

# Parietal Area 5 Activity Does Not Reflect the Differential Time-Course of Motor Output Kinetics During Arm-Reaching and Isometric-Force Tasks

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Submitted 27 July 2005; accepted in final form 11 February 2006

**Hamel-Pâquet, Catherine, Lauren E. Sergio, and John F. Kalaska.** Parietal area 5 activity does not reflect the differential time-course of motor output kinetics during arm-reaching and isometric-force tasks. *J Neurophysiol* 95: 3353–3370, 2006. First published February 15, 2006; doi:10.1152/jn.00789.2005. Many single-neuron recording studies have examined the degree to which the activity of primary motor cortex (M1) neurons is related to the kinematics and kinetics of various motor tasks. This has not been explored as extensively for arm movement-related neurons in posterior parietal cortex area 5. We recorded the activity of 78 proximal arm-related neurons in area 5 of two monkeys while they used their whole arm to make reaching movements toward eight targets on a horizontal plane against an inertial load or to generate isometric forces at the hand in the same eight horizontal directions. The overall range of measured output forces was similar in the two tasks. The forces increased monotonically in the desired direction in the isometric task. In the movement task, in contrast, they showed a rapid initial increase in the direction of movement, followed by a transient reversal of forces as the hand approached the target. Many task-related area 5 neurons were tuned for the direction of motor output in the tasks, but most area 5 neurons were more strongly active or exclusively active in the movement task than in the isometric task. Furthermore, their activity at either the single cell or population level did not reflect the transient reversal of output forces during movement. In contrast, M1 neuronal activity was typically strong in both tasks and showed task-related changes that reflected the differences in the time course and directionality of force outputs between both tasks, including the transient reversal of forces in the movement task. These results show that area 5 neurons are less strongly related to the time-course of task kinetics than M1 during isometric and arm-movement tasks.

## INTRODUCTION

Many behavioral studies suggest that reaching movements are first planned in terms of their extrinsic spatial kinematics (e.g., target location, directions, hand path) and transformed into a representation of the associated intrinsic kinematics (joint and limb segment motions) (Abend et al. 1982; Bhat and Sanes 1998; Gordon et al. 1994a,b; Krakauer et al. 2000; Morasso 1981; Soechting and Flanders 1989a,b). To execute the planned movement, those hypotheses presume that the reach plan in kinematic parameters is subsequently converted into a representation of the causal kinetics (e.g., static and dynamic forces, joint torques) necessary to determine the required muscle activity patterns. The nature of these representations and of any intervening transformations, as well as

the neural populations that are involved in these operations, all continue to be the topic of vigorous debate (Andersen and Buneo 2002, 2003; Battaglia-Mayer et al. 2003; Burnod et al. 1999; Colby and Goldberg 1999; Feldman and Levin 1995; Georgopoulos and Ashe 2000; Kalaska et al. 2003; Feldman and Latash 2005; Moran and Schwartz 2000; Ostry and Feldman 2003; Rizzolatti and Luppino 2001; Todorov 2000). Nevertheless, it is evident from everyday experience that we have considerable voluntary control over all aspects of the metrics of reaching movements, including hand paths and final endpoint locations, joint rotations, arm segment motions and orientations, output forces, and muscle activity. To achieve that control, it is reasonable to presume that neuronal representations of these different movement attributes should exist in one form or another within the distributed arm motor control system.

The primary motor cortex (M1) and area 5 of the posterior parietal cortex are both involved in the control of arm movements. M1 is generally assumed to play a prominent role in generating the final cerebral cortical motor output command (Cheney and Fetz 1980; Evarts 1968, 1969; Hepp-Reymond et al. 1978, 1999; Lemon et al. 1986). In contrast, area 5 may contribute to the sensorimotor guidance of motor behavior, including the integration of multimodal sensory information and some of the early sensorimotor transformations implicated in the planning of movement (Andersen and Buneo 2002, 2003; Andersen et al. 1997; Batista et al. 1999; Battaglia-Mayer et al. 2001, 2002, 2003; Buneo et al. 2002; Caminiti et al. 1998, 1999; Colby and Goldberg 1999; Ferraina et al. 2001; Graziano and Gross 1998; Graziano et al. 2000; Kalaska 1996; Kalaska et al. 1990, 2003; Mascaró et al. 2003; Rizzolatti and Luppino 2001; Sakata 2003; Snyder et al. 1997).

Neurophysiological studies have shown that M1 activity is modulated by task kinetics, including both static and dynamic forces (Boline and Ashe 2005; Cheney and Fetz 1980; Evarts 1968, 1969; Georgopoulos et al. 1992; Gribble and Scott 2002; Hepp-Reymond et al. 1978, 1999; Kalaska et al. 1989; Lemon et al. 1986, 1998; Li et al. 2001; Maier et al. 1993; McKiernan et al. 1998; Taira et al. 1996; Thach 1978). Other studies have shown that M1 activity also covaries with the kinematics of motor output (Caminiti et al. 1990, 1991; Georgopoulos et al. 1982; Kalaska et al. 1989; Moran and Schwartz 1999; Reina et al. 2001; Schwartz et al. 1988; Scott and Kalaska 1995, 1997). By using an external load to dissociate kinetics from kinemat-

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ics during a reaching task, Kalaska et al. (1989) showed that the activity of many M1 neurons was modulated both by the direction in which the arm was pulled by the external forces and by the direction of movement and the static posture of the arm during unloaded arm movements. Furthermore, the directionality of arm movement-dependent and load-dependent response modulations were strongly coupled, suggesting a functional link or even a common causal origin for those two response properties in those neurons (Kalaska et al. 1989). Nevertheless, many other M1 neurons were strongly directionally tuned for movement direction but were relatively insensitive to the presence and direction of external loads, indicating that the response properties of M1 neurons and their contributions to performance of the task were not homogeneous (Kalaska et al. 1989).

In contrast, area 5 neuron discharge is highly modulated by the direction of movement and by the posture of the arm in reaching tasks (Battaglia-Mayer et al. 2001, 2003; Buneo et al. 2002; Ferraina et al. 2001; Kalaska et al. 1983, 1990; Lacquaniti et al. 1995; Mascaro et al. 2003; Scott et al. 1997), but is much less influenced than M1 by external forces during static posture and arm movement (Kalaska and Hyde 1985; Kalaska et al. 1990). Also in contrast to M1, the directionality of movement-dependent and load-dependent response modulations of area 5 neurons were not strongly coupled (Kalaska et al. 1990). Ashe and Georgopoulos (1994) found that area 5 activity was most strongly correlated to the direction and velocity of movement but poorly correlated to movement acceleration, which is the kinematic parameter most closely correlated to movement forces through the Newtonian laws of motion. These various findings suggest that the arm movement representation in area 5 expressed primarily the kinematic attributes of motor outputs. In at least one preliminary report, however, both area 5 and M1 neurons were found to be modulated to similar degrees by the level of force exerted during an isometric task (Boline and Ashe 1998).

To re-examine the nature of motor output representations in the motor cortex, Sergio and Kalaska (1998) and Sergio et al. (2005) studied the activity of M1 neurons during two tasks specifically designed to dissociate the kinematics and kinetics of motor output. Monkeys displaced a cursor on a screen from a central target to one of eight peripheral targets by moving a weighted handle (movement task) or applying forces to a fixed handle (isometric task). The isometric task required the monkeys to generate monotonically increasing force ramps in eight directions in the horizontal plane. In contrast, the combined inertia of the arm and weighted handle in the movement task required the monkeys to transiently reverse the direction of output forces at the hand to apply a brief braking pulse to the handle to decelerate it as it approached the target. M1 neurons were strongly active in both tasks but showed changes in their response time-course that paralleled the differences in the temporal patterns of forces in the two tasks (Sergio and Kalaska 1998; Sergio et al. 2005). These results complement the previous study (Kalaska et al. 1989) in which external forces were applied at the hand during reaching movements.

In this study, we recorded the activity of area 5 neurons in the same monkeys from which motor cortex recordings had been made (Sergio and Kalaska 1998; Sergio et al. 2005). If parietal neurons are primarily processing information about movement kinematics, as found in earlier studies (Ashe and

Georgopoulos 1994; Kalaska et al. 1990), area 5 neurons should be active and vary with movement direction and static postures in the arm movement task, but should not show activity that varies with the moment-to-moment changes in forces during movement. Furthermore, area 5 neurons should be significantly less active and less directionally tuned in the isometric task, which involves only minor changes in arm geometry and no displacement of the hand. Preliminary results of this study have been reported previously (Hamel-Pâquet et al. 2002, 2003).

Terms borrowed from mechanics (e.g., kinematics, kinetics, dynamics) are used throughout this paper. However, they are used here only in a general sense as convenient descriptors to express the degree to which neuronal activity covaries with the externally observable spatiotemporal form of motor outputs (task kinematics) or to their underlying causal forces, torques, and muscle activity (task kinetics), while the system is in equilibrium (statics) and while in transition between static states (dynamics). Their use does not imply that parietal cortex neuronal activity explicitly codes any particular Newtonian mechanical parameter.

## METHODS

### Task apparatus

Two juvenile male rhesus monkeys (*Macaca mulatta*; monkey A: 3.4–6.1 kg; monkey B: 3.4–7.0 kg) were trained to perform an isometric-force task, and an arm-movement task against an inertial load (Fig. 1). In the isometric task, the manipulandum was a rigid

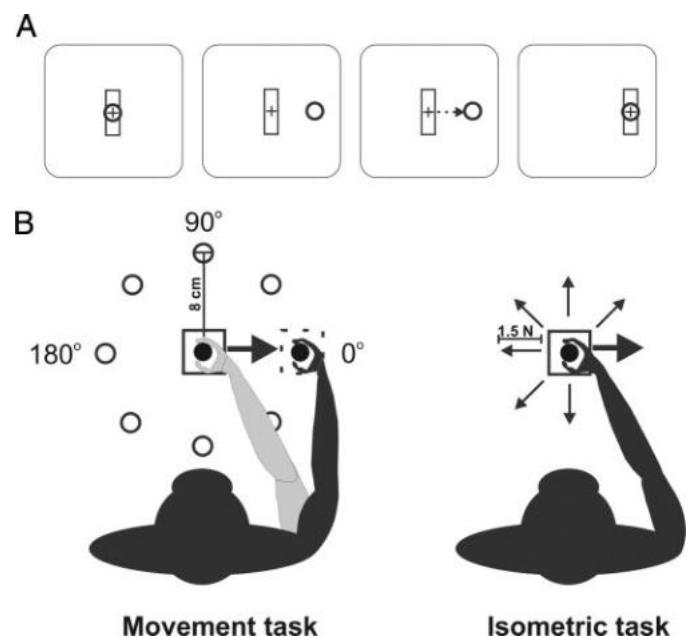


FIG. 1. *A*: behavioral task. Circles on the monitor indicate positions of targets. During performance of the task, only 1 target circle was visible at any one time. + represents the cursor the monkey had to control, and box around it indicates acceptable range of  $z$ -axis (vertical) forces the monkey was permitted to apply to the handle (Sergio and Kalaska 1998, 2003; Sergio et al. 2005). *B*: to move cursor, the monkey either displaced a movable handle (movement task) or generated force against a rigid handle (isometric task). Note that target circles in movement-task figure (*B*) are presented for convenience to show spatial distribution of targets in both tasks. There were no visible targets in the hand workspace, and the monkey's behavior was guided entirely by visual feedback on the monitor.

handle attached to a 6-df force/torque transducer (F3/T10 system, Assurance Technologies) fixed at waist level 20 cm in front of the monkey. The monkey held onto the handle with its hand and used its whole arm to generate 1.5-N force ramps in different directions in the horizontal plane. In the movement task, an identical handle/force transducer assembly was installed in a box at the free end of a 1.6-m-long weighted pendulum. Extra weights were added empirically to the transducer assembly box to ensure that the ranges of dynamic and static forces were comparable in the two tasks (Sergio et al. 2005). The transducer and box weighed 1.3 kg and the pendulum itself weighed a further 1.3 kg. To localize the position of the free end of the pendulum in the horizontal ( $x$ - $y$ ) workspace of the task, the stylus of an ultrasonic digitizer was attached to the pendulum base and its spatial location was sampled at 55 Hz (0.1-mm resolution; GP-9, Science Accessories Corp.). The spatial location of the monkey's hand in the isometric task and its starting position in the movement task were identical.

A cursor on a computer monitor positioned at eye level, 60 cm in front of the monkey, gave continuous visual feedback to guide task performance. In the isometric task, cursor position corresponded to the current force the monkey exerted with its hand on the rigid handle in the horizontal plane. In the movement task, cursor position corresponded to the  $x$ - $y$  position of the free end of the pendulum in the workspace (for more details, see Sergio and Kalaska 1998; Sergio et al. 2005). Forces applied to the pendulum handle in the  $x$ - $y$  plane during the movement task were measured by the force transducer installed in the handle but were not used to control the cursor position on the monitor, unlike in the isometric task. Vertical ( $z$ -axis) forces were measured in both tasks and controlled so that they remained within a small range about the horizontal plane of each task (Sergio and Kalaska 1998, 2003; Sergio et al. 2005).

### Behavioral tasks

A circle representing the central target first appeared on the monitor at the start of each trial (Fig. 1). The monkey generated a small static force of 0.3 N directed away from its body on the rigid handle (isometric task) or pushed the pendulum from its natural rest position to a location slightly further away from its body (movement task) to hold the cursor in the central target for a variable period of time ( $2,000 \pm 500$  ms). After this initial hold period, the central target disappeared and one of eight peripheral targets arrayed in a circle around the central target appeared. The eight targets were spaced at  $45^\circ$  intervals, starting from  $0^\circ$  at the right. The monkey generated the isometric force or the arm movement required in the horizontal plane to displace the cursor from the center to the peripheral target and held it there for 2 s to receive a liquid reward. One data file comprised 40 successful trials of one of the tasks, corresponding to five trials to each target, in a randomized-block design. The two tasks were performed in separate consecutive files of 40 trials. The order in which the tasks were performed varied from neuron to neuron. In a number of neurons, duplicate files of each task were collected to verify the stability of neuronal activity.

Four behavioral epochs were defined for the trials in both tasks. The first epoch, center-hold time (CHT), ended when the peripheral target appeared. The interval between the appearance of the peripheral target and the first significant change in force applied to the manipulandum in both tasks was called reaction time (RT). The dynamic-force time epoch (DFT) of the isometric task ended when the cursor stabilized at a constant target force direction and level. The equivalent movement-time epoch (MT) of the movement task ended when the pendulum stabilized at a constant spatial position in the peripheral target. The target-hold time (THT) epoch corresponded to the remaining period of static hold in the target circle in both tasks.

### Data collection

The monkeys were implanted with a recording cylinder over area 5 of the posterior parietal cortex using standard aseptic surgical techniques and stereotaxic coordinates. These same animals were also used for a parallel study of M1 neuron activity in these same tasks (Sergio and Kalaska 1997, 1998, 2003; Sergio et al. 2005).

Conventional techniques were used to isolate and record the activity of single neurons in posterior parietal area 5 (Kalaska et al. 1989, 1990). A glass-insulated platinum-iridium microelectrode was used and advanced through the cortex to isolate neurons. Each neuron was tested in the task to see if it was active and directionally tuned in the tasks. The passive response of each neuron was then tested, if possible, to determine its peripheral input. If a neuron responded to active or passive movements of the contralateral proximal joints but not to more distal inputs, and was directionally tuned in at least one of the tasks, it was recorded and used for further analysis.

Near the end of data collection in each cylinder, small electrolytic lesions were made ( $5\text{--}20 \mu\text{A}$ , 10 s) in selected penetrations. When the experiment was finished, the monkeys were deeply anesthetized with barbiturates and perfused with buffered saline and formalin for monkey A or with saline, and 4% paraformaldehyde for monkey B. Pins were inserted into the cortex at known grid coordinates to delimit the cortical area from which neurons were recorded. The cortex was sectioned to permit localization of the marked penetrations.

Activity was recorded from 16 proximal arm muscles in both monkeys in recording sessions separate from the neural recordings. In each EMG recording session, two muscles were implanted percutaneously with pairs of Teflon-coated single-stranded stainless steel wires. The recorded signal was amplified (1,000–5,000 times), rectified, integrated (5-ms bins), and digitized on-line at 200 Hz.

### Data analysis

An unbalanced repeated-measures ANOVA was used to test for a significant main effect of task or direction and for direction-task interactions on the mean neuron discharge rate during RT, MT, and THT epochs ( $P < 0.01$ ; 5V program, BMDP Statistical Software, Los Angeles, CA). A  $\chi^2$  test assessed if the frequency of effects was different between epochs ( $P < 0.05$ ).

The direction-related dynamic range of neuron activity across the eight directions of motor output was determined to compare the overall effect of motor output direction on the activity of the neurons between the two tasks. For each neuron, the direction-related dynamic range was defined as the difference in mean discharge rate recorded for the two directions of motor output that showed the maximum and minimum discharge rates across the eight directions of output in a given epoch of a given task.

To compare these results between area 5 and M1, a contrast ratio analysis was performed. The contrast ratio values were calculated from the dynamic range values (DR) obtained for the movement (mvt) and the isometric (iso) tasks during each trial epoch, using the following equation

$$\text{Contrast ratio} = (\text{DR}_{\text{mvt}} - \text{DR}_{\text{iso}}) / (\text{DR}_{\text{mvt}} + \text{DR}_{\text{iso}})$$

The values ranged from  $-1$  to  $+1$  and were binned in 10 groups of 0.2 units. The two resulting distributions were then compared with each other with a Kolmogorov-Smirnov (KS) test ( $P < 0.05$ ). Each distribution was also tested for a significant deviation from equal activity in each task (i.e., mean contrast ratio of 0.0;  $t$ -test,  $P < 0.05$ ).

To compare the incidence of significant directional tuning of neurons between tasks, the directionally tuned neurons, determined by a bootstrap test (Crammond and Kalaska 1996, 2000; Sergio and Kalaska 1998, 2003), were counted, and a  $\chi^2$  test was performed. To test if the distribution of preferred directional tuning of the neurons was uniform across the population, a Rao's spacing test ( $P < 0.05$ ) was done on the distribution of the preferred directions (PDs) of the sample population (Batschelet 1981).

In addition, a sliding-window analysis was performed for the isometric and movement tasks to describe the time-varying profile of the apparent instantaneous directionality of each neuron on moment to moment basis. Spike data for each trial in each task were aligned to the moment of force onset. A window of 50-ms duration was defined and advanced by steps of 10 ms, beginning 400 ms before force onset and ending 1,200 ms after force onset. The momentary mean activity of the neuron was calculated in each successive window of each trial, using whole and partial spike intervals rather than simple spike counts (Coe et al. 2002; Georgopoulos et al. 1982; Sergio and Kalaska 1998, 2003; Sergio et al. 2005). The PD of the activity was calculated in each window, using standard methods (Sergio and Kalaska 1998, 2003). A bootstrapping procedure was used to evaluate if neuron activity in each window was significantly directionally tuned with a confidence level of 95% (Crammond and Kalaska 2000; Sergio and Kalaska 2003; Sergio et al. 2005).

To evaluate the moment-to-moment net directional signal at the population level, a population-vector analysis was performed. For this analysis, momentary neuronal activity was calculated in 20-ms non-overlapping windows, after all single-trial data were aligned to force onset. The apparent PD of a neuron can change from window to window, in part because the stochastic nature of neuron activity is accentuated when examined at such short time intervals. Furthermore, the apparent directionality of M1 neurons often changed dramatically during the MT epoch of the movement task (Sergio and Kalaska 1998; Sergio et al. 2005). This raises the question of how to identify the presumed directional influence of a given neuron on motor output at a given moment in time, and thus its contribution to the evolving population signal.

To address this question, we assumed that this directional influence on peripheral motor output remains stationary, at least over the time frame of single trials and single data files. We observed that the apparent directional tuning of muscles and single M1 neurons was generally similar between isometric and movement tasks during the RT and especially the THT epochs. Because the THT epoch is substantially longer than the RT epoch, we decided that this would give a more stable estimate of the overall directional tuning of M1 neurons. Therefore we calculated the preferred direction of the M1 neurons using the average discharge of each neuron during the THT epoch in each task and used it as the canonical PD of the neuron for the reconstruction of population vectors in the corresponding task (Sergio et al. 2005). We retained that same general approach for this study, but had to adapt it to the response patterns of parietal cortex neurons. Because parietal cortex neurons were typically most active during the dynamic (MT or DFT) phase of each task, the canonical PD of each neuron was calculated during the MT epoch of the movement task and the DFT epoch of the isometric task, rather than during THT as had been done for the M1 data (Sergio et al. 2005). Irrespective of the apparent directional tuning of the neuron in a given 20-ms time window, its presumed contribution to the population-vector signal was based on its PD during the MT or DFT of the corresponding task. Population vectors were reconstructed from the summed directional contributions of all neurons in the sample, using standard methods (Sergio et al. 2005).

## RESULTS

### *Measured forces exerted at the hand against the task manipulandum*

Forces were measured at the hand while the monkeys performed the movement and the isometric tasks. In the isometric task, forces were monotonically increasing ramps directed at the target that rose progressively and smoothly up to a stable force maintained throughout the remainder of the trial (Fig. 2A). In the movement task, the monkeys made corresponding monotonic ramp displacements of the arm toward targets.

However, the forces applied by the hand showed a more complex “triphasic” pattern (Fig. 2B). An initial accelerative force was directed toward the targets, followed by a transient rapid reduction and change in direction of exerted force of almost 180° before the peak of velocity to slow the handle as it approached the target. This was followed by a second reversal of force direction so that it again pointed in the direction of the target. This latter force was sustained for the remainder of the trial to hold the mass of the pendulum over the target against the force of gravity.

### *Muscle activity*

Muscle activity was recorded from a total of 57 sets of EMG records collected from 16 proximal arm muscles in each monkey (see Sergio and Kalaska 2003; Sergio et al. 2005 for more details). The distribution of the preferred directions of the muscles was uniform in all epochs in both tasks (Rao’s spacing test,  $P < 0.05$ ). The profile of activity of muscles appeared to parallel the differences in force profiles in both tasks. For almost all the muscles studied, such as the middle deltoid (Fig. 2), the EMG activity changed monotonically during force-ramp generation and was directionally tuned in the isometric task (Fig. 2A). In the movement task, in contrast, the muscle activity showed a reciprocal “triphasic-burst” pattern in the movement task, including a brief reduction or pause in activity during movement in the directions in which the muscle was an agonist, and a delayed burst during movements in directions in which the muscle acted as an antagonist (Fig. 2B). These transient changes in EMG activity were not seen in the isometric task (Sergio and Kalaska 1998; Sergio et al. 2005). In these highly practiced animals, EMG activity was characterized by precisely timed reciprocal activation of antagonist muscles in both tasks, with little evidence of extended periods of co-activation of antagonist muscles.

### *Parietal area 5 neuronal activity*

Neuronal activity was recorded in posterior parietal area 5 in the intraparietal sulcus of two monkeys (Fig. 3). Seventy-eight area 5 neurons that were directionally tuned in at least one task and that were related to the proximal arm were included in the sample. A large number of other task-related neurons were tested in the two tasks, but could not be held long enough to collect complete data files in both tasks, and so are not presented here. However, their properties were similar to those of the neurons reported in this paper. A few of the most rostral and medial penetrations in the left hemisphere of monkey B may have encroached on area 2 of SI. However, the cytoarchitectonic border between area 5 and area 2 is difficult to determine in cresyl-violet stained sections. The majority of neurons were recorded in penetrations made in the medial bank of the IPS, clearly in area 5 (Fig. 3).

The most striking finding overall was that many area 5 neurons, unlike the case in M1 (Sergio et al. 2005), were significantly more active in the movement task than in the isometric task (Fig. 4).

Area 5 neurons showed a continuum of temporal response patterns in the movement task. However, most neurons could be subjectively classified into one of three general temporal response profiles based on their overall pattern of activity in the

## A Isometric task

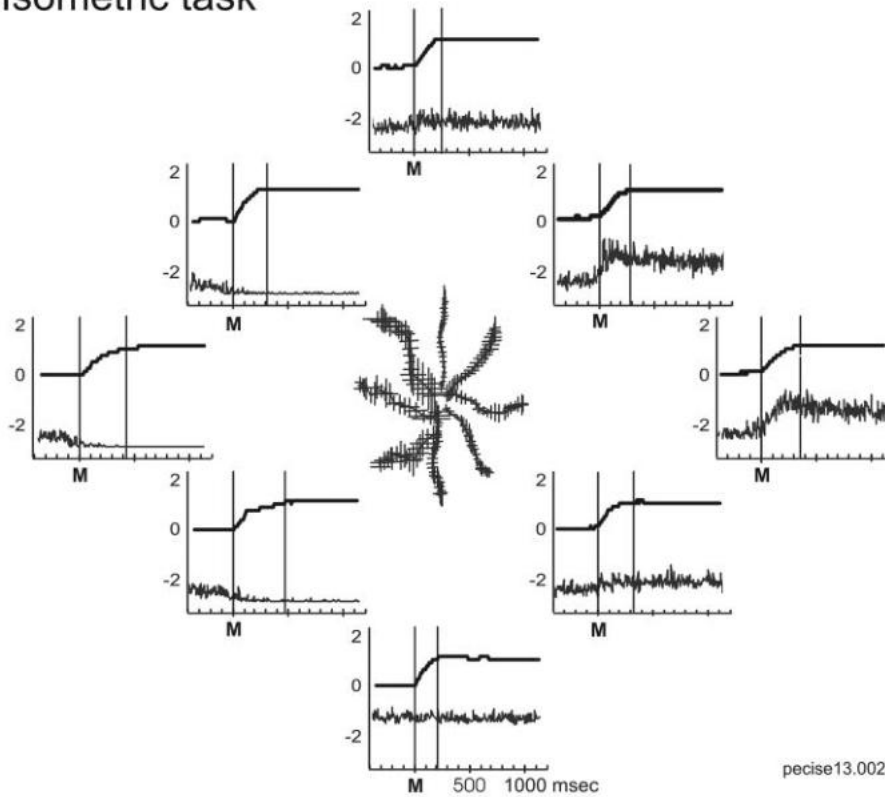
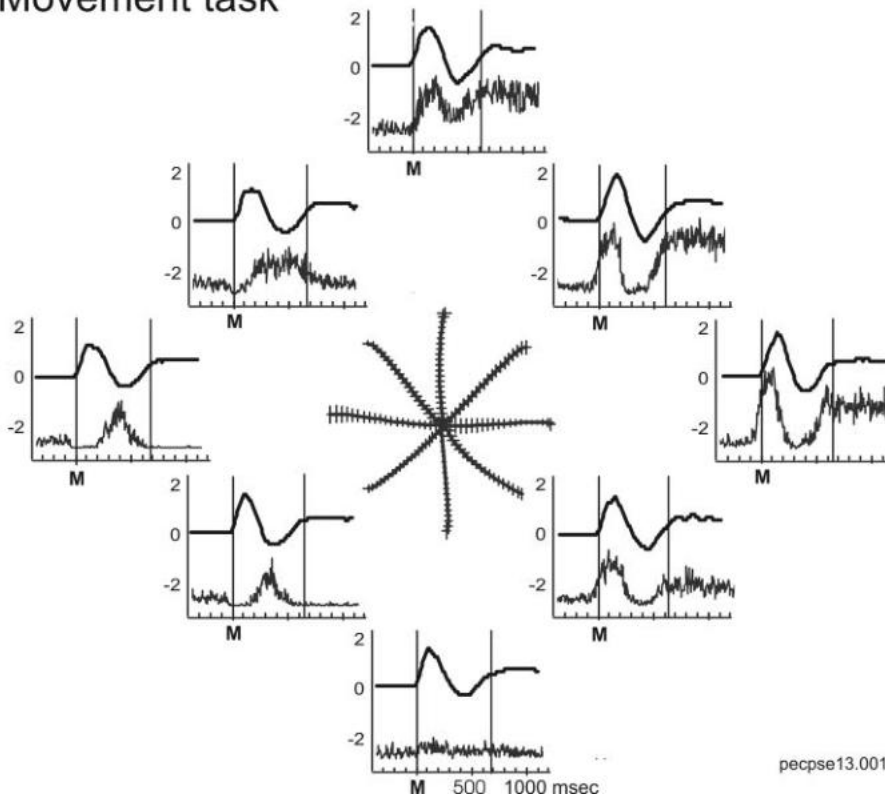


FIG. 2. EMG activity of the right middle deltoid muscle during isometric (A) and movement (B) tasks. Histograms represent average rectified and integrated EMG activity (arbitrary units) from 5 trials in each output direction. Curves above each histogram show time-course of the mean magnitude of component of the measured force output vector exerted on the task handle that was oriented along the axis from the central starting location toward each target in that data file. Force scale (y-axis, in N) refers to force curves. Data are aligned at 1st significant force change in each trial (M). The 2nd vertical line, to *right* of force onset alignment line, corresponds to mean time of last significant change in force or position and indicates end of dynamic force time (DFT; isometric task) or movement-time epoch (MT; movement task) and beginning of target-hold time (THT) epoch. Mean isometric forces (A) and hand movement paths (B) for those particular data files are shown at the center of each group of histograms.

## B Movement task



movement task (Fig. 4, Table 1). Phasic neurons (33/78; 42%) primarily showed a phasic burst during movement in their preferred direction (Fig. 4A). Tonic neurons (23/78; 30%)

showed a simple ramp or step increase in their tonic rate, beginning at different times relative to movement onset in different neurons, that was sustained until the end of the trial

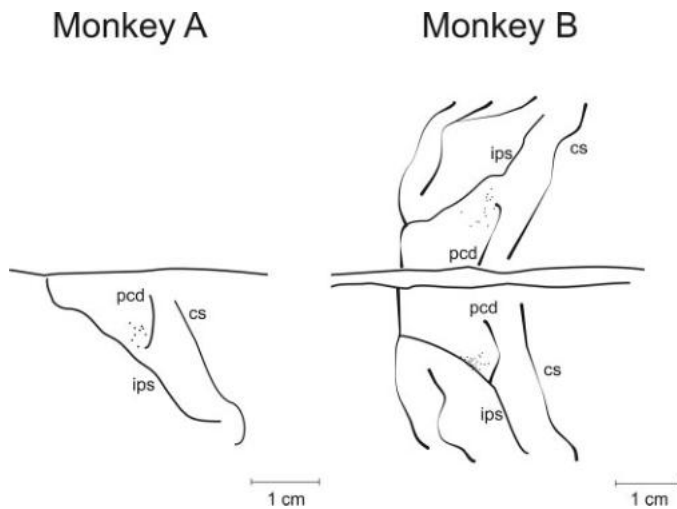


FIG. 3. Locations of recording sites made in area 5 of posterior parietal cortex of both monkeys (right hemisphere only for monkey A). Rostral is to the right and caudal to the left for each brain map. ips, intraparietal sulcus; pcd, postcentral dimple; cs, central sulcus.

(Fig. 4B). Phasic-tonic neurons (16/78; 21%) were intermediate in properties, showing an initial phasic burst followed by tonic activity without an intervening pause in activity (Fig. 4C). In addition, a few “reversal” neurons (5/78; 6%) showed an initial phasic burst at the onset of movement in one direction and a late ramp increase in activity during target hold time in the opposite direction (data not shown; Kalaska et al. 1990). One neuron (1/78; 1%) showed a modest “triphasic-burst” pattern reminiscent of EMG activity (Sergio et al. 2005).

In the isometric task, many of the area 5 neurons that had been active in the movement task were relatively or completely inactive (35/78; 45%; Fig. 4, A–C). Other neurons were active in the task and showed either phasic (25/78; 32%), tonic (15/78; 19%), or phasic-tonic (3/78; 4%) patterns. While nearly one-half of the sample of area 5 neurons were active almost exclusively in the movement task, there was no evidence of a significant population of neurons with the opposite task preference for nearly exclusive activation in the isometric task.

An ANOVA assessed the effect of task and direction on neuron discharge (Table 2). The results showed significant differences in overall discharge rate between the two tasks (main effect of task) for many area 5 neurons during RT (40/78; 51%), MT (56/78; 72%), and THT (49/78; 63%). Single-neuron discharge was also influenced by the direction of movement across tasks (main effect of direction) during RT (48/78; 62%), MT (67/78; 86%), and THT (68/78; 87%). Most strikingly, far more neurons showed differences in directional properties between the two tasks (significant task–direction interaction) in MT (61/78; 78%) and THT (62/78; 80%) than in RT (28/78; 36%). These last results in particular indicated that area 5 neurons tended to show progressively greater differences in their relation to output direction between the two tasks with time after the appearance of the output targets in the trials. For all three effects studied, the proportion of neurons showing a significant effect was different between epochs ( $\chi^2$ ,  $P < 0.05$ ). The analyses in the following sections provide further insight into the origin and functional implications of these ANOVA results.

### Dynamic range and contrast ratio analysis

A task-direction interaction can be caused by a difference in the gain of direction-dependent discharge modulation between the two tasks. To assess this possibility, we compared the direction-related dynamic range (see METHODS) of neuronal activity for different directions of motor output in the movement and the isometric tasks (Fig. 5) for all three trial epochs. The scatter plots show that most of the data points fell below the diagonal identity line, indicating a larger direction-related dynamic range in the movement task than in the isometric task for most neurons. The slope of the regression function was far below 1.0 (the identity line) in each trial epoch and decreased from RT (0.339) to MT (0.195) and THT (0.179).

To further compare the differences in responses of area 5 neurons in both tasks, a contrast ratio analysis was performed on the dynamic range values obtained for the two tasks during the RT, MT, and THT periods (Fig. 6, solid lines). The values ranged from  $-1$  to  $+1$ , with a value of  $-1$  signifying that the neuron was only active in the isometric task and  $+1$  signifying that the neuron was only active in the movement task. For the parietal neurons, the distribution on average shifted significantly toward  $+1$  at all times during the trial (mean of the distribution was significantly different from 0.0 in RT, MT, and THT,  $t$ -test,  $P < 0.05$ ), which further shows that area 5 neurons were systematically more active in the movement task than in the isometric task.

A contrast ratio analysis was also performed on M1 activity recorded from those same monkeys (Fig. 6, dashed lines; data from Sergio et al. 2005). Whereas the distributions of ratios of area 5 neurons shifted toward  $+1$  for all three trial epochs, the distributions for M1 neurons were slightly biased toward  $-1$  for the RT and MT/DFT epochs (significantly different from 0.0,  $t$ -test,  $P < 0.05$ ). This indicated that the dynamic ranges of M1 neurons were slightly larger on average during the isometric than the movement task for those two epochs. For the THT epoch, the M1 distribution was slightly biased toward  $+1$ , like the parietal neurons, but to a lesser degree. For all three epochs, the distributions of contrast ratios of area 5 and M1 neurons were significantly different (Kolmogorov-Smirnov test,  $P < 0.05$ ), with a systematic bias toward larger positive contrast ratios (i.e., relatively greater activity in the movement task than in the isometric task) for area 5 compared with M1.

### Temporal analysis of single-neuron directionality

Another potential cause of a task-direction interaction is a task-dependent change in the directionality of motor output tuning of the neurons, independent of their discharge levels in the two tasks. To examine this possibility, we first compared the incidence of the directional tuning of neurons between the two tasks in each of the three epochs. More area 5 neurons were significantly directionally tuned (bootstrap test) in the movement task (RT: 33/78, 42%, MT: 66/78, 85%, THT: 62/78, 80%) than in the isometric task (RT: 11/78, 14%, MT: 34/78, 44%, THT: 35/78, 45%). The frequency of neurons that were directionally tuned was significantly different between the two tasks for each of the three epochs ( $\chi^2$  test,  $P < 0.05$ ). The distribution of the PDs of significantly directionally tuned neurons, calculated from the mean activity during the entire RT, MT, and THT epochs, was uniform in all three epochs in the isometric task and for the MT and THT epochs in the

TABLE 1. Temporal response profiles of area 5 neurons in isometric and movement tasks

Isometric Task	Movement Task					Total
	P	T	PT	R	TB	
P	17 (22)	2 (3)	6 (8)	0 (0)	0 (0)	25 (32)
T	1 (1)	7 (9)	2 (3)	4 (5)	1 (1)	15 (19)
PT	1 (1)	1 (1)	1 (1)	0 (0)	0 (0)	3 (4)
I	14 (18)	13 (17)	7 (9)	1 (1)	0 (0)	35 (45)
Total	33 (42)	23 (30)	16 (21)	5 (6)	1 (1)	78 (100)

Classification of area 5 neurons. Table shows the number (and percentages) of neurons in each category in each task. P, phasic; T, tonic; PT, Phasic-tonic; R, Reversal neuron; TB, triphasic-burst; I, inactive.

movement task (Fig. 7; Rao's spacing test,  $P < 0.05$ ). During the RT epoch in the movement task, however, the distribution was nonuniform, showing a significant bimodal distribution (Rao's spacing test,  $P < 0.05$ ).

To look more closely at the temporal response pattern of activity of single neurons in each task, a sliding-window analysis was performed that gives information about the temporal evolution of the apparent instantaneous PD of a single neuron. A bootstrap test was also applied to evaluate if neuronal activity was significantly directionally tuned in each 50-ms time window. For the neuron shown in Fig. 4C, the directionality of activity in the movement task remained relatively constant and was significant from about 100 ms before the onset of the movement to the end of the trial (Fig. 8A). In contrast, in the isometric task, the neuron was not significantly tuned at any given moment for most of the trial (Fig. 8B). A brief period of directional tuning from about 650–1,000 ms after force onset (Fig. 8B) can be explained by small clusters of spikes in the 135° and 180° directions (Fig. 4C).

Many neurons showed this trend of a greater probability of directional tuning at a given moment in time in the movement task than in the isometric task. To summarize this trend at the population level, the bootstrap test used in the preceding analysis was performed to test for the significance of directional tuning of neurons in a given window in a given task (Fig. 9). Neurons began to be directionally tuned before movement onset in both tasks. By the time of force onset in each task, however, nearly twice as many neurons were directionally tuned in a 50-ms time window in the movement task than in the isometric task and this difference persisted for the remainder of the trial.

### Population-level analysis

Two population analyses were performed to see how the observations reported at the single neuron level are reflected at the population level.

In the first, population histograms were generated of the activity of all area 5 neurons that were directionally tuned in a given epoch (Fig. 10). Only the significantly directional neurons in a given epoch and task were included in the corresponding histogram. The histograms show that, in the movement task, the activity of the population of area 5 neurons increased rapidly before motor output onset and peaked at about 100 ms after output onset. The activity decreased to reach a plateau where it stayed until the end of the trial. In the isometric task, a similar pattern was observed, but the discharge rate was much lower. Note also the progressive change in the shape of the population histogram profiles when the neuronal data are aligned to the PD calculated in different epochs.

The population histograms seem to be predominantly phasic in the movement task when aligned to the PD during the RT epoch, and there is relatively little difference in late tonic activity at the end of the trials in the PD and opposite direction (Fig. 10). The initial phasic component becomes less prominent and less strongly directionally tuned, and a directionally tuned late tonic discharge becomes more evident as the activity is aligned to the PD of each neuron during MT and then THT (Fig. 10). Similar trends are seen for the data in the isometric task, but the task-related responses were much smaller on average than in the movement task.

The mean profile of forces applied on the task handles was also calculated while recording the activity of each population of neurons (Fig. 10). The differences between the histograms of neuronal activity for the two tasks do not reflect the large task-related changes in the temporal patterns of output forces between the two tasks. In particular, there was no evidence of a neuronal response component that paralleled the transient reversal of output forces during the decelerating phase of the movement task.

Note that the population histograms presented in Fig. 10 tend to exaggerate the amount of activity evoked in the area 5 population during the isometric task relative to that during the movement task, because they were generated using only those neurons that were significantly directionally tuned in a given trial epoch in the corresponding task. Far fewer neurons overall were significantly directional in the isometric task in each trial epoch. If histograms had been generated from the total sample population rather than just the directionally tuned neurons, the differences in activity level between the two tasks would have been even greater than is indicated in Fig. 10 (data not shown).

Next, a population–vector analysis was performed using the activity of the entire sample, and was compared with the average temporal profile of forces applied to the rigid manipulandum in the isometric task or the moving handle in the movement task (Fig. 11).

The population–vector representation showed the moment-to-moment net directional signal generated by a population of

TABLE 2. Effect of task, direction and T-D interactions on area 5 neurons

Epoch	Task	Direction	T-D Interaction
RT	40 (51)	48 (62)	28 (36)
MT	56 (72)	67 (86)	61 (78)
THT	49 (63)	68 (87)	62 (80)

Unbalanced repeated-measure ANOVA, Wald test  $P < 0.01$ . Table shows the number (and percentages) of neurons that had a significant effect in each experimental epoch. RT, reaction time; MT, movement time; THT, target-hold time; T-D, task-direction.

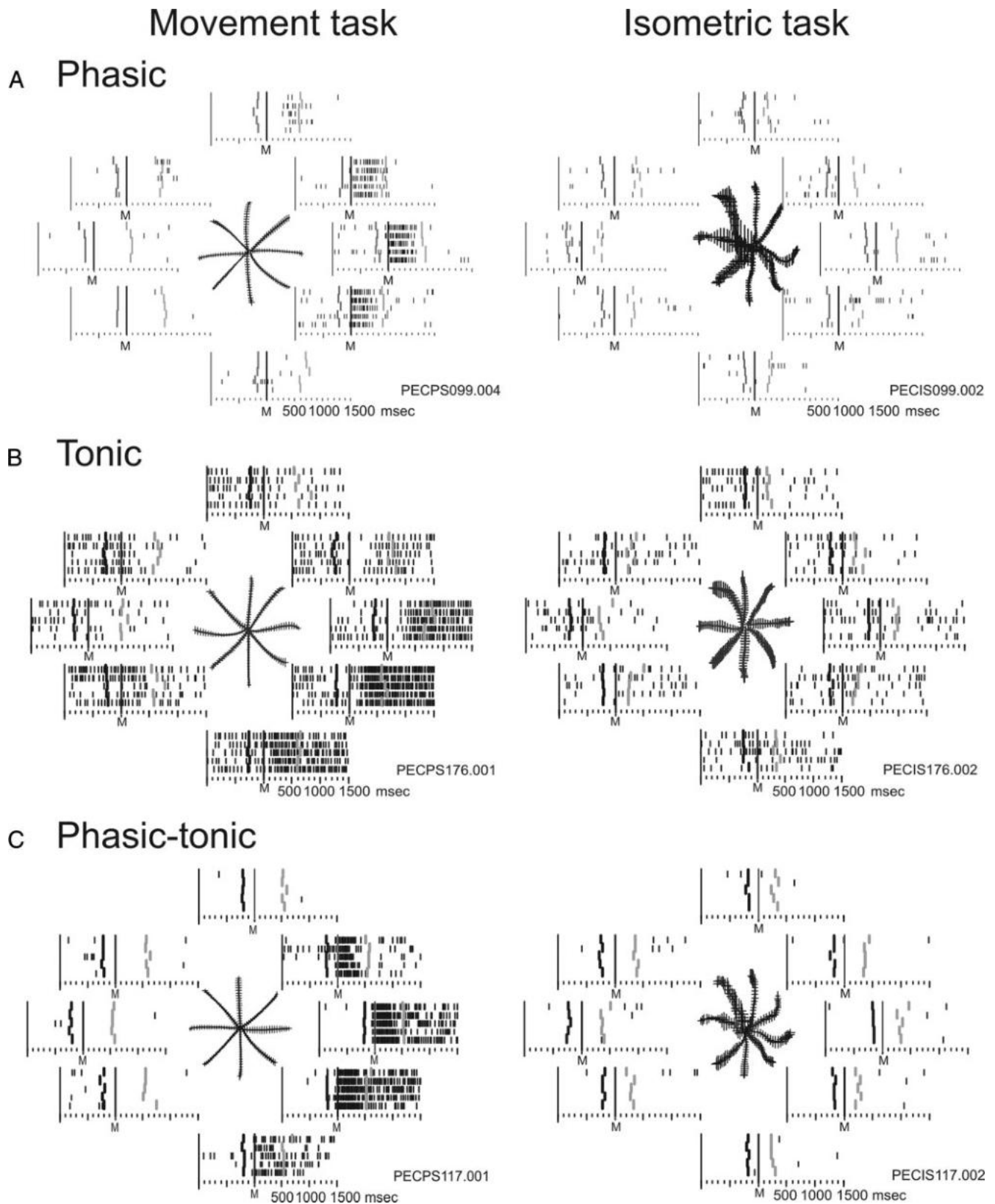


FIG. 4. Rasters of discharge patterns of 3 proximal arm-related parietal area 5 neurons of monkey B during movement and isometric tasks. Neurons shown here had phasic (A), tonic (B), and phasic-tonic (C) temporal response profiles during movement task. Each raster shows 5 trials to 1 of the 8 directions. Data are aligned on the 1st significant force change, indicated by the solid vertical line (M). Thick tick marks to the left of that line show time of target onset and thick gray marks to the right show end of DFT or MT epoch, which corresponds to the moment the final static level of force or position within the peripheral target was reached in each trial. Mean force/movement paths for each data file are shown at the center of each set of rasters.

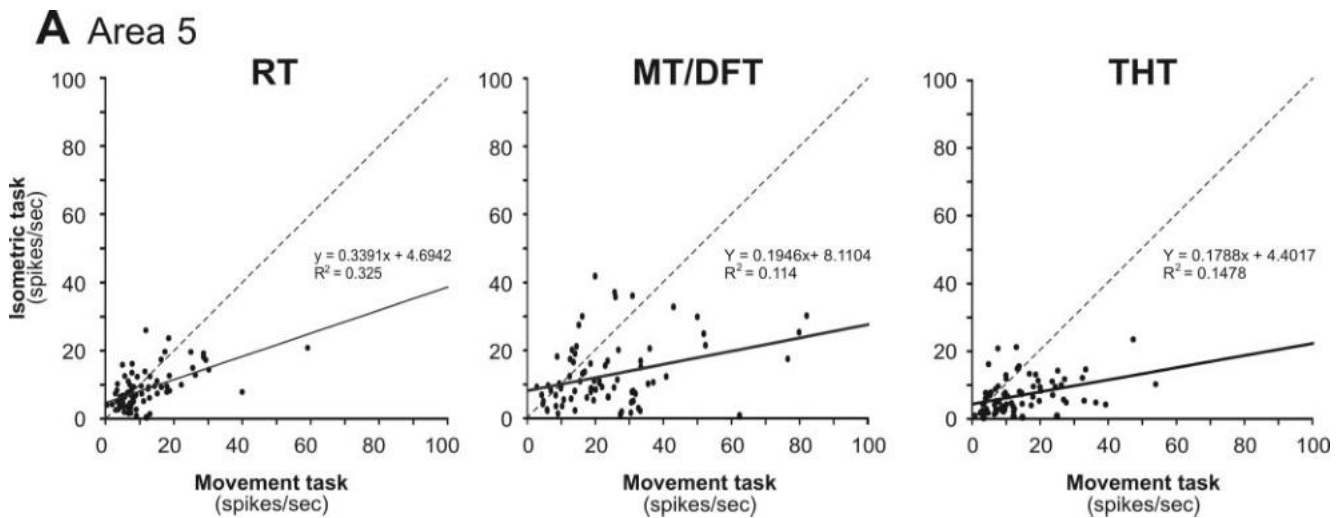


FIG. 5. Scatter plots comparing the direction-related dynamic range of neuron activity for different directions of motor output in the movement and isometric tasks for RT, MT/DFT, and THT epochs in area 5. Solid line represents regression line and dashed line represents identity line.

78 area 5 parietal neurons during arm movement and isometric-force tasks. Each vector represented the direction and the strength of the net population signal during a 20-ms sliding-window that was advanced in nonoverlapping 20-ms steps. The population vector representation differed between the two tasks. In the movement task, there was a rapid increase in the length of the vectors prior to and during movement, which decreased and remained relatively constant for the remainder of the trial (Fig. 11C). Furthermore, the direction of the vectors varied systematically with and corresponded fairly well to the direction of movement, despite the relatively small neuron sample size. The directionality of the vectors also remained nearly constant throughout the trial, reliably signaling the direction of movement or change in arm posture at all times. There was no evidence of a neural correlate of the complex time-course and reversal in directionality of the output forces measured at the hand during movement (Fig. 11A). In contrast, the population vector signal generated by the neurons was substantially smaller in the isometric task but also tended to correspond to the direction of force output (Fig. 11D). Similar results were obtained when the population-vector analysis was repeated using the directional tuning of neurons during the THT epoch (data not shown).

These trends were shown more clearly when the individual 20-ms population vectors were joined tip-to-tail to form neural trajectories (Georgopoulos et al. 1988). In the movement task (Fig. 11E), the neural trajectories started near the direction of desired motor output and continued along that direction for the duration of the trial, without any major inflections or reversals of direction. The same was also observed for the neural trajectories of the area 5 population in the isometric task, but the overall scale of the motor output representation was substantially smaller (Fig. 11F).

#### Comparison with neuronal activity in primary motor cortex in the same task conditions

Neuronal recordings were made from the caudal part of the primary motor cortex in the same tasks in these same monkeys. Those results are described in detail elsewhere (Sergio et al. 2005). The findings showed that the M1 population showed prominent temporal correlates of the differences in the time-course of output kinetics in the two tasks, including the reversal of output forces and the triphasic response patterns of many prime-mover muscles in the movement task against a heavy inertial load, that were not evident in the area 5 sample population.

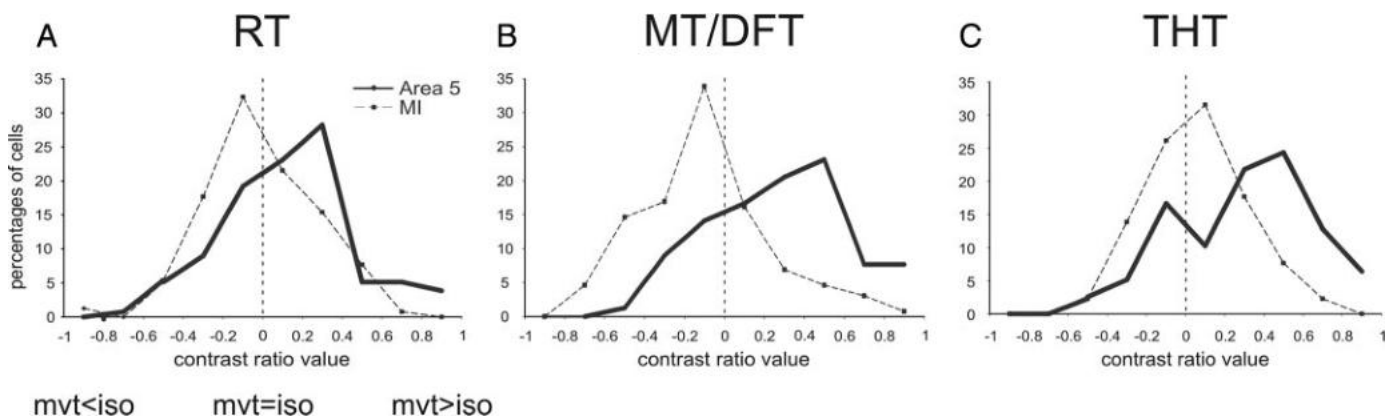


FIG. 6. Contrast ratio analysis. Frequency distributions, in percentages, of the contrast ratios of task related-dynamic ranges of neurons in area 5 (solid line) and M1 (dashed line), for RT (A), MT/DFT (B), and THT (C) epochs. Contrast ratio values were calculated from dynamic range values obtained for both tasks. Positive contrast ratios indicate a larger dynamic range in the movement task than in the isometric task, and negative ratios indicate the opposite.

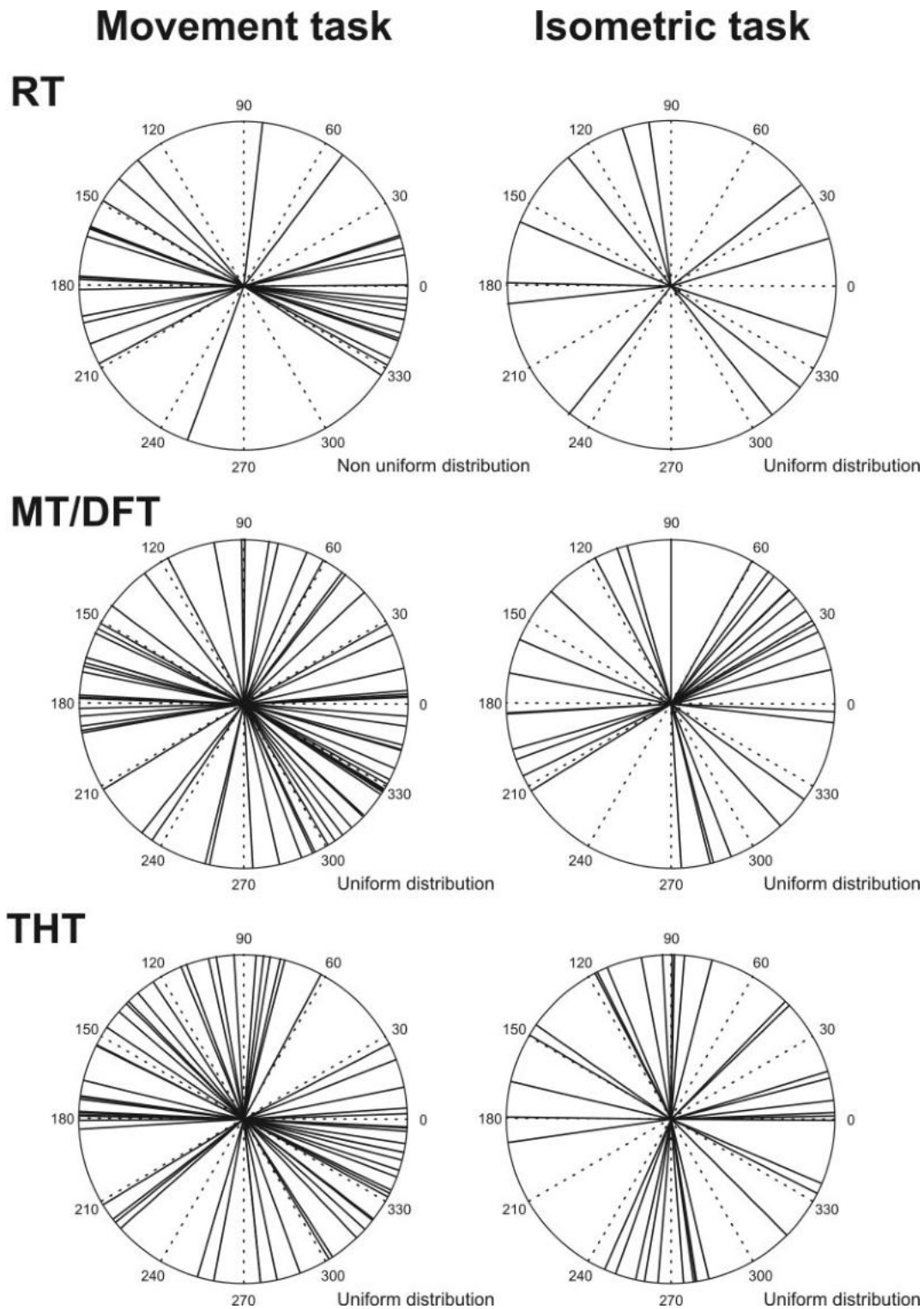


FIG. 7. Polar plots representing the distributions of PDs of directionally tuned area 5 neurons (solid lines) during the movement and the isometric tasks for the RT (A), MT/DFT (B), and THT (C) epochs. Rao's spacing test ( $P < 0.05$ ; Batschelet 1981) assessed if the distributions showed a significant deviation from directional uniformity.

To facilitate comparison of results, we present some of the M1 results here. Figure 6 compared the distributions of contrast ratios of dynamic ranges of activity from the two tasks in the two cortical areas. As already noted, there was a systematic shift in the distributions from M1, reflecting the

greater activation of M1 cells in the isometric task compared with area 5. Figures 12 and 13 provide further direct contrasts of the major differences in the temporal patterns of neuronal activity in the two cortical areas during the movement task.

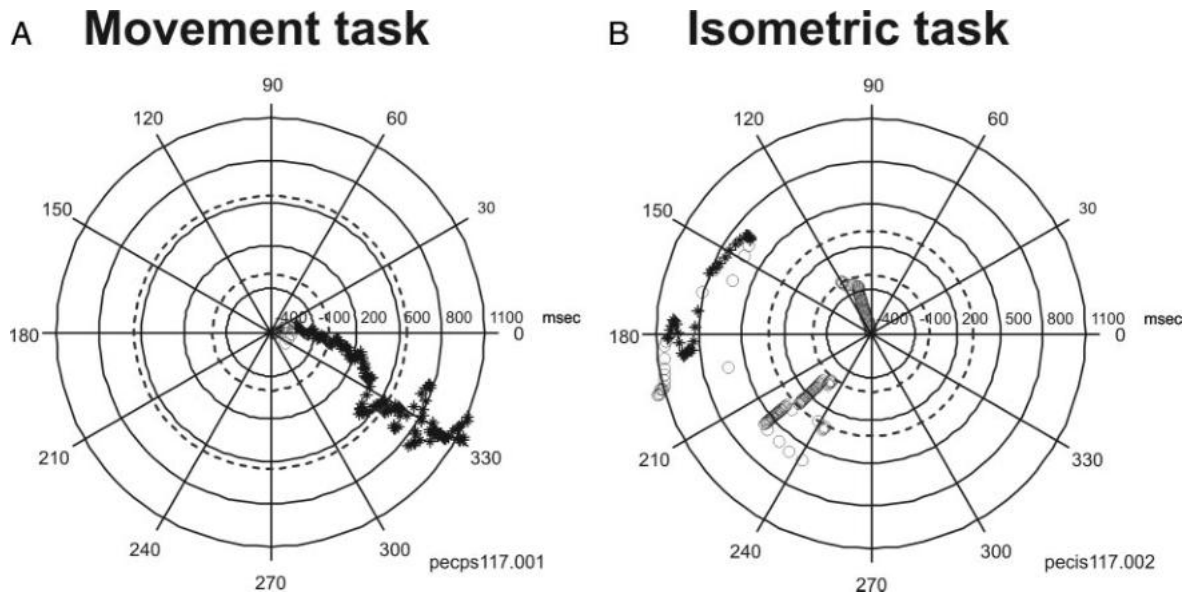


FIG. 8. Temporal evolution of the apparent instantaneous preferred direction (PD) of the neuron shown in Fig. 4C in the movement (A) and the isometric (B) tasks, determined by a 50-ms sliding windows analysis. Time window within which the neuron was significantly related to direction (bootstrap test) is represented by a \*. Time window within which the neuron was not significantly related to direction is shown by an "o". Inner and outer dashed circles represent onset and offset, respectively, of movement and force ramps.

Figure 12 presents the mean population histograms of the samples of neurons that were directionally tuned during the RT epoch in area 5 (cf. Fig. 10) and in M1 (modified from Fig. 8A of Sergio et al. 2005). The area 5 population (Fig. 12, thick lines) emitted a single phasic response before and during movements in the preferred direction of each neuron and relatively little change in mean activity for movements in the opposite direction. In contrast, the corresponding M1 population showed an early phasic burst peaking at movement onset in the preferred direction (Fig. 12, thin lines), followed by a brief decrease in mean activity and a second increase in activity. In the opposite direction, the M1 population showed an initial decrease in activity followed by a brief strong phasic burst preceding and during the deceleration phase of the

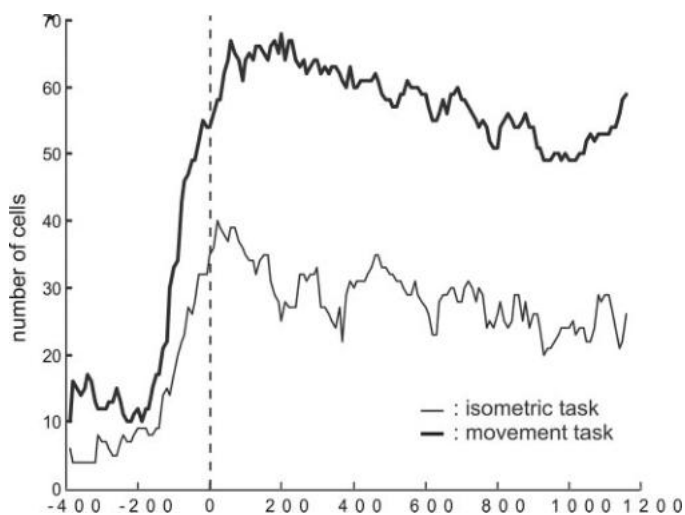


FIG. 9. Number of significantly directionally tuned neurons (bootstrap test) in each task over time, within successive 50-ms windows that were stepped forward in 10-ms increments. Thick solid line represents data from the movement task, whereas thin line corresponds to the isometric task.

movements. This delayed burst was completely absent in the area 5 population (Fig. 12, thick lines).

Figure 13 shows the temporal evolution of the distribution of directionally tuned activity of single cells and the net resultant population vector at 40-ms time intervals during the movement task in area 5 (cf. Fig. 11) and in M1, during arm movements in one direction, 180° (modified from Fig. 10B of Sergio et al. 2005). The area 5 population became directionally tuned before movement onset. Although the overall magnitude of the net population signal varied with time, its direction remained relatively constant and oriented near 180° at all times after the population became directionally active. In contrast, the net directional signal in M1 initially pointed near the direction of desired movement, but diminished and reversed in direction during the time period from ~200 to 400 ms after movement onset, before reversing direction again to point back in the desired direction of movement.

## DISCUSSION

The goal of this study was to examine the relation of the activity of parietal area 5 neurons to the kinematics and kinetics of motor output during an arm-movement and an isometric-force task. The two tasks were designed to dissociate motor output kinematics (e.g., direction and velocity of movement, static arm positions) from output kinetics (e.g., direction and time course of static and dynamic forces, EMG patterns). The isometric task required the monkeys to generate monotonic ramps of output forces in different directions in the horizontal plane against a rigid task handle, but no hand displacements. In contrast, the movement task required monotonic ramp-like displacements of the hand in the horizontal plane, that were produced by exerting a complex nonmonotonic pattern of output forces at the hand against the inertial load of a movable task handle. The nonmonotonic output forces in the movement task included a transient reversal of the

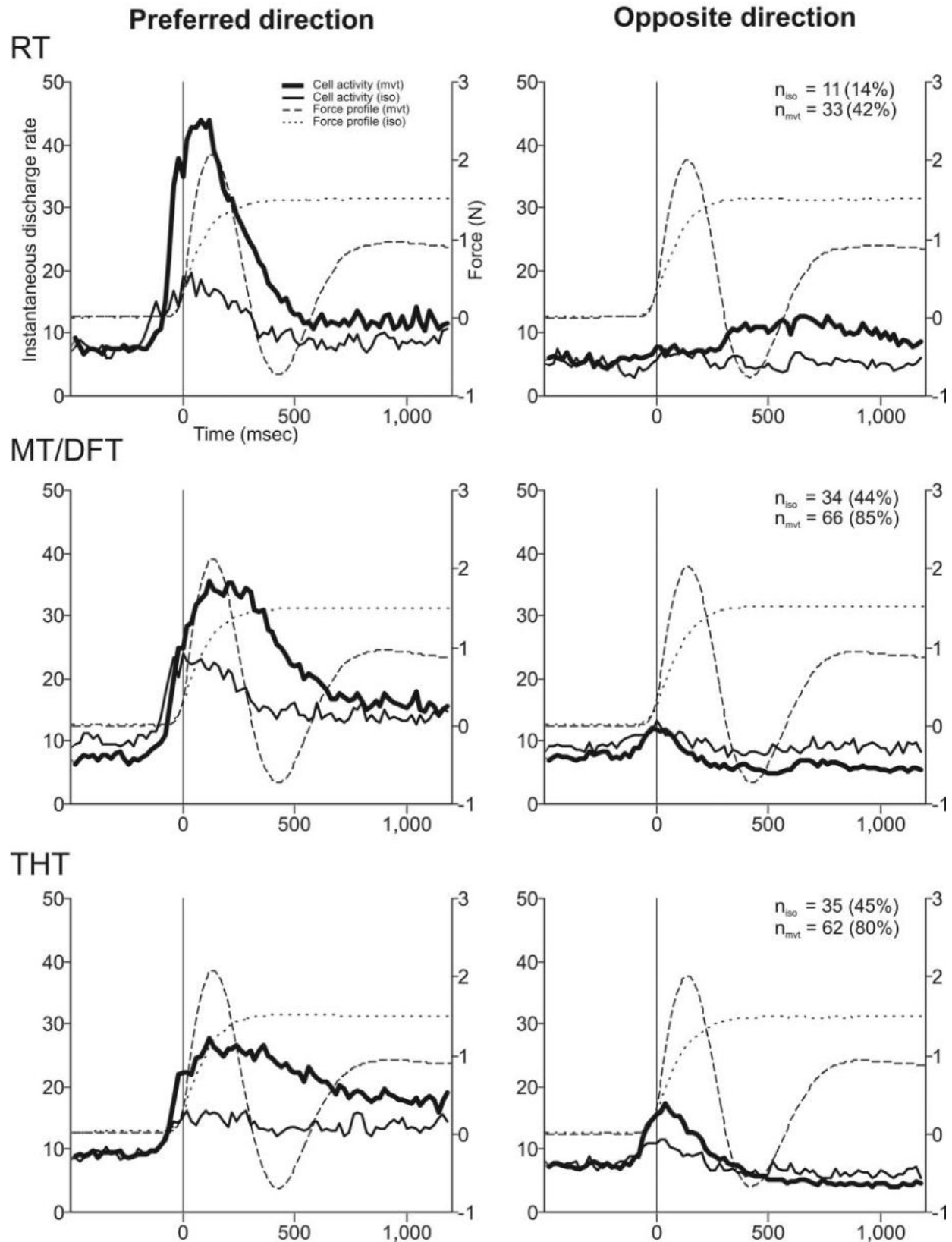


FIG. 10. Population histograms of area 5 neuronal activity and mean forces in isometric and movement tasks at the PD and direction opposite to the PD of neurons in RT, MT/DFT, and THT epochs. All histograms are aligned to force onset (0) in both tasks. Force traces show time-course of mean magnitude of component of measured force output vector exerted on task handle that was oriented along axis from central starting location toward each target in that data file. Negative force values indicate a force component oriented in direction opposite to motor output target.  $n$ , number of directionally tuned neurons in that trial epoch that contributed to population histograms for isometric (iso) and movement (mvt) tasks.

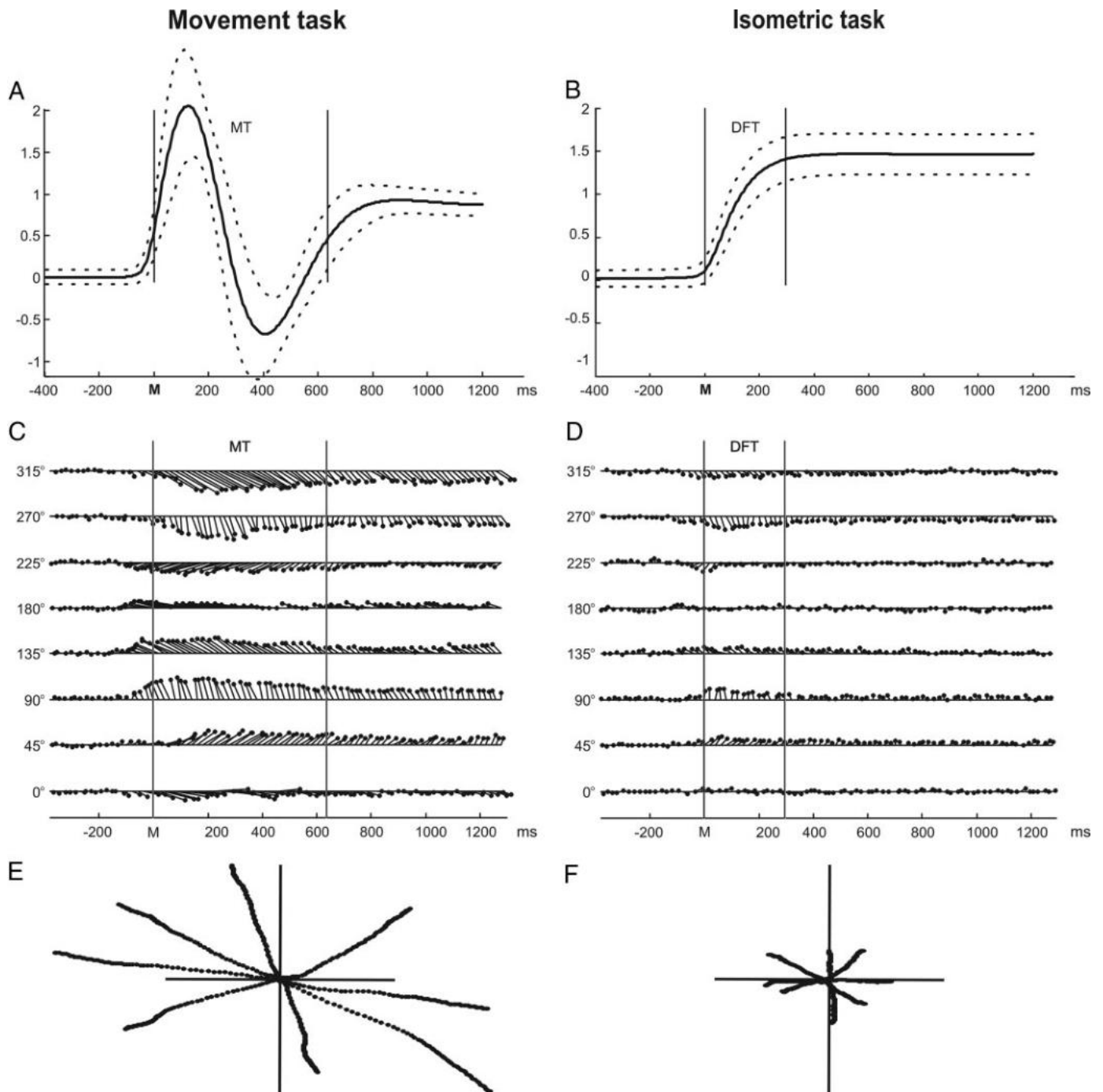


FIG. 11. *A* and *B*: mean temporal profile of forces applied to the manipulandum in the direction of desired motor output, averaged across all 8 output directions from all data files in movement (*A*) and isometric (*B*) tasks, respectively. Solid line is mean value of component of measured force output vector that was oriented along the axis between start position and target, calculated every 20 ms, and dotted lines indicate SD of mean force values. Negative force values indicate a force component oriented in direction opposite to target. Left vertical line indicates onset of the MT/DFT epoch and the right vertical line shows average time of their end. *C* and *D*: population-vector representation of area 5 activity in movement (*C*) and isometric (*D*) tasks for each of the 8 targets. Each vector represents direction and strength of net population signal generated by all neurons during a sliding 20-ms window that was advanced in nonoverlapping 20-ms steps. *E* and *F*: neural trajectory representation of area 5 activity for each motor output direction in movement (*E*) and isometric (*F*) tasks, formed by joining the 20-s population vectors (*C* and *D*) tip-to-tail.

direction of forces applied to the handle to decelerate it as it approached the targets. During the decelerating phase of the movements, the directions of hand motions and hand-centered output forces were temporarily dissociated. The monkeys also had to generate muscular forces that acted against the mass and inertia of different limb segments during the arm movements,

but we have no direct measure of these internally-acting forces. Finally, during the terminal (target-hold) epoch of each trial, the monkeys generated comparable static hand-centered output forces in the same eight horizontal directions but the latter were also associated with large changes in static arm postures in the movement task but not in the isometric task.

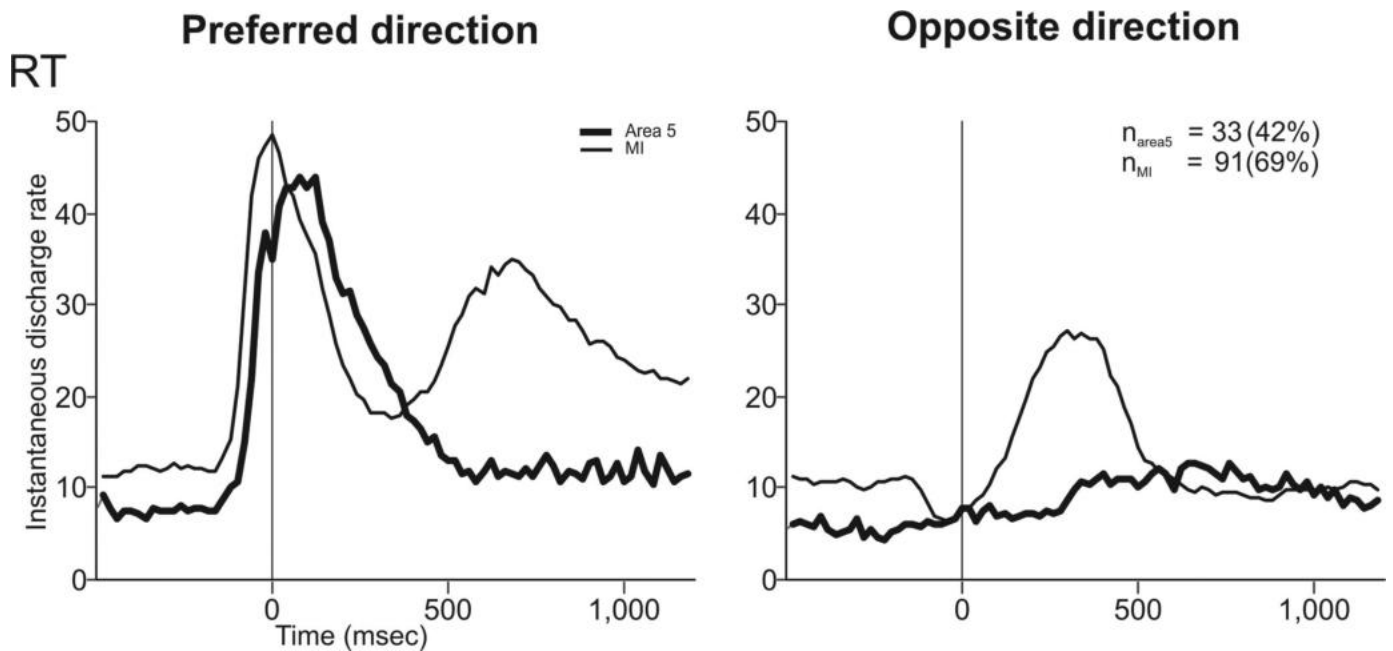


FIG. 12. Comparison of the mean population histograms of neurons that were directionally tuned during RT epoch in area 5 (thick lines) and primary motor cortex (thin lines) of the same monkeys for movements at preferred direction (*left*) and opposite direction (*right*). Area 5 population histograms are reproduced in modified form from Fig. 10, and M1 histograms are reproduced in modified form from Fig. 8A of Sergio et al. (2005).

One notable finding of this study is that the presence of a large inertial load did not significantly alter the overall relation of area 5 activity to arm movement kinematics. The present sample population showed the same broad tuning as a function of the direction of movement and the final arm postures that has been described in many earlier studies (Battaglia-Mayer et al. 2001, 2003; Buneo et al. 2002; Caminiti et al. 1998; Ferraina et al. 2001; Georgopoulos et al. 1984; Kalaska and Crammond 1995; Kalaska and Hyde 1985; Kalaska et al. 1983, 1990; Lacquaniti et al. 1995; Scott et al. 1997). This shows that the underlying movement-related tuning functions of the cells were robust to the perturbation imposed by the inertial loads.

There were two principal findings in this study. First, area 5 neurons were typically more active, and often exclusively active, in the movement task than in the isometric task, even though the latter required similar overall levels of hand-centered output forces and EMG activity as in the movement task. Nearly one-half of the sample population (45%) were active and directionally tuned in the movement task but relatively or completely inactive in the isometric task. Second, the temporal pattern of area 5 activity in the movement task did not reflect the time course of the forces and muscle activity during the arm movements. In the movement task, the temporal pattern of output forces at the hand showed an initial rapid increase of force exerted against the task handle in the desired direction of movement, followed by a transient reversal of forces to decelerate the motion of the handle as the monkey approached the target. The transient reversal of forces was also clearly reflected in the muscle activity, which typically showed the classic reciprocal triphasic-burst pattern during arm movement. Area 5 activity, at both the single-neuron and population level, showed little or no evidence of the transient reversal of the directionality of output forces and muscle activity during movement. The preferred direction of each neuron, if it was directionally tuned in the movement task, tended to remain

relatively constant throughout the trial, as shown by a sliding-window analysis. Only 1 of the 78 area 5 neurons showed a weak “triphasic” response pattern in the movement task. Furthermore, a population–vector analysis of the activity of the sample population showed that the net directional signal generated by the population remained oriented in the direction of movement throughout its duration. In summary, area 5 neurons were typically much more active in the movement task than the isometric task, and there was no correlate at either the single-neuron or population level of the transient braking pulse of forces that is a prominent feature of the time course of motor output in the movement task.

These results complement an earlier study of parietal area 5 (Kalaska and Hyde 1985; Kalaska et al. 1990). Kalaska and Hyde (1985) showed that constant external loads applied to the arm in different directions had only a modest effect on area 5 activity when monkeys actively held their arm in a fixed posture against the loads, compared with the much greater sensitivity of M1 neurons to the same loads. Similarly, the movement-related activity of the area 5 neurons was relatively unaffected at the single-neuron and particularly at the population level, when the monkeys made reaching movements along constant spatial hand paths while the arm was pulled in different directions by the external loads (Kalaska et al. 1990). The earlier and present studies show that parietal area 5 activity is far less modulated by constant loads during active postural maintenance, by constant or inertial loads during arm movements, and by isometric force generation than it is by arm movements and by different arm postures themselves. In other words, area 5 activity showed far weaker correlations with the time course and directionality of static and dynamic output forces and muscle activity (task kinetics) across those different task conditions than it did with the spatiotemporal form (task kinematics) of the arm motor output.

Ideally, if the arm movement representation in area 5 only signaled properties of the spatiotemporal form of the output and not about its causal forces and muscle activity, one would expect all area 5 neurons to be inactive during the isometric task. However, about one-half of the neurons were modestly active and directionally tuned in the isometric task when no limb movements are presumably being planned or executed. A

number of possible explanations related to peripheral motor events or to central processes could account for this activity.

For instance, it could partly reflect the fact that the hand and the arm are not completely rigid, and that small movements and postural changes of the hand, arm, shoulder or trunk occurred while the monkeys generated the isometric forces in different directions. An indeterminate amount of the activity during the isometric task could reflect proprioceptive signals about the kinematics of these uncontrolled small motions and posture changes. Furthermore, ascending proprioceptive inputs to the primary somatosensory cortex (S1) do not signal purely kinematic information only about arm movements and changes in posture. On the contrary, the activity of many S1 neurons is also modulated by the changes in the forces and muscle activity required to compensate for external loads during arm movements or to generate isometric output forces (Fromm and Evarts 1982; Jennings et al. 1983; Prud'Homme et al. 1994; Wannier et al. 1991). Part of the area 5 activity in the isometric task could have been a residual trace of any kinetics-related information encoded in the peripheral afferent input, and relayed into area 5 via cortico-cortical projections from S1. This may have been compounded by the possibility that some of the recorded neurons may have been in the caudal part of S1 (area 2) itself, rather than in area 5 proper (Fig. 3).

Alternatively, the activity in the isometric task might be of central origin. For instance, it could be an efference copy of the isometric motor output command that is used in area 5 to deconvolve kinematics and kinetics signals, or to contribute to on-line error-correction mechanisms or other possible functions (Kalaska 1996; Kalaska et al. 2003). It could represent an abstract central signal related to the behavioral goal to generate a directional output to displace the cursor to the targets, independent of the causal kinetics required to accomplish the goal, and even though no physical displacement of the arm is intended in the isometric task (Crammond and Kalaska 1989; Ferraina and Bianchi 1994; Kalaska and Crammond 1995; Snyder et al. 1997). Finally, part of the isometric task-related modulation of area 5 neurons may have been caused by visual inputs about cursor motions or target locations or signals about the direction of gaze as the monkeys observed task events displayed on the computer monitor during the dynamic phases of each task, rather than to arm-related output (Batista et al. 1999; Battaglia-Mayer et al. 2001; Buneo et al. 2002; Ferraina et al. 2001; Graziano et al. 2000). However, visual and oculomotor influences have been documented primarily in parts of the superior parietal cortex that are located medial to the recording sites in this study.

Any combination of these peripheral and central factors could have contributed to the area 5 activity during the isometric task.

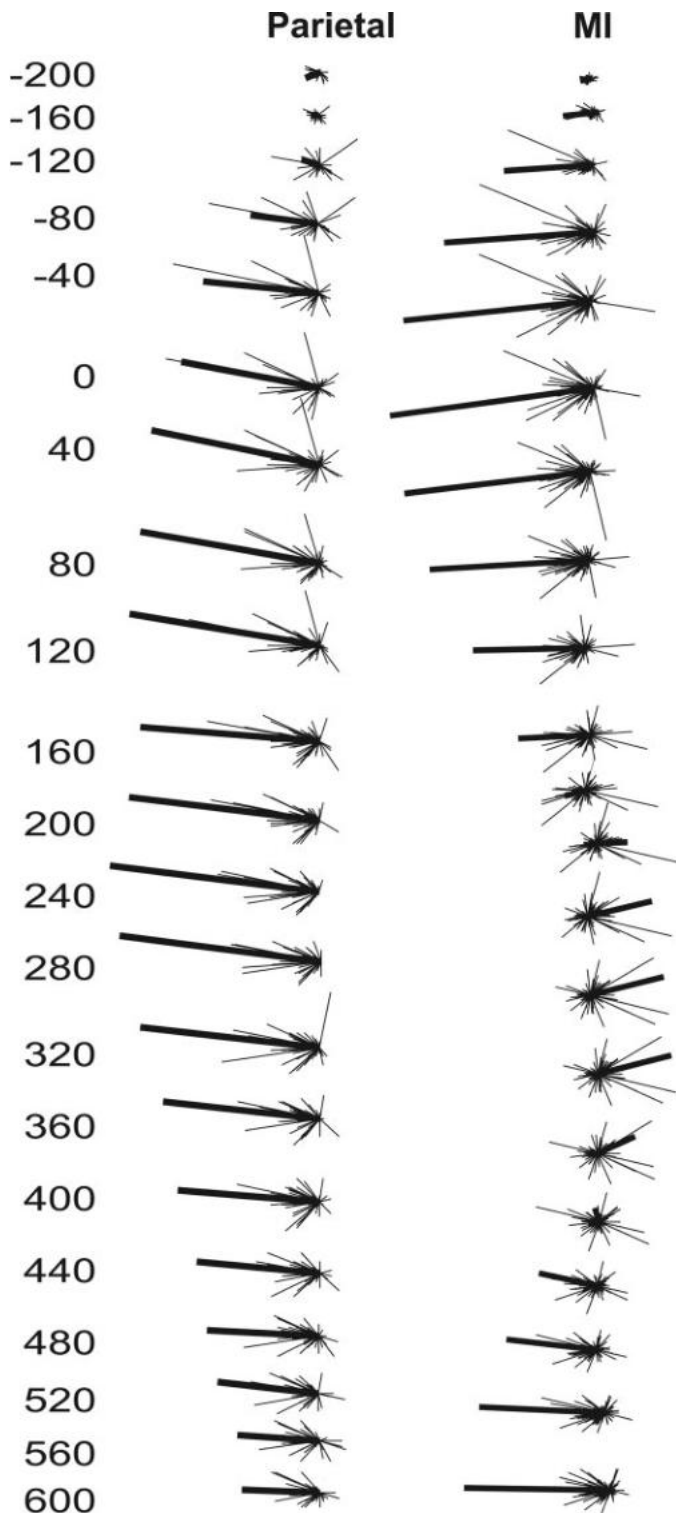


FIG. 13. A time series representation of the temporal evolution of the directionally tuned activity of sample populations of area 5 and M1 single neurons (thin lines) and net resultant population vector signal (thick lines) during arm movements in the 180° direction. Each vector cluster represents pattern of activity of all neurons in each sample during a 20-ms time window sampled at 40-ms time intervals centered on time indicated by each cluster. Activity of each neuron is represented by a vector oriented in the neuron's preferred direction during MT epoch (area 5) or THT epoch (M1) (see METHODS for justification for choice of canonical PD for each neuron). Length of each single-neuron vector is proportional to change in activity of the neuron during that 20-ms interval and mean activity of the neuron during the CHT epoch before appearance of movement target. By convention, if the change in a neuron's activity during a given time window was negative in sign, the direction of its single-neuron vector was inverted. Net resultant population vectors (thick lines) were calculated by vectorial summation of all the single-neuron vectors at each time interval. M1 data are modified from Fig. 10B of Sergio et al. (2005).

We suggest that this activity is largely nonfunctional biological noise in a predominantly kinematic representation of motor behavior, but we cannot categorically reject the possibility that it indicates a role for area 5 in the control of motor output in an isometric-force task or has some other undetermined function.

#### *Comparison of neuronal response properties between parietal area 5 and primary motor cortex*

The behavior of the parietal area 5 neurons in this study is in sharp contrast to the activity of neurons recorded in the caudal half of the primary motor cortex (M1) of the same monkeys. M1 neurons were typically as active and often more active in the isometric task than in the movement task (Sergio and Kalaska 1997, 1998, 2003; Sergio et al. 2005), and showed changes in their temporal pattern of activity that captured the differing time course of output dynamics between the two tasks (Sergio and Kalaska 1998; Sergio et al. 2005). In particular, many M1 neurons showed a complex “triphasic” response pattern reminiscent of the muscle activity during the movement task with a heavy inertial load (Sergio et al. 2005). Neurons with a triphasic response pattern during arm movements were also prominent in an earlier study of M1 activity during unloaded arm movements or movements against a constant external load (Kalaska et al. 1989). That study also found that the activity of those “triphasic” neurons was more strongly modulated by different directions of static external loads during posture and arm movement than any other type of M1 neuron (Kalaska et al. 1989). These complementary findings from the two different studies indicate that the caudal part of M1 contains a significant population of neurons whose activity covaries with critical aspects of the kinetics of the tasks. At the same time, it is also clear that the M1 neurons showed significant systematic deviations from the measured output forces and were not explicitly encoding a Newtonian mechanical parameter of task kinetics (Sergio et al. 2005).

In contrast to M1, cells with triphasic response patterns were virtually absent in area 5 during arm movements with a heavy inertial load (present study) and without external loads (Kalaska et al. 1990). Area 5 neurons also showed weak modulation of movement-related activity during arm movements perturbed by static external loads (Kalaska et al. 1990), and significantly weaker modulations of activity in the isometric task compared with the movement task (present study). Collectively, these findings all suggest that area 5 neurons are preferentially implicated in the representation of the spatiotemporal form (the kinematics) of motor output.

Although the response properties of area 5 cells suggest that they are preferentially related to movement kinematics, it is still possible that they are in fact generating a higher-order control signal that ultimately determines the output kinetics without reflecting their temporal details to the same degree as M1 neurons. These results indicate that this control signal would have to be largely monophasic, of greater magnitude in the movement task than the isometric task, and not reflect either the transient reversal of output forces during the deceleration phase of arm movements or the changes in forces and EMG activity required to compensate for constant external loads. Equilibrium point models argue that the central motor system cannot explicitly specify the kinetics of motor output (Feldman and Levin 1995; Feldman and Latash 2005; Ostry and

Feldman 2003). They propose instead that limb movements and isometric forces are both generated by largely monotonic central commands that signal shifts in the desired viscoelastic equilibrium state of the limb. The activity in area 5 could be a neuronal correlate of the equilibrium shifts required to produce forces and movements in the two tasks. This could possibly account for the lack of correlates with the transient reversal of forces and triphasic EMG activity during arm movements in the present study (see further discussion of this issue in Sergio et al. 2005). However, the much lower activity of area 5 cells in the isometric task would imply that the equilibrium shifts were correspondingly smaller in the isometric task than the movement task, but it is not immediately apparent why that would be the case. In particular, the level of static output forces at the hand during the target-hold epoch of the isometric task was somewhat larger than in the movement task, not smaller (Fig. 10). In contrast, the static directional signal generated by area 5 cells during the target-hold epoch of the isometric task was very weak (Figs. 10 and 11). Similarly, this hypothesis would not explain why area 5 activity is relatively insensitive to the presence of external loads that induce large changes in muscle activity during kinematically invariant arm movements (Kalaska et al. 1990). Equilibrium point models argue that the generation of arm movements and isometric forces as well as the compensation for external loads are all functionally unified through the control of the desired equilibrium state of the arm. That proposed functional unity is not evident in the responses of area 5 neurons in the different task conditions.

Admittedly, many of the arguments presented here for a representation of the spatiotemporal form of motor output in area 5 are negative in nature. They are based on the absence of prominent neuronal correlates of major features of the kinetics of several different tasks. This study does not provide direct evidence for a causal relation between area 5 activity and any particular kinematic output parameter. Furthermore, the modest directional activity during the isometric task is not consistent with an exclusive representation of motor output kinematics in the strictest sense. Nevertheless, other studies have also described strong quantitative correlations of area 5 activity with a variety of parameters of the spatiotemporal kinematics of arm movements, such as direction, velocity, and current and intended arm positions (Andersen and Buneo 2003; Ashe and Georgopoulos 1994; Buneo et al. 2002; Kalaska et al. 1983, 1990; Lacquaniti et al. 1995; Scott et al. 1997). As was the case with the M1 correlations with task kinetics, however, the correlations of area 5 activity with kinematics parameters should not be interpreted as evidence of a movement representation in some arbitrary Euclidian spatial or Newtonian mechanical reference frame. The term kinematics is not being used here in its literal meaning from physics and mechanics. It is being used here in a more figurative sense to capture the general character of the area 5 movement representation rather than its exact nature and form.

#### *Implications for the role of area 5 in visuomotor control*

Many current hypotheses suggest that arm movements are first planned in terms of some attribute or other of their spatiotemporal form (kinematics) before being transformed into neuronal signals that eventually generate the causal forces and muscle activity required to execute the movement (Abend

et al. 1982; Bhat and Sanes 1998; Krakauer et al. 2000; Morasso 1981; Riehle and Requin 1989; Soechting and Flanders 1989a,b). Area 5 is implicated in the integration of multimodal sensory inputs and centrally generated signals to perform some of the early sensorimotor transformations that convert spatial information about targets into intended arm movements (Andersen and Buneo 2002, 2003; Andersen et al. 1997; Batista et al. 1999; Battaglia-Mayer and Caminiti 2002; Battaglia-Mayer et al. 2001, 2003; Caminiti et al. 1998; Colby and Goldberg 1999; Ferraina et al. 2001; Graziano and Gross 1998; Kalaska et al. 1997, 2003; Lacquaniti et al. 1995; Marconi et al. 2001; Mascaró et al. 2003). Alternatively, area 5 neurons may be integrating peripheral feedback signals about limb motions with efference copies of motor output commands to generate a representation of posture and movement that may contribute to kinesthetic sensation or the on-line control of movement (Kalaska et al. 2003). These findings support the hypothesis that these processes occur in a predominantly kinematic parameter space, that is, a representation of the spatio-temporal form of movements that is relatively devoid of signals about the causal forces and muscle activity.

#### ACKNOWLEDGMENTS

We thank L. Girard and N. Michaud for expert technical assistance. C. Leger (Département de Mathématiques et Statistiques, Université de Montréal) suggested the bootstrap test for significant changes in directional tuning. G. Richard built the task apparatus. R. Albert, S. Dupuis, É. Clément, C. Valiquette, and J. Jodoin provided software and electronics support.

#### GRANTS

This study was supported by Canadian Institutes of Health Research (CIHR) Group Grant in Neurological Sciences GR-15176, CIHR Individual Operating Grants MT-14159 and MOP-62983 to J. F. Kalaska, and postdoctoral fellowships from the Fonds de la Recherche en Santé de Québec and the Fonds pour la Formation de Chercheurs et l'aide à la Recherche Groupe de Recherche sur le Système Nerveux Central to L. E. Sergio.

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