Exp Brain Res (2007) 176:652–657
DOI 10.1007/s00221-006-0818-7

RESEARCH NOTE

Coordinate system representations of movement direction in the premotor cortex

Wei Wu · Nicholas G. Hatsopoulos

Received: 3 July 2006 / Accepted: 21 November 2006 / Published online: 19 December 2006

Abstract Recently, we compared the encoding of movement direction in primary motor cortex (MI) under three coordinate systems, an extrinsic cartesian (CA), an intrinsic joint angle (JA), and an intermediate shoulder-centered (SC) and found that no single coordinate system was uniquely represented in MI. Here we extend this investigation to the premotor area which is regarded as a major source of input to the MI. Multiple single units were simultaneously recorded from the caudal portions of dorsal premotor (PMd) and ventral premotor (PMv) cortices as a behaving monkey moved its hand over the horizontal work space. We compared the mutual information between the neuronal firing rate of each unit and hand movement direction under each of the three coordinate systems. As in the MI study, the results showed that there was no evidence for a unique coordinate system representation. There was a bias towards the SC system in PMd, albeit weaker than the SC bias observed in MI. In PMv, there was a strong bias for both SC and JA coordinate systems as compared to a CA coordinate system. These results provided further evidence against a unique coordinate system for movement direction within the motor cortex. However, the directional information within both PMd and PMv was significantly less than that of MI suggesting that factors other than the detailed motion of the arm account for much of the variance of activity within the premotor cortex.

Introduction

Goal-directed arm movements are widely acknowledged as a complex process which involves sensorimotor transformations in a number of sensory and motor regions such as primary motor cortex (Georgopoulos et al. 1982; Caminiti et al. 1990; Kakei et al. 1999), premotor cortex (Caminiti et al. 1991; Kakei et al. 2001), area five of the parietal cortex (Kalaska et al. 1983; Lacquaniti et al. 1995), supplementary motor cortex (Hocherman and Wise 1991), and cerebellum (Fortier et al. 1989). Different coordinate reference frames have been proposed in the motor and premotor cortices to explain behavioral outcomes and neural modulation patterns during visuo-motor behavior of the arm (Soechting and Flanders 1992; Ajemian et al. 2000). In a recent study, we investigated the coordinate representation of movement direction in single units of the primary motor cortex (MI) by comparing the degree of directional tuning variance and the mutual information between firing rate and movement direction in the cartesian (CA), joint-angle (JA), and shoulder-centered (SC) coordinate systems (Wu and Hatsopoulos 2006). It was found that none of the coordinate systems was uniquely represented in MI.

Here we extend our investigation by using the same paradigm to study the coordinate system encoding of

W. Wu
Department of Statistics, Florida State University,
1015 W Call St, Tallahassee, FL 32306-4330, USA
e-mail: wwu@stat.fsu.edu

N. G. Hatsopoulos (✉)
Department of Organismal Biology and Anatomy,
University of Chicago, 1027 E 57th St,
Chicago, IL 60637, USA
e-mail: nicho@uchicago.edu

movement direction in the caudal portions of dorsal premotor (PMd) and ventral premotor (PMv) cortices. Anatomical studies have shown corticospinal projections from premotor cortex as is found in MI as well as strong horizontal connectivity between premotor cortex and MI (Muakkassa and Strick 1979; Martino and Strick 1987; Dum and Strick 1991, 2002, 2005). Thus, it is of scientific interest to determine whether the premotor cortex provides a qualitatively different coordinate system representation of movement direction.

We used the same behavioral paradigm as in the MI study to examine the coordinate representation in the PMd and PMv. Due to the relatively poor cosine-tuning in the premotor area, spatial invariance of preferred directions over the workspace could not be robustly estimated as was done in the MI study. We therefore, only focused on estimating the mutual information between firing rate of single units and movement direction in the three coordinate systems.

Materials and methods

The electrophysiological recording, the behavioral paradigm, and the quantitative description of the three coordinate systems were described in our previous work (Wu and Hatsopoulos 2006). Here we provide a brief summary. Silicon microelectrode arrays containing 100 platinized-tip electrodes (1.0 mm electrode length; 400 μm inter-electrode separation; Cyberkinetics Inc., Salt Lake City, UT) were implanted in the arm area of caudal portions of the dorsal premotor cortex (PMd) and/or ventral premotor cortex (PMv; area F4 (Matelli et al. 1985) in three adult macaque monkeys (*Macaca mulatta*), where in addition to an implant in MI, monkey RJ had an implant in PMd, monkey NI had an implant in PMv, and monkey VE had an implant in both premotor areas (Fig. 1a). Single units were manually extracted by the contours and templates methods using offline sorter (Plexon Inc., Dallas, TX). To ensure good single unit isolation, we only studied the single units whose signal-to-noise ratio was larger than 3. A total of 403 PMd and 484 PMv neuron samples were recorded and analyzed in eight data sets (two recording sessions per area in each animal). Specifically, the number of simultaneously recorded PMd single units in each of the two data sets was 48 and 40 from monkey RJ, and 160 and 155 from monkey VE. Likewise, the number of PMv units was 94 and 72 from monkey NI, and 152 and 166 from monkey VE. Note that because the recordings were made from the same array in each monkey, the data over sessions for each monkey are not entirely independent.

The monkeys were trained to perform a random-sequence task by moving a cursor via contralateral arm movements using a two-joint robotic arm to a set of randomly positioned targets presented sequentially (Fig. 1b). The shoulder joint was abducted 90° such that shoulder and elbow flexion and extension movements were made in the horizontal plane. All of the surgical and behavioral procedures were approved by the University of Chicago's IACUC and conform to the principles outlined in the guide for the care and use of laboratory animals (NIH publication no. 86–23, revised 1985).

We studied the encoding of movement direction in three coordinate systems. The first one was an extrinsic, cartesian (CA) space (x, y) of the hand position; the second one was a joint angle (JA) space (θ, ϕ) at the shoulder (θ) and elbow (ϕ); and the third one was a shoulder-centered (SC) coordinate system (u, v) whose main axis rotated with the line connecting the shoulder to the hand (Fig. 1b) (see Wu and Hatsopoulos 2006).

The firing rates (spike counts) of single cell were computed in non-overlapping 50 ms bins. To match time scales, the kinematics data, particularly the movement direction, in all three systems were down-sampled every 50 ms. For each neuron, we examined the mutual information between its firing rate modulation and the kinematics in each coordinate system and compared the results over the three systems. Movement direction was regarded as better encoded in a system in which the mutual information was larger.

Results

To estimate the mutual information between firing activity in the premotor cortex and movement direction, we first needed to determine the optimal latency between them. We estimated the peak mutual information between each neuron's firing rate and direction across a range of time leads/lags from −500 to 500 ms at 50 ms step size in the cartesian system (see estimation in one example neuron in Fig. 1c). In contrast to MI (Wu and Hatsopoulos 2006), we found that the optimal lags were significantly more broadly distributed (Moran and Schwartz 1999; Kakei et al. 2001) and the associated mutual information values were significantly lower in PMd and PMv neurons (Fig. 1d). Quantitatively, the standard deviation in optimal latencies from MI neurons was 106 ms and the average mutual information was 0.018 bits (using data in Wu and Hatsopoulos 2006). However, the standard deviation in optimal latencies and the average mutual information were 170 ms and 0.013 bits within PMd, and 156 ms

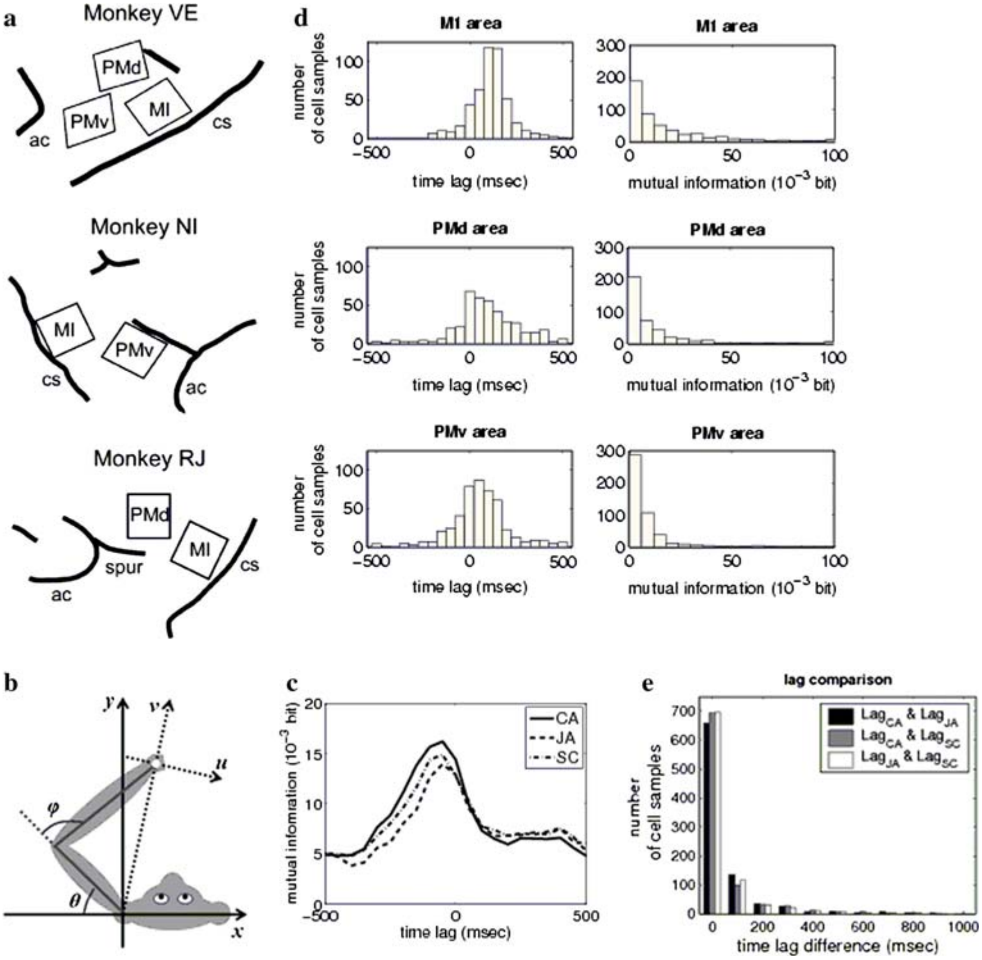
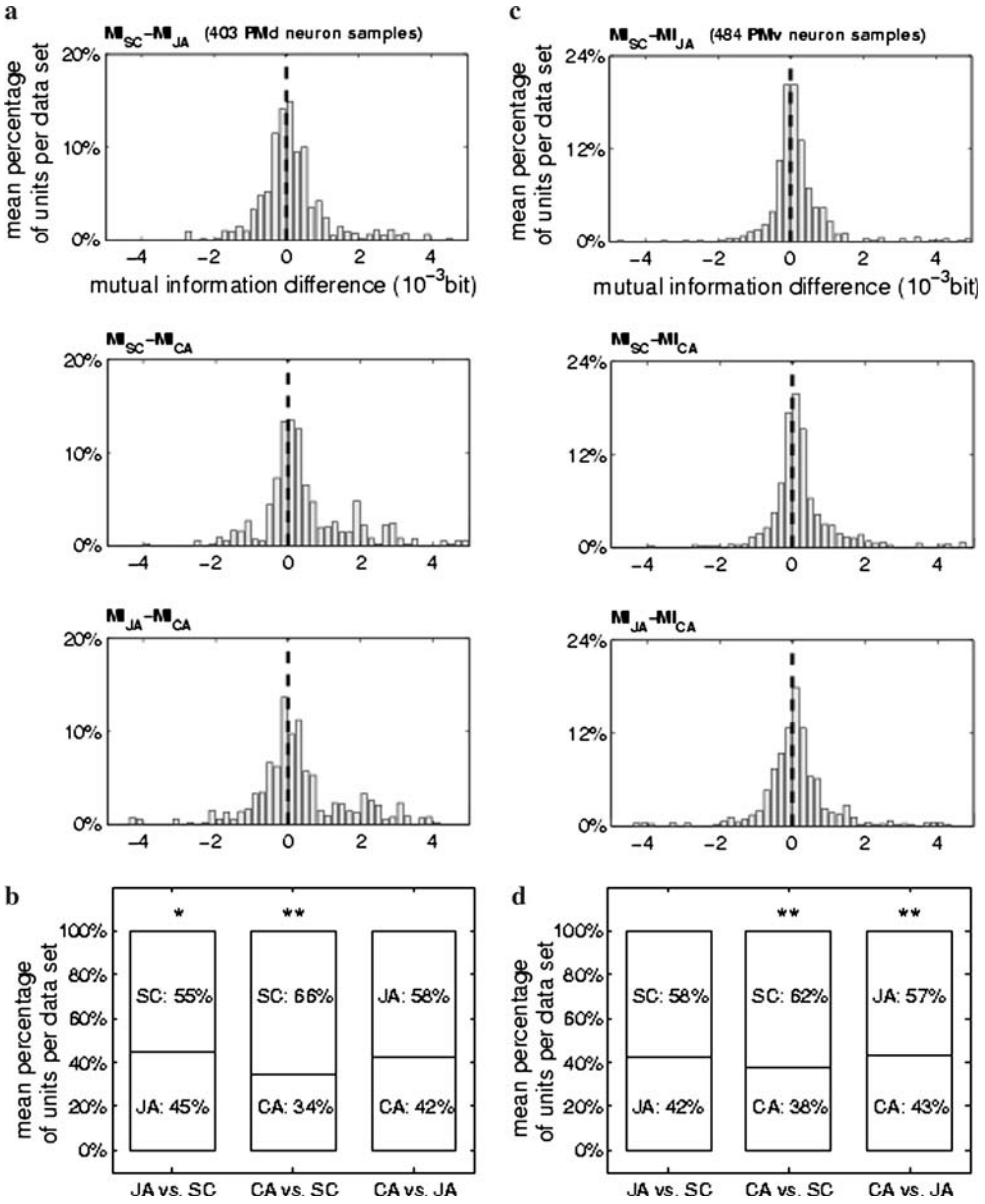


Fig. 1 Experimental paradigm and optimal time lags between firing rate and movement direction. **a** Illustration of the location of the array implantation in motor cortex in three monkeys. **b** The monkey's arm was constrained to move in a two-dimensional plane which resulted in a one-to-one mapping between hand position (x, y) and shoulder (θ) and elbow angle (ϕ). (u, v) denote the axes of the shoulder-centered coordinate system. **c** The mutual information as a function of time lag of one example neuron in the CA, JA, and SC coordinate systems. **d** Distribution of the optimal lags and the associated mutual information of all MI neuron samples (*top panels*, using data from Wu and Hatsopoulos 2006), of all PMd neuron samples (*middle panel*), and of all PMv neuron samples (*bottom panel*) in the cartesian system. **e** Comparison of optimal lags in the three coordinate systems. *Black*, *gray*, and *white bars* denote pair-wise comparison between CA and JA, between CA and SC, and between JA and SC, respectively

and 0.009 bits within PMv. The relatively lower mutual information between premotor cortex and kinematics suggested the encoding mechanism between them might be more indirect and complex than that between MI and kinematics. The result also indicated that the latency in premotor cortex was not as consistent as that in MI and led us to employ a unique optimal latency for each neuron separately. In addition to the CA system, we performed the same latency analysis in the JA and SC systems and found that the difference in optimal latencies between the three systems were nearly zero (Fig. 1e). This showed that for each neuron the latency was very consistent over the three coordinate systems, and therefore we could take the average latency over the three systems.

Using the optimal time latency for each neuron, we computed the mutual information between the firing rate and movement direction in each of the three coordinate systems in PMd and PMv. The distributions of mutual information differences over all PMd and PMv neurons revealed that they were all unimodal and the peaks were all near zero (Fig. 2a, c). This indicated that none of the three coordinate systems was dominantly represented in the PMd and PMv, which is consistent with the results we obtained in our MI study. However, on a statistical level, we found that there were significantly more PMd neurons with higher mutual information values in the SC coordinate system as compared to the JA ($P < 0.05$, sign test) and CA coordinate systems ($P < 0.01$, sign test). There was no

Fig. 2 The comparison of mutual information between firing rate and movement direction in the CA, JA, and SC coordinate systems. **a** The distribution of the mutual information differences between SC and JA (*top panel*), between SC and CA (*middle panel*), and between JA and CA (*bottom panel*) coordinate systems over all 403 PMd neuron samples. **b** Percentage of neurons with larger directional mutual information values within pairs of coordinate systems. Each *stack bar* denotes one comparison with total percentage of 100. *Single star* denotes a significance *P*-value < 0.05, and *double star* denotes a significance *P*-value < 0.01. **c, d** Same as (**a**, **b**) except for all 484 PMv neuron samples



difference in population sizes between JA and CA coordinate systems ($P = 0.18$, sign test) (Fig. 2b). The same comparison was also applied to all PMv neurons. It was found that there were significantly more neurons with higher mutual information in the SC and JA systems as compared to the CA system ($P < 0.01$, sign test) while there was no statistical difference in population sizes between JA and SC coordinate system ($P = 0.06$, sign test) (Fig. 2d).

Discussion

As a natural extension of our recent study in MI, we investigated the coordinate representation of movement direction among neurons in the premotor cortex, which is known to be a major source of input to MI. We used a standard information-theoretic approach to examine the mutual information between firing rate and movement direction in each of the CA, JA and SC systems. This method offered the advantage that it is a model-free approach to directly estimate the encoding of movement direction without depending on measuring tuning curves with prescribed functional forms. It was found that none of the coordinates showed strong dominance over the others in the PMd and PMv. This result was consistent with what we obtained in the MI study and provided further evidence against a single coordinate system representation in the motor cortex. Although a bias towards the SC system was still observed in premotor area, it was small and not likely to be functionally significant.

Note that our study focuses on the comparison of the three coordinate systems under same framework. By using the KINARM system, the monkey's hand movements were constrained to two dimensions in the horizontal plane, and such a constraint provides the necessary framework under which there is a one-to-one mapping between the three systems (Wu and Hatsopoulos 2006). If the movements were unconstrained the cartesian coordinate system would have three degrees of freedom, while the joint angle coordinate system could have up to seven degrees of freedom. In that case, we would not have a direct mapping between the coordinate systems and the comparisons over coordinate systems would be difficult although not impossible to perform.

Our results are consistent with those found by Caminiti and colleagues (1991) who examined the spatial shifts in direction tuning of PMd neurons. They found that PMd and MI neurons exhibited similar shifts in preferred direction as monkeys performed a center-out task from three different initial starting positions in the workspace. However, the fact that the average directional information in PMd and PMv activity was ~30 and 50% less than that of MI activity, respectively, suggests that premotor activity may be more related to parameters other than the kinematics of the arm such as the target or goal of the movement as others have suggested (Alexander and Crutcher 1990; Kakei et al. 2001; Schwartz et al. 2004; Pesaran et al. 2006). In particular, Schwartz and colleagues devised a clever experimental paradigm that uncoupled the actual movement from the visually perceived movement of the arm using a motor illusion (Schwartz et al. 2004). By applying population vector decoding, they found an interesting double dissociation such that the primary motor cortex reconstructed the actual arm trajectory more accurately whereas the ventral premotor cortex predicted the perceived trajectory. In our study, we did not dissociate vision from action so a direct comparison with that study is difficult. However, the broader distribution of optimal mutual information lags (including negative lags indicating that the cursor motion leads cortical modulation for some neurons) seen in both PMv and PMd as compared to MI is consistent with the view that premotor cortex provides a complex combination of movement and sensory-related information. Recently, a study has suggested that neurons in PMd encode target position relative to both a hand-centered and an eye-centered coordinate system (Pesaran et al. 2006). In that study, the focus was on the coding of the target of a reach prior to movement onset during an instructed delay period. Unlike that study, our focus was on the coding of movement execution and not the target and therefore, the two studies are not directly comparable. All these studies including our own suggest that premotor cortex has complex sensory, movement planning, and movement execution responses that may be using a variety of different coordinate systems in different contexts.

Acknowledgments We thank S. Francis, Z. Haga, D. Paulsen, and J. Reimer for training the monkeys and collecting the data. This work was supported by NIH-NINDS R01 NS45853-01. N. Hatsopoulos has stock ownership in a company, Cyberkinetics Inc., that is commercializing neural prostheses for severely motor disabled people.

References

Ajemian R, Bullock D, Grossberg S (2000) Kinematic coordinates in which motor cortical cells encode movement direction. J Neurophysiol 84:2191–2203

Alexander GE, Crutcher MD (1990) Neural representations of the target (goal) of visually guided arm movements in three motor areas of the monkey. J Neurophysiol 64:164–178

Caminiti R, Johnson P, Urbano A (1990) Making arm movements within different parts of space dynamic aspects in the primate motor cortex. J Neurosci 10:2039–2058

Caminiti R, Johnson P, Galli C, Ferraina S, Burnod Y (1991) Making arm movements within different parts of space the premotor and motor cortical representation of a coordinate system for reaching to visual targets. J Neurosci 11:1182–1197

Dum RP, Strick PL (1991) The origin of corticospinal projections from the premotor areas in the frontal lobe. J Neurosci 11:667–689

Dum RP, Strick PL (2002) Motor areas in the frontal lobe of the primate. Physiol Behav 77:677–682

Dum RP, Strick PL (2005) Frontal lobe inputs to the digit representations of the motor areas on the lateral surface of the hemisphere. J Neurosci 25:1375–1386

Fortier PA, Kalaska JF, Smith AM (1989) Cerebellar neuronal activity related to whole-arm reaching movements in the monkey. J Neurophysiol 62:198–211

Georgopoulos AP, Kalaska JF, Caminiti R, Massey JT (1982) On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. J Neurosci 2:1527–1537

Hocherman S, Wise S (1991) Effects of hand movement path on motor cortical activity in awake, behaving rhesus monkeys. Exp Brain Res 83:285–302

Kakei S, Hoffman DS, Strick PL (1999) Muscle and movement representation in the primary motor cortex. Science 285:2136–2139

Kakei S, Hoffman DS, Strick PL (2001) Direction of action is represented in the ventral premotor cortex. Nat Neurosci 4:1020–1025

Kalaska JF, Caminiti R, Georgopoulos AP (1983) Cortical mechanisms related to the direction of two-dimensional arm movements relations in parietal area 5 and comparison with motor cortex. Exp Brain Res 51:247–260

Lacquaniti F, Guigon E, Bianchi L, Ferraina S, Caminiti R (1995) Representing spatial information for limb movement role of area 5 in the monkey. Cereb Cortex 5:391–409

Martino AM, Strick PL (1987) Corticospinal projections originate from the arcuate premotor area. Brain Res 404:307–312

Matelli M, Luppino G, Rizzolatti G (1985) Patterns of cytochrome oxidase activity in the frontal agranular cortex of the macaque monkey. Behav Brain Res 18:125–136

Moran DW, Schwartz AB (1999) Motor cortical activity during drawing movements: population representation during spiral tracing. J Neurophysiol 82:2693–2704

Muakkassa KF, Strick PL (1979) Frontal lobe inputs to primate motor cortex evidence for four somatotopically organized ‘premotor’ areas. Brain Res 177:176–182

Pesaran B, Nelson M, Andersen R (2006) Dorsal premotor neurons encode the relative position of the hand, eye, and goal during reach planning. Neuron 51:125–134

Schwartz AB, Moran DW, Reina GA (2004) Differential representation of perception and action in the frontal cortex. Science 303:380–383

Soechting JF, Flanders M (1992) Moving in three-dimensonal space frames of reference, vectors and coordinate systems. Annu Rev Neurosci 15:167–191

Wu W, Hatsopoulos N (2006) Evidence again a single coordinate system representation in the motor cortex. Exp Brain Res 175:197–210