

Temporal Encoding of Movement Kinematics in the Discharge of Primate Primary Motor and Premotor Neurons

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SUMMARY AND CONCLUSIONS

1. Several neurophysiological studies of the primary motor and premotor cortices have shown that the movement parameters direction, distance, and target position are correlated with the discharge of single neurons. Here we investigate whether the correlations with these parameters occur simultaneously (i.e., parallel processing), or sequentially (i.e., serial processing).

2. The single-unit data used for the analyses presented in this paper are the same as those used in our earlier study of neuronal specification of movement parameters. We recorded the activity of single neurons in the primary motor and premotor cortices of two rhesus monkeys (*Macaca mulatta*) while the animals performed reaching movements made in a horizontal plane. Specifically, the animals moved from a centrally located start position to 1 of 48 targets (1 cm²) placed at eight different directions (0–360° in 45° intervals) and six distances (1.4–5.4 cm in 0.8-cm increments) from the start position.

3. We analyzed 130 task-related cells; of these, 127 (99 in primary motor cortex, 28 near the superior precentral sulcus) had average discharges that were significantly modulated with the movement and were related to movement direction, distance, or target position. To determine the temporal profile of the correlation of each cell's discharge with the three parameters, we performed a regression analysis of the neural discharge. We calculated partial R^2 's for each parameter and the total R^2 for the model as a function of time.

4. The discharge of the majority of units (73.2%) was significantly correlated for some time with all three parameters. Other units were found that correlated with different combinations of pairs of parameters (21.3%), and a small number of units appeared to code for only one parameter (5.5%). There was no obvious difference in the presence of correlations between cells recorded in the primary motor versus premotor cortices.

5. On average we found a clear temporal segregation and ordering in the onset of the parameter-related partial R^2 values: direction-related discharge occurred first (115 ms before movement onset), followed sequentially by target position (57 ms after movement onset) and movement distance (248 ms after movement onset). Some overlap in the timing of the correlation of these parameters was evident. We found a similar sequential ordering for the latency of the peak of the R^2 curves (48, 254, and 515 ms after movement onset, respectively, for direction, target position, and distance). The partial R^2 profile for direction had a higher peak value but a shorter duration than that for both target location and distance. An additional set of univariate regression analyses demonstrated that the sequential ordering of the correlations was preserved, with direction occurring first and distance last.

6. For some cells that were related to two or more parameters, the partial R^2 's waxed and waned in a reciprocal manner during the transition period. A high partial R^2 for one parameter at a given moment in time was often associated with a low partial R^2 for the other parameter. We developed an index of simultaneity and measured the degree to which cell firing was correlated signifi-

cantly with the two parameters during these transition periods. During the transition period from direction to target position, a large number of cells had a low index of simultaneity, indicating that the discharge of these cells is correlated with only one parameter at a time.

7. The timing differences in the parameter-related discharge of motor and premotor neurons have three implications. First, these parameters are processed serially. Second, because each parameter has a relatively distinct time course, the correlations with direction, X-Y position of the target, and movement distance exhibit considerable independence. Third, the observation that distance modulation mostly occurs after the time of peak velocity suggests that the distance coding does not specify the movement velocity. These results demonstrate that single cells can encode multiple parameters by a temporal parcellation scheme. This scheme avoids the ambiguities of firing rate simultaneously encoding more than one parameter.

INTRODUCTION

The parameters or variables that are controlled by the nervous system during reaching movements, and the means by which this control is achieved, have been subjects of much debate and experimentation (e.g., Hollerbach and Atkeson 1987; Kalaska 1991; Soechting and Flanders 1991; Stein 1982). Psychophysical studies have suggested that the kinematic parameters direction and distance are coded as distinct variables (Favilla et al. 1989; Larish and Frekany 1985; Rosenbaum 1980; Soechting and Flanders 1989a). Both parameters have been incorporated into theoretical schemes (Bullock and Grossberg 1988; Soechting and Flanders 1989a,b). However, there has been some disagreement regarding the order and importance of these two parameters (Favilla et al. 1989; Goodman and Kelso 1980; Larish and Frekany 1985; Rosenbaum 1980; Soechting and Flanders 1989a,b).

How and where are distance and direction encoded or represented in the CNS? Modulation of neuronal discharge with changes in movement amplitude has been observed in the globus pallidus and subthalamic nucleus of monkeys (Georgopoulos et al. 1983b). In the motor cortex only a weak correlation of neuronal firing with amplitude was found in a two-dimensional reaching task (Georgopoulos 1990; Schwartz and Georgopoulos 1987), and no correlation was found in a study of single-joint movement (Hamada and Kubota 1979). Using a monoarticular wrist flexion/extension task, Riehle and Requin (1989) identified a small number of neurons in premotor cortex whose activity was modulated by prior information about movement amplitude. Using a multiarticular task, Kurata (1993) reported that a majority

of cells in premotor cortex had set-related and movement-related discharge that was modulated with movement direction and distance. We identified a large proportion of task-related cells whose discharge was correlated with movement direction and distance in the motor and premotor cortices of monkeys (Flament et al. 1993; Fu et al. 1993b). By fitting the neural responses to movement distance and direction using a multivariate regression model, we defined the significance, strength, and form of the relationship between the neuronal modulation and the controlled parameters (Fu et al. 1993b).

In the primary motor cortex, directional tuning of many cells' discharge is firmly established. Neuronal modulation related to movement direction has been documented during single-joint movements (Evarts et al. 1968; Fetz et al. 1980; Hamada and Kubota 1979; Schmidt and Jost 1975; Tanji and Evarts 1976) as well as in two- and three-dimensional reaching tasks (Georgopoulos et al. 1982; Schwartz et al. 1988). The tonic discharge of some cells was found to vary with the position of the hand in three-dimensional space (Kettner et al. 1988). Given the rather broad cosine tuning of cell firing, it has been shown that a population code can be used to predict movement direction accurately (Georgopoulos et al. 1983a, 1988). A similar vectorial population code can accurately describe movement direction for cell firing in the premotor cortex (Caminiti et al. 1991), parietal cortex (Kalaska et al. 1983), and cerebellum (Fortier et al. 1989).

Because direction, distance, and target position are all correlated to some degree with the discharge of cells in the premotor and primary motor cortices, the question of how these structures encode multiple movement parameters needs to be asked. Other parameters of movement that may be encoded in the primary cortex include force (Maier et al. 1993; Montgomery et al. 1992; Wannier et al. 1991), muscle activity (Crutcher and Alexander 1990; Maier et al. 1993), and movement velocity (Burbaud et al. 1991; Flament and Hore 1988; Schwartz 1992). Similarly, several studies of the premotor cortex have argued for the encoding of movement- and motor set-related information (Kurata 1989, 1993; Kurata and Wise 1988; Weinrich and Wise 1982; Wise and Kurata 1989). It has also been reported that, as well as being related to direction of limb movement, the activity of some premotor cells is also related to the position of the target or stimulus (di Pellegrino and Wise 1993). Correlation with target position has also been described for the tonic post-movement firing of motor cortex cells (Kettner et al. 1988). In our earlier study (Fu et al. 1993b) it emerged from fitting the responses to direction and distance that the firing of most cells was also correlated strongly with target position (i.e., the target's *X* and *Y* coordinates).

How do the primary motor and premotor cortices encode multiple movement parameters? One obvious scheme is to encode individual parameters in spatially distinct areas or in different cell populations. Although our previous study (Fu et al. 1993b) found some evidence for spatial segregation of direction- and distance-related information, there was a fair number of cells with considerable spatial intermixing of direction-, distance-, and target position-related firing. Moreover, segregation of information did not occur at the single-cell level. On the basis of an analysis of the average firing in either the premovement or movement periods, the

discharge of most cells was correlated significantly with more than one parameter.

Another possible scheme is to parcellate temporally information related to different parameters. In this scheme, a cell's firing would elaborate information serially. Our earlier analysis of parameter encoding in the primary motor and premotor cortices revealed differences in the timing of the correlations with direction and amplitude (Fu et al. 1993b). The average premovement discharge was more likely to be correlated significantly with the direction of the upcoming movement, whereas the average activity occurring during the movement was correlated with both direction and distance (Fu et al. 1993b). Correlations of cell discharge with target position were also more prevalent during the movement than before it. Additional support for this hypothesis lies in the results of several earlier psychophysical studies that suggest that a serial elaboration of direction and distance information occurs (Goodman and Kelso 1980; Larish and Frekany 1985; Rosenbaum 1980). Recently it has been shown that the amount of information about the direction of a remembered target's position was greater than the amount about its distance (Soechting and Flanders 1989b). Thus both the neuronal and psychophysical results suggest that direction and distance representations may differ in their time courses.

In this study we extend our previous analysis of the correlations between movement parameters and the neuronal activity that immediately precedes and occurs during the execution of two-dimensional reaching movements (Fu et al. 1993b). The raw data used for the current analyses are taken from this earlier report. We have refined the regression analyses relating the discharge of primary motor and premotor cortex neurons to movement direction, distance, and target position, enabling us to extract and quantify the temporal features of the correlations with these parameters. An abstract of this work has been presented (Fu et al. 1993a).

METHODS

Behavioral paradigm

The behavioral paradigm, hardware, and recording procedures are described fully in previous publications (Fu et al. 1993b; Ojakangas and Ebner 1991). Only a brief account of the essential details is included here. Two (*A* and *B*) female rhesus macaques (*Macaca mulatta*) weighing 4–5 kg were trained using operant conditioning to make visually guided multiarticulate reaching movements. These were the same two monkeys used previously (Fu et al. 1993b). The task required the animals to superimpose a cross-hair cursor onto 1-cm² targets displayed on a horizontally placed video screen, using a draftsman's arm-style manipulandum (Ojakangas and Ebner 1991). In each trial the animals were first required to hold the cursor in a start position (also a 1-cm² video display), located ~15 cm in front of the midline. Targets were circumferentially placed around the start position at 45° intervals (8 directions) at distances ranging from 1.4 to 5.4 cm, in 0.8-cm increments (6 distances). After a randomized hold period of 1.0–1.5 s, 1 of 48 pseudorandomly selected targets was presented. The successful completion of a trial required accurate movement to the newly displayed target in ≤2,000 ms after its appearance and maintenance of the cursor within the target for a further 750 ms. Success was rewarded with the delivery of fruit juice.

Chamber implantation, electrophysiological recording, and histological procedures

After 5–6 mo of intensive training, the monkeys were stereotactically implanted with a stainless steel chronic recording chamber. The chamber was placed over the contralateral premotor and primary motor cortices and attached to the skull with acrylic cement. All surgical procedures were performed under aseptic conditions and with full surgical anesthesia [Ketamine ($20 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) and Xylazine ($1.0 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$)]. In the immediate postoperative period the animals received an analgesic (Nubain, 0.05 mg/kg) and for several days also received prophylactic doses of antibiotics (Ampicillin, $250 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$). After recovery, extracellular single-unit recordings were made using paralyene-coated tungsten microelectrodes (tip impedance $3\text{--}10 \text{ M}\Omega$). Signals were amplified, discriminated using a time-amplitude window discriminator, and converted to transistor-transistor logic (TTL) pulses before being digitized and stored to computer at 1 kHz . We studied cells only if their discharge was task-related during active reaching or occurred in response to passive rotation of the shoulder or elbow joints. The position of the manipulandum was also stored on computer (sampling rate 250 Hz) using potentiometers located at its joints. Velocity of hand movement was calculated by numerical differentiation of the position signal.

We have described both the histological procedures for reconstruction of electrode recording sites and the criterion used to distinguish premotor from primary motor cortex in a previous paper (Fu et al. 1993b).

Data and statistical analyses

The raw data used in this study are the same as those used in Fu et al. (1993b). Here we present a series of novel analyses to describe further and characterize the temporal profiles of the correlations with different movement parameters. We used SAS software for statistical analyses (SAS Institute 1988).

Neuronal discharge and kinematic data were aligned to movement onset for the various analyses (Fu et al. 1993b). We defined movement onset and termination as the times when tangential velocity first reached and then returned to a threshold of 1.0 cm/s , respectively. Response histograms of cell discharge were generated by averaging sets of five movements to each target.

A multivariate regression model was used to define, for each cell's discharge, the contributions of direction and distance. This model's development is described in detail in Fu et al. (1993b). Two terms, $[\sin(\theta) \cdot d]$ and $[\cos(\theta) \cdot d]$, that describe the "interaction" of direction and distance were also included. Geometrically, these terms reduce to the X - Y coordinates of the target position. In this report the regression analysis was extended, calculating the regression as a function of time. The firing rate, f , at time t was fitted to a linear, quadratic polynomial function, as follows

$$f(t) = k_0(t) + k_1(t) \sin(\theta) + k_2(t) \cos(\theta) + k_3(t)d + k_4(t)d^2 \\ + k_5(t)[\sin(\theta) \cdot d] + k_6(t)[\cos(\theta) \cdot d]$$

where d is the constant distance between the start position and the final position reached for each movement, k_i are constants, and θ is the constant movement direction vector between the start and target locations. The term d^2 was included because it significantly improved the model fit, indicating that there is some nonlinearity in the coding of distance. The regression analysis was calculated in 20-ms bins for the firing obtained from all movement directions and distances, using the average of 5 movements to each of 48 targets for a total of 240 trials. Before fitting firing rate into the time regression model, we used a data smoothing procedure (3-point moving average) on the average cell discharge for each target.

We calculated statistical significance of the total R^2 as well as partial R^2 values for each parameter as a function of time using

an analysis of variance (ANOVA, F test, $P < 0.01$). The former gives the amount of variance in the discharge explained by the entire model and the latter the variance accounted for by individual terms in the model. The directional terms in the equation above were combined to yield the partial R^2 for direction (R_{dir}^2), the two distance terms were combined to generate the partial R^2 for distance (R_{dis}^2), and the target location terms were combined to calculate the partial R^2 for target position (R_{tar}^2). The criterion for the existence of a correlation with one of the three parameters was arbitrarily set so that three consecutive bins have a significant partial R^2 (F test, $P < 0.01$); this reduced the number of spurious correlations. Cells whose time regression analysis did not meet this criterion were excluded from further analysis. Onset latency of parameter-related correlation was defined as the time at which the first of three consecutive bins had significant partial R^2 values. The time of peak correlation for each parameter was also measured.

For cells in which the partial R^2 's were significantly related to at least two parameters, the amplitude of the partial R^2 's sometimes appeared to be reciprocal; that is, a large R^2 in one parameter was associated with a low R^2 in the other, and vice versa (e.g., Fig. 2). This phenomenon occurred during the transition period between two parameters. Stated differently, the discharge of these cells appeared to be correlated with only one parameter at a time. To study this property we defined and determined an index of simultaneity, I_S , between pairs of parameters. First, the transition period was determined for the correlated cell activity for any two parameters. We defined this as the interval spanning the onset time of significant correlation for the temporally later parameter to the end of the period of significant correlation for the temporally earlier parameter. For some cells this period was too short to analyze meaningfully; therefore the analysis was arbitrarily restricted to transition periods of $\geq 100 \text{ ms}$. Within this transient period, I_S was defined as the fraction of bins in which both parameters were significantly correlated with the firing. Therefore $I_S = 0.0$ implies that at no time in the transition period were both parameters significant, and $I_S = 1.0$ implies that for the entire transition period both parameters were significantly correlated.

RESULTS

Temporal profile of unit discharge and parameter correlation

From the two monkeys in which complete sets of five movements to each of the 48 targets were obtained, the temporal profile of the firing of a total of 130 cells was fitted into the time regression model. Of these, the discharge of 127 showed a significant correlation (ANOVA, $P < 0.01$ for 3 consecutive bins) with at least one of the model parameters. Figure 1 illustrates the discharge of a cell that was correlated with movement direction and distance. Each outer block of histograms represents the discharge frequency of a single cell at a given target direction for the six distances from the central starting position. This cell's firing was broadly tuned to the direction of the movement, with higher-frequency discharge at 0° , 45° , and 90° . It can also be appreciated that the firing rate increased with increasing distance along several movement directions (0° , 45° , and 90°). Qualitatively this increase in discharge is most apparent during movement, particularly near the end of movement. The center block shows the firing rate profiles fitted to the regression model. Average movement velocity, total R^2 , and individual R_{tar}^2 , R_{dir}^2 , and R_{dis}^2 terms are shown. This unit's firing demonstrated a significant directional component beginning 220 ms before movement onset. The R^2 for direction increased to a maximum value during the premovement period and

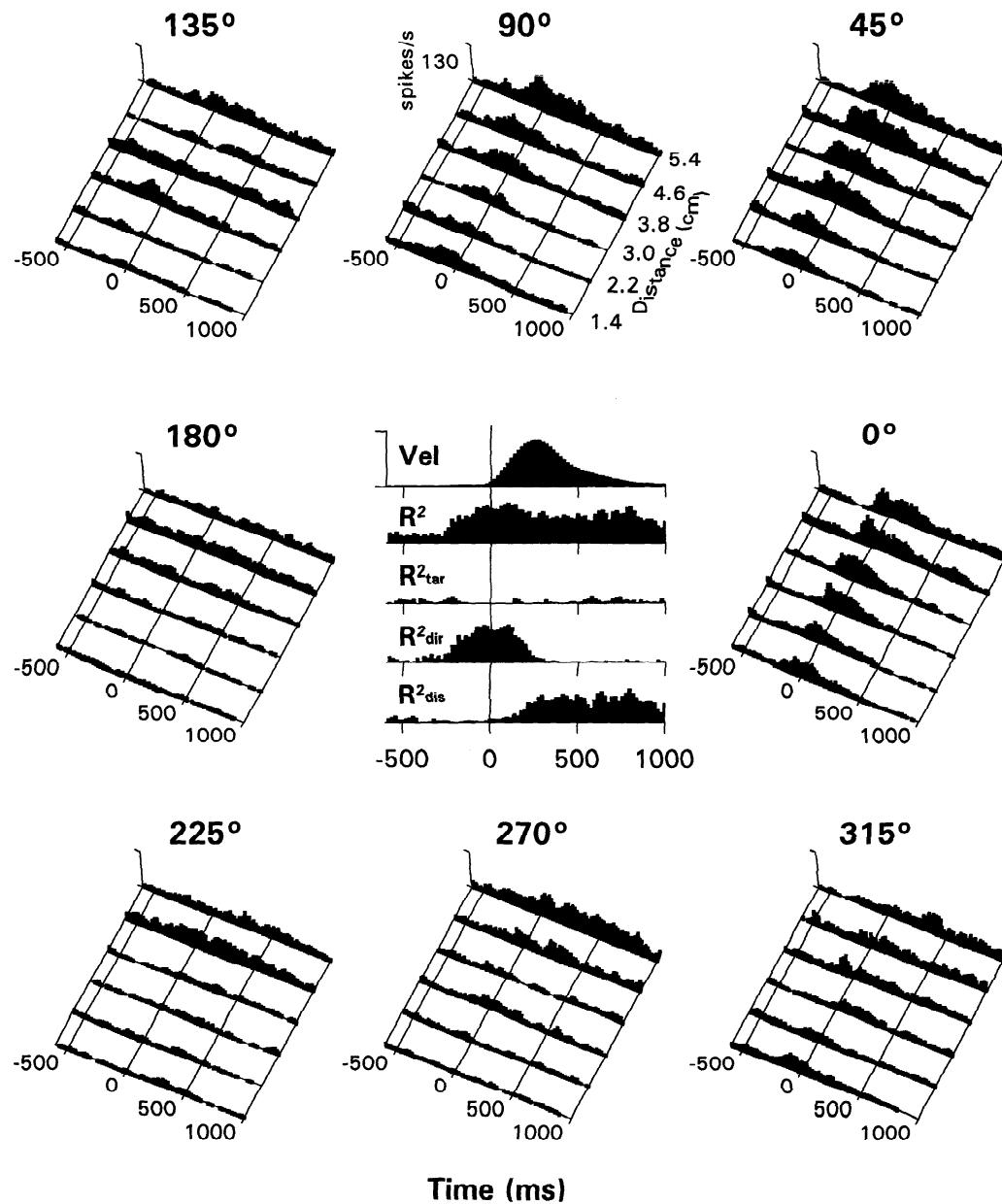


FIG. 1. Example of a cell showing discharge modulation with direction and distance but not with target position. *Middle illustration:* partial R^2 's for distance (R^2_{dis}), direction (R^2_{dir}), and target position (R^2_{tar}), the total R^2 calculated as a function of time, and the average velocity profile (Vel) for all movements to the 48 targets. R^2 values are from the model described in METHODS. Arranged circumferentially around this plot are the response histograms for the cell's discharge generated from groups of 5 movements made in 8 directions (0–315° in 45° intervals). Each set of histograms at a given direction shows the modulation in discharge that occurred for movements of different distances (1.4–5.4 cm in 0.8-cm increments). All illustrations are aligned to movement onset (time = 0 ms) and both the R^2 profiles and histograms use 20-ms bins. Unit recorded in premotor cortex from monkey B. Calibration bar for *middle illustration*: $R^2 = 1.0$; velocity = 10 cm/s.

then gradually decreased after movement onset. This cell's firing also had a distance-related component beginning near the time of movement onset that gradually increased and continued for almost 1,000 ms, persisting beyond the end of the movement (compare with velocity profile). There is a period of overlap (from ~100 to 250 ms after movement onset) during which the correlations with direction and distance are both significant. Note that this transition period between these parameters was smooth, with R^2_{dir} gradually decreasing as R^2_{dis} gradually increased. The X and Y coordinates of the target position, based on the R^2 from the interaction terms, did not account for any significant portion of the

variance in this unit's firing. The overall degree of fit of the firing to the model can be appreciated by the total R^2 regression profile. The total R^2 is maintained at a high level throughout the movement.

A cell whose discharge was correlated with movement direction and the X-Y position of the targets, but not target distance, is illustrated in Fig. 2. This cell's firing was also broadly tuned to movement direction, with the largest firing around the 315–0° targets. As can be seen in the *middle illustration*, the direction component of the correlated activity began 140 ms before movement onset and decreased ~250 ms after movement onset. Correlation of the firing

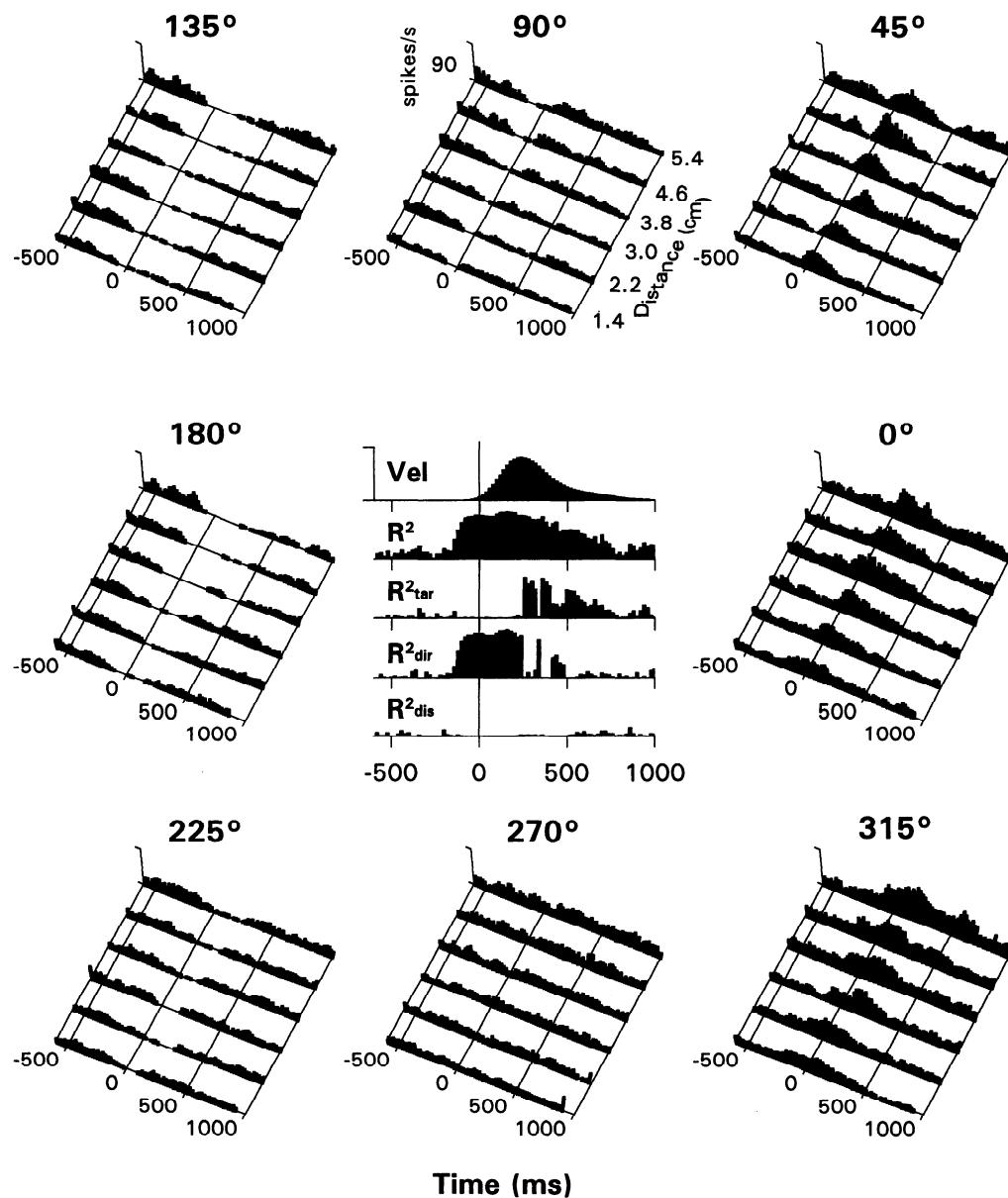


FIG. 2. Example of a unit whose firing is correlated sequentially with direction and target position, but not movement distance. Same conventions as in Fig. 1. Note the "switching"-like change in the R^2_{dir} and R^2_{tar} in the transition period between these two parameters. Unit recorded in primary motor cortex from monkey *B*.

with target position began 260 ms after movement onset and gradually decreased as the movement proceeded. Notice the rather rapid transition from significant correlation of firing with direction to target position in the period between these two parameters.

More typically a unit's discharge was related to all three parameters in varying degrees. A neuron with this type of firing is illustrated in Fig. 3. This cell fired most vigorously for movements made in directions 180° and 225° from the center hold position. The earliest significant partial R^2 occurred for direction (160 ms before movement onset), followed by the target X-Y coordinates (80 ms before movement onset) and finally by distance (560 ms after movement onset). After movement onset there were two 20-ms time periods in which R^2_{dir} increased with a corresponding decrease in the correlation with target position. During the transition period between direction and target position, the

changes in correlations could be very abrupt, as is also seen for the cell depicted in Fig. 2. A more gradual transition in the strength of correlation occurred near the end of movement as the distance correlation increased but the correlation with target position decreased. The temporal profile of the total R^2 was smooth with a high level of fit of the firing with the model.

Polar plots of unit discharge: temporal series

To visualize better the relationship between cell discharge and movement direction, distance, and target position as a function of time, we illustrate the data from two cells using a series of contour polar plots (Figs. 4 and 5). In these polar plots, movement distance is given by the position along the radius and movement direction by the angle of the radius arm. The intensity of neural discharge is proportional to the

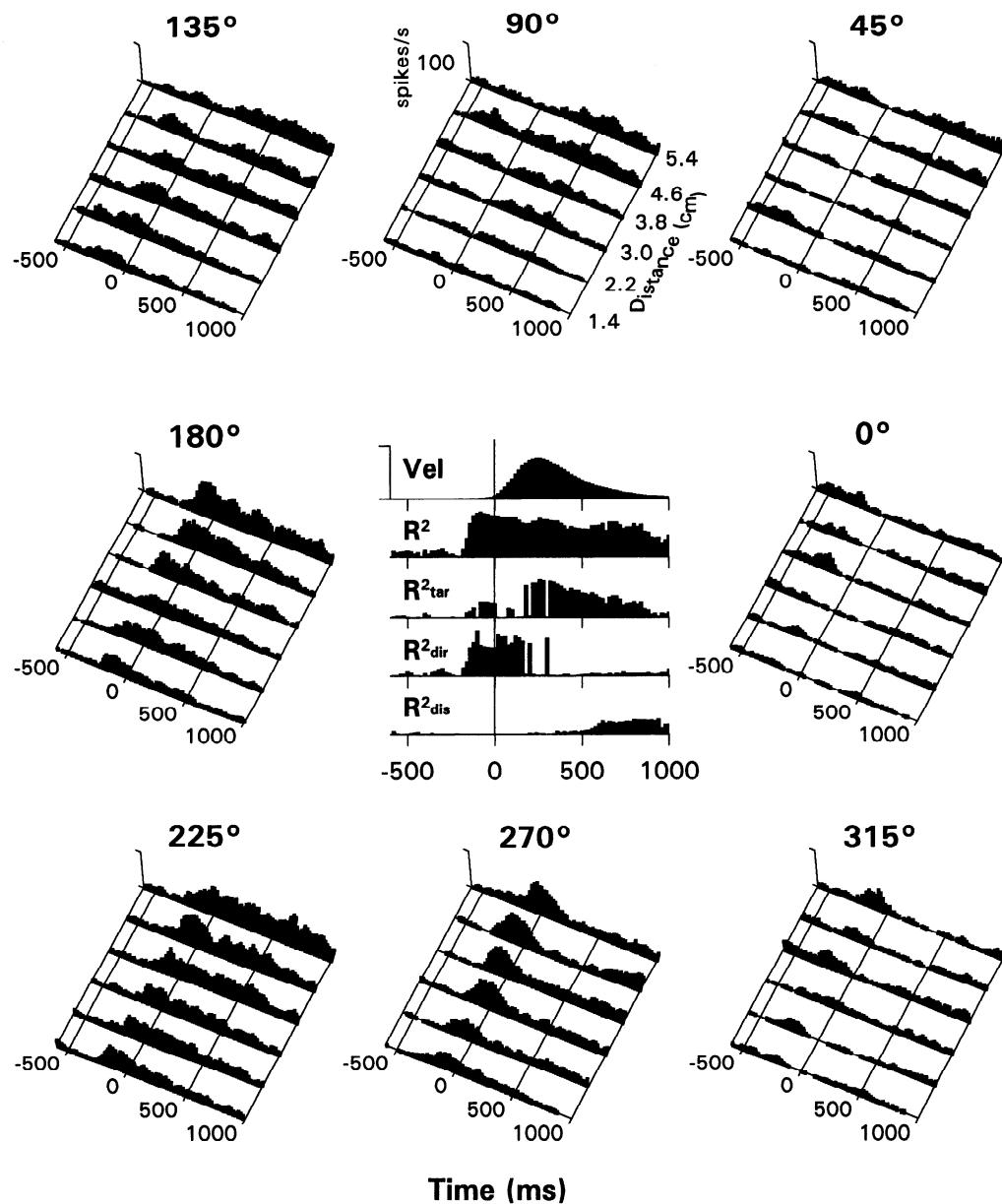


FIG. 3. Example of a unit with sequential correlation of its discharge with direction, target position, and distance. Switchlike changes in the partial R^2 between direction and target position occur, but a gradual transition is observed from the target position to distance. Same conventions as in Fig. 1. Unit recorded in primary motor cortex from monkey B.

intensity of shading. The data in Fig. 4 are from the same unit shown in Fig. 1, which had direction- and distance-related discharge only. A series of 12 contour plots illustrating the changes in neural discharge over time is depicted in Fig. 4. At 350 ms before movement onset the discharge is relatively low; it gradually increases and becomes directionally tuned at ~ 150 ms before movement onset. A gradual transformation to a predominantly distance-related pattern occurs by 350 ms after movement onset. At 50 ms before movement onset, the cell's discharge was significantly correlated with direction only (preferred movement direction $\approx 45^\circ$). The coefficients from the regression at this time were used to generate the idealized contour plot for pure direction-related neural discharge for this unit (crescent-shaped pattern, Fig. 6A). Similarly, at 650 ms this cell's firing was almost exclusively correlated with movement distance, and the coefficients from the regression at this time were used

to generate the idealized plot for pure distance-related discharge (bullseye pattern, Fig. 6A). Note the similarity between the model results (Fig. 6A) and the actual firing (Fig. 4) for the 50- and 650-ms contour plots. Figure 5 shows the shifting in the pattern of neural discharge as a function of time for the unit shown in Fig. 3. Figure 6B illustrates idealized contour plots for movement direction (crescent-shaped pattern), target position (striped pattern), and movement distance (bullseye pattern), respectively, based on the coefficients obtained from the regression model at -50, 250, and 650 ms. The unit's contour plots in Fig. 5 show that the earliest parameter-related pattern indicates a strong relationship with movement direction at -150 ms (preferred direction $180-225^\circ$). By 250 ms the unit begins to acquire some of the characteristics of a target position-related pattern, and at 550 ms distance-related discharge is apparent. However, as seen in the partial R^2 plots in Fig. 3, some overlap between

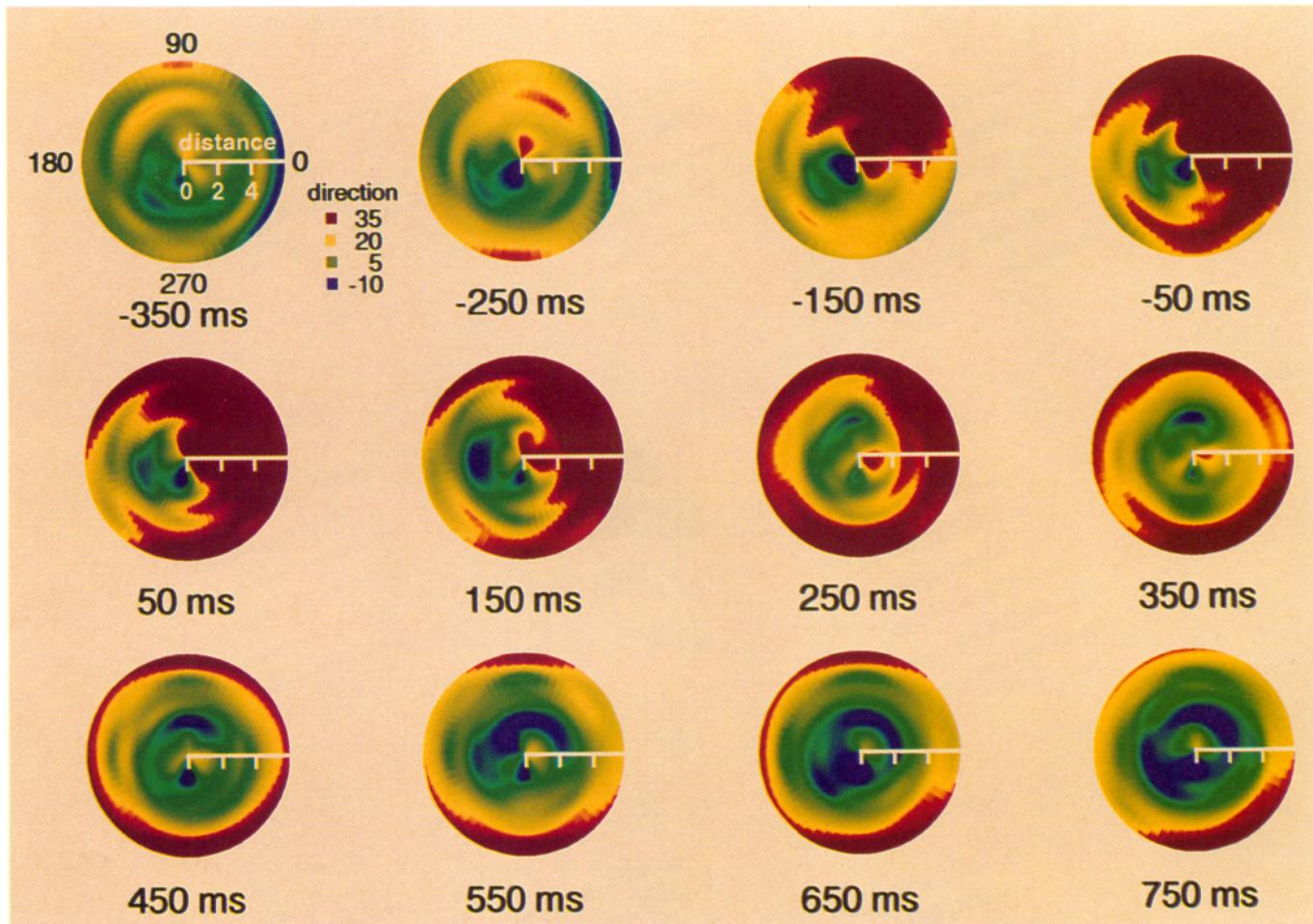


FIG. 4. Contour plots showing relation between cell discharge and movement direction and distance as a function of time for the same unit illustrated in Fig. 1. Each plot is of the actual neural activity averaged over a 100-ms interval centered on the time shown below each plot. Movement onset occurred at time 0. Calibrations: movement distance is in centimeters, direction in degrees, and discharge rate in impulses per second.

target position and distance exists; this overlap is also clearly seen in the contour plots.

Population statistics for parameter correlations

Table 1 shows the distribution of parameter-related cells in primary motor and premotor cortex. The firing of the majority of cells (93 of 127, 73.2%) was significantly correlated with all three parameters at some time during the pre-movement or postmovement periods. The firing was correlated with a single parameter in only seven cells; these neurons were all located in primary motor cortex. Other than this, there were no obvious differences between premotor and motor cortical cells based on the existence of parameter encoding.

The average total and partial R^2 's as a function of time are shown in Fig. 7 for all cells in which a significant correlation occurred for a given parameter. Each point represents the averaged R^2 and is shown with its SD. The profiles of the R^2 's averaged for all cells do not differ markedly from those observed for the individual neurons described in Figs. 1–5. R^2_{dir} (Fig. 7A) begins to increase, rises steeply, and peaks before movement onset (vertical dotted line at time 0). R^2_{tar} (Fig. 7B) begins to rise slightly later, rises more slowly,

and peaks during the movement. R^2_{dis} (Fig. 7C) begins near or shortly after movement onset and reaches a plateau late in the movement. Notice that neither the correlation with distance nor with target position has returned to pre-movement baseline by the end of the 1,000-ms analysis period. Because this time period represents the vast majority of the movement time (see velocity profiles in Figs. 1–3), this implies a significant coding of movement parameters at the end of the movement. The total R^2 (Fig. 7D) is an approximate sum of the individual three parameters. Inspection of the partial R^2 profiles (Fig. 7, A–C) reveals that target position and distance coding have lower peak values than direction. However, the duration over which their R^2 values are above baseline is prolonged.

The partial R^2 temporal profiles shown in Fig. 7 demonstrate that, on average, a serial ordering of the correlation with direction, target position, and distance occurs, in that order. The same temporal ordering is also evident if one examines the onsets or peaks of the various partial R^2 's for these three parameters. The frequency distributions of onset latency relative to movement initiation at time 0 for the different partial R^2 's are shown in Fig. 8, A–C. Latencies were binned into 100-ms epochs. For onset of direction correlation (Fig. 8A), the distribution is relatively narrow, with

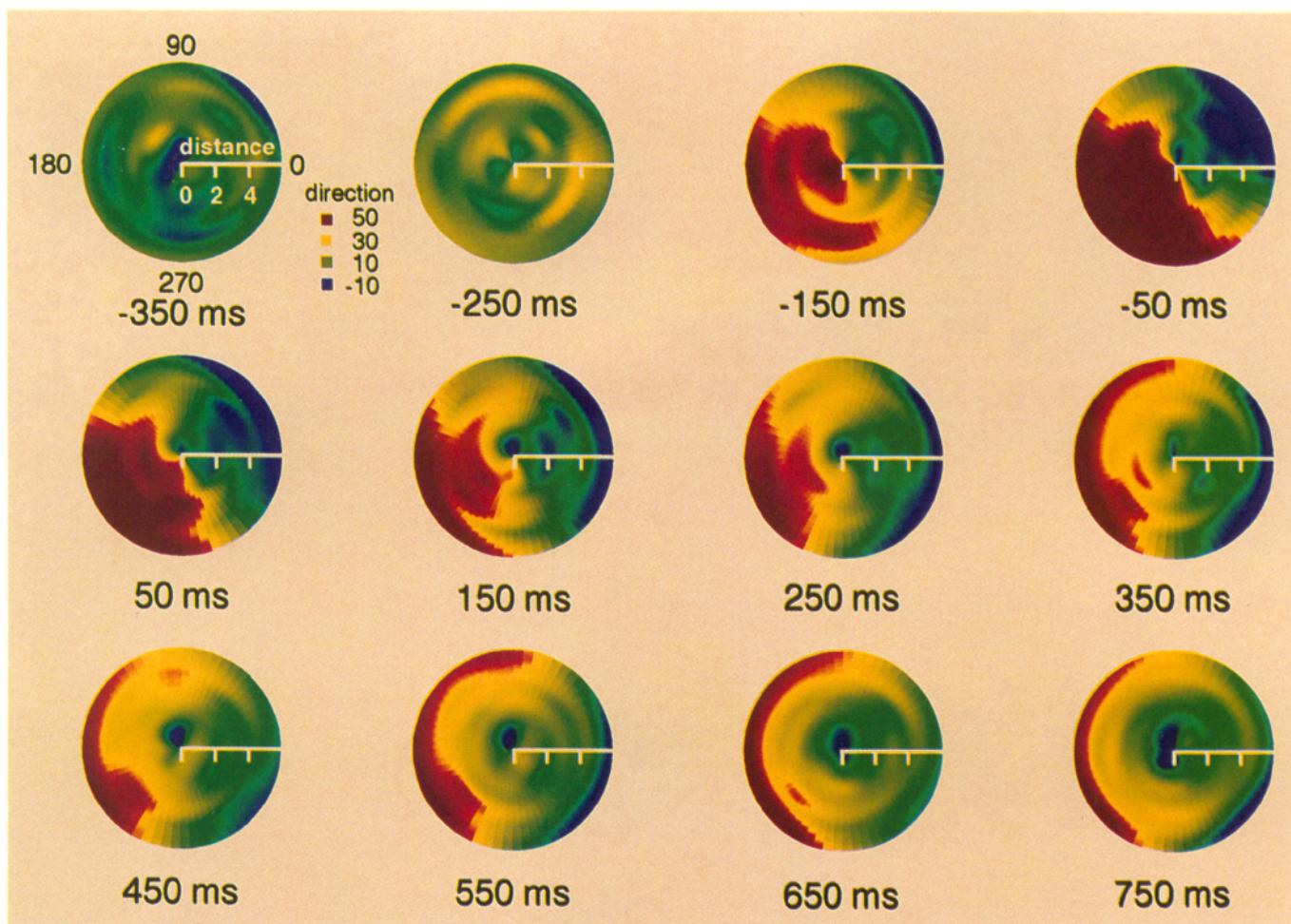


FIG. 5. Contour plots as a function of time, showing relation between cell discharge and movement direction, target position, and movement distance for the same unit as illustrated in Fig. 3. Same conventions as in Fig. 4.

most latencies falling in the interval between 250 and 50 ms before movement onset. The distributions for distance (Fig. 8B) and target position (Fig. 8C) are broader than for direction. For target position, the onset of the significant correlation begins in some cells before movement onset, with a large peak at -100 ms. For target distance, a minority of the cells had latencies that occurred before movement onset. The means \pm SD of the latencies (Fig. 8D) progressively increase for direction [-115.5 ± 167.9 (SD) ms], target position (57.5 ± 205.8 ms), and distance (248.5 ± 284.4 ms). The means of the onset latencies for the three groups were significantly different (ANOVA, $P < 0.0001$). The distribution of times at which peak partial R^2 values are reached is illustrated in Fig. 9, A–D. Similar to that for onset latency, the distribution for direction correlation is narrower (Fig. 9A) and peaks near movement onset. The R^2_{dis} correlation (Fig. 9B) peaks at 650–750 ms, near the end of movement. For target position correlation, the partial R^2 was equally likely to reach a maximum at any time from 50 ms before movement onset to 450 ms into the movement (Fig. 9C). The average time of peak correlation (Fig. 9D) increases for direction (48.5 ± 209.0 ms), target position (253.9 ± 297.5 ms), and distance (515.5 ± 355.2 ms), similar to the onset latency. The means of the peak latencies for the three groups differed significantly (ANOVA, $P < 0.0001$).

To confirm that the population results truly represent the order of the parameter correlation that occurs in individual cells, we analyzed the temporal order for each cell that encoded more than one parameter. From the group of 120 cells, 63 had sequential onsets of partial R^2 with the order $R^2_{\text{dir}}, R^2_{\text{tar}}, R^2_{\text{dis}}$. Another 26 cells had the order of the first two reversed with distance remaining last (i.e., $R^2_{\text{tar}}, R^2_{\text{dir}}, R^2_{\text{dis}}$). Twenty-one cells had R^2_{dir} occur first, but had a reversed order of target position and distance (i.e., $R^2_{\text{dir}}, R^2_{\text{dis}}, R^2_{\text{tar}}$). Only 10 cells did not fall within one of these categories. Therefore by all measures including averages of the partial R^2 profiles, and the onset and peak latencies for significant correlations, a consistent temporal ordering occurs in the correlation of the cell's firing with these three parameters.

We considered the possibility that the onset latency of the partial R^2 's was in some way related to the reaction time. For example, in a movement with a short reaction time, the direction-related neural discharge might occur closer to movement onset than in a movement with a longer reaction time (such a relationship may suggest that more lead time was available in which to "set" the neuron for the required direction). Distance and target position components of the neural discharge may be similarly affected. To test this possibility, we plotted the relationship between onset latency of significant partial R^2 values and reaction time (Fig. 10A).

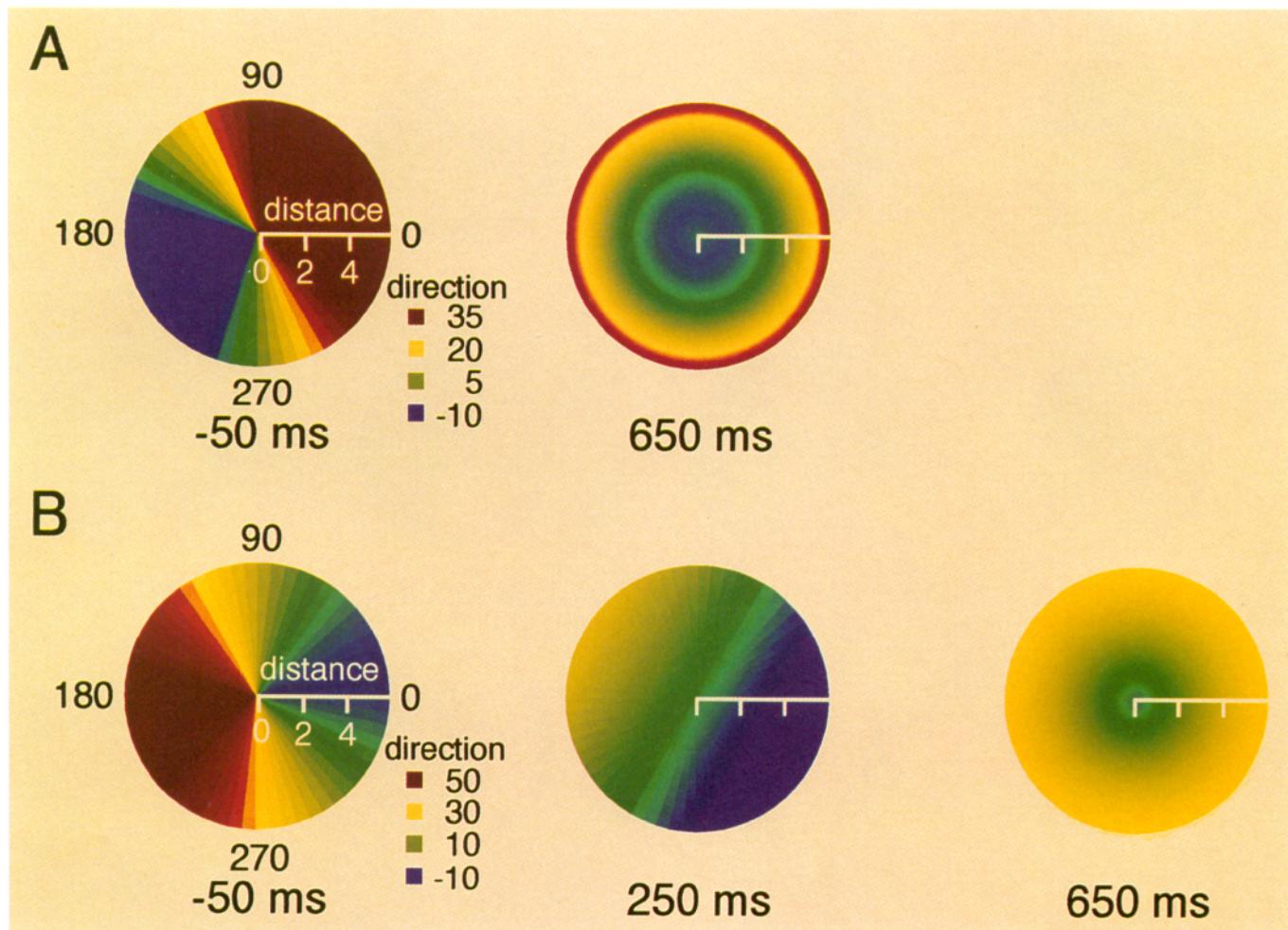


FIG. 6. A: Contour plots predicted by the model at 2 selected times in which the discharge was solely correlated with direction (-50 ms) and solely with distance (650 ms). The coefficients of the model were averaged from the 20-ms time bins in the 100-ms interval. B: 3 selected time periods from the model show the predicted pattern of firing for direction (-50 ms), target position (250 ms), and distance (650 ms). Same conventions as in Fig. 4.

Reaction times ranged from 207 to 399 ms, with a mean \pm SD of 312 ± 43 ms. No correlation was found between reaction time and partial R^2 onset latency for any of the tested parameters. Following similar reasoning, we also evaluated the relationship between the time of peak partial R^2 and peak velocity time. The results of this analysis, illustrated in Fig. 10B, show that no such correlation existed. An im-

portant point to note is that the peak correlation with distance generally lagged behind the time of peak velocity. Therefore the timing of the correlation between neural discharge and movement distance, direction, and target position is independent of reaction time and peak velocity.

We undertook two additional analyses of the correlations with target position. The first determined the "directionality" of this target position correlation in the two-dimensional work space. The contour plots of Fig. 6B demonstrate that the neural discharge related to target position takes the form of a linear gradient or a plane of a particular orientation (e.g., Fig. 6B, middle plot). To determine whether the orientation of these gradients favored a particular direction or was uniformly distributed, the orientation of the gradient was represented as a vector whose length was proportional to the slope of the gradient (Fig. 11). The slopes cover a sizable range ($1.1\text{--}9.2 \text{ impulses} \cdot \text{s}^{-1} \cdot \text{cm}^{-1}$), and although the directions of these gradients are distributed over a wide area of the work space, they were found to be nonuniform (Watson's test, $U^2 = 44.21$, $P < 0.01$, $n = 118$). A comparison of these vectors with those for the cells' preferred directions showed that for 50% of all cells ($n = 112$), the difference between vector orientations was $<27^\circ$, with an average difference of $49.4 \pm 58.6^\circ$ for all cells.

TABLE 1. Distribution of parameter-related cells in primary motor and premotor cortices

Parameter	Primary Motor Cortex	Premotor Cortex
Dir	3 (3.0)	—
Dis	2 (2.0)	—
Tar	2 (2.0)	—
Dir, Dis	2 (2.0)	3 (10.7)
Dir, Tar	14 (14.0)	4 (14.3)
Dis, Tar	2 (2.0)	2 (7.1)
Dir, Dis, Tar	74 (75.0)	19 (67.9)
Total cells	99 (100)	28 (100)

Values in parentheses are percentages. Distribution of all cells with a statistically significant discharge modulated with movement direction (Dir), movement distance (Dis), target position (Tar), and combinations thereof, located in the primary motor and premotor cortices.

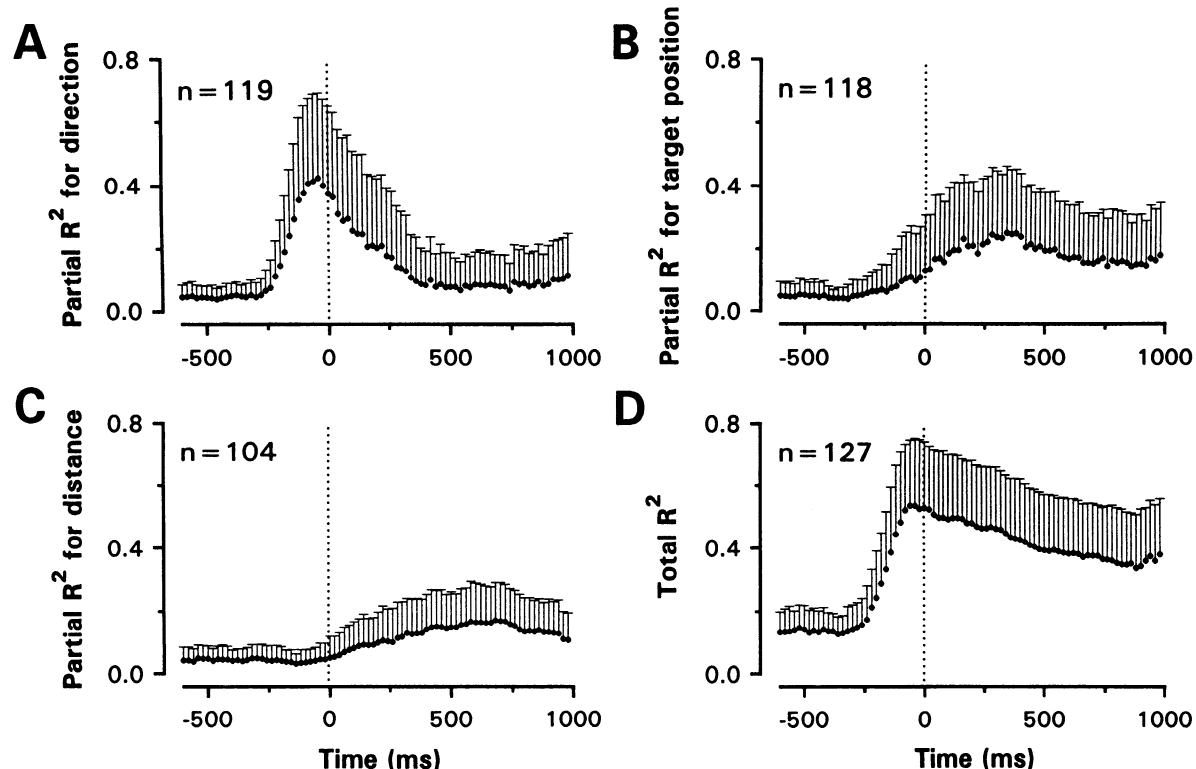


FIG. 7. Averaged (mean \pm SD) partial and total R^2 's for all units that showed significant modulation of discharge related to the plotted parameter. Significance criterion required 3 consecutive bins in the R^2 plot to be greater than baseline [analysis of variance (ANOVA), F test, $P < 0.01$]. The number of cells constituting each average is given in the top left corner of each plot. Graphs are aligned to movement onset (vertical dotted line at time 0). On average, the correlations with direction occurred first, followed by target position and then distance.

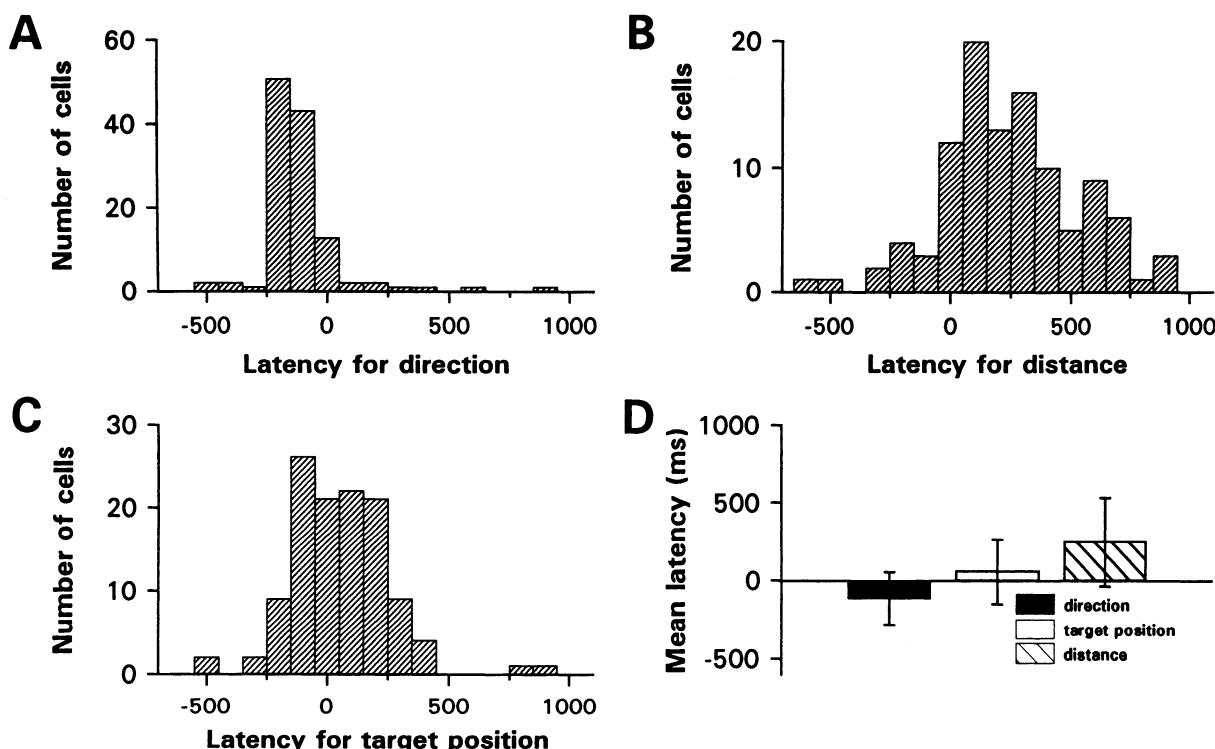


FIG. 8. A–C: frequency distributions of partial R^2 onset latencies for all units having discharge significantly correlated to the given parameter. Onset latencies were grouped into 100-ms bins. Movement onset at time 0. D: means \pm SD of R^2 onset latencies for the parameters and cells described in A–C. Positive mean latencies denote occurrence after movement onset, negative latencies before movement onset.

The second analysis of target position encoding was based on the fact that each target position may be represented as a pair of X - Y coordinates. We have decomposed the contribution of these individual components to the partial R^2 calculated for target position to determine whether the individual partial R^2 latencies of the X and Y components were independent. Frequency distribution histograms for the onset latency of the various target position components are illustrated in Fig. 12A. These latencies are depicted for the X component ($n = 66$), for the Y component ($n = 89$), and for the cells in which the X and Y components occurred at the same latency ($n = 33$). The distributions of the X and Y components are similar, with a slightly delayed correlation for cells in which the latency of the X and Y components was identical. This interpretation is confirmed by an examination of the mean latencies and the SDs, as shown in the bottom graph of Fig. 12A. The times of onset of the correlations with the Y and X components are similar, followed by simultaneous X - Y correlations 150 ms later (153.7 ± 267.4 , 150.9 ± 235.6 , and 327.8 ± 220.9 ms, respectively). This difference was significant (ANOVA, $P < 0.05$). Distributions of times for the peak correlations of the individual components are illustrated in Fig. 12B (401.1 ± 298.7 , 380.9 ± 300.7 , and 526.6 ± 258.6 ms, respectively, for the Y , X , and X - Y components). There were no significant differences in the mean times of the peak correlation (ANOVA, $P > 0.05$). Besides the delay in the onset of the simultaneous X and Y correlations, the target position components occurred and peaked at similar times.

Single-cell correlations with multiple parameters: simultaneous versus reciprocal

In units whose discharge was correlated with two or more parameters, the correlations sometimes fluctuated in a reciprocal manner during the transition periods. High partial R^2 's in one parameter occurred when low values were present in the other parameter, and vice versa. This reciprocal behavior is illustrated in Figs. 2 and 3, in which the later correlations with direction (e.g., the interval from 250 to 500 ms after movement onset in Fig. 2) are associated with a large decrease in R^2_{tar} . The indices of simultaneity (I_S) for direction and target position coding for the cells in Figs. 2 and 3 are 0.50 and 0.54, respectively. On the other hand, a priori it is equally likely that graded changes in parameter correlations occur, with one parameter gradually decreasing as one or more increases. In this case the cell's firing can "simultaneously" code two parameters. The cell illustrated in Fig. 1 exhibited such a relationship for direction and distance coding ($I_S = 1.0$), as did the cell in Fig. 3, where $I_S = 1.0$ for the transition period between target position and distance.

The I_S distributions for the three possible pairs of parameters from the population of cells are shown in Fig. 13. For the transition period between direction and target position (Fig. 13A) the I_S for the vast majority of cells was <0.5 . The mean I_S was 0.33 ± 0.28 , suggesting that these two parameters are in general not correlated simultaneously with a cell's firing. The mean I_S for direction and distance (Fig. 13C) was also quite low (0.38 ± 0.29). Although the average I_S for the transition period between target position and distance (Fig. 13B) was the largest of the three pairs (0.55 ± 0.25), a cell was simultaneously correlated with both param-

eters for an average of only half of the transition time. Therefore, for the transition periods, reciprocal correlations between parameters are a common observation.

Univariate model analysis of temporal sequence of direction and distance correlations

It should be emphasized that the multivariate analysis used was intended to identify correlations between unit discharge and movement parameters that occurred globally; that is to say, for the entire range of movement, directions and distances, and target locations studied. This technique could potentially fail to detect correlations that occur over limited areas of the work space. For example, distance-related activity that occurs at only one movement direction might yield an R^2 too low to reach statistical significance. To confirm that the multivariate model did not produce a misleading picture of the parameterization taking place, we also processed the data using a simple linear model for distance and a cosine tuning model for direction. These models are described fully in Fu et al. (1993b). Briefly, for distance, cell discharge was fitted to movement distance as a function of time by a linear equation where the intercept and slope were dependent on firing rate, as follows

$$f(t) = a_0(t) + a_1 d(t)$$

where a_0 is the intercept, a_1 is the slope, and d is the distance. For direction, discharge as a function of time was fitted to movement direction by a cosine tuning function where the intercept and amplitude of the cosine were dependent on firing rate, as follows

$$f(t) = b_0(t) + c_1(t)[\cos(\theta - \theta_p)]$$

where b_0 is the intercept, c_1 is the change in firing rate of the cell as a function of direction, and θ_p represents a cell's preferred direction.

An example of these analyses for one cell is shown in Fig. 14. This is the same unit illustrated in Fig. 2, which was shown by the multivariate model to have an early direction-related discharge, a later target position-related discharge, and no relation to movement distance. The plots of R^2 for direction at each movement distance are illustrated in Fig. 14A. Significant R^2 values are marked with a dot above the significant bin. Using our criterion of three consecutive significant bins ($P < 0.01$), it can be seen that direction-related discharge began before movement onset at four of six movement distances (1.4, 3.8, 4.6, and 5.4 cm). The direction-related discharge persisted for 200–300 ms after movement onset for the various distances, in agreement with the results from the multivariate regression models. Also in agreement with the multivariate model, there was no distance-related activity at any movement direction that met our three-bin criterion (Fig. 14B). An occasional isolated bin reached significance, but no significant correlation with distance was maintained along any direction for three consecutive bins. The distributions of onset latency of direction and distance coding based on the univariate models, for the whole cell population, are shown in Fig. 15. The number of sets (ordinate) is calculated from the combinations of eight movement directions and six distances for each cell. For example, a cell with a direction-related discharge at four distances and a distance-related

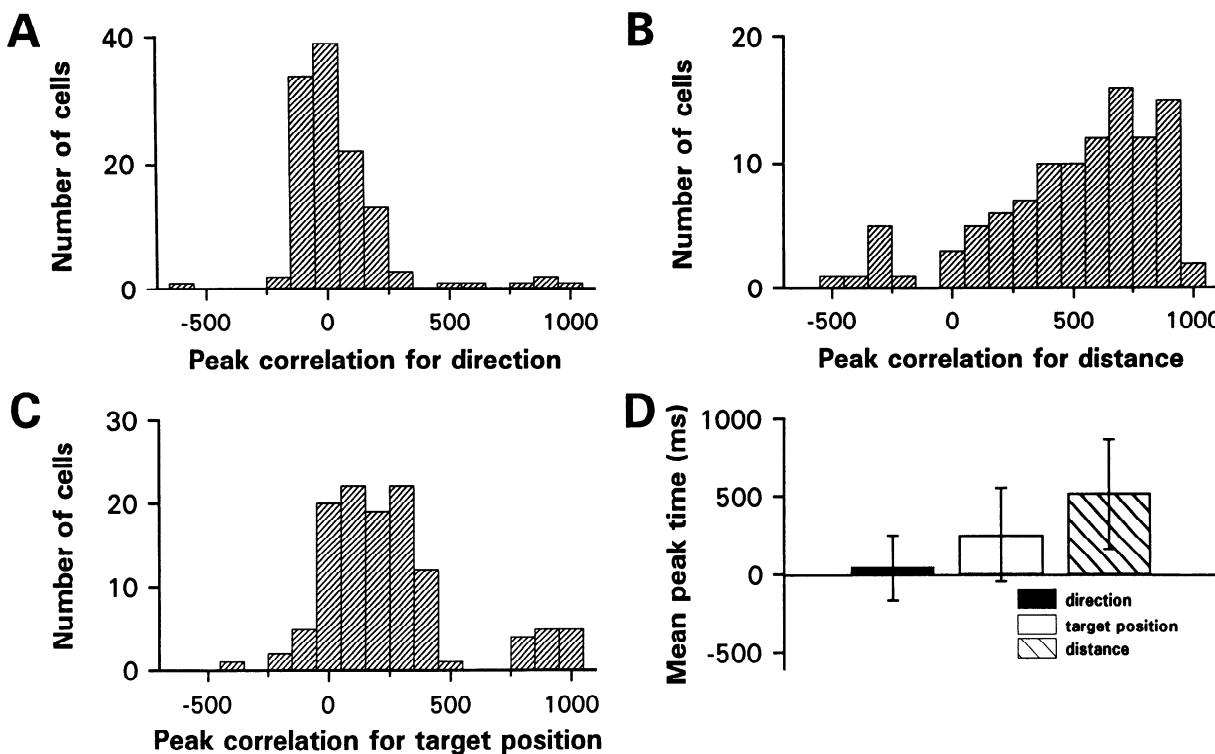


FIG. 9. A–C: frequency distributions of partial R^2 peak latencies for all units having discharge significantly correlated to the given parameter. R^2 peak latencies were grouped into 100-ms bins. Movement onset at time 0. D: means \pm SD of R^2 peak latencies for parameters and cells described in A–C. Positive mean latencies denote occurrence after movement onset, negative latencies before movement onset.

discharge at five directions would contribute four sets to the histogram in Fig. 15A and five sets to the histogram in Fig. 15B. The distribution for direction correlation peaked before movement onset, with several sets having very late onsets for the direction. Only for a small number of sets was there significant correlation with distance before movement onset (for example, for the cell discharge shown in Fig. 1 along 270°, regression data not shown), and the onset latency of the vast majority of sets with significant distance correlations began after movement onset. The mean latency and SD for the correlations with direction was 123 ± 307 ms ($n = 306$) and for distance 414 ± 284 ms ($n = 119$). These means were statistically different from each other ($t = 9.29, P < 0.0001$) and from the means obtained using the multivariate model (cf. Fig. 8. Direction: -115.5 ± 167.9 ms, $t = 10.23, P < 0.0001$. Distance: 248.5 ± 284.4 ms, $t = 4.37, P < 0.0001$). In fact, the onsets of the correlations with discharge for the single-variable regressions were ~ 150 – 200 ms later than for the multivariate regression analyses. Therefore the multivariate model was actually more sensitive in defining the timing of the correlations. However, the sequential nature of the correlations was similar to that obtained using the multivariate model. The timing of the correlations observed was not an epiphenomenon of the multivariate model used.

DISCUSSION

Temporal parcellation of movement parameter encoding

Encoding of movement direction in the discharge of cortical neurons has been established for the primary motor cor-

tex (Alexander and Crutcher 1990a; Fu et al. 1993b; Georgopoulos et al. 1983a, 1984, 1988; Kettner et al. 1988; Schwartz et al. 1988; Tanji and Evarts 1976), the premotor cortex (Caminiti et al. 1991; Fu et al. 1993b; Kurata 1993; di Pellegrino and Wise 1993; Riehle and Requin 1989), and the parietal cortex (Alexander and Crutcher 1990a; Kalaska et al. 1983). Georgopoulos and colleagues demonstrated that a population hypothesis based on a vectorial sum can accurately predict movement direction (Georgopoulos et al. 1983a, 1988). Although the degree and strength of movement distance tuning in the motor cortical areas were reported to be limited (Riehle and Requin 1989; Schwartz and Georgopoulos 1987), distance-related modulation of the discharge of premotor neurons has recently been described (Kurata 1993). However, the latter study only documented that the discharge of premotor cortical neurons differed in relationship to a single-joint movement of two amplitudes. No explicit relationship between discharge and amplitude was described. In our previous paper (Fu et al. 1993b) we reported that in both the premotor and primary motor cortices the neuronal activity was correlated linearly with distance. Use of a multiple regression model showed that, in addition to being correlated with movement direction and distance, cell discharge could be correlated with target position. Taken together these findings suggest that considerable kinematic and/or spatial information is encoded in the discharge of these neurons. These findings expand the concept, formulated by Georgopoulos and colleagues (Kettner et al. 1988), that the motor cortex can act as a processor of spatiomotor information. Thus, in addition to movement direction, target position and movement distance must be considered as relevant parameters.

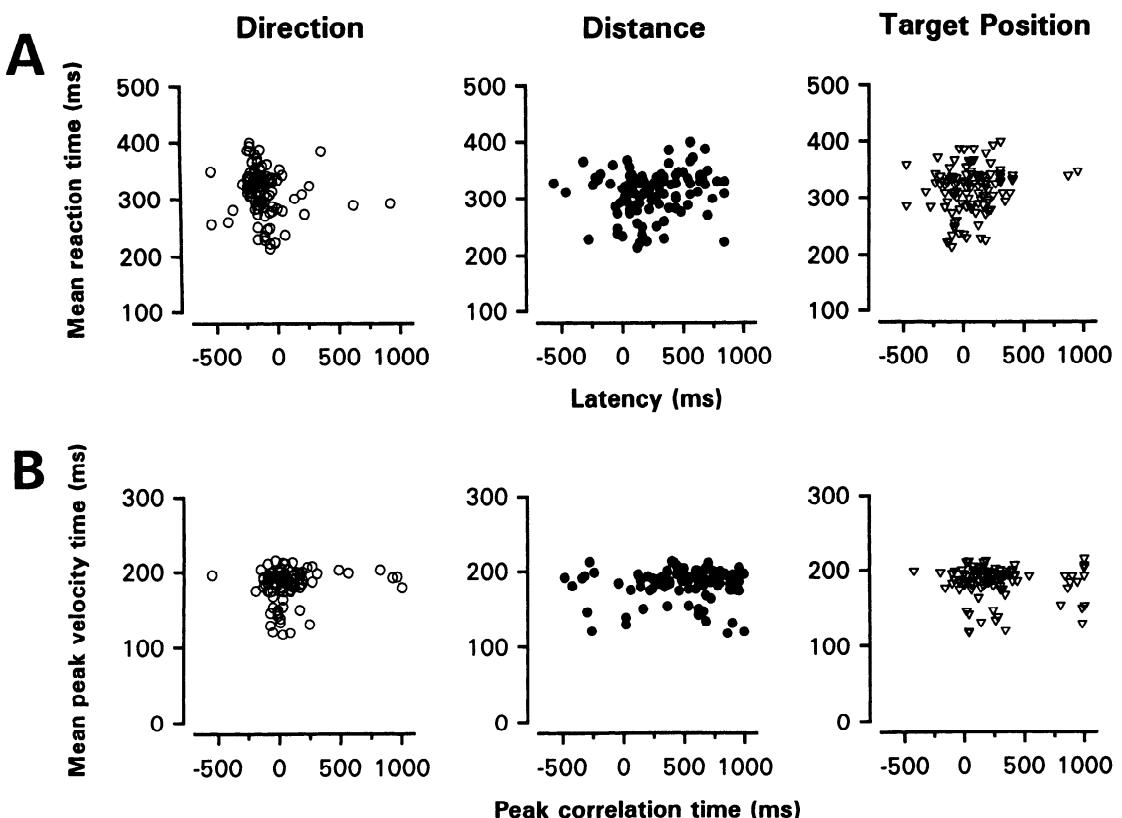


FIG. 10. A: scatter plot of reaction time as a function of partial R^2 onset latency for all units having parameter-related discharge modulation. B: plot of time of peak movement velocity as a function of the time of the peak R^2 value for same units. No correlation was found between these parameters.

Before the present study, the time course of any movement parameter encoding had been evaluated primarily for direction. In a reaching task, the population vector for movement direction not only developed during the reaction time period (Georgopoulos et al. 1988; Schwartz 1993; Schwartz et al. 1988), but accurately predicted direction in memory and programmed movement delay period tasks (Georgopoulos et al. 1989a; Smyrnis et al. 1992). One of the more intriguing demonstrations was the rotation in time of the population

vector associated with a mental rotation task (Ashe et al. 1992; Georgopoulos et al. 1989b; Lurito et al. 1991).

Precise timing relationships for correlations with the various other kinematic parameters have not been described. For example, in a three-dimensional reaching task, correlation of the cell's tonic firing with target position has been described (Kettner et al. 1988), but further details about the timing of the relationship between target position and the movement were not discussed. Although the distance and direction of a movement influenced the cell's discharge both in the pre-movement and movement periods, the onset or peak of these effects was not described (Kurata 1993).

In the study reported here, the temporal profiles of the correlations between cell discharge and direction, target position, and distance yielded a consistent relationship both at the single-cell level and for the population statistics (Figs. 1–3 and 7–9). Over the entire analysis period, direction-related discharge occurred first, target position-related discharge second, and distance-related discharge last. Similar temporal profiles were found for the means and distributions of the onset and peak correlations for the partial R^2 for each parameter. The same temporal parcellation of kinematic information occurs in the activity of single cells (Figs. 1–3). Cells with a relatively low I_s primarily encoded only one parameter at a time (Fig. 13). The same temporal ordering of direction followed by distance was also found when the analysis was restricted to specific distances and directions (Figs. 14 and 15). Therefore movement direction, target position, and distance are processed in primary motor and premotor cortices as relatively independent parameters and

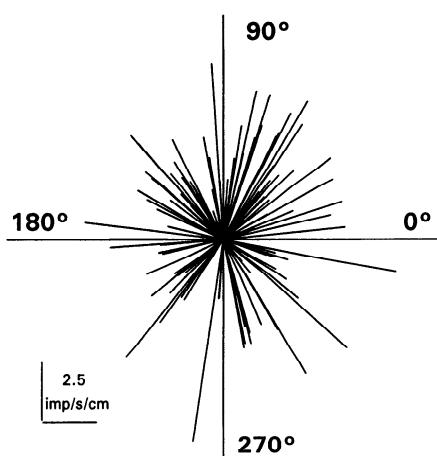


FIG. 11. Vectors representing the orientation of the linear gradient of contour plots related to target position for all cells with a significant R_{tar}^2 . Each vector was calculated from the k_5 and k_6 terms of the model [$\theta = \arctan(k_5/k_6)$]. Vector length represents the cell firing rate per unit distance at the time of peak R_{tar}^2 .

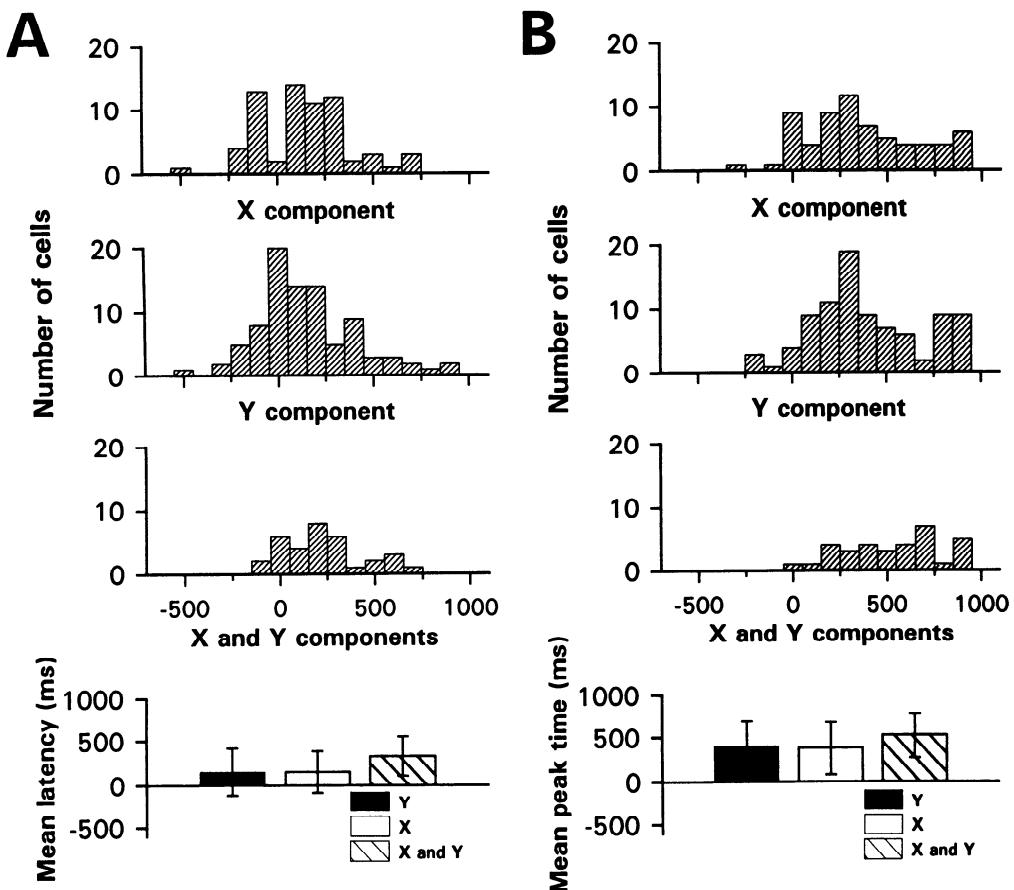


FIG. 12. A: frequency distributions for the latency of onset of the partial R^2 as a function of time for the X component, for the Y component, or for the X and Y components for the target position when the latency of both components was simultaneous. Bottom graph: mean \pm SD of the distributions above. B: Same as A, but for the time of the peak of the partial R^2 s.

are hypothesized to be encoded in a well-defined temporal order.

For some individual neurons, and for the population of cells, there was some overlap in the sequential correlations with the parameters. The discharge of some cells showed early correlation with distance; in other cells it showed late correlation with direction (Figs. 8 and 15). Although such overlap is not unexpected in a biological system, the consistency of the sequential ordering of the correlations is striking at the single-cell or population level, regardless of whether the single or multivariate regression analyses were used. An important issue is the role this overlap plays. For example, do the few cells with distance-related discharge before movement onset contribute significantly to the specification of movement amplitude?

The relative contributions to the observed correlations from centrally generated signals versus those generated from sensory feedback are not directly addressed by the present study. The earliest direction signals occur well before movement onset and are probably, in part, centrally generated. Because the directional tuning is evident in memory and programmed movement delay tasks (Georgopoulos et al. 1989a; Smyrnis et al. 1992) and is modified during a mental rotation task (Ashe et al. 1992; Georgopoulos et al. 1989b), it follows that a significant component of the directional signal may be centrally generated. The later discharge correlations with target position and distance are hypothesized to

have a significant contribution from sensory feedback. This is suggested not only by the later onset latencies, but also by the observation that accuracy in movement distance requires visual feedback (Soechting and Flanders 1989b). The neural substrate exists in the premotor and primary motor cortex for significant sensory feedback (for reviews, see Lemon 1990; Wise 1985). Identifying the relative contributions of centrally generated input from peripherally derived input (i.e., sensory feedback) remains an important, unsolved problem.

The relative independence of these parameters and the temporal ordering of the coding suggest several new insights into the processing of kinematic information by the motor cortical areas. As reviewed above, directional tuning of neuronal discharge is prevalent in the cerebral cortex. In the reaction time task of this study, we found that the correlation with movement direction dominates the premovement period (Figs. 7 and 8). This finding clarifies why others have furnished little evidence for distance-related discharge in the premotor (Riehle and Requin 1989) and primary motor cortices (Schwartz and Georgopoulos 1987). These earlier studies concentrated on analyzing the premovement period. As shown in the present study, priority is given to direction in this period. It should be noted, however, that Kurata (1993) found a small percentage of neurons with distance-related discharge in premotor cortex during the premovement period.

Our observation that a cell's firing was correlated with

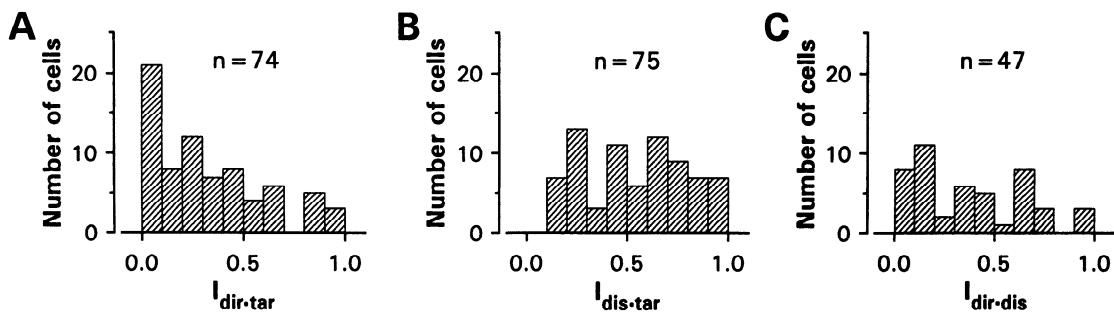


FIG. 13. Distribution of simultaneity indices for the statistically significant partial R^2 s that occurred during the transition periods for direction and target position (A), distance and target position (B), and direction and distance (C). The total number of cells used in generating the distributions is given as n .

target position was somewhat of an unanticipated finding. In the initial study (Fu et al. 1993b) these correlations arose from the need to consider the interactions between direction and distance. Although target position correlations have been shown previously for the tonic activity of primary motor cortical cells (Kettner et al. 1988), the present findings clarify the temporal characteristics of this relationship. Correlations with target position begin as early as movement onset and peak before holding at the final position. One possible interpretation is that target position encoding reflects the transition or overlap between direction and distance coding. However, several findings do not favor that interpretation. First, the I_S for many cells is small (<0.5) for both the simultaneous correlations with direction and target position and the simultaneous correlations with distance and target position. Second, the target position components of the correlations act as a unit. The onset and peak of the X and Y components of the correlation occur concurrently. The only difference is the delay in the onset of the simultaneous correlations with the X and Y of target position (Fig. 12). This delayed correlation may only reflect the added difficulty of having two components reach significance simultaneously. Therefore the X and Y correlations have some degree of independence from both direction and distance coding.

The correlation with movement distance develops last; this finding raises questions about the way in which this "late" information is used. One possibility is that this distance information is utilized for some type of final position control for obtaining and holding the target. Alternatively, this information may be used as a measure of final position from which subsequent movements are initiated. Target position information could also be utilized for the latter purpose.

One difference between the present results and those previously reported (Fu et al. 1993b) is that in the earlier study there was a higher percentage of cells with distance coding in the premovement period. There are two reasons for this apparent inconsistency. First, in the earlier report the premovement regression analysis was performed over a 200-ms period. In the present study, the temporal analysis evaluated for correlated cell activity in 20-ms bins. It would therefore be expected that the influence of random noise is greater in the present case. Second, we required that three consecutive bins have a statistically significant partial R^2 before accepting a parameter as correlated with the discharge. Both of these factors would be expected to make it somewhat more difficult to reach significance, especially given the lower partial R^2 values for distance. However, the major

contributor to the lower distance correlations is the 10-fold difference in time epochs (20 vs. 200 ms). This discrepancy should not be construed as a question of the validity of the two models. Instead, it asks the question of what is the time epoch used by the CNS to encode this information.

Correlation versus coding and covariation of movement parameters

The regression model and techniques used in this report were developed to evaluate further the hypothesis that movement direction, distance, and target location are represented in the discharge of motor and premotor neurons (Fu et al. 1993b). The presence of significant correlations between these parameters and neural discharge supports our hypothesis. Causality is not necessarily implied, but the possibility should not be excluded. Ideally, one wishes to determine the most parsimonious description of the discharge of these cells. One must recognize that other parameters of movement may be tightly coupled to the parameters analyzed in this report. Also, the possibility exists that an analysis in a different space than the Cartesian coordinates could yield a better fit to the data.

The temporal correlations uncovered by these analyses will aid in identifying the best descriptors. The delayed nature of the distance coding has such implications. Kinematic parameters such as velocity and acceleration covary with movement amplitude (Bouisset and Lestienne 1974; Cooke 1980; Flament et al. 1984; Freund and Budingen 1978), as do other parameters such as movement time (Fitts 1954) and force (Flanders and Hermann 1992). Furthermore, the muscles used and their patterns of activation also vary for movements of different amplitudes (Flanders 1991). In the present study, the relative accuracy requirements of the task also covaried with movement amplitude because target size was constant. In our previous publication we could not rule out the possibility that the relationship between neural discharge and amplitude was the consequence of the parallel changes in other movement parameters (Fu et al. 1993b). This was problematic because it has been demonstrated that the discharge of premotor neurons may have some weak modulation of the premovement discharge in relation to movement velocity (Kubota and Hamada 1978) and acceleration (Weinrich et al. 1984). It has also been shown that the firing of primary motor cortical cells is velocity related (Schwartz 1992, 1993). The finding of the temporal parcellation of movement parameter coding has considerable

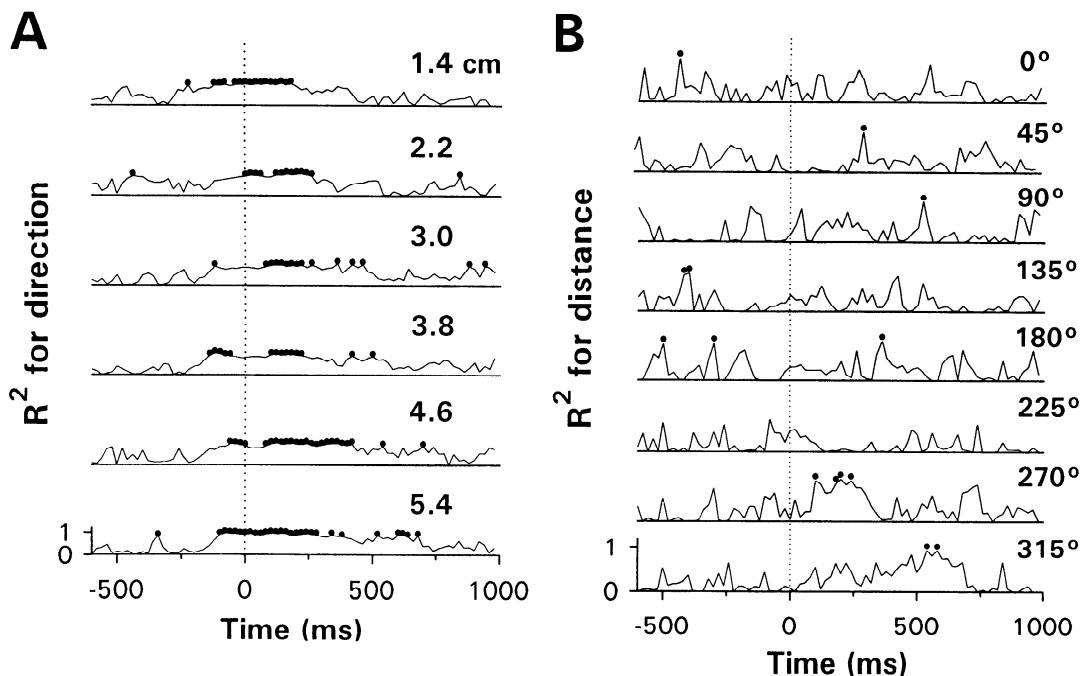


FIG. 14. Univariate model analyses as a function of time for direction and distance coding. Temporal profiles of the R^2 calculated from the cosine tuning model for direction-related activity (*A*) and from the linear regression model for distance-related activity (*B*). Dots: significant bins ($P < 0.01$).

bearing on this issue. The late timing of the correlations with distance makes it unlikely that velocity or its derivatives are specified by the distance correlation observed. The timing of the distance correlation lagged considerably behind the peak of hand velocity (Fig. 10*B*, middle plot). Similar arguments could apply to the major propulsive force or electromyographic activity, which could be expected to precede the late correlations observed with distance (Buneo et al. 1994; Flanders 1991).

Information processing in the motor and premotor cortices: serial or parallel?

There is debate as to whether the cortex processes parameter information, particularly direction and distance information, serially or in parallel (Goodman and Kelso 1980; Keele 1968; Larish and Frekany 1985; Megaw 1972; Rosenbaum 1980). In our previous investigation of parameter coding in motor and premotor cortices based on average firing rates (Fu et al. 1993b), we suggested that distance and direction were being processed to some degree in parallel. Two pieces of evidence led to this suggestion: 1) the relative independence of movement direction with distance-related modulation and a cell's preferred movement direction and 2) the encoding of both direction and distance in the premovement period by 47% of the cells recorded and the encoding of these parameters during the movement by 80% of the cells. We noted, however, that there was a tendency for the premovement discharge to be dominated by movement direction, whereas distance dominated the discharge during the movement, suggesting that an ongoing elaboration of kinematic information was occurring.

The present results now lead us to reinterpret the processing mechanisms involved in specifying kinematic parameters. It should be stressed that this study differs from

several others (Alexander and Crutcher 1990a,b; Fu et al. 1993b; Kurata 1993) in explicitly determining the time course of the various parametric correlations. The temporal difference between the onsets and peaks of direction, target position, and distance coding suggests that these parameters are processed primarily in a serial manner (Figs. 1–3, 8, and 9). This finding is consistent with the earlier psychophysical observations of Soechting and Flanders (1989a,b) that large distance errors occurred when moving to a remembered target (i.e., in the absence of continual updating of target information), whereas directional errors were much smaller. Thus more information about movement direction, compared with movement distance, appears to be specified in the premovement period by visual targeting.

Recent psychophysical findings suggest that direction and amplitude are specified in parallel (Favilla et al. 1989, 1990). It should be noted, however, that these studies were of isometric contractions of elbow muscles and that amplitude here refers to contractile force and not movement amplitude (i.e., distance). Parallel processing of information during both the preparation and execution of visually guided limb movements has been suggested by Alexander and Crutcher (1990b). In a thorough study of the primary motor cortex, the supplementary motor area, and the putamen in monkeys, these investigators analyzed cell discharge related to the movement itself and to the target (goal) of the movement. All three motor areas contained neurons whose discharge was modulated by the target of the movement as well as the direction of the limb movement, and this was true in both the preparatory and execution phases of the task. Because these variables were represented simultaneously in all three areas, parallel processing was suggested. The present study does not rule out this latter type of parallel processing. The serial processing hypothesis has been described in two forms. The first form is hierarchical, where a hierarchically

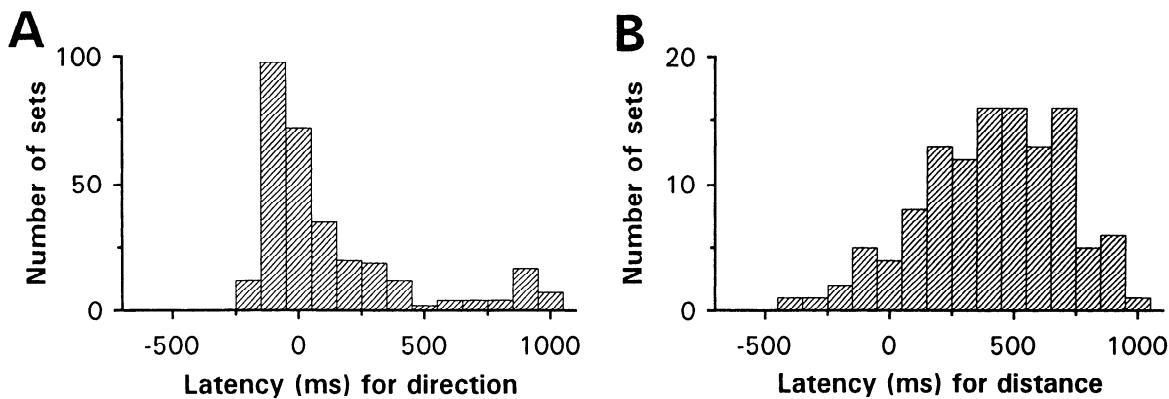


FIG. 15. Distribution of onset latency for direction (A) and distance (B) coding, based on the univariate regression model. For direction coding, the sets represent the number of cells and movement distances at which direction coding occurs; for distance coding, the sets represent the number of cells and movement directions at which distance coding occurs. Latencies, mean \pm SD: direction 123 ± 307 ms, distance 414 ± 284 ms.

lower parameter is processed in a top-down fashion (Larish and Frekany 1985; Megaw 1972). The second is a "distinctive-feature" form, where different parameters may be specified independently and, in its most general form, in any order (Rosenbaum 1980). Our data do not fit neatly into either form for a number of reasons. The independence of the correlations with direction, distance, and target position is clear at both the single-unit and population levels. Discharge of different cells was correlated with any single parameter or combination thereof. In this respect the data might be argued to fit the distinctive-feature form. However, the overwhelming temporal ordering of the parameters argues for a hierarchical organization. A strict classification, however, is probably unwarranted at this time for two reasons. First, overlap in the partial R^2 values occurs in the population statistics as well as in some cells. Second, the experimental design did not attempt to manipulate the requirements for direction, distance, or target position information. Conceivable in tasks demanding that distance information be used earlier, changes in the serial ordering of the correlations could be observed. Nonetheless, the temporal parcellation of the parameter encoding is evident, showing that the CNS utilizes this strategy in this reaching task.

Encoding of multiple movement parameters

There is a tendency for studies evaluating the encoding of movement parameters in the primary motor or premotor cortex to emphasize the encoding or representation of only a single movement parameter. Several studies have concentrated on the relationship of cells in these regions with force or muscle activation (Cheney and Fetz 1980; Evarts et al. 1968; Evarts and Fromm 1983; Fetz and Cheney 1980). Others have emphasized the correlation with direction (Georgopoulos et al. 1982, 1984, 1988). Two recent papers have argued that the coding of more than one parameter is occurring. Schwartz (1992, 1993) showed that both direction and velocity are represented, whereas we demonstrated that direction, distance, and target position are encoded (Fu et al. 1993b). Even in the latter study only 60% of the variance in cell discharge could be accounted for by direction and distance, leaving the possibility for the encoding of additional movement parameters. It should be emphasized that, even with the inclusion of distance and target position, a

large component of the cells' variance remains unaccounted for, indicating that other parameters must also be encoded in the cells' discharge.

How are multiple parameters encoded? An obvious possibility is by segregating parameters spatially or in different cells. On the basis of our earlier analysis of average firing rates there is some segregation of distance- and direction-related information in this population of cells, with distance-related firing more anteriorly located in the premotor areas (Fu et al. 1993b). However, no spatial segregation of the target position-related cells was observed, and the distance- and direction-related cells still showed considerable intermixing. As described in this paper, the discharge of most cells when analyzed temporally is correlated with all three parameters (Table 1). The potential for considerable ambiguity in interpreting the firing of the cells would seem to exist. The results described here suggest a novel mechanism by which the encoding of multiple parameters occurs; that is, by temporal parcellation. Although some overlap was observed in the population, distinct temporal profiles for the correlations were found. Equally interesting are the correlations with different movement parameters found in a single cell. Even in the transition periods between two different parameters, many single cells tended to be correlated with only one of the variables at a time. Therefore, both at the single-cell and the population level, the encoding schemes utilize a temporal parcellation mechanism. The net result is a reduction in the ambiguity associated with the encoding of the different parameters.

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