Movement Parameters and Neural Activity in Motor Cortex and Area 5

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The relations of ongoing single-cell activity in the arm area of the motor cortex and area 5 to parameters of evolving arm movements in two-dimensional (2D) space were investigated. A multiple linear regression model was used in which the ongoing impulse activity of cells at time $t + \tau$ was expressed as a function of the $\{X, Y\}$ components of the target direction and of position, velocity, and acceleration of the hand at time t, where τ was a time shift (-200 to $+200$ msec). Analysis was done on 290 cells in the motor cortex and 207 cells in area 5. The time shift at which the highest coefficient of determination (R^2) was observed was determined and the statistical significance of the model tested. The median R^2 was 0.581 and 0.530 for motor cortex and area 5, respectively. The median shift at which the highest R^2 was observed was -90 and $+30$ msec for motor cortex and area 5, respectively. For most cells statistically significant relations were observed to all four parameters tested; most prominent were the relations to target direction and least prominent those to acceleration.

An important question in motor neurophysiology concerns the parameters of the motor output to which cell activity within areas involved in motor function might relate. This problem has been investigated mainly by correlating the average frequency of cell discharge to aspects of motor parameters, including their intensity and direction (see Evarts, 1981; Georgopoulos, 1991; Kalaska and Crammond, 1992). However, little attention has been paid to an analysis of the time course of the ongoing cell activity in relation to evolving motor parameters. Humphrey et al. (1970) were able to predict the time course of the force, velocity, and displacement during flexion-extension movements of the wrist, using suitably added temporal profiles of three to eight simultaneously recorded cells in the motor cortex of the monkey. Flament and Hore (1988) studied the time course of activity of cells the discharge of which changed reciprocally with imposed flexion-extension movement perturbations about the elbow. It was found that in the majority of cases the time course of neural activity resembled that of acceleration, whereas in other cases it resembled that of velocity. Finally, Beddingham and Tatton (1985) found that the activity of some cells in the motor cortex of the cat related to the acceleration and jerk components of passive movements about the elbow.

In the present study we reexamined the issue of the relations of ongoing single-cell activity to the evolving parameters of movement for 2D movements made toward eight visual targets in a reaction time task (Georgopoulos et al., 1982). For that purpose we used a multiple linear regression model that assessed the relations between single-cell activity and the $\{X, Y\}$ components of the visually defined direction of the target, relative to the origin of the movement, and the $\{X, Y\}$ components of the position, velocity, and acceleration of the movement. We performed these analyses for cells recorded in the arm area of the motor cortex (Georgopoulos et al., 1982) and area 5 of the parietal cortex (Kalaska et al., 1983).

Materials and Methods

Database

The data analyzed came from single-cell recordings performed previously in our laboratory. The data consisted of impulse activity of 290 cells recorded in the arm area of the motor cortex (five hemispheres of

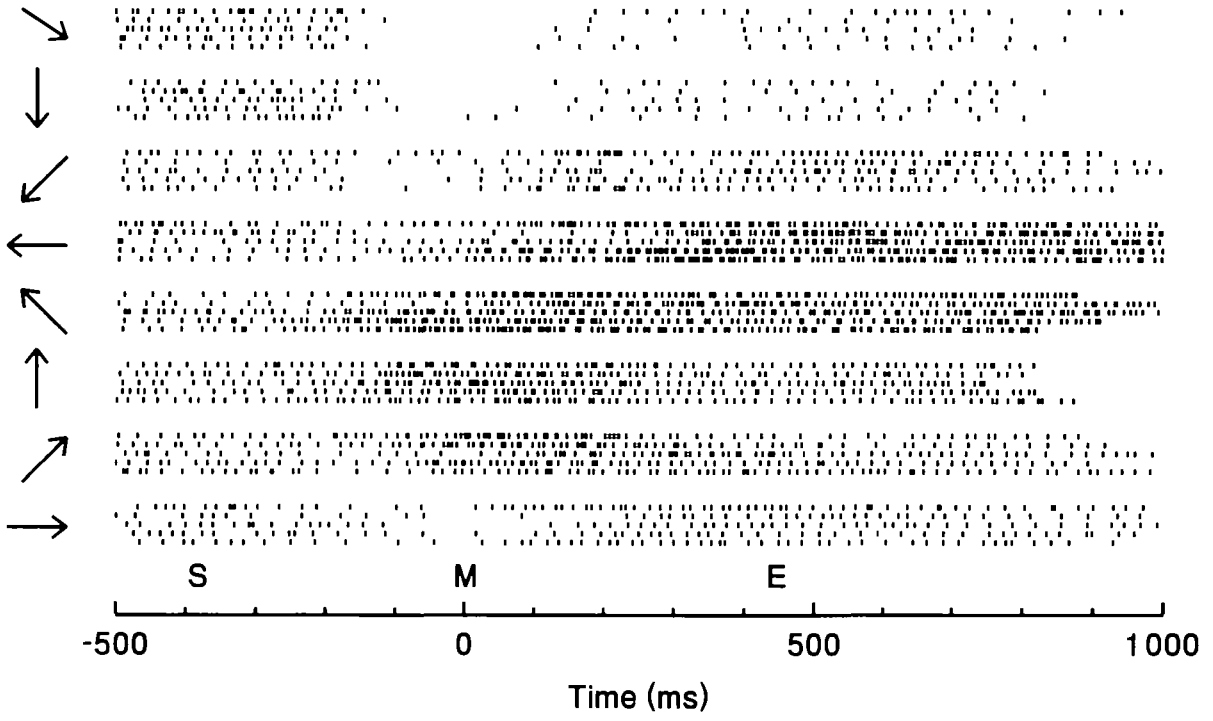

Figure 1. Spike trains from one cell are illustrated as 40 rasters corresponding to 40 trials. Rasters are arranged in eight sets of five rasters each, each set corresponding to a movement direction indicated by the arrows. *M*, onset of movement; *S* and *E*, average time of target onset and end of movement, respectively.

four monkeys; see Georgopoulos et al., 1982) and 207 cells recorded in the arm area of area 5 (three hemispheres of three monkeys; see Kalaska et al., 1983). The monkeys moved a handle on a planar working surface in eight radially arranged directions, from the center to light-emitting diodes serving as visual targets in a reaction time task. The behavioral procedures, surgical operations (performed under general pentobarbital anesthesia, 28 mg/kg), and data collection techniques are described elsewhere (Georgopoulos et al., 1982). Neuronal impulse activity was collected with a time resolution of 0.1 msec. The $\{X, Y\}$ components of the position of the distal end of the handle were recorded every 10 msec with a spatial resolution of 0.125 mm.

Data Analysis

The data analyzed consisted of 40 single trials per cell, five for each of the eight directions mentioned above. The exit of the manipulandum from a 10-mm-diameter circular positional window centered on the starting point indicated the approximate onset of the movement, and the entrance of the manipulandum into a 35-mm-diameter circular positional window centered on the target of the movement indicated the approximate end of the movement (Georgopoulos et al., 1982); a liquid reward was delivered 500 msec later. We call T the time from the onset of the target until the delivery of the reward.

An example of spike train data from one cell is shown in Figure 1. The spike train was binned (0.01 sec binwidth) and the time-varying frequency of cell discharge, *d*, computed using fractional interspike intervals. The resulting intensity function, $f(t)$, was smoothed using a digital low-pass filter, and the square root taken and divided by 0.01 to convert it to units of impulses/sec:

$$f(t) = \sqrt{d(t)}/0.01 \qquad (1)$$

The square root transformation was used to stabilize the variance (Cox and Lewis, 1966, p 44). The $\{X, Y\}$ position data were smoothed using a digital low-pass filter; velocity and acceleration were obtained from the smoothed position data by single and double digital differentiation, respectively, using a five-point Lagrange polynomial approximation. Records from a single trial are shown in Figure 2. The following analyses were carried out.

Multiple Linear Regression

A multiple linear regression was performed (Draper and Smith, 1981) in which the trial-by-trial time course of the square-rooted frequency of cell discharge, f, at time $t + \tau$ (τ is a time shift, from -200 to $+200$ msec at 10 msec intervals) was expressed as a function of the target direction (expressed as the cosine and sine functions of the target polar angle), and of the position (x, y in meters), velocity ($\dot{x}$, $\dot{y}$ in m/sec), and acceleration ($\ddot{x}$, $\ddot{y}$ in m/sec^2) of the hand at time t, measured from the onset of the movement:

$$f_{t+\tau} = b_0 + b_1\cos(\phi) + b_2\sin(\phi) + b_3x_t + b_4y_t + b_5\dot{x}_t + b_6\dot{y}_t + b_7\ddot{x}_t + b_8\ddot{y}_t + \epsilon_t, \quad t + \tau \le T, \qquad (2)$$

where b_0–b_8 are regression coefficients, ϵ is an error term, and T is the period of time from the onset of the target until the delivery of reward. The inequality above means that the neural data included within the

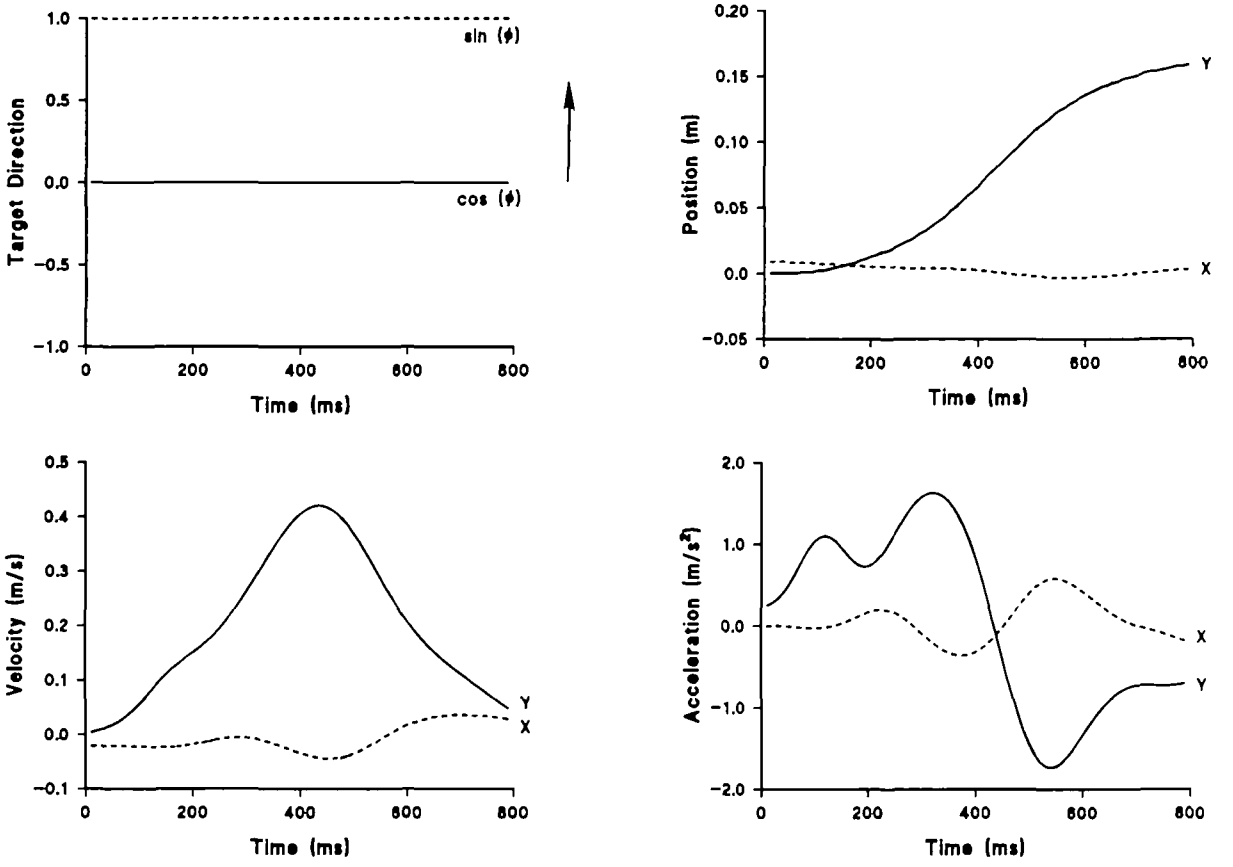

Figure 2. Examples of the time course of the movement parameters used from a single trial of a movement toward 12 o'clock (see *arrow*).

shifted spike train were always contained within the behaviorally meaningful time period T. The shifting operation is illustrated in Figure 3. Finally, it should be noted that target direction has been entered in Equation 2 as a time-invariant constant because it did not vary with time within a given trial, and therefore did not provide time-related information. However, it was a controlled, fixed variable that differed for trials in different directions, and therefore qualified as an independent variable in that context.

For every time shift, the standardized regression coefficients were also calculated. These are coefficients obtained when observations are expressed as Z scores (i.e., in standard deviation units), and are therefore dimensionless. The standardized coefficients allow a comparison among variables and provide information about the importance of a given variable in the regression equation. Since all variables above consist of X and Y components, the resultant of the standardized coefficient pair was computed for each variable as the square root of the sum of the squares of the standardized regression coefficients corresponding to the {X, Y} components of a parameter. The length of this resultant indicates the relative importance of the variable. Therefore, the four resultants (one for each parameter) were rank ordered and the number of cells for which each parameter was ranked first was calculated.

The detailed construction of the model for the analysis of the data from one cell was as follows. Let 1, 2, 3, . . . , k be single trials, each consisting of [1, 2, 3, . . . , $n(1)$], [1, 2, 3, . . . , $n(2)$], [1, 2, 3, . . . , $n(3)$], . . . , [1, 2, 3, . . , $n(k)$] 10 msec time bins; then the total number N of bins is

$$N = n(1) + n(2) + n(3) + \ldots + n(k) = \sum_{i=1}^{k} n(i) \quad (3)$$

In matrix notation, Equation 2 can be written as

$$\mathbf{F}(t + \tau) = \mathbf{M}(t)\boldsymbol{\beta} + \boldsymbol{\epsilon}, \quad (4)$$

where $\mathbf{F}$ is an $N \times 1$ vector containing the time-varying neural frequency of discharge, $\mathbf{M}$ is an $N \times 9$ matrix containing the data for trial-related, constant target direction and the time-varying movement parameters, $\boldsymbol{\beta}$ is a 9×1 vector containing the regression coefficients, and $\boldsymbol{\epsilon}$ is an $N \times 1$ vector containing the error term. The extended form of Equation 4 for one time shift τ is shown in Figure 4. It is noteworthy that the target direction [cos(ϕ) and sin(ϕ)] has been entered in the matrix of independent variables ($\mathbf{M}$) as a trial-related, but not time-varying, variable since it differed for movements in different directions but did not vary with time within a given trial.

The coefficient of determination, R^2 (proportion of variance explained), was measured at each shift (−200 to +200 msec, every 10 msec), and the shift for which the highest R^2 was obtained was noted. The

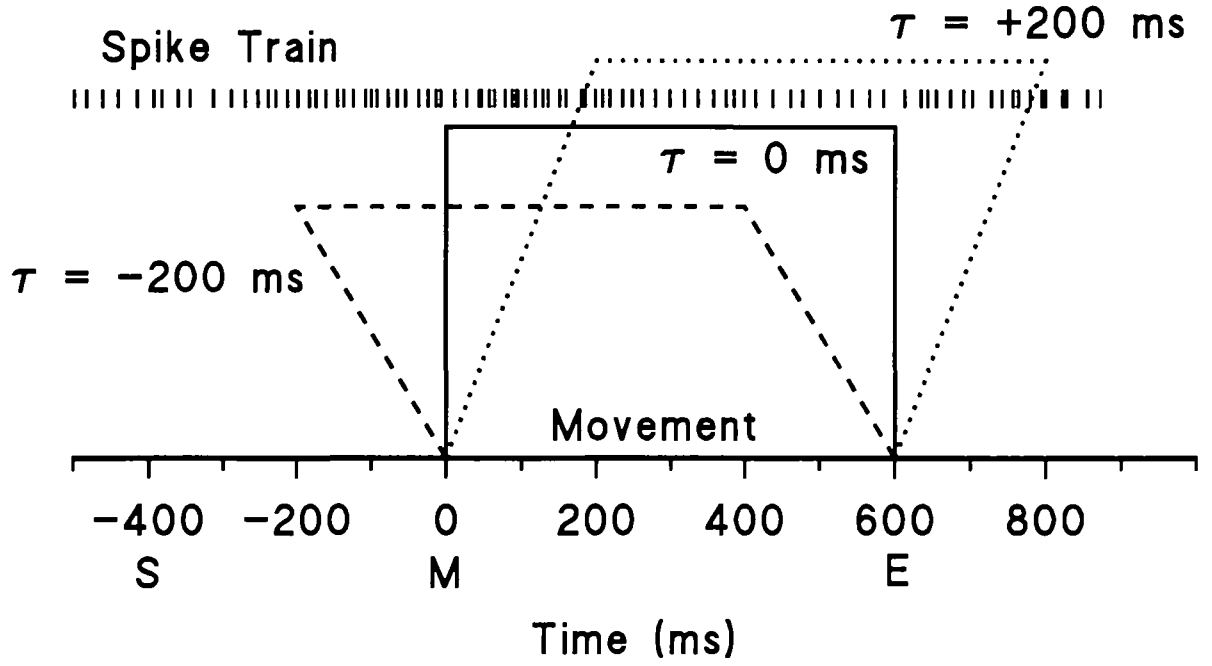

Figure 3. Schematic diagram illustrating the time shift of the neural data, relative to the movement data for a single trial. The movement data are delimited between the onset (*M*) and end (*E*) of the movement; *S*, time of target onset. The neural data (spike train) are systematically shifted between the range of −200 to +200 msec; the 0 msec shift case is also shown (intermediate shifts every 10 msec are not illustrated).

beginning and end of t in Equation 2 above was at the onset and the end of the movement, respectively (see above) It should be noted that the time shift τ in Figure 4 (F) above is the same for all trials, and that all shifting was done separately within each trial and did not extend across adjacent trials (see inequality in Eq. 2 above).

Statistical Significance of the Model

The statistical significance of the model was tested using two different methods. In the first method, the F test was calculated and its statistical significance determined. In the second method, a bootstrapping procedure was used in which the bins of the spike train were shuffled randomly and the regression was redone and the R^2 recalculated. This was done 100 times, each with a different random shuffling of the bins of the spike train. Then the 100 R^2 values thus obtained were rank ordered and the number of these that were higher than the R^2 actually obtained from the original, unshuffled data was noted. this number indicated the probability (as percentage, since 100 random shufflings were performed) that the actually observed R^2 could be due to chance. For both the F test and the bootstrapping procedure a level of $P < 0.05$ was taken to indicate that the regression model was statistically significant. The regression analysis was repeated using the $\{X, Y\}$ components of only one variable at a time (target direction, position, velocity, acceleration) to determine which variable yielded the highest R^2.

The t statistic and its probability level were calculated for each coefficient. Since eight simultaneous comparisons were performed, the nominal probability level of $\alpha = 0.05$ was adjusted according to the Bonferroni inequality (Snedecor and Cochran, 1980) to $\alpha' = 0.05/8 \approx 0.005$, so $P < 0.005$ was considered statistically significant. A cell was deemed to be significantly related to a parameter if at least one of the two coefficients (corresponding to the $\{X, Y\}$ component of the parameter) was statistically significant.

Predicted Frequency of Discharge

Using Equation 2 the predicted frequency of discharge was obtained. The differences between the observed and predicted discharge rates for each time bin are the regression residuals. An analysis of the residuals showed that, although they were approximately normally distributed and were approximately constant for the range of predicted values, they were frequently correlated, as expected from the time-domain data analyzed; plots of the autocorrelation function and the partial autocorrelation function of the residuals indicated that typically the residuals fit a first-order autoregressive process. Therefore, the analyses concerning the statistical significance of the regression coefficients above were supplemented by an additional regression analysis appropriate for correlated errors. For that purpose, the program AREG of the SPSS/PC+ statistical package for Windows (SPSS Inc., Chicago, IL) was used; trials in Figure 4 were separated by a single row of missing data values and the regression was carried out using the exact maximum-likelihood estimation method of the program.

Overall Statistical Comparison

Finally, the results obtained from the motor cortical and area 5 population were compared using standard statistical methods (Snedecor and Cochran, 1980).

$$\mathbf{F} = \begin{vmatrix} f_{1(1+\tau)} \\ f_{1(2+\tau)} \\ f_{1(3+\tau)} \\ \vdots \\ f_{1(n(1)+\tau)} \\ \hline f_{2(1+\tau)} \\ f_{2(2+\tau)} \\ f_{2(3+\tau)} \\ \vdots \\ f_{2(n(2)+\tau)} \\ \hline f_{3(1+\tau)} \\ f_{3(2+\tau)} \\ f_{3(3+\tau)} \\ \vdots \\ f_{3(n(3)+\tau)} \\ \hline \vdots \\ \hline f_{k(1+\tau)} \\ f_{k(2+\tau)} \\ f_{k(3+\tau)} \\ \vdots \\ f_{k(n(k)+\tau)} \end{vmatrix} \quad \mathbf{M} = \begin{vmatrix} 1 & \cos(\phi)_1 & \sin(\phi)_1 & x_{11} & y_{11} & \dot{x}_{11} & \dot{y}_{11} & \ddot{x}_{11} & \ddot{y}_{11} \\ 1 & \cos(\phi)_1 & \sin(\phi)_1 & x_{12} & y_{12} & \dot{x}_{12} & \dot{y}_{12} & \ddot{x}_{12} & \ddot{y}_{12} \\ 1 & \cos(\phi)_1 & \sin(\phi)_1 & x_{13} & y_{13} & \dot{x}_{13} & \dot{y}_{13} & \ddot{x}_{13} & \ddot{y}_{13} \\ \vdots & & & \vdots & & & & & \\ 1 & \cos(\phi)_1 & \sin(\phi)_1 & x_{1n(1)} & y_{1n(1)} & \dot{x}_{1n(1)} & \dot{y}_{1n(1)} & \ddot{x}_{1n(1)} & \ddot{y}_{1n(1)} \\ \hline 1 & \cos(\phi)_2 & \sin(\phi)_2 & x_{21} & y_{21} & \dot{x}_{21} & \dot{y}_{21} & \ddot{x}_{21} & \ddot{y}_{21} \\ 1 & \cos(\phi)_2 & \sin(\phi)_2 & x_{22} & y_{22} & \dot{x}_{22} & \dot{y}_{22} & \ddot{x}_{22} & \ddot{y}_{22} \\ 1 & \cos(\phi)_2 & \sin(\phi)_2 & x_{23} & y_{23} & \dot{x}_{23} & \dot{y}_{23} & \ddot{x}_{23} & \ddot{y}_{23} \\ \vdots & & & \vdots & & & & & \\ 1 & \cos(\phi)_2 & \sin(\phi)_2 & x_{2n(2)} & y_{2n(2)} & \dot{x}_{2n(2)} & \dot{y}_{2n(2)} & \ddot{x}_{2n(2)} & \ddot{y}_{2n(2)} \\ \hline 1 & \cos(\phi)_3 & \sin(\phi)_3 & x_{31} & y_{31} & \dot{x}_{31} & \dot{y}_{31} & \ddot{x}_{31} & \ddot{y}_{31} \\ 1 & \cos(\phi)_3 & \sin(\phi)_3 & x_{32} & y_{32} & \dot{x}_{32} & \dot{y}_{32} & \ddot{x}_{32} & \ddot{y}_{32} \\ 1 & \cos(\phi)_3 & \sin(\phi)_3 & x_{33} & y_{33} & \dot{x}_{33} & \dot{y}_{33} & \ddot{x}_{33} & \ddot{y}_{33} \\ \vdots & & & \vdots & & & & & \\ 1 & \cos(\phi)_3 & \sin(\phi)_3 & x_{3n(3)} & y_{3n(3)} & \dot{x}_{3n(3)} & \dot{y}_{3n(3)} & \ddot{x}_{3n(3)} & \ddot{y}_{3n(3)} \\ \hline \vdots & & & \vdots & & & & & \\ \hline 1 & \cos(\phi)_k & \sin(\phi)_k & x_{k1} & y_{k1} & \dot{x}_{k1} & \dot{y}_{k1} & \ddot{x}_{k1} & \ddot{y}_{k1} \\ 1 & \cos(\phi)_k & \sin(\phi)_k & x_{k2} & y_{k2} & \dot{x}_{k2} & \dot{y}_{k2} & \ddot{x}_{k2} & \ddot{y}_{k2} \\ 1 & \cos(\phi)_k & \sin(\phi)_k & x_{k3} & y_{k3} & \dot{x}_{k3} & \dot{y}_{k3} & \ddot{x}_{k3} & \ddot{y}_{k3} \\ \vdots & & & \vdots & & & & & \\ 1 & \cos(\phi)_k & \sin(\phi)_k & x_{kn(k)} & y_{kn(k)} & \dot{x}_{kn(k)} & \dot{y}_{kn(k)} & \ddot{x}_{kn(k)} & \ddot{y}_{kn(k)} \end{vmatrix}$$

$$\beta = \begin{vmatrix} b_0 \\ b_1 \\ b_2 \\ b_3 \\ b_4 \\ b_5 \\ b_6 \\ b_7 \\ b_8 \end{vmatrix} \quad \varepsilon = \begin{vmatrix} \varepsilon_{11} \\ \varepsilon_{12} \\ \varepsilon_{13} \\ \vdots \\ \varepsilon_{1n(1)} \\ \hline \varepsilon_{21} \\ \varepsilon_{22} \\ \varepsilon_{23} \\ \vdots \\ \varepsilon_{2n(2)} \\ \hline \varepsilon_{31} \\ \varepsilon_{32} \\ \varepsilon_{33} \\ \vdots \\ \varepsilon_{3n(3)} \\ \hline \vdots \\ \hline \varepsilon_{k1} \\ \varepsilon_{k2} \\ \varepsilon_{k3} \\ \vdots \\ \varepsilon_{kn(k)} \end{vmatrix}$$

Figure 4. Extended form of Equation 4 (see Materials and Methods) for one time shift τ. The *first* and *second subscripts* denote the trial and time bin, respectively. Individual trials are separated by *dashed lines*.

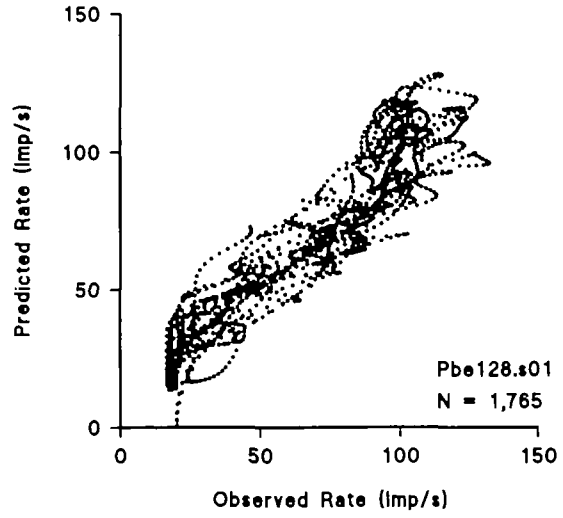

Figure 5. Discharge rate (in 10 msec bins; N = 1765, 40 trials) predicted by the regression model (Eqs. 2, 5) is plotted against that observed for the motor cortical cell for which data are illustrated in Figures 1–3 above. Cell Pbe128.s01.

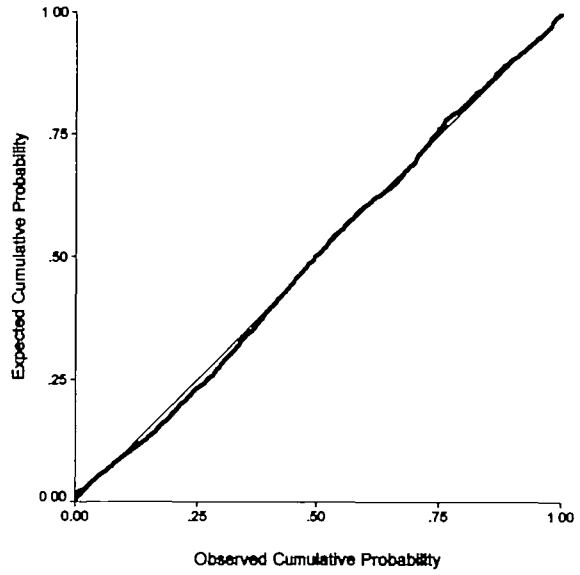

Figure 6. Normal cumulative probability–probability plot (*thick line*) of the observed regression residuals against those expected from a normal distribution. The *thin line* along the diagonal indicates the case for a perfect normal distribution. Data are from the cell illustrated in Figure 5 (see Eq. 5).

Results

Regression Model

In all cases, the regression model above (Eq. 2) was statistically significant (F test, $P < 0.05$) at the shift with the highest R^2. An example is shown in Figure 5, in which the predicted frequency of discharge is plotted against the observed one. It can be seen that the points are spread along the diagonal (perfect prediction). The regression equation was

$$f_{t-\tau} = 69.84 + 6.60\cos(\phi) + 13.28\sin(\phi) - 210.68x - 69.29y - 25.59\dot{x} + 91.85\dot{y} - 5.81\ddot{x} - 1.55\ddot{y} + \epsilon_t, \quad (5)$$

where $R^2 = 0.864$ and $\tau = -110$ msec The distribution of the regression residuals ϵ_t approximated closely a normal distribution (Fig. 6). Finally, all regression coefficients were statistically significant ($P < 10^{-5}$).

Proportion of Variance Accounted for by the Model

The R^2 indicates the proportion of variance in cell activity accounted for by the regression model. The R^2 was higher, overall, in motor cortex than in area 5; the median R^2 was 0.581 and 0.530 for motor cortex and area 5, respectively. The cumulative frequency distributions of R^2 are shown in Figure 7 (top); they differ significantly ($P < 0.001$, Kolmogorov-Smirnov test).

Time Shift

The neural time shifts at which the highest R^2 were observed were appreciably earlier in the motor cortex than in area 5; the median shifts were −90 and +30 msec, respectively. The cumulative frequency distributions are shown in Figure 7 (bottom); they differ significantly ($P < 0.001$, Kolmogorov-Smirnov test).

Movement Parameters

The question of the relations of neural activity to the time-varying movement parameters and the time-in-

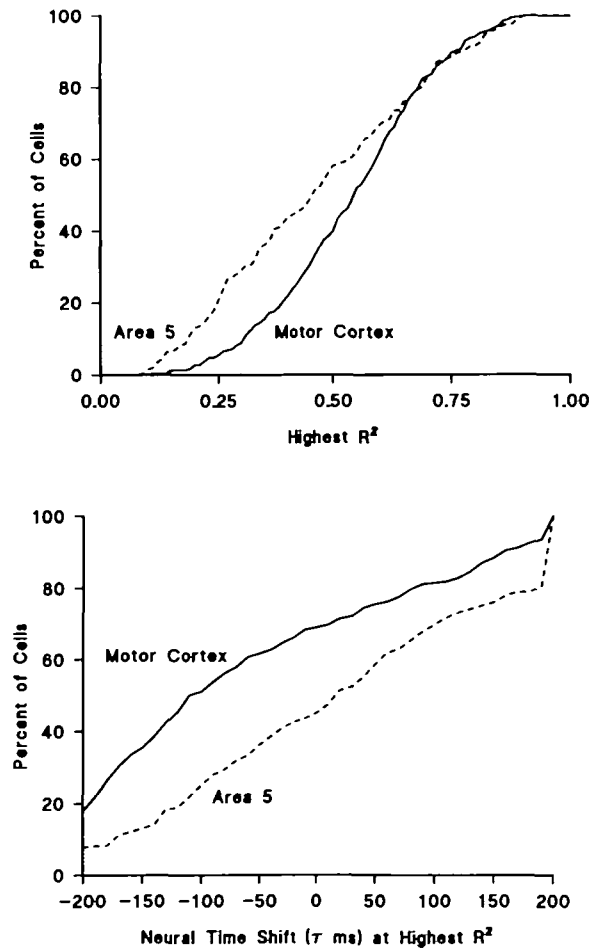

Figure 7. Cumulative frequency distributions of the proportion of variance explained (R^2) (*top*) and of the time shift at which the highest R^2 was observed (*bottom*).

Table 1
Numbers and percentages (in parentheses) of cells for which the noted variable yielded the highest R^2

Variable	Motor cortex	Area 5
Target direction	135 (46.55)	88 (42.51)
Velocity	115 (39.66)	91 (43.96)
Position	21 (7.24)	20 (9.66)
Acceleration	19 (6.55)	8 (3.87)
Total	290 (100%)	207 (100%)

variant target direction was investigated using four different approaches. First, the explanatory power of each parameter *independently of the other parameters* was assessed by calculating the R^2 in a regression model in which only the {*X*, *Y*} components of that parameter were entered as independent variables. The results of this analysis are given in Table 1, which shows that target direction and movement velocity possessed the highest explanatory power in motor cortex and area 5, respectively. Second, the explanatory power of each parameter *within the context of the other parameters* was assessed by calculating the standardized coefficients in the multiple regression model in which all the parameters were entered as independent variables (Eq. 2). The results of this analysis were very similar in both areas studied. They are illustrated in Figure 8, which shows that target direction was the most important parameter in >50% of cells, followed by velocity and position; acceleration did not rank first in any area 5 cell and in only 1.7% of cells in the motor cortex. Third, the question was investigated whether neuronal activity *related to one or more of the parameters tested*; this was evaluated by testing the statistical significance of the regression coefficients. The main result was that in the large majority of cases, all four parameters tested contributed significantly to the variation in neuronal activity, as shown in Figure 9. Very similar results were obtained when the statistical significance of the coefficients was tested using the AREG program (see Materials and Methods). Finally, a different question concerns *the percentage of cells for which a given parameter was statistically significant*, irrespective of the rank or importance of that parameter relative to the other parameters Table 2 shows that any of the four movement parameters tested was significant in over 80% of cells in both areas studied.

Discussion

In this study we examined the relations between the time course of cell activity in the motor cortex and area 5, and various parameters of movement using a multiple linear regression model. In previous studies, direction has been shown to be a major determinant of single-cell activity in motor cortex (Georgopoulos et al., 1982) and area 5 (Kalaska et al , 1983). In those studies, the regression model consisted of the average frequency of cell discharge, as the dependent variable, and the trial-related constant direction, as the independent variable. Under those conditions, the direction accounted for a significant portion of the variance in average cell activity. However, that model did not incorporate any information about the time course of cell activity during a trial because the target direction did not vary with time and therefore could not have served as an independent variable in that context. Since reaching movements evolve in time, they do comprise time-varying parameters, including position, velocity, and acceleration. These parameters not only vary with time but also encompass an adequate spectrum of movement-related information, including kinematic and kinetic information. Therefore, we incorporated these parameters in our present

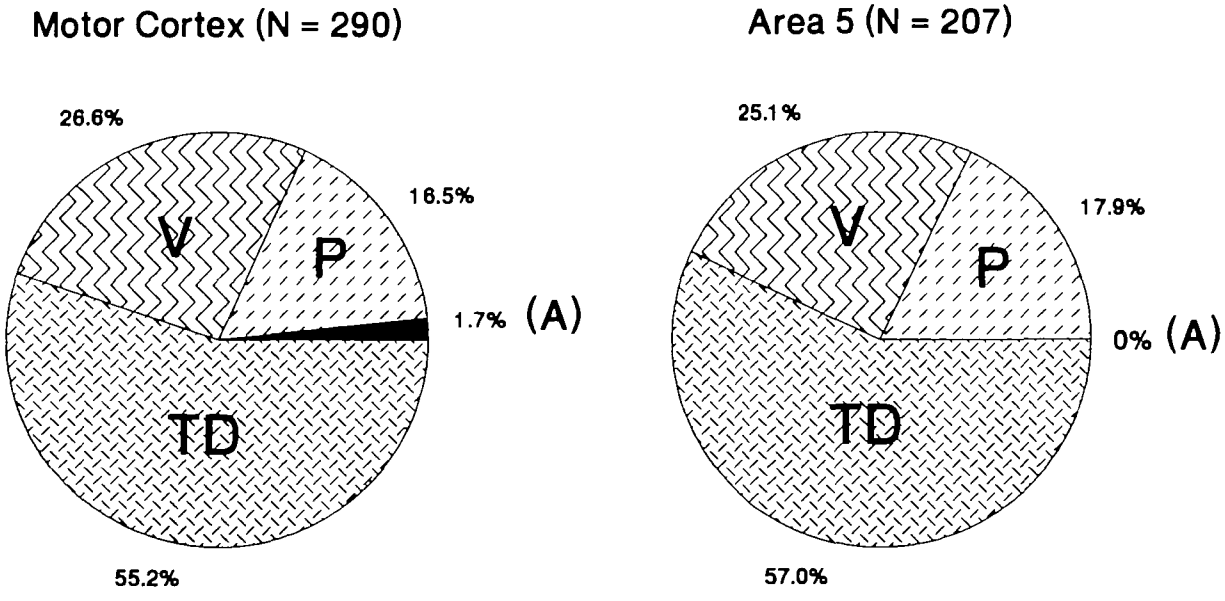

Figure 8. Percentages of cells for which the noted movement parameter was ranked first in the standardized coefficients analysis (see Materials and Methods). *TD*, target direction; *V*, velocity; *P*, position; *A*, acceleration.

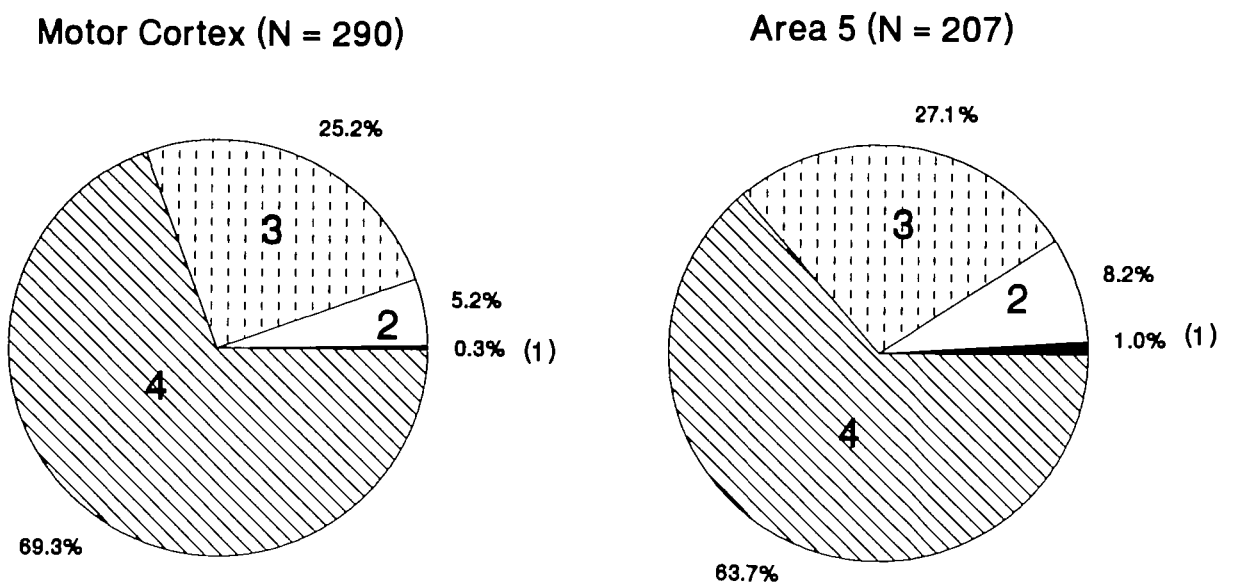

Figure 9. Percentages of cells that showed significant relations to one or more parameters of movement (*numbers inside slices or in parentheses*)

model and tested the hypothesis that the time-varying cell activity is a function of both a constant target direction as well as of time-varying movement parameters. The salient findings of the study were that (1) most cells in both areas studied related significantly to all of the parameters tested, (2) the target direction was the most important determinant of the variation in cell activity in both areas studied, followed by velocity and position, and (3) there were significant differences between the motor cortex and area 5 regarding the proportion of the variance of cell activity accounted for by the model and the time shift at which these relations were strongest. We discuss these findings separately below.

Methodological Considerations

The multiple linear regression analysis we used in this study is a standard statistical technique. Theoretically, a polynomial regression model and/or a regression model nonlinear in the parameters could have been used, but our purpose was not to fit a curve but to quantify the explanatory power of the parameters used within the context of a linear model. The parameters incorporated in the model comprised a reasonable range of time-varying movement parameters, including position, velocity, and acceleration, and the time-invariant target direction which, in the behavioral task employed, provided the information for the direction and amplitude of the movement. All of these parameters were entered in the model as X and Y components, for it has been shown that the relations of cell activity to the amplitude of the movement can differ for different movement directions (Fu et al., 1993).

Finally, it should be noted that other factors, unaccounted for in the present analysis, might also be important determinants of cell activity; there is always room for improvement, so that, by inclusion of novel factors, the R^2 distributions in Figure 7 (top) might be raised to higher levels. However, the analysis of the residuals indicated that the errors in prediction were random and did not vary systematically at different levels of the dependent (or predicted) variable; this suggests a noisy relation rather than an incorrect model.

Table 2
Numbers and percentages (in parentheses) of cells for which the noted variable yielded a statistically significant regression coefficient in the X or Y component of the variable

Variable	Motor cortex	Area 5
Target direction	278/290 (95.8)	187/207 (90.3)
Velocity	275 (94.8)	192 (92.7)
Position	265 (91.4)	180 (86.7)
Acceleration	236 (81.4)	169 (81.6)

Parameters of Movement and Cell Activity

A major finding of this study was that a large proportion of cells in both motor cortex and area 5 related significantly to all the parameters tested (Fig. 9), and, conversely, any of the parameters tested had a statistically significant effect in a large percentage of cells in both areas studied (Table 2). This is in essential agreement with the original observations of Humphrey et al. (1970), and the more recent findings of Schwartz (1992), and suggests a distributed system of representation of the various visuomotor parameters; namely, there are hardly any cells specific for a particular parameter but, instead, each cell codes for several parameters. Therefore, a given parameter is coded in the discharge of the neuronal population. Other studies of the time course of neuronal activity (Flament and Hore, 1988) did not analyze the data by multiple regression, and therefore could not evaluate the relative contributions of different motor parameters within the same model.

The discussion below is focused on the relative importance of the movement parameters tested using the model described above.

Direction

A clear finding of this study was the prominence of the target direction as the single most important explanatory parameter for accounting for variation in cell activity in >50% of cells in motor cortex and area 5 (Fig. 8). This result is in accord with those of previous studies (Georgopoulos et al., 1982; Kalaska et al., 1983). This finding is noteworthy because it was derived from the regression model in which all parameters were entered as independent variables (Eq. 2), and, therefore, reflects more closely the true state of affairs than the model in which each parameter was tested alone (Table 1). However, it should be noted that target direction was entered in the regression model as a trial-related but time-invariant constant (see Eq. 2; Fig. 4, **M**), because it differed for movements in different directions but did not change with time within a given trial. Since the experimentally controlled target direction provided the instruction for the direction of the upcoming movement, the inclusion of this information in the model is necessary; however, since this parameter is not a temporal variable, its contribution to the model should be qualified as the contribution of a fixed variable, and therefore distinguished from that of the remaining time-varying parameters discussed below.

Velocity

In addition to direction, the velocity of the movement was an important explanatory variable (Fig. 8, Table 1). The importance of both of these variables for the time course of cell activity in the motor cortex was documented recently in a 2D drawing task (Schwartz, 1992). There have been four studies in the motor cortex which explicitly addressed the relation between velocity and cell activity in primate motor cortex (Humphrey et al., 1970; Hamada and Kubota, 1979; Hamada, 1981; Flament and Hore, 1988). Humphrey et al (1970) used a function based on the time course of cell activity to predict the time course of various movement parameters The predictive value of this function was strongest when based on the activity of several simultaneously recorded neurons. Under these conditions the correlation between observed and predicted values was statistically significant for force, velocity and displacement. There are a number of significant methodological differences among the studies above. Humphrey et al. (1970) used the correlation coefficient derived for each individual parameter as a multiplier of the time course of cell activity to predict the time course of that parameter. Flament and Hore (1988) identified a number of cells whose activity resembled, in its time course, the speed of movement. Hamada and Kubota (1979) found 20% of pyramidal tract neurons in which the average firing frequency in the reaction time correlated with the peak velocity during the movement. In a later study, Hamada (1981) did not find any relation between the activity of 41 pyramidal tract cells and velocity. In summary, the results of the various studies discussed above and those of this study indicate that cell activity in the motor cortex and movement velocity is well related in the temporal domain, but this relation may not be strong in other analyses; for example, the intensity of cell discharge during the reaction time may not predict well the peak velocity of the ensuing movement (Kubota and Hamada, 1979; Hamada, 1981). It is interesting that a temporal association has also been described in the eye movement system between saccadic eye velocity and the ongoing discharge of cells in the superior colliculus (Berthoz et al., 1986).

Position

The position was, overall, third in importance as an explanatory variable for the time course of cell activity in both areas studied (Fig. 8, Table 1). Although the relations of cell activity in motor cortex and area 5 to hand position in 2D space are well established under static conditions (Georgopoulos et al., 1984), these relations have not been examined under dynamic conditions. In studies of the relations between neural activity in motor cortex and the amplitude of the movement (Schwartz and Georgopoulos, 1987; Georgopoulos, 1990; Fu et al., 1993), the amplitude covaried with the velocity of the movement and the position of the target. By contrast, the time course analysis in the present study effectively distinguished these different parameters. The results of the present study essentially confirmed those of previous studies, including the recent study of Fu et al. (1993), namely, that amplitude is a significant variable for cell activity but quantitatively less important than direction.

Acceleration

In the present study, the relations of cell activity to acceleration were not very prominent. Acceleration, considered independently of the other parameters, was the most important parameter in only a small proportion of cells (Table 1), although this proportion was almost twice as high in the motor cortex (6.55%) than in area 5 (3.87%), a finding in accord with the idea that motor cortex may be more involved with kinetics than area 5 (Kalaska et al., 1990). However, in the analysis of standardized coefficients, acceleration was ranked first in only 1.7% of motor cortical cells and in none of area 5 cells (Fig. 8). These results do not mean that acceleration was not a significant variable, for a large proportion of cells related to all four parameters tested (Fig. 9, Table 2); instead, these findings show that, when comparisons and rankings were made, the time course of cell activity was dominated by the other three parameters.

Given that the time course of the $\{X, Y\}$ acceleration generally resembles the time course of the corresponding components of force acting on the manipulandum, and that the latter has been calculated previously on the basis of the former (Massey et al., 1986), the present results suggest that force is not a dominant factor in determining the time course of cell activity under dynamic conditions of generation and

execution of reaching movements. Under those conditions, direction, velocity, and position seem to be the major factors involved. This could reflect both feedforward motor commands and feedback signals from peripheral receptors in the contracting muscles and the moving limb. It is likely that the high proportion of motor cortical cells related to acceleration reported by Flament and Hore (1988) could be due to the criteria employed to select cells for study, namely, cells whose activity changed in a reciprocal fashion (i.e., increase vs decrease of activity) with flexion-extension movements about the elbow.

Processing in Area 5 and Motor Cortex

Area 5 and motor cortex are interconnected anatomically and they both have separate connections with other motor and sensory areas, in addition to projections to the spinal cord. The primary somatosensory cortex projects to area 5 (Jones and Powell, 1969, 1970; Pandya and Kuypers, 1969; Vogt and Pandya, 1978), and area 5, in turn, projects to the motor cortex (Strick and Kim, 1978; Zarzecki et al., 1978; Caminiti et al., 1985) and to premotor areas (Jones and Powell, 1969, 1970; Jones et al., 1978). Although many cells within area 5 probably subserve a sensory function, a proportion of cells relate to active movement (Mountcastle et al., 1975, MacKay et al., 1978; Kalaska et al., 1983; Chapman et al., 1984), even in deafferented animals (Bioulac and Lamarre, 1979; Seal et al., 1982).

The results of the present study underscore the similarities in the relations of cell activity to movement parameters in the areas studied. Thus, the large majority of cells in both areas showed significant relations to all parameters tested (Fig. 9). This similarity is in accord with previous observations (Kalaska et al., 1983) and supports the idea that there is a similar mode of processing of sensorimotor information in these areas (Kalaska et al., 1983). The main, and consistent, difference between the motor cortex and area 5 lies in the time shift of cell activity with respect to the movement for which relations to these parameters were strongest. The onset of changes in cell activity is, in general, earlier in the motor cortex than in area 5 (Kalaska et al., 1983; Kalaska and Crammond, 1992; see also Evarts, 1974), which is consistent with our finding that the time shift for obtaining the highest R^2 was also earlier in the motor cortex (median = −90 msec) than in area 5 (median = +30 msec). It is noteworthy that the optimal time shift (−90 msec) above for the motor cortex is very similar to average time shift values obtained in other studies (Humphrey et al., 1970; Schwartz, 1993).

Finally, it should be noted that these findings refer to dynamic conditions, that is, to neural activity recorded during arm movements. Under static conditions (e.g., when holding against a constant load), clear differences have been described between these areas, as evidenced by the lower activity of area 5 cells as compared to motor cortex (Kalaska et al., 1990). This finding led to the hypothesis that area 5 deals with movement kinematics and motor cortex with movement kinetics (or *dynamics*, in the nomenclature used by Kalaska et al., 1990). This idea may hold under static conditions but its validity under dynamic conditions of change in force, and movement of the arm, remains to be tested.

The present findings suggest a strong relation of both areas to target direction and movement velocity, less to position, and even less to acceleration. It should be noted that these findings do not come from subsets of cells preselected specifically according to particular criteria (Flament and Hore, 1988; Kalaska et al., 1992) but instead come from the whole ensemble of cells related to arm movements. As such, the findings of this study provide information about the functional composition of the ensemble rather than the behavior of a restricted subset of its components.

Notes

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