waiting period. The *filled circle* on the abscissa indicates the time after the beginning of the delay (130 ms) at which the population vector reached statistical significance

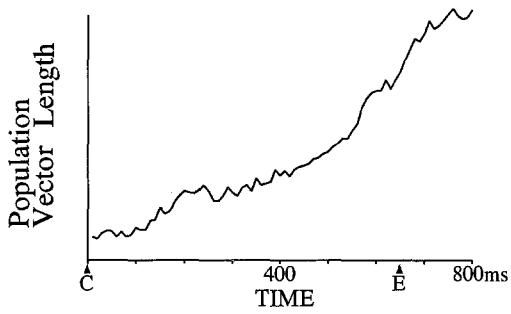


**Fig. 8.** The length of the population vector vs time. *C*, onset of delay; *E*, end of waiting period.

Fig. 8, showing that the signal increased gradually during the waiting period. The population vector reached statistical significance ($P<0.05$, modified Rayleigh test, see Materials and methods) 130 ms after the beginning of the delay. Figure 7 shows that at this point the population vector was pointing in the leftward direction, similar to the direction of the final part of the movement in the memorized trajectory.

*Directional engagement of cells during the waiting period.* The analyses above dealt with the neuronal population vector. However, a different insight into the process unfolding during the waiting period can be gained by analyzing the directional properties of cells engaged during that period. Given that directionally tuned cells were preferentially engaged during the waiting period (Table 2; see above), we analyzed the distributions of the directional influences exerted by the cells that changed activity during each of the three 200-ms epochs of the waiting period (see Materials and methods): if the cell activity increased, the cell was taken to exert a unit-length directional influence in its preferred direction; if the activity decreased, the opposite direction was taken. Frequency distributions of these directions were then constructed and plotted. The following can be seen in Fig. 9. First, the directional influences of cells recruited in each of the three epochs are widely distributed. Second, the distribution of the directional influences of cells recruited during the first 200 ms of the waiting period is skewed towards a leftward direction; indeed, the mean direction (Mardia 1972) of this distribution is at 186.5° and it is statistically significant (mean resultant 0.379, $n=22$, $P<0.05$, Rayleigh test). Third, there is a clockwise shift in the directional influences of cells recruited during the second 200 ms of the waiting period; the mean direction is now at 116.8° (length of mean resultant 0.475, $n=27$, $P<0.01$, Rayleigh test). Finally, there is a further clockwise shift in the directional influences of cells recruited during the last 200 ms of the waiting period, but this is not statistically significant. Of course, the ongoing weighted contributions of all these cells are combined to yield the neuronal population vector (see above); but this analysis showed (a) that the directional contributions by single cells were distributed and not restricted to a narrow set of directions and (b) that there was a shifting directional engagement of cells, from the leftward (←) to the upward direction (↑).

*Location of recordings.* The recording sites for both animals were in the crown and the exposed part of the precentral gyrus (Brodmann's area 4; Fig. 10).

## *Human studies*

The mean ($\pm$SD) of the immediate premovement time in the memorized movement trials was $204\pm38$ ms. Con-

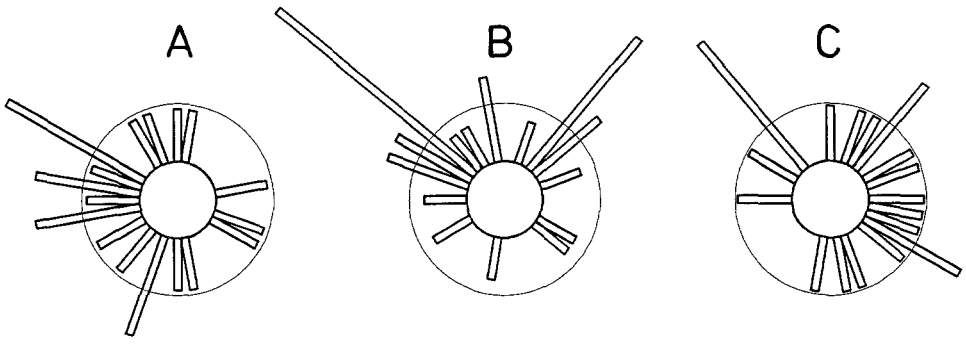


**Fig. 9A–C.** Polar plots of directional influences of single cells during the first three successive 200-ms epochs of the waiting period. **A** 0–200 ms; **B** 200–400 ms; **C** 400–600 ms. *Bars* are plotted in the middle of 10° directional bins. The length of a bar indicates the percentage of cells making directional contributions within a particular bin. The *center circle* represents 0 and the *outer circle* 5% change

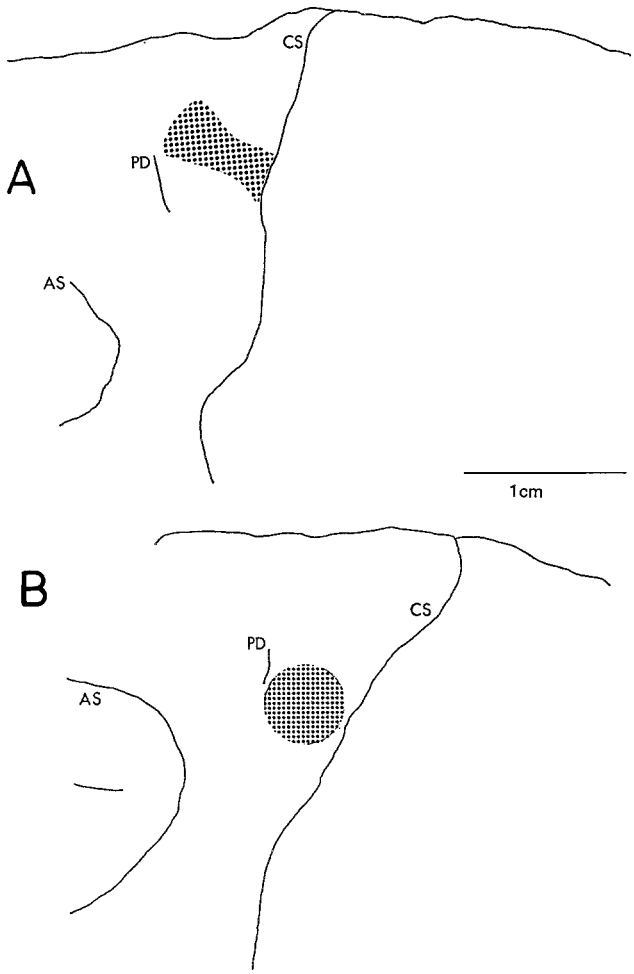


**Fig. 10A,B.** Sites in the cortex of the two monkeys from which recordings were made. *CS*, central sulcus; *PD*, precentral dimple; *AS*, arcuate sulcus

cerning the RT for the visually triggered trials, there were two main findings. First, the RT to the visually triggered stimuli was longer by $188 \pm 69$ ms ($P < 0.0001$, $F$ test in the analysis of variance) when the trials were made within the context of the *memorized task* (RT $504 \pm 65$ ms; zero delay – see Materials and methods) than within the *visually triggered task* (RT $316 \pm 38$ ms). Second, the RT to the visual stimuli generally decreased as the delay increased (delay main effect, $P < 0.0001$, $F$ test). Moreover, the change of RT with the delay depended on the direction (delay × direction interaction, $P < 0.0001$, $F$ test). The reduction of the RT between the 0- and 200-ms delay conditions was significant (paired $t$-test with $P < 0.05$) for all upward directions ($90 \pm 45°$). However, the reduction in the RT between the 200- and 400-ms delay conditions was significant for the directions of 90° and 270°. These effects can be observed in Fig. 11, in which radial plots are used to compare the RT of the visually triggered responses for all directions at zero delay within the memorized task and in the visually triggered task, and also to compare the RT of the responses at a delay of 0, 200, and 400 ms within the visually triggered responses in the memorized task.

## Discussion

The neural mechanisms underlying the planning and execution of complex movement trajectories with directional bends are largely unknown. The importance of the parietal cortex in this process has been shown by the results of lesion experiments (Petrides and Iversen 1979). On the other hand, the involvement of the motor cortex in the specification of the direction of movement is well documented (Georgopoulos et al. 1982, 1984, 1988; Kalaska et al. 1989; Caminiti et al. 1990), as is that of other motor structures (Kalaska et al. 1983; Fortier et al. 1989; Caminiti et al. 1991). It is thus reasonable to suppose that many structures cooperate in this process. Hocherman and Wise (1991) produced strong evidence for the involvement of motor and premotor cortical areas in planning movements through memorized trajectories in 2D space. The memorized movement task we used in these experiments was unique in several respects. First, the animal had to generate from memory a complex movement trajectory involving a change in direction. Second, the movement was truly internally generated: there was no "go" signal to trigger the movement. And third, there was never a visual signal, either during the recordings or during the training of the animals, to indicate the endpoint of the movement: therefore, the movement was internally

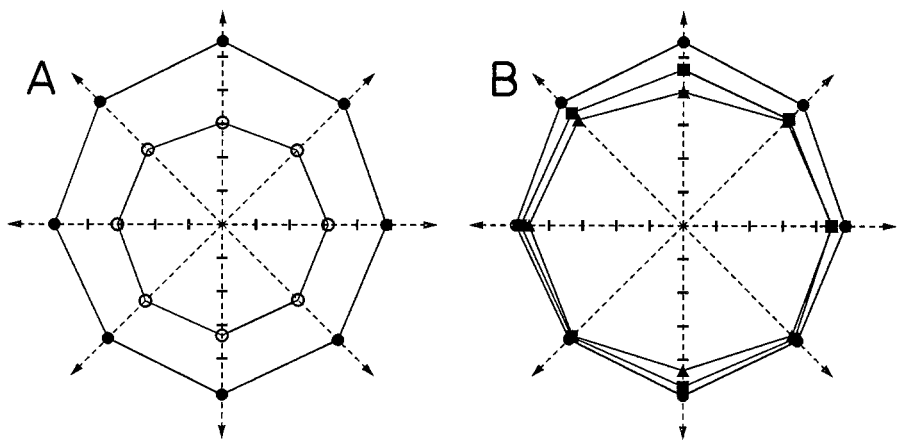


**Fig. 11A,B.** Human studies. **A** Radial plots of the averaged reaction time for all subjects in the visually triggered movement task performed (a) outside the memorized movement task (*open circles*) and (b) at zero delay in the memorized movement task (*filled circles*; see text for explanation). **B** Radial plots of the averaged reaction time for all subjects in the visually triggered movement task performed at 0 (*filled circles*), 200 (*filled squares*) and 400 ms (*filled triangles*) delay during the memorized movement task (see text for explanation). *Arrows* indicate direction of movement. The center of each plot is at 0 ms and each division is 100 ms

planned. We hoped that the activity of some cells, in the waiting period before the movement, might reflect the strategies used for the generation of the memorized trajectory.

A variety of patterns of cell activity was observed during the different epochs in the memorized movement task. For example, some cells changed activity in the memorized task, but only after the waiting period (Fig. 3). Therefore a change in activity during the waiting period was not a prerequisite for the successful performance of the task or for movement related activity during it. Occasional cells showed a change in activity almost exactly 600 ms after the beginning of the delay period (Fig. 4), as if signaling the end of the imposed waiting period. These observations provide neurophysiological evidence for the hypothesis concerning the independence of the processes involved in the planning and triggering of motor responses, as suggested on psychophysical grounds (Favilla et al. 1989).

Finally, the observation that cells could be active exclusively in the memorized (Fig. 5) or in the visually triggered task (Fig. 6) supports the idea that different processes may underlie the generation of the motor output in these tasks. It is possible that in the memorized task the two movements were grouped in a new behavioral unit rather than being merely the composite of the upward and leftward movements, as they were performed in the visually triggered task. In addition, there was a difference in the kinematics of the movements in the two tasks: the average peak velocity of the upward movement in the memorized task was twice that of the upward movement in the visually triggered task. This finding may relate to the greater amplitude of the movement in the memorized task (8.3 cm) than in the visually triggered task (4 cm) or may reflect different underlying processes in the two movements. The difference in peak velocity, though it could obviously affect cell activity, may not fully account for the presence of relatively brisk movement-related activity in the one case and its complete absence in the other.

### *Neural activity during waiting*

One of the main findings of this study was that 62.8% of the cells studied showed changes in activity during the waiting period. This is in accordance with the results of previous studies that have shown involvement of motor cortical cells in memorized movement tasks (Alexander and Crutcher 1990; Hocherman and Wise 1991; Smyrnis et al. 1993). In the present study there were several factors to which the change seen in the activity of single cells during the waiting period could relate, such as motor attention, preparation for the upcoming movement, internal timing, activation of muscles, memory-related processes, a mental rehearsal of the upcoming movement, etc. The exact contribution of each one of these factors is unclear. A plausible explanation for the cell activity observed during the waiting period could be that it relates to changes in the activity of some muscles. Since we did not record muscle activity in this study, we cannot reject this possibility. However, we deem it unlikely, since in previous studies we have not observed consistent changes in EMG activity during the waiting period in instructed (Georgopoulos et al. 1989) or memorized (Smyrnis et al. 1993) delay tasks. Moreover, several other workers recording in the motor cortex have also failed to find concomitant EMG activity during a delay period prior to movement (Tanji and Evarts 1976; Kubota and Hamada 1979; Godschalk et al. 1981; Kubota and Funahashi 1982; Weinrich et al. 1984; Lecas et al. 1986; Wise et al. 1986; Riehle and Requin 1989; Alexander and Crutcher 1990; Mushiake et al. 1991). The activity of the cells that we observed may well relate to preparation for movement, but this explanation in itself gives little information about the process involved.

### *Processing of directional information*

Since the memorized trajectory involved two movement directions, it is reasonable to expect that the activation seen during the waiting period might reflect the processing of directional information. This idea was supported by the results of human studies in which we measured the RT of movements toward visual targets presented randomly at the beginning of and during the waiting period in the memorized trajectory task. The results obtained suggest two points. First, the finding that the RT was longer for the visually triggered trials when they were embedded in the *memorized task* suggests that the process of the memorized movement interfered in some way with the processing of the visually triggered movements; for example, the subjects could have been processing continuously some information during the delay period, although the up-and-to-the-left movements were quite simple and well practiced. Second, the kind of information processed seemed to change during the delay period, as the RT was influenced both by the delay and the direction of the visual stimulus.

The hypothesis that the neural activation seen during the waiting period relates to processing of directional information is strengthened by the observation in the monkey that directionally tuned cells were preferentially recruited during this period (Table 2). It was then worth examining the directional contributions of these cells. Overall, these contributions initially pointed in a leftward direction and then shifted clockwise toward the upward direction (Fig. 9); these directions are those of the second and first component of the bent trajectory, respectively. Therefore, it seems as if a directional processing of the upcoming movement directions did occur during the waiting period, but this processing was *in a reverse order* to the temporal sequence of the directions in the actual movement. This finding was further validated by observing the changes in the direction of the neuronal population vector (which is the weighted vector sum of directional cell contributions): the population vector showed a similar shift, from a leftward direction initially to an upward direction later in the waiting period. Whether this process reflects a true backward rehearsal of the upcoming trajectory or another process is unclear. The im-

portant point is that, whatever the *true* nature of the process (e.g., attention, motor set, etc.), at face value it does involve the processing of directional information, and this information is processed in a particular order.

The fact that at the end of the waiting period the population vector should point, and indeed pointed, in the direction (upward) of the initial part of the upcoming movement is not surprising, since this has been shown previously to be the case in instructed (Georgopoulos et al. 1989) and memorized delay tasks (Kettner et al. 1991; Smyrnis et al. 1993). But this requirement should not limit a commonly contemplated forward rehearsal of the trajectory, as the time for the required rotation of the population vector should be well within the 600-ms waiting period. If, however, the mental rehearsal needs to be *temporally* as well as *spatially* congruent with the upcoming movement, and if the population vector at the end of the waiting period must point in the direction of the initial direction of the movement trajectory, then the rehearsal in reverse is the only way in which the problem can be solved. This could be an explanation of the present findings, given that the minimum waiting period *imposed* was 600–700 ms and the average *performed* movement time of the bent trajectory was 650 ms (see Results). Thus, the results obtained could reflect the adaptation of a rehearsal strategy to the specific timing requirements of the task.

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