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RESEARCH ARTICLE

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# On the relations between single cell activity in the motor cortex and the direction and magnitude of three-dimensional dynamic isometric force

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**Abstract** The role of the motor cortex in the control of both the direction and magnitude of dynamic force, when both are allowed to vary in 3D, is not known. We recorded the activity of 504 cells in the motor cortex of two monkeys during a behavioral task in which the subjects used a manipulandum to vary both the direction and magnitude of isometric force in 3D space. The majority (86%) of cells active in the task related to the direction, a tiny number (2.5%) to the magnitude, and a moderate number (11.5%) to both the direction and magnitude of dynamic force output. Finally, we compared neural activity in the same population of neurons during dynamic and static force output and found that the relations to direction and magnitude were very similar in both epochs. Our results indicate that during dynamic force production, cells in the motor cortex are primarily concerned with specifying the direction of force. The magnitude signal is not prominent in motor cortex neurons, and in general, magnitude and direction of force are specified together. Furthermore, the data suggest that the control of static and dynamic motor systems is based, to a great extent, on a common control process.

**Keywords** Force · Motor cortex · Monkey · Isometric Direction · Static · Dynamic

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## Introduction

The production of force in appropriate muscle groups is necessary to generate goal-directed movements. Force is a vector and, as such, is defined both by its direction and magnitude. How the direction and magnitude of force are controlled by the brain, particularly by the motor cortex, has been a subject of study since the pioneering experiments of Evarts (1968, 1969). One can think of force output by the motor system in terms of static force, which relates primarily to the control of posture and dynamic force, which is responsible for movement. The cortical control of static force, which is experimentally more tractable, has been extensively studied. These studies have shown that cells in the motor cortex may relate to the magnitude (Evarts 1968, 1969; Evarts et al. 1983; Hepp-Reymond et al. 1978; Fromm 1983; Cheney and Fetz 1980) or to the direction of static force (Kalaska et al. 1989). The relative contributions of the direction and magnitude of static force to neural activity have not been clear because of the practice of studying these parameters separately. We recently examined the relative contribution to cell activity of the magnitude and direction of static force and found that the direction signal was the most important determinant of cell activity, and that cells relating to the magnitude of force alone were uncommon (Taira et al. 1996).

In the current study, we extend our investigation to the relations between neural activity and the direction and magnitude of force under *dynamic* conditions. To date, the majority of studies of dynamic force coding have concentrated on magnitude (Evarts 1969; Evarts et al. 1983; Hepp-Reymond et al. 1978; Fromm 1983; Cheney and Fetz 1980; Smith et al. 1975; Humphrey and Reed 1983; Martin and Ghez 1985). These studies have found the most consistent relations were, not to magnitude *per se*, but to the rate of change in force. However, the direction of dynamic force has also been shown to be an important determinant of motor cortex

cell activity (Georgopoulos et al. 1992). Although much of our motor behavior is dependent on our ability to continuously vary both the direction and magnitude of dynamic force, to our knowledge, there have not been any studies in which this issue has been explicitly examined.

In the work described here, we addressed the following issues. First, are both the magnitude and direction of force encoded during dynamic isometric force output? Second, what is the relative importance of direction and magnitude in determining cell activity? Third, what are the quantitative relations between neural activity and the direction and magnitude of force output? Fourth, we were in a position to compare, in the same population of cells, neural activity during dynamic and static components of the task and thus address the question of whether there may be a common control process relating to both static and dynamic motor output. Finally, we explicitly do not address the neural correlates of rates of change in force and their derivatives; this is best done using a time-based analytic approach (Ashe and Georgopoulos 1994) and will be the subject of a separate report.

## Methods

Two rhesus monkeys (*Macaca mulatta*, 6–7.5 kg body weight) were used in these experiments. Care and treatment of the animals during all stages of the experiment conformed to the principles outlined in "Principles of Laboratory Animal Care" (NIH publication No. 86–23, revised 1995) and was approved by the local institutional animal care committee.

### Apparatus

A 3D isometric manipulandum and a video monitor were used in the task. The manipulandum has been described previously (Massey et al. 1988), and consisted of a vertical rigid metal rod with a disc attached to the top. XYZ forces exerted on the disc were read with a resolution of 0.04 N and sampled every 5 ms. Conventions for the coordinates of the force vector followed the left hand rule. The positive $X$ axis pointed to the left of the subject, the positive $Y$ axis pointed toward the subject, and the positive $Z$ axis pointed downward. The animals sat 60 cm from the monitor and used the pronated right hand to control the manipulandum, which was in front, and slightly to the right of the midsagittal plane. By exerting force on the manipulandum, the animals controlled the movement of a force-feedback cursor on the video screen. If no force was applied, the force-feedback cursor returned to an initialized zero point in the middle of the screen. Targets displayed on the monitor were used to instruct the direction and magnitude of $XY$ force. The application of 1 N of force on the manipulandum, in the $X$ or $Y$ direction, caused a movement of 3.5 cm of the force- feedback cursor, in the same direction, on the screen. Although $Z$ forces were collected, they were not controlled during this task.

### Behavioral task

At the beginning of each trial, a circular target appeared within a center-force window (0.3 N radius) on the display. The animal was required to hold the force-feedback cursor at this center target for a variable period (600–1,000 ms). The last 400 ms of this period was defined as the *control period* (CP). At the end of the CP, the target jumped to a peripheral location which could be in any one of eight different directions (every 45°) and at one of three different magnitudes (1.5 N, 2.0 N, and 2.5 N) giving a total of 24 potential targets. The animal was required to exert a force pulse toward the target, within a 25° direction window, and maintain the cursor within the peripheral target window (0.4 N radius) for a variable period (600–1,000 ms). The last 300 ms of this period was defined as the *static hold period* (SH). Therefore, this task comprised a dynamic force generation period (FG) and a static component. Correct performance was rewarded at the end of each trial with drops of water or juice. A complete data set consisted of 120 successful trials, 5 repetitions of 8 directions and 3 steps. Each repetition comprised 24 pseudo-randomly presented trials (3 steps X 8 directions).

### Surgical procedures

When the animals reached a criterion performance level in the task, a 19-mm recording chamber and a head restraint system (Nakasawa Works Co. Tokyo) were surgically implanted on the skull, under aseptic conditions, using general anesthesia. The correct location of the recording chamber was determined using stereotaxic coordinates derived from anatomic MR images of the animals' brain. Following surgery, the animals were given acetaminophen with codeine orally and Xylocaine gel topically for analgesia.

### Neural recording

We recorded the extracellular electrical signals from single neurons in the motor cortex during task performance using a 7 microelectrode recording system (Thomas Recording, Marburg, Germany). This device allowed for independent control of each of the seven electrodes. The electrophysiological techniques used to record the electrical signs of single cell activity were described previously (Georgopoulos et al. 1982; Mountcastle et al. 1991). Neural impulses were discriminated on-line either manually using a dual time-amplitude window discriminator (BAK Electronics,

MD) or semiautomatically with an on-line spike sorting system (Alpha Omega, Nazareth, Israel). The spike trains were stored as interspike intervals measured with a resolution of 0.1 ms. The neural activity from each cell was recorded during the performance of the task. Following the collection of data from a group of cells, we examined the animals to test the activity of each cell during active and passive movements of the contralateral arm. Only cells related to movement of the elbow, upper arm or shoulder were used in further analysis. We also excluded from analysis cells which had a very low firing rate (less than 20 impulses during the performance of the task).

## Euthanasia

At the end of the experiment, the animals were premedicated with ketamine (10 mg/Kg) and the area of recording on the cortical surface demarcated, using several pins, inserted into the cortex at known locations. The animals were then sacrificed with an overdose of sodium pentobarbital (250 mg/kg).

## Electromyographic recordings (EMG)

These sessions were separate from neural-recording sessions. The EMG activity was sampled during performance of the tasks using intramuscular, Teflon-coated, multistranded, stainless steel wires. The following proximal muscles were sampled in both monkeys (SA and SB), supraspinatus, infraspinatus, anterior deltoid, posterior deltoid, biceps, lateral head of triceps, pectoralis, and latissimus dorsi. The EMG signals were recorded differentially, amplified through a Grass amplifier system with an amplification of 10,000–20,000, bandpass filtered at 30–300 Hz, rectified, low-pass filtered at 16 Hz, and sampled at a rate of 200 Hz with an analog-to-digital converter.

## Data analysis

### *General approach*

Standard analysis (Mardia 1972; Draper and Smith 1981; Snedecor and Cochran 1989) and display techniques were used to inspect, evaluate, and analyze the data. The level of $a = 0.05$ (i.e., $P < 0.05$) was regarded as statistically significant in all tests performed. This level was adjusted for multiple comparisons when needed, using the Bonferroni inequality (Snedecor and Cochran 1989). A repeated measures analysis of variance (ANOVA) and both a step-wise multiple linear and nonlinear regression were used to analyze the activity of cells and muscles. For the ANOVA and the step-wise multiple linear and nonlinear regression analyses, the neural, EMG, and force data were averaged over the epoch of interest. The duration of the various epochs was as follows: CP was 400 ms, the immediate RT period was 100 ms, and the duration of the FG period depended on behavioral performance.

### ANOVA

This analysis was used to determine whether there was a significant change in the activity during an epoch, when compared to the CP activity. The program 5 V of the commercially available package BMDP DYNAMIC (BMDP Statistical Software Inc. Los Angeles, CA, USA 1993) was used to perform a repeated measures ANOVA. The average cell activity was regarded as the rate of cell discharge (impulses/s) computed from counts of fractional interspike intervals (Taira et al. 1996) during that period.

The model included the following terms: Epoch, Target Direction, Target Step and their Interactions. The Epoch term was defined as the contrast between the average activity in a particular epoch (RT, FG) and the activity in the preceding CP epoch. Each cell could have a significant change in activity in any combination of the model variables. If any of the model variables reached significance in the ANOVA, that cell was classified as being task related.

### The 3D force space

The forces exerted by the animals during the behavioral task were defined by a 3D force space. The characteristics of this space have been previously described (Taira et al. 1996).

### *Step-wise multiple regression*

The regression analysis was performed only on cells or muscles that reached significance in the ANOVA. We used a linear regression model as our primary analysis. However, we also fit a nonlinear model in a separate analysis for the purposes of comparison (see below). The BMDP program 2R was used in both cases. This program fit a multiple regression equation in a step-wise manner, by entering or removing one variable at a time, from the list of the independent variables. Only forward stepping was used, i.e., beginning with no predictors. The default values (for the program) of the $F$ statistic to enter or remove a predictor in a step were used ($F$-to-enter = $F$-to-remove = 4.0). The default tolerance level of 0.01 was used that provided a safeguard against possible colinearity effects.

The average frequency of cell discharge, or the average EMG activity for each epoch (see above), was used as the dependent variable. In this task, there were three sets of independent (predictor) variables: the average CP activity (co-variate), the force magnitude $M$, and the direction cosines $[x, y, z]$ of the force vector $\boldsymbol{F}$.

The inclusion of the CP activity as an independent variable allowed the estimation of the effects of the force parameter on cell activity during the RT or FG epoch, independently of any possible relation between these values and the center hold activity. Since this variable was not related to the output of force, this effect will not be addressed further.

The variables relating specifically to force were analyzed more rigorously for their relations to cell output in the following manner. After running the stepwise linear regression equation, we noted the following final outcomes: a) either none of the two sets of force predictors had a significant effect, in which case the regression model did not reach significance, or b) at least one set of the force predictor variables had a significant effect, in which case there was a statistically significant regression model. More specifically, if only the direction effect was significant, this indicated a *pure direction effect*; if only the magnitude effect was significant, this indicated a *pure magnitude effect*; and if both the directional and magnitude effects were significant, this indicated a *combined direction + magnitude effect*.

The general model we tested in all cells was :

$$d = b_0 + b_x x + b_y y + b_z z + b_f F + e \quad (1)$$

where $d$ is the frequency of discharge, $b_0$ is the intercept, $b_x$ - $b_z$, $b_f$ are partial regression coefficients, [$x$, $y$, $z$] are the direction cosines and F is the magnitude of the 3D force vector, and $e$ is an error term. The model in Eq. 1 is clearly additive. However, because there is some debate as to whether direction and magnitude are best described by an additive or a multiplicative model, we also fit a multiplicative, or non-linear, model to the data as follows:

$$d = b_0 + F(b_x x + b_y y + b_z z) + e \quad (2)$$

or equivalently,

$$\log(\mathrm{d}) = b_0 + b_1 F + b_2 Dir \quad (3)$$

where Dir $= b_x\, x + b_y\, y + b_z\, z$. The respective merits of each model are discussed below.

### Index of directional modulation ($I_d$)

This index was used to quantify the directional modulation of each cell's firing rate during an epoch, and it was computed using the following equation:

$$(\mathrm{Max}\ D - \mathrm{Min}\ D)/C \quad (4)$$

where Max D is the maximum average firing rate, and Min D the minimum average firing rate of the cell during the epoch of interest, and C is the average firing rate of the cell during the CP. For statistical testing, $\boldsymbol{I}_d$ was log transformed to normalize the distribution of the ratios.

### Preferred direction equal area projection plots

Equal area projection plots (Mardia 1972) were used to illustrate the distribution of the preferred directions of the cells. To illustrate the complete unit sphere, two equal area projection plots were used. The top plots showed the preferred directions of the cells in the upper $Z$ hemisphere, or for forces exerted upward; the lower plot showed the preferred directions of the cells in the lower $Z$ hemisphere, or for forces exerted downward.

## Results

### Neural activity

#### *General overview*

We recorded the impulse activity of 504 cells in 189 penetrations in the proximal arm area of motor cortex contralateral to the performing arm (left hemisphere, right arm) in two animals during the performance of the task described above. The locations of the recordings are shown in Fig. 1; all the penetrations were within the proximal arm areas of the motor cortex (Woolsey et al. 1958). The majority of penetrations were on the crown rather than in the bank of the motor cortex. All penetrations were approximately orthogonal to the cortical surface. The majority of neurons recorded were at a depth of between 500 and 1250 microns from the first sign of neural activity. Each cell changed activity in relation to movements of the shoulder and/or elbow area of the contralateral arm, as judged by the examination of the animal outside the behavioral task. The average activity of these cells was analyzed for a change in activity related to force output. Cells activated purely in relation to distal (hand or finger) limb movement were not included in this sample.

#### *Behavioral performance*

The time-course of the XY force output by one of the animals during the task is shown in Fig. 2. The Z forces were not controlled and were generally more variable than the X and Y forces. The range and average forces produced in the different dimensions were as follows: $F_x$: range (−2.04–2.08 N), mean 0.01 N; $F_y$ range (−2.13–2.02 N), mean −0.01; $F_z$ (−0.38–4.18 N), mean 1.20 N. The force vector F ranged from 0.7 to 4.5 N with an average of 1.85 N.

#### *Changes in cell activity related to dynamic force output*

The activity of all the cells was analyzed for a significant change during the RT and FG periods from the CP using ANOVA. In the task, 429/504 (85.1%) cells showed a significant change in activity during the RT,

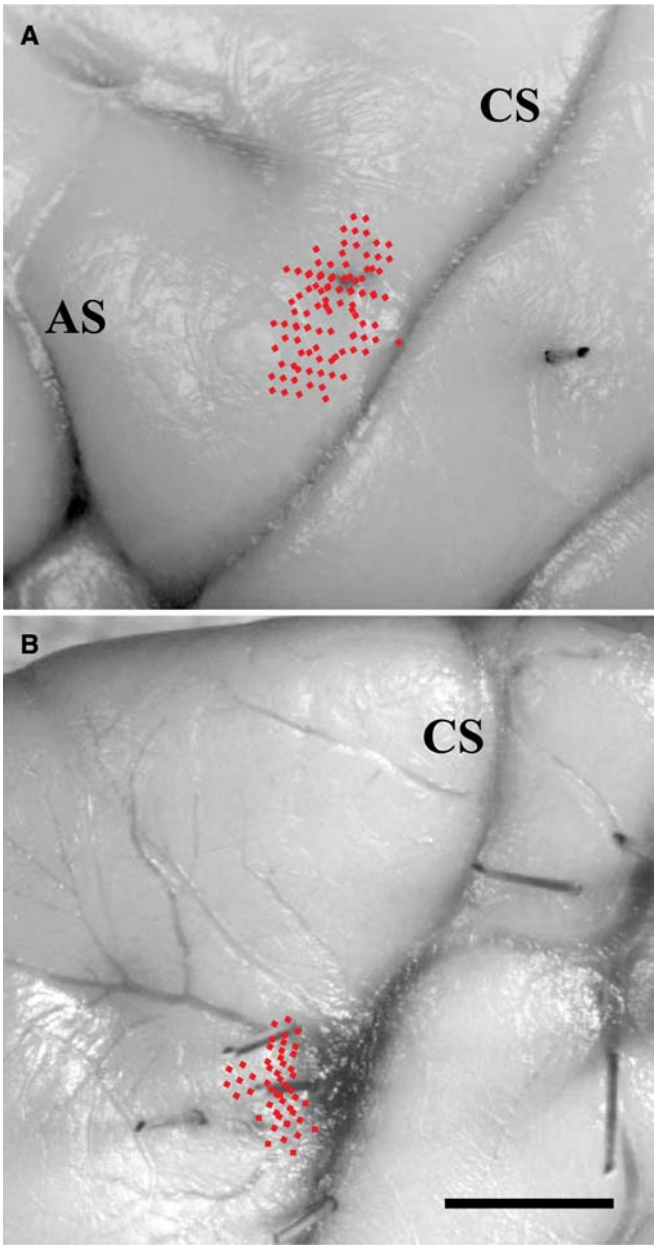



**Fig. 1** The entry points of the electrode penetrations in each animal (**A** = SA; **B** = SB) superimposed on a photograph of the brain. *AS* = arcuate sulcus, *CS* = central sulcus. The *bar* on the bottom right = 5 mm. It can be seen that all penetrations are within the *motor cortex*

and 470/504 (93.3%) cells showed a change in activity during the FG period.

We further analyzed the activity of the cells with significant effects in the ANOVA using both additive and multiplicative step-wise multiple linear regression models as outlined in Eqs. 1 and 2. As can be seen in Table 1, the results from both models were quite similar. The effect of magnitude was not large in either model and both were equivalent in accounting for the variance in neural activity. Since there appeared to be little difference between the models, we decided to use the results from the simpler additive one in the presentation of the remainder of the results. The relevance of both models for the interpretation of the results will be discussed below.

In this task, 329/429 (76.7%) cells in the RT epoch, and 408/470 (86.8%) cells in the FG epoch showed significant relations in the regression model described in Eq. 1. The distribution of significant main effects in the regression model is shown graphically in Fig. 3. During the RT 307/329 (93.3%) of cells showed a direction effect, 6/329 (1.8%) a magnitude effect, and 21/329 (6.4%) both a direction and magnitude effect. During the FG epoch 351/408 (86.0%) of cells showed a direction effect, 10/408 (2.5%) a magnitude effect, and 47/408 (11.5%) a direction and magnitude effect.

### *Effect of force direction*

*Preferred direction* Many cells in the motor cortex had a significant direction effect. The activity of one such cell is shown in Fig. 4. The observed firing rate against that predicted for the same cell by the regression model is seen in Fig. 5a and the normal cumulative probability-probability plot in Fig. 5b. The null hypothesis that the preferred directions were uniformly distributed was not rejected in the RT (Rayleigh test, RT: $P > 0.05$, $\chi^2_{[3]} = 7.27$) but was rejected during the FG epoch (Reyleigh test, FG: $P < 0.05$, $\chi^2_{[3]} = 13.31$). Figure 6 shows an equal area projection plot of the preferred force directions of the cells during the FG epoch (Upper hemisphere: $n = 168$; Lower hemisphere: $n = 216$). The pattern of distribution was similar during the RT period, although fewer cells were activated. During both epochs, the preferred force directions of the cells were somewhat clustered in the anterior part of the lower hemisphere and the posterior part of the upper hemisphere.

*Index of modulation* The average index of modulation ($I_d$) was computed for all cells with a direction effect during both the RT and the FG epochs (see Table 2). We were interested in whether the directional modulation of cells was different in cells that only related to direction, compared with cells that related to both direction and magnitude. During the RT epoch, the $I_d$ of the cells with a pure direction effect was less than the cells with a combined direction + magnitude effect ($P < 0.05$, $t = 2.02$, $df = 321$). However, in the FG epoch, the $I_d$ was not significantly different between the cells with a pure direction effect, and cells with a combined direction + magnitude effect ($P > 0.05$, $t = 0.31$, $df = 396$). Therefore, although there were some differences in $I_d$ between cells when grouped on the basis of functional cell types, these differences were not large.

### *Effect of force magnitude*

Cells with a significant magnitude effect were found during both epochs of the task. The average change in firing rate per Newton of force for cells with a

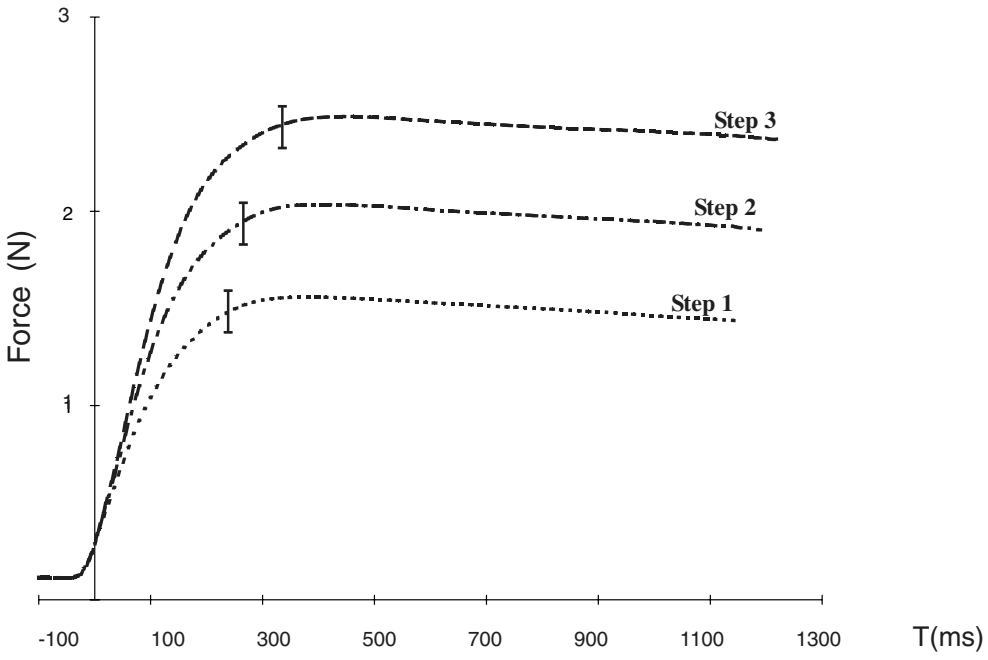



**Fig. 2** The *XY* force output by in one animal *(SA)* as a function of time. The forces are aligned to the onset of force. The *vertical markers* denote the end of the force generation (FG) period

**Table 1** The results of the step-wise linear regression using additive and multiplicative models on cells ($n = 504$) recorded in motor cortex. Significant, refers to all cells that fit the models; D + M, direction and magnitude

| | Significant | Direction | Magnitude | D + M | $R^2$ median, (25–75, centile) |
|---|---|---|---|---|---|
| Additive | | | | | |
| RT | $n = 329$ | 302 (91.8%) | 6 (1.8%) | 21 (6.4%) | 0.18 (0.17–0.25) |
| FG | $n = 408$ | 351 (86.0%) | 10 (2.5%) | 47 (11.5%) | 0.23 (0.20–0.28) |
| Multiplicative | | | | | |
| RT | $n = 287$ | 251 (87.4%) | 20 (7.0%) | 16 (5.6%) | 0.19 (0.16–0.25) |
| FG | $n = 357$ | 294 (82,3%) | 20 (5.6%) | 43 (12.4%) | 0.22 (0.17–0.31) |

magnitude effect is shown in Table 3. The absolute value of the average positive slopes was greater than the negative slopes within an epoch (RT: $P < 0.05$, $t = 7.31$, $df = 25$; FG: $P < 0.05$, $t = 11.03$, $df = 55$). In general, the quantitative relations of cells to magnitude (whether positive or negative) were greater among cells that were also modulated by direction (Fig. 7). An example of a cell showing a positive relation to the magnitude of force is shown in Fig. 8. A cell with a negative relation to the magnitude of force is shown in Fig. 9.

*Comparison between relations to dynamic and static force*

The task design enabled us to directly compare the relations to static and dynamic force in the same population of cells. The overall relation between neural activity and the direction and magnitude of force was very similar under dynamic and static conditions (Table 4). Although we had previously reported the relations to static force (Taira et al. 1996) in another population of cells, we thought it was important that the main effects of force direction and magnitude should be compared during both static and dynamic behavior in the same population.

Muscles

*Overview*

We recorded the electromyographic (EMG) activity of eight muscles of the shoulder girdle and upper arm, while each animal performed the task. The average activity of these muscles was measured in arbitrary units and analyzed in an identical manner to the cells. We pooled the EMG data from the two monkeys giving a total of 16 muscles. The behavioral performance in both animals during the EMG recording sessions was similar to that during the neural recording.

*Changes in muscle activity related to dynamic force output*

The activity of all the muscles was examined for a significant change in activity during dynamic force output. Among the muscles, 12/16 (75%) and 13/16 (81%) were active in the RT and FG, respectively. These muscles were further analyzed, for a direction or magnitude effect, using a step-wise multiple linear regression model. During the RT, 11/12 (92%) of the muscles had a direction effect, 1/12 (8%) had a pure magnitude effect,

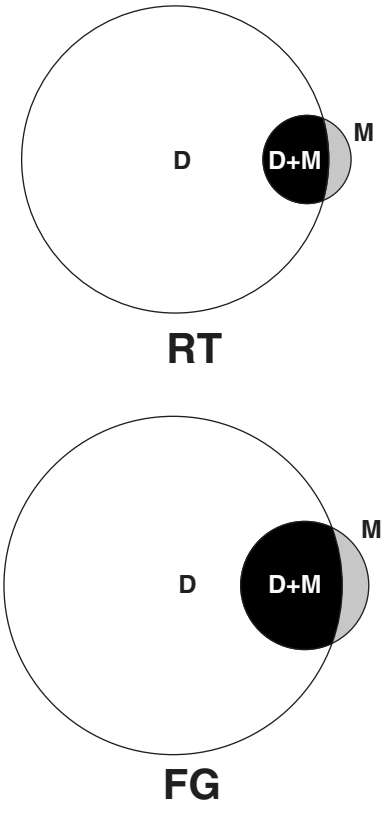
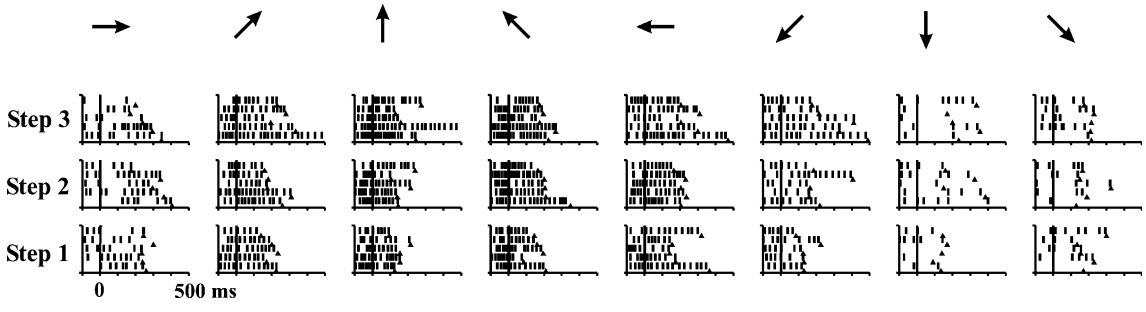



**Fig. 3** Distribution of direction (*D*), magnitude (*M*) and combined direction + magnitude (*D* + *M*) effects during behavioral epochs in the task among cells with a significant change in activity during dynamic force output

and none of the muscles had a combined direction and magnitude effect. In the force-generation period, the respective values were direction 7/13 (54%), pure magnitude 0/13 (0%), and direction and magnitude 6/13 (46%). The majority of muscles related to direction during both behavioral epochs, while the effect of magnitude was less prominent and generally tied to direction. However, the percentage of muscles with some magnitude effect was much greater than that seen in the cells (Chi-Square, 15.46, $P = 0.0004$).

**Fig. 4** Neural activity of a motor cortex cell during dynamic isometric force output. *Arrows* indicate the instructed *XY* force direction. This cell showed a significant direction effect. The rasters are aligned to force onset (*vertical line*) and are truncated at the end of the dynamic FG. The regression equation during the FG epoch was: $d = 25.99 + 8.04\ x + 14.74\ y + 7.13\ z$ ($R^2 = 0.796$, $P < 0.0005$), where *x*, *y*, and *z* are direction cosines. (Cell Chi067 11#180)




## Discussion

The principal findings in this study, which systematically varied both the direction and magnitude of dynamic isometric forces in 3D space, were as follows: (i) the discharge of the majority of cells in the motor cortex was related only to the direction of dynamic force output, (ii) coding of the magnitude of dynamic force alone was reflected in a tiny proportion of cells, (iii) an intermediate number of cells processed information about both the magnitude and direction of force, and (iv) the relations to dynamic force were very similar to those seen for static force in a separate epoch of the task.

### Methodological considerations

The examination of visually guided 3D isometric force is fraught with methodological difficulties (see Taira et al. 1996). In this study, we adopted a practical alternative to the full 3D specification of isometric force, namely to instruct force on a plane (X,Y force space), so that two force components were controlled, while still measuring all three components of force output. This design resulted in 3D forces which varied in both direction and magnitude.

In choosing a regression model, we decided to use a polar rather than a Cartesian coordinate system to express the forces, as there is adequate evidence, both from neural and psychophysical data, that direction and magnitude may be coded independently (Fu et al. 1993; Taira et al. 1996; Ghez et al. 1997). When modeling the changes in neural activity associated with force output, we primarily employed an additive rather than a multiplicative regression model. We took this approach for several reasons: (i) the linear model is a simpler one from a conceptual point of view, (ii) preliminary analysis using ANOVA showed that less than 5% of cells were significant for an interaction between direction and magnitude, and (iii) data suggest that changes in the amplitude of movement may have additive effects on the direction properties of neurons (Turner and Anderson 1997). However, since there are also compelling experimental (Moran and Schwartz

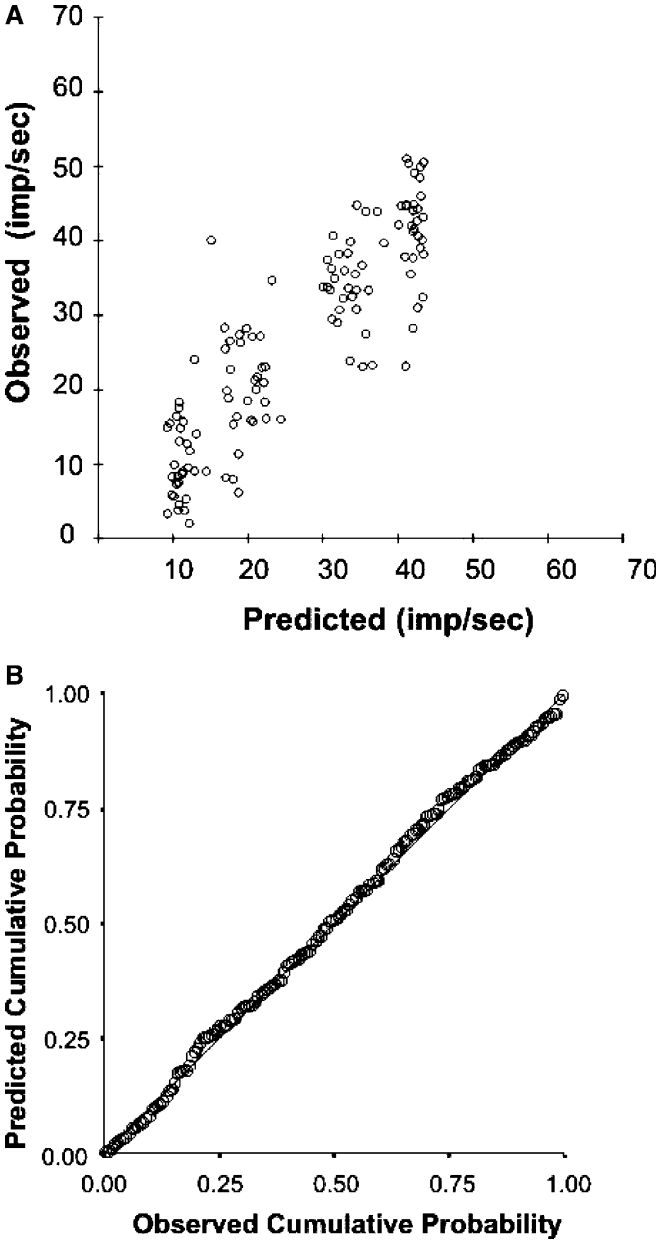



**Fig. 5** (**A**) The observed firing rate is plotted against the firing rate predicted by the regression model for the cell (Chi067 11#180). (**B**) Normal cumulative probability-probability plot of the observed regression residuals against those expected from a normal distribution for one same cell. The *line along the diagonal* indicates the expected residuals from a normal distribution

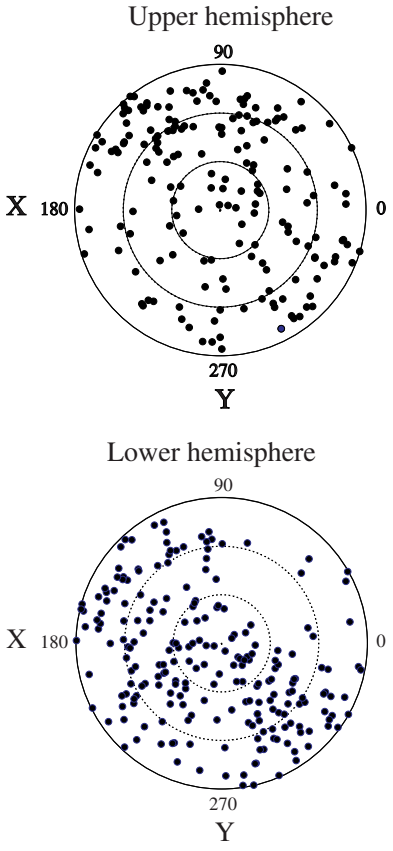



**Fig. 6** Equal area projection plots of the preferred directions of cells during the FG period. These are pseudo 3D plots in which the preferred directions of individual cells are treated as unit vectors with the origin at the center of a unit sphere and then projected onto the upper and lower hemisphere of that sphere. The center of each hemisphere signifies the pole of the *Z* axis and each *concentric circle* is 30° farther from the axis

1999) and theoretical (Todorov 2000) arguments for considering a multiplicative model, we performed both analyses. Our finding of similar results using either model (Table 1) does not allow us to make strong conclusions about these different approaches. The magnitude of force had such a small influence on neural activity in the population of cells we recorded that it probably mattered little whether this factor was included as an additive or a multiplicative term. It is likely that in cases in which the magnitude of force was a more important determinant of cell activity then the choice of model would make a crucial difference to the results.

### *Coding of direction and magnitude*

The finding that the vast majority of cells sampled in the motor cortex related to the direction rather than the magnitude of dynamic force might seem to be at variance with previous work since many studies have shown a strong correlation between activity in the motor cortex and the magnitude of force output. However, when one looks critically at the large number of earlier studies (Evarts 1969; Humphrey et al. 1970; Evarts et al. 1983; Hepp-Reymond et al. 1978; Fromm 1983; Cheney and Fetz 1980; Smith et al. 1975; Humphrey and Reed 1983; Martin and Ghez 1985; Wannier et al. 1991; Maier et al. 1993), only a few focused on dynamic force (Cheney and Fetz 1980; Smith et al. 1975; Humphrey et al. 1970), and only one showed a clear relation to the magnitude of dynamic force (Humphrey et al. 1970). The relative importance of magnitude and direction has been difficult to determine as these variables have either been examined in separate studies or direction was varied in only

**Table 2** The index of direction modulation (*Id*) during the response time (RT) and force generation (FG) time for those cells in the task with significant direction effects alone (D) or with effects of direction and magnitude (D + M)

| | RT (*Id*) | FG (*Id*) |
|---|---|---|
| D | 11.36 ± 0.79 ($n=302$) | 9.74 ± 0.66 ($n=351$) |
| D + M | 13.85 ± 1.96 ($n=21$) | 11.18 ± 2.52 ($n=47$) |

**Table 3** The average increase and decrease, in impulses per second per Newton force (Imp.$S^{-1}$.$N^{-1}$), for cells showing significant positive and negative effects of magnitude in the reaction time (RT) and force generation period (FG)

| | *n* | Percentage | Imp $S^{-1}$ $N^{-1}$ |
|---|---|---|---|
| RT Epoch | | | |
| Positive | 21 | 77.78 | 6.50 ± 0.72 |
| Negative | 6 | 22.22 | −3.68 ± 0.57 |
| Total | 27 | 100 | |
| FG Epoch | | | |
| Positive | 30 | 52.63 | 5.93 ± 0.78 |
| Negative | 27 | 47.37 | −5.06 ± 0.59 |
| Total | 57 | 100 | |

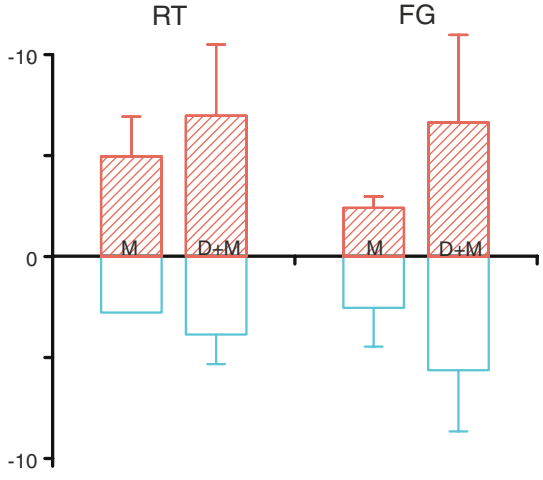



**Fig. 7** Quantitative relations in impulses per second per Newton force (Imp.$S^{-1}$.$N^{-1}$) plotted on the ordinate during the RT and FG epochs for cells with significant relations to magnitude alone (*M*) and to both magnitude and direction (*D + M*)

one dimension. To our knowledge, this is the first study of motor cortex activity during the production of dynamic forces of different magnitudes in more than one dimension, making it more similar to the normal physical environment. In the current study, the number of cells that related exclusively to the magnitude of force was modest by any criterion. It could be argued that this small percentage may be due to the range of forces produced in the task (0.71–1.85 N). This is not likely, however, as other studies, albeit under static conditions, have shown that motor cortex cells have maximal sensitivity to force within that range and few cells are recruited at higher forces (Evarts et al. 1983; Wannier et al. 1991; Maier et al. 1993). In addition, our findings on the importance of force direction get some indirect support from the clinical literature which shows that it is the impairment of movement dexterity, often involving rapid coordinated changes in direction, rather than the inability to produce a specific magnitude of force that is most troublesome for patients following motor cortex lesions (Wenzelburger et al. 2005).

Given the relatively small proportion of cells involved *specifically* with force magnitude at the level of the motor cortex, how then is the magnitude of force specified? One possibility is that other cortical areas, such as posterior parietal or premotor cortex, might generate that signal. However, our data from parietal area 5, failed to reveal strong evidence of such coding (Boline and Ashe 1997). In addition, premotor cortex studies, in either one (Riehle et al. 1994; Kurata 1993) or two dimensions (Riehle et al. 1994; Kurata 1993, Fu et al. 1993, 1995; Messier and Kalaska 2000) have not, in general, supported a role for that structure in amplitude coding. Perhaps the amplitude of force is specified in conjunction with direction or requires only a small population of neurons in motor cortex. If so, these cells may have disproportionately large effects on spinal motor neurons. The most parsimonious explanation for the prominence of the direction signal is that the specification of the direction of force ultimately involves the weighted activation of a large set of muscles, which is more computationally demanding and requires a greater amount of cortical resources. Once the direction of force has been established, the activation need only be scaled to produce forces of varying magnitude (Flanders and Soechting 1990).

In the cells that did show relations to the magnitude of dynamic force, the quantitative relations to magnitude (approximately 6 Imp.$S^{-1}$.$N^{-1}$) were similar to those previously described for static forces of comparable range (Evarts et al. 1969; Thach 1978; Fetz and Cheney 1980; Taira et al. 1996). In addition, these relations were consistently greater among cells that were also modulated by direction, lending further support to the idea that a common network of cells is primarily responsible for regulating both parameters. Motor cortex cells with a negative correlation to the magnitude of force, have also been seen in previous studies of static force (Smith et al. 1975; Hepp-Reymond et al. 1978; Hepp-Reymond and Diener 1983; Wannier et al. 1991; Maier et al. 1993). It is likely that such cells project to muscles antagonistic to the set of muscles necessary to perform the behavioral task (Maier et al. 1993) or to shoulder girdle muscles that relax as higher forces are generated.

Although the focus of the current work is on the coding of dynamic force, we also had the opportunity to examine the coding of static force (Table 4) in the same population of cells. We found that there was extensive overlap in the population of cells active during static and dynamic processes which indicate that the neural control of these physiological states is not nearly as distinct as

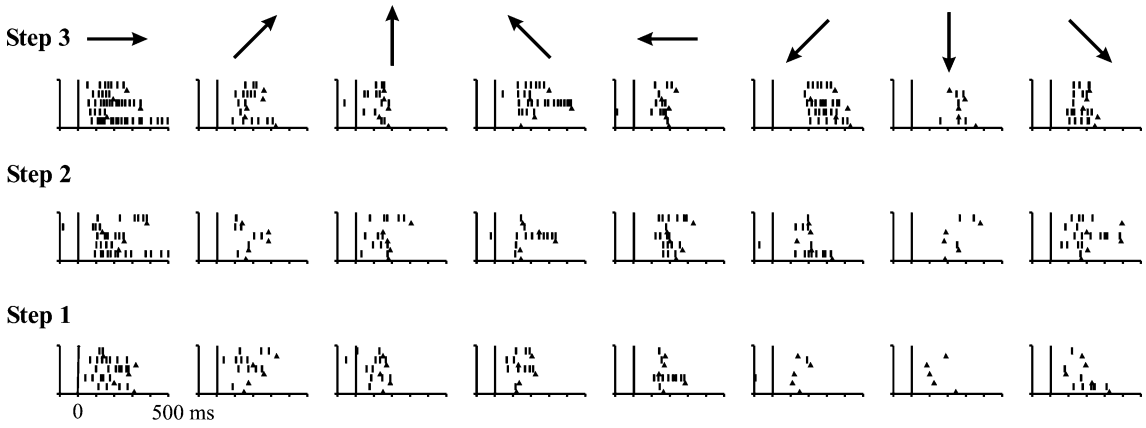



**Fig. 8** Neural activity of a motor cortex cell showing a significant direction effect and a positive relation to the magnitude of dynamic force. Format and conventions as in Fig. 4. *Arrows* indicate instructed *XY* force. The regression equation was: $d = 6.82 + 1.69\ x$ $0.86\ y + 17.23\ z + 11.95\ k$ ($R^2 = 0.422$, $P = 0.001$). Cell Chi079 7#236

others have suggested (Kurtzer et al. 2004). In addition, the distribution of direction and magnitude effects in both populations was very similar. Finally, the findings during static force output were almost identical to those we had previously documented (Taira et al. 1996).

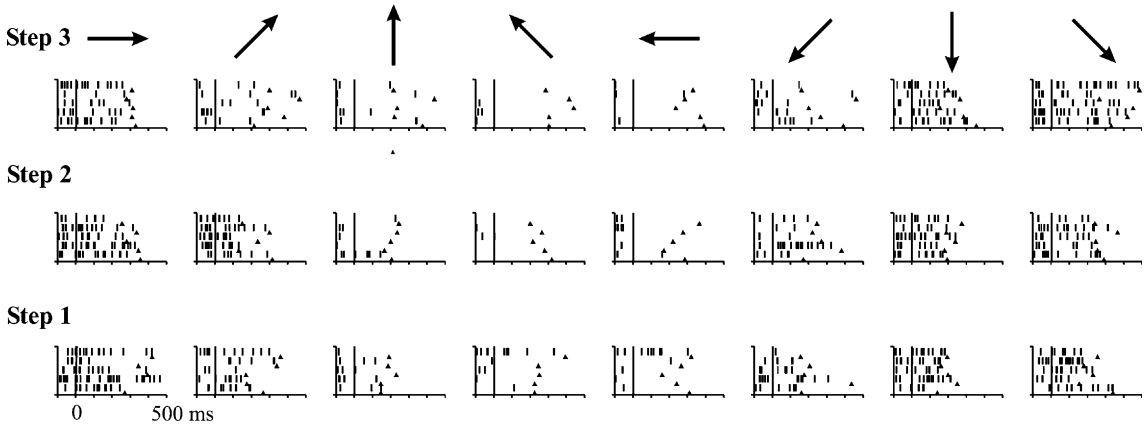
*Direction and magnitude: separate processing channels?*

It has been proposed, on the basis of the results of psychophysical studies of movement, that direction and amplitude are specified through separate processing channels (Goodman and Kelso 1980; Larish and Frekany 1995; Rosenbaum 1980; Soechting and Flanders 1989; Bhat and Sanes 1998). Another view is that these controlled parameters share a "common neural resource" (Favilla et al. 1989; Ghez et al. 1990, 1997) within the brain, implying that there is an interaction in their specification. Our data provide some support for both views, while being more strongly in favor of the latter. We found that although the magnitude of force could be specified independently of direction, this was relatively uncommon. By contrast, among the cells which showed a relation to force magnitude, 80% also reflected information about direction. This last finding is in keeping with neural recording data during movement from the motor (Fu et al. 1993, 1995, Riehle et al. 1994; Riehle and Requin 1989) and premotor cortex (Fu et al. 1993, 1995; Messier and Kalaska 2000), which showed that the amplitude signal was embedded in the direction signal.

*Kinetic or kinematic coding in the motor cortex*

There has been much debate as to whether the motor cortex codes motor output in terms of its kinetics (forces) or kinematics (Evarts 1969; Cheney and Fetz 1980; Georgopoulos et al. 1982; Kalaska et al. 1989; Alexander and Crutcher 1990; Caminiti et al. 1990, 1991; Georgoupoulos et al. 1992; Ashe and Georgopoulos 1994; Scott and Kalaska 1997; Kakei et al. 1999; Todorov 2000; Georgopoulos and Ashe 2000; Scott et al. 2001; Sergio and Kalaska 2003). A common experimental approach has been to dissociate the behavioral goal, be it the direction of movement or force, from the muscles involved in the task. Unfortu-

**Fig. 9** Neural activity of a motor cortex cell showing a significant direction effect and a negative relation to the magnitude of dynamic force. Format and conventions as in Fig. 4. The regression equation was: $d = 30.19 + 9.17\ x + 10.40\ y + 10.04\ z - 11.08\ k$ ($R^2 = 0.662$, $P < 0.0005$). Cell Chi024 9#49



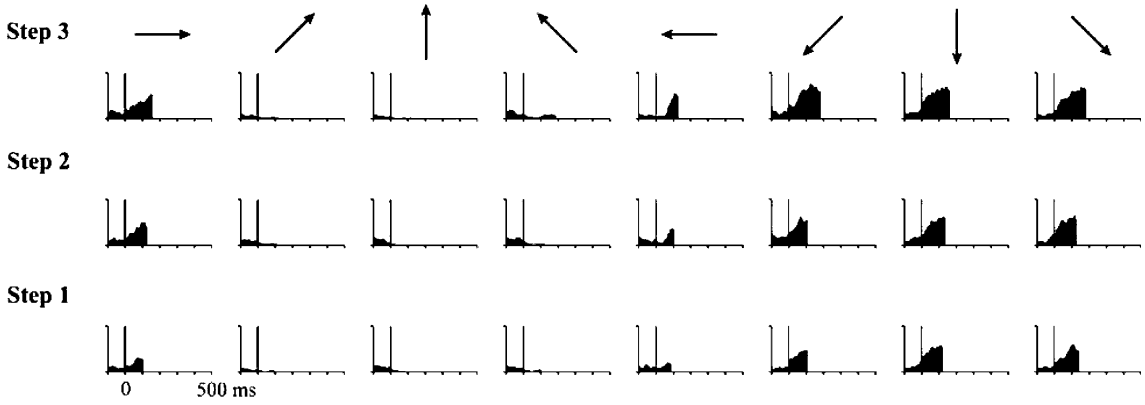



**Fig. 10** EMG activity of a muscle during dynamic isometric force output that showed significant effects of both direction and magnitude of force. The regression equation was : $d = 0.26 + 0.02\ x + 0.54\ \ y + 0.06\ \ z + 0.26\ \ k$ ($R^2 = 0.900$, $P < 0.0005$). Muscle: Bbe043#8, lattisimus dorsi

nately, a harmonious conceptual understanding of motor cortex has not developed as a result of such work. Although pure spatial signals are strongly represented in motor cortex, it is impossible to ignore the clear effect of biomechanical factors on cell activity (Caminiti et al. 1990, 1991; Scott and Kalaska 1997; Scott et al. 2001; Sergio and Kalaska 2003). On the other hand, studies that categorically dissociate the motor behavior from muscle activation, either during movement (Kakei et al. 1999; Alexander and Crutcher 1990) or during the production of isometric force (Georgopoulos et al. 1992) have given little support to concept that muscles are strongly represented. Although the current study is not designed to resolve the "muscles versus movement" conundrum, it and other similar isometric studies (Georgopoulos et al. 1992; Taira et al. 1996; Sergio and Kalaska 2003) in which there was a strong relation to the spatial component of the behavior in the absence of overt movement provide some insight into the issue. First, it would seem that the motor cortex might code for either kinetics or kinematics depending on the behavioral context; it is not really an issue of muscles versus movement. In the current experiment, there was no movement and the behaviorally relevant output was the net force at the hand. Consequently, the neural activity was related primarily to this variable, which was, as the summed output of the arm muscles, purely kinetic. In our view, the cumulative results of these experiments support the idea that it is neither kinetics nor kinematics *per se* that are coded in motor cortex, but rather the variable crucial for controlling the motor output trajectory. In conclusion, we propose that coding in the motor cortex is in terms of the spatially most meaningful (i.e., relevant or important) task variable, which may be in muscle space or in "world" space and is in a coordinate frame most appropriate for effective behavioral control.

**Table 4** Distribution of regression effects in the total population of motor cortex cells ($n = 504$) during the static and dynamic epochs of the task. D + M, direction and magnitude

| | Significant | Direction | Magnitude | D + M |
|---|---|---|---|---|
| Dynamic RT | $n = 329$ | 302 (91.8%) | 6 (1.8%) | 21 (6.4%) |
| Dynamic FG | $n = 408$ | 351 (86.0%) | 10 (2.5%) | 47 (11.5%) |
| Static FG | $n = 305$ | 247 (81.0%) | 13 (4.2%) | 45 (14.8%) |

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