Exp Brain Res (2006) 175: 197–210
DOI 10.1007/s00221-006-0556-x

RESEARCH ARTICLE

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Evidence against a single coordinate system representation in the motor cortex

Received: 30 January 2006 / Accepted: 7 April 2006 /

Abstract Understanding the coordinate systems in which the motor cortical cells encode movement parameters such as direction is a fundamental yet unresolved issue. Although many studies have assumed that motor cortex encodes direction in an extrinsic, Cartesian (CA) coordinate system, other studies have provided evidence for encoding in intermediate coordinate systems such as a shoulder-centered (SC) or in a purely intrinsic, joint-angle-based (JA) coordinate frame. By simultaneously recording from multiple single units in primary motor cortex, we examined movement direction encoding under each of these three coordinate systems. We directly compared the degree of directional tuning invariance over multiple sub-regions in the workspace. We also compared the mutual information between neuronal firing rate and movement direction in the three systems. We observed a broad range of directional invariance in all three coordinate systems with no strong dominance of any single coordinate system. The mutual information analyses corroborated this observation. However, we found a small but significant bias toward the SC coordinate frame, which was also supported by population vector decoding. Similar results were found when we compared hand/torque force direction encoding in all three coordinate systems. These results suggest that the motor cortex employs a coordinate system that is yet to be discovered or perhaps that the motor cortex should not be viewed as a substrate for any coordinate system representation.

Introduction

Planning and executing an arm movement to a visually presented target would appear to require a set of coordinate transformations between retinally based representations of the target to joint-based and ultimately muscle-based commands of arm movement such as direction to attain the target. One viewpoint places the motor cortex near the top of this chain of coordinate transformations whereby the motor cortex forms a neural substrate of movement direction in an extrinsic, body-centered coordinate system (Georgopoulos et al. 1982; Kakei et al. 1999), implying that the transformation to a joint-centered coordinate system occurs downstream from the motor cortex. At the other extreme, there is experimental evidence that suggests that the motor cortex lies near the end of this set of transformations and represents movement direction in an intrinsic, joint-based or muscle-based coordinate system (Scott and Kalaska 1997; Morrow and Miller 2003). Finally, there is an intermediate perspective, which suggests that the motor cortex, in particular, represents movement direction in a shoulder-centered (SC) system whose main axis is oriented with respect to a line between the shoulder joint and the hand (Soechting and Flanders 1989; Caminiti et al. 1990; Soechting et al. 1990; Flanders et al. 1992). Unlike an extrinsic, Cartesian (CA) coordinate system, a SC coordinate system rotates relative to the body as the shoulder-hand axis changes orientation. However, unlike a joint-based coordinate system, it remains unchanged for all joint angle (JA) positions that keep the shoulder-hand axis fixed.

Evidence exists that suggests that the motor cortex does not represent movement direction in a purely extrinsic, body-centered coordinate system. By having monkeys move in different directions from one of three initial positions, Caminiti et al. (1990) demonstrated that the directional tuning of single motor cortical neurons did not remain invariant with respect to a

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body-centered coordinate system but rather shifted in a systematic fashion implying that motor cortex does not represent direction in a purely extrinsic coordinate system. More recently, Scott and Kalaska (2000) also demonstrated that the direction tuning of motor cortical neurons exhibited significant changes in orientation when a monkey was required to move its hand under two different postural configurations of the arm again implying that the motor cortex encodes direction in some form of coordinate system that depends on the configuration of the joints.

Results of a recent simulation study have indirectly suggested that motor cortical neurons encode direction in a JA coordinate system (Ajemian et al. 2000). In that study, a set of model neurons were developed that represented movement direction in each of the three coordinate systems. By using data from an experimental study that examined the effects of different hand paths on neural activity (Hocherman and Wise 1991), Ajemian et al. (2000) found that model neurons with invariant direction encoding in a JA coordinate system more closely replicated the proportions of experimental neurons that were selective to clockwise, counter-clockwise, and straight paths.

We present evidence that none of these three coordinate systems strongly dominates within the motor cortex although there exist small subpopulations of neurons that appear to encode direction in each of these coordinate systems. We directly compared the encoding of movement direction under a body-centered, “CA” coordinate system, a JA elbow-shoulder coordinate system, and a SC coordinate system. We explored to what degree the preferred directions (PDs) of motor cortical neurons remained invariant under any of these coordinate systems as a behaving monkey moved its hand through a set of randomly positioned targets thereby covering multiple regions of the workspace (Fig. 1a,b). By assessing the degree of directional tuning invariance over multiple regions, we found a unimodal and broad distribution of invariance that was similar across all three coordinate systems. However, we did find a significantly larger number of neurons that invariantly represented movement direction in a SC coordinate system as compared to either CA or JA coordinate system. Those neurons that invariantly represented direction in one coordinate system generated systematic shifts in directional tuning (clockwise and counterclockwise) in the other coordinate systems that could be explained by the geometric coordinate transformation between the coordinate systems. Mutual information estimates between neuronal firing rate and direction measured over the whole workspace also demonstrated an encoding bias of the SC coordinate system. Finally, using the population vector decoding algorithm to predict direction (Moran and Schwartz 1999), we observed a slight bias in the SC coordinate system. Similar analyses in the kinetic domain (Evarts 1968; Thach 1978) supported the findings that none of the three coordinate

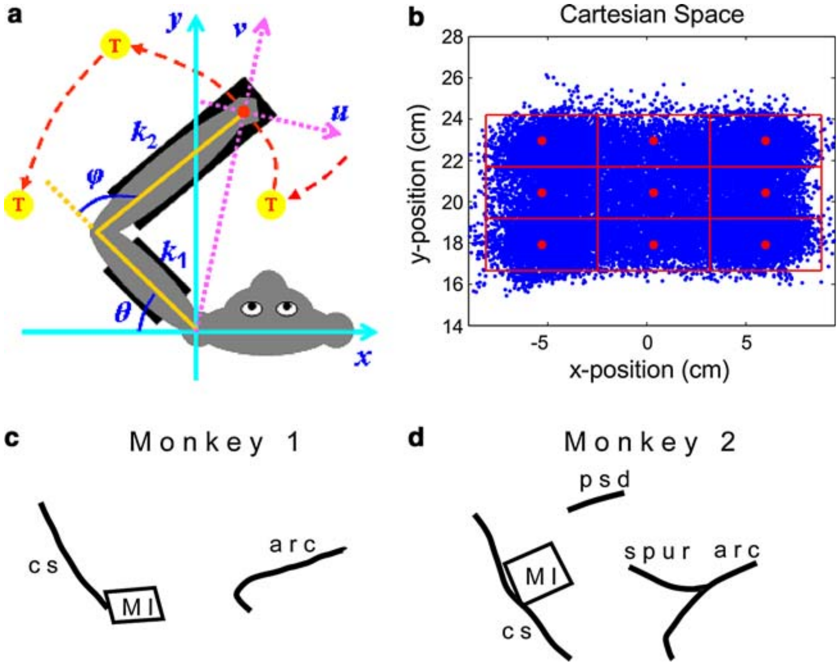


Fig. 1 The “RS” behavioral paradigm used in this study. **a** The monkey was operantly trained to move a cursor (*red dot*) by moving its hand to a set of randomly-positioned targets (*yellow dots labeled with a “T”*). The monkey’s arm was constrained to move in a two-dimensional plane, which resulted in a one-to-one mapping between hand position (x, y) and shoulder (θ) and elbow angle (φ). k_1, k_2 denote the upper and lower arm lengths, respectively (u, v) denote the axes of the SC coordinate system. **b** Position samples visited by the hand over a complete set of trials in the RS task. An overall selection region of x- and y-position samples was chosen (mean ± 1.8×standard deviation) and partitioned into nine (3 × 3) equally-sized sub-regions. The *red dots* are the centers of the sub-regions. **c, d** Illustration of the location of the array implantation in primary motor cortex (MI) in both monkeys

systems dominated although there was a weak but significant bias in the SC as well as in the CA coordinate systems. Taking the movement and kinetic direction results together, the evidence argues against the viewpoint that primary motor cortex uniquely encodes direction in any of these three coordinate systems.

Materials and methods

Electrophysiological recording

Silicon microelectrode arrays containing 100 platinized-tip electrodes (1.0 mm electrode length; 400 µm inter-electrode separation; Cyberkinetics Inc., Salt Lake City, UT, USA) were implanted in the arm area of primary motor cortex (MI) in two juvenile male macaque monkeys (*Macaca mulatta*) (Fig. 1c). Signals were filtered, amplified (gain, 5,000) and recorded digitally (14-bit) at 30 kHz per channel using a Cerebus acquisition system (Cyberkinetics Inc.). Only waveforms (1.6 ms in duration) that crossed a threshold were stored and spike-sorted using Offline Sorter (Plexon Inc., Dallas, TX, USA). Single units were manually extracted by the Contours and Templates methods. Inter-spike interval histograms were computed to verify single-unit isolation by ensuring that less than 0.05% of waveforms possessed an inter-spike interval less than 1.6 ms. The number of units in each electrode varied from one to five. To ensure good single unit isolation, we only studied the single units whose signal-to-noise ratio was larger than three. Raster plots from one neuron are shown in Fig. 2 when the monkey's hand moved in different directions during the execution of the task. A total of 680 neuron samples in six data sets (three data sets per animal) were recorded over a 3 month period and analyzed where the numbers of distinct units within each of the three data sets were 108, 124, and 133 for the first monkey, and 90, 100, and 125 for the second one. We decided to use the term "neuron samples" when aggregating units over multiple data sets to make clear that these represent independent samples but may or may not represent different neurons. Given the chronic nature of our multi-electrode recordings, it is uncertain whether recordings on the same electrodes over different sessions represent the same or different neurons. Clearly within each data set, we are sure that the units recorded on different electrodes are different. Therefore, our major results are reported in terms of the percentage of units recorded per data set.

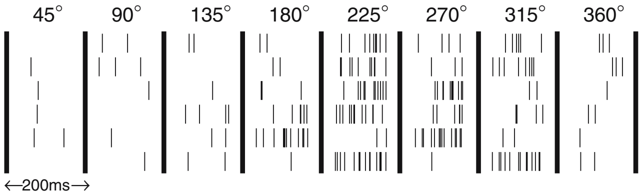


Fig. 2 Examples of spike trains across six instances of movements executed in different directions during the task. Six spike trains of a neuron are shown in raster display when the monkey's hand consistently moved in one of eight directions (45, 90, ..., 360°) during a 200 ms period

Random-sequence task

The monkeys were operantly trained to perform a random-sequence task (RS) by moving a cursor to targets via contralateral arm movements. The cursor and a sequence of seven targets (target size: 1×1 m) appeared on a horizontal projection surface. At any one time, a single target appeared at a random location in the workspace, and the monkey was required to reach it within 2 s. As soon as the cursor reached the target, the target disappeared and a new target appeared in a new, pseudo-random location (see Fig. 1a). After reaching the seventh target, the monkey was rewarded with a drop of water or juice. A new set of seven random targets was presented on each trial. On average, the monkey finished more than 400 trials in each session. We deliberately arranged more targets in the boundary area of the rectangle workspace so that sufficient hand position data over the full working space were collected. The kinematic sample points of one data set are shown in Fig. 1b.

The monkey's arm rested on cushioned arm troughs secured to links of a two-joint robotic arm (KINARM system, see Scott 1999) underneath the projection surface. The shoulder joint was abducted 90° such that shoulder and elbow flexion and extension movements were made in the horizontal plane. The robotic arm contained two motor encoders that directly measured the shoulder and elbow JAs of the monkey's arm at a sampling rate of 500 Hz. 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).

Joint angle coordinate system

Due to the constraints imposed by the KINARM, the monkey's wrist was fixed, and therefore there exists a one-to-one correspondence between the hand position (x, y) measured in CA coordinates and JAs at the shoulder (θ) and elbow (φ) (see Fig. 1a). The mapping from the JA to the hand position is described by the forward kinematics equations:

$$\begin{aligned} x &= -k_1 \cos(\theta) - k_2 \cos(\theta + \varphi) \\ y &= k_1 \sin(\theta) + k_2 \sin(\theta + \varphi) \end{aligned} . \tag{1}$$

Here, k_1 and k_2 denote the upper and lower arm lengths. In Monkey 1, $k_1 = 13.0$ cm, $k_2 = 19.0$ cm; in Monkey 2, $k_1 = 12.8$ cm, $k_2 = 19.0$ cm.

The mapping from the hand position to the JA is described by the inverse kinematics equations:

$$\begin{aligned}\varphi &= \arccos\frac{x^2+y^2-k_1^2-k_2^2}{2k_1k_2}\\ \theta &= 180-\arctan\frac{y}{x}-\arccos\frac{x^2+y^2+k_1^2-k_2^2}{2k_1\sqrt{x^2+y^2}}.\end{aligned}\tag{2}$$

From Eq. 1, we can derive the velocity mapping from the CA to the JA coordinate system:

$$\begin{pmatrix}\mathrm{d}\theta/\mathrm{d}t\\ \mathrm{d}\varphi/\mathrm{d}t\end{pmatrix}=\begin{pmatrix}k_1\sin(\theta)+k_2\sin(\theta+\varphi) & k_2\sin(\theta+\varphi)\\ k_1\cos(\theta)+k_2\cos(\theta+\varphi) & k_2\cos(\theta+\varphi)\end{pmatrix}^{-1}\begin{pmatrix}\mathrm{d}x/\mathrm{d}t\\ \mathrm{d}y/dt\end{pmatrix}.\tag{3}$$

Shoulder-centered coordinate system

This is a coordinate frame whose main axis rotates with the line connecting the shoulder to the hand. The mapping from CA to SC coordinate systems (u, v) is described in the velocity domain:

$$\begin{pmatrix}\mathrm{d}u/\mathrm{d}t\\ \mathrm{d}v/\mathrm{d}t\end{pmatrix}=\begin{pmatrix}\frac{y}{\sqrt{x^2+y^2}} & -\frac{x}{\sqrt{x^2+y^2}}\\ \frac{x}{\sqrt{x^2+y^2}} & \frac{y}{\sqrt{x^2+y^2}}\end{pmatrix}\begin{pmatrix}\mathrm{d}x/\mathrm{d}t\\ \mathrm{d}y/\mathrm{d}t\end{pmatrix}.\tag{4}$$

Analysis

The firing rates of single cell were computed in non-overlapping 50 ms bins. To match time scales, the kinematics data (hand position, as well as shoulder and elbow angles) were down-sampled every 50 ms. To determine the optimal latency between firing activity in MI and hand movement, we estimated the peak mutual information (Eq. 8) between each neuron's firing rate and direction across a range of time lags. Consistent with previous studies (Moran and Schwartz 1999; Paninski et al. 2004), we found that the mean (across neurons) peak information value occurred at a time lag of ~ 100 ms in all CA, JA, and SC coordinate systems (Fig. 3). Therefore, in all our analyses we compared the neural activity in a 50 ms bin with the instantaneous direction of the arm measured 100 ms later (i.e. a two time bin delay).

To examine the degree of spatial invariance of directional tuning in the CA coordinate system, the workspace was partitioned into nine (3 × 3) sub-regions (see Fig. 1b). Within each sub-region, we computed the firing rate every 50 ms of each neuron for each of 16 direction bins equally-spaced around the circle (typically 250 direction samples per direction bin). We only considered 664 (98% of the 680 recorded neuron samples) task-related neuron samples that modulated their firing rate with movement direction in at least one of the nine sub-regions ($p < 0.05$, ANOVA). 16 out of the total 680 MI neuron samples were not task-related and were not studied further.

Each time step was assigned to one of the nine sub-regions in the CA coordinate system. Within each sub-region, we also computed the average firing rate of each neuron for each of 16 direction bins in each of the three coordinate systems, and then fit the tuning curves with a cosine function to estimate the PDs (Georgopoulos et al. 1982).

Due to the periodic nature of direction, we used circular statistical methods to estimate the statistical moments of the directional data. The mean μ and standard deviation σ of given directions $\alpha_1, \alpha_2, \ldots, \alpha_n$ are estimated as follows:

$$\mu=\arctan\left(\frac{\sum\sin\ \alpha_i}{\sum\cos\ \alpha_i}\right),\tag{5}$$

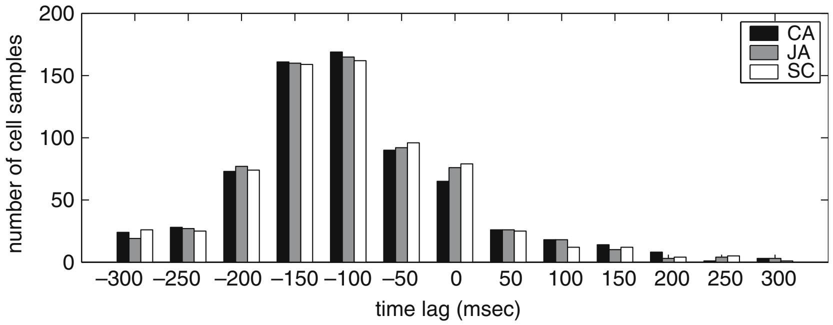


Fig. 3 The distribution of optimal time lags in mutual information between each neuron's firing rate and movement direction over the entire neuronal population. The optimal time lag of each neuron is estimated as the largest mutual information between firing rate and direction across a lead/lag time range from −300 to 300 ms in the CA coordinate system (*black bars*), the JA coordinate system (*gray bars*), and the SC coordinate system (*white Bars*) for all 680 neuron samples. The distributions in the three systems are nearly the same with an average around 100 ms

$$\sigma = \sqrt{\frac{1}{n}\sum_{i=1}^{n}\arccos^2\left(1-\frac{1}{2}\left((\cos\alpha_i-\cos\mu)^2+(\sin\alpha_i-\sin\mu)^2\right)\right)}. \tag{6}$$

Shift quantifications

The curl was locally computed at each of the nine sub-regions to describe the rotational trend in the preferred direction vector field. In a vector field $\mathbf{v}=(v_x, v_y)$, the curl is defined as

$$\mathrm{curl}\,\mathbf{v} = \frac{\partial v_y}{\partial x} - \frac{\partial v_x}{\partial y}. \tag{7}$$

A positive curl implies a local counterclockwise shift, and a negative curl implies a clockwise shift. We counted the number of positive curl values (*POS)* over the nine sub-regions to describe the overall rotational trend in the space:

$$\text{The PD vector field shifts} \begin{array}{ll} \text{clockwise} & \text{if POS} = 0,\ldots,4 \\ \text{counterclockwise} & \text{if POS} = 5,\ldots,9. \end{array}$$

The curl of each sub-region was numerically estimated from its nearest (horizontal and vertical) spatial neighbors. Note that the center sub-region has four nearest neighbors, the ones at the edges have three, and the ones at the corner only have two nearest neighbors.

Mutual information estimates

We measured the mutual information between the firing rate and the movement direction in each of the three coordinate systems. The firing rate or more properly the spike count, R (number of spikes within 50 ms bin) was typically a small integer (always less than ten in the data) and the direction D was also a small integer representing one of the 16 directional bins. Therefore the joint distribution $p(R, D)$ and marginal distributions $p(R)$ and $p(D)$ could be directly estimated from the raw data using non-parametric density estimation method. The mutual information is defined as:

$$\mathrm{MI}(R,D) = \sum_R\sum_D p(R,D)\log_2\frac{p(R,D)}{p(R)p(D)}. \tag{8}$$

Coordinate systems in the kinetic domain

The shoulder and elbow torques generated by the animal were estimated by feeding the kinematics of motion into the inverse dynamics equations of the exoskeletal robot together with the animal's arm (Scott 1999). Let (f_x, f_y) denote the force at the hand in CA coordinates, and (t_s, t_e) denote the torques at the shoulder and elbow (f_x, f_y) corresponds to the hand velocity $(\mathrm{d}x/\mathrm{d}t, \mathrm{d}y/\mathrm{d}t)$, and (t_s, t_e) corresponds to the joint velocity $(\mathrm{d}\theta/\mathrm{d}t, \mathrm{d}\varphi/\mathrm{d}t)$ in the kinematic domain. Similar to Eq. 3, the mapping from the joint-based to CA coordinate systems in the kinetic domain is (Wolovich 1987):

$$\begin{pmatrix} f_x \\ f_y \end{pmatrix} = \begin{pmatrix} k_1\sin(\theta)+k_2\sin(\theta+\varphi) & k_1\cos(\theta)+k_2\cos(\theta+\varphi) \\ k_2\sin(\theta+\varphi) & k_2\cos(\theta+\varphi) \end{pmatrix}^{-1} \begin{pmatrix} t_s \\ t_e \end{pmatrix}. \tag{9}$$

The SC coordinate system in the kinetic domain is defined by rotating the force (f_x, f_y) with the line connecting the shoulder to the hand. As in Eq. 4, the mapping from CA to SC coordinate system (f_u, f_v) is described as follows:

$$\begin{pmatrix} f_u \\ f_v \end{pmatrix} = \begin{pmatrix} \frac{y}{\sqrt{x^2+y^2}} & -\frac{x}{\sqrt{x^2+y^2}} \\ \frac{x}{\sqrt{x^2+y^2}} & \frac{y}{\sqrt{x^2+y^2}} \end{pmatrix} \begin{pmatrix} f_x \\ f_y \end{pmatrix}. \tag{10}$$

Population-vector decoding

The population-vector algorithm depends on cosine-tuning encoding of single neurons and can be expressed in the following equation (Moran and Schwartz 1999):

$$\mathrm{PV}_k = \sum_{i=1}^{C}\frac{r_{i,k}-\bar{r}_i}{r_{\max_i}-\bar{r}_i}\cdot\frac{\vec{B}_i}{r_{\max_i}-\bar{r}_i}, \tag{11}$$

where PV_k is the population vector at time $t_k=k\Delta t$, $k=1, \ldots, M$; $r_{i,k}$ is the firing rate of neuron i at time $t_k\bar{r}_i$; and $r_{\max_i}$ are the average and maximum firing rates of neuron i over all time bins, respectively; and $\vec{B}_i$ is the 2D unit-length vector pointing in the preferred direction of neuron i, $i=1, \ldots, N$, .

Assume V_k is the true velocity at time t_k, $k=1, \ldots, M$. The average decoding error is estimated as the averaged angular distance:

$$\mathrm{Err} = \frac{1}{M}\sum_{k=1}^{M}\arccos\left(\frac{\mathrm{PV}_k}{||\mathrm{PV}_k||}\bullet\frac{V_k}{||V_k||}\right), \tag{12}$$

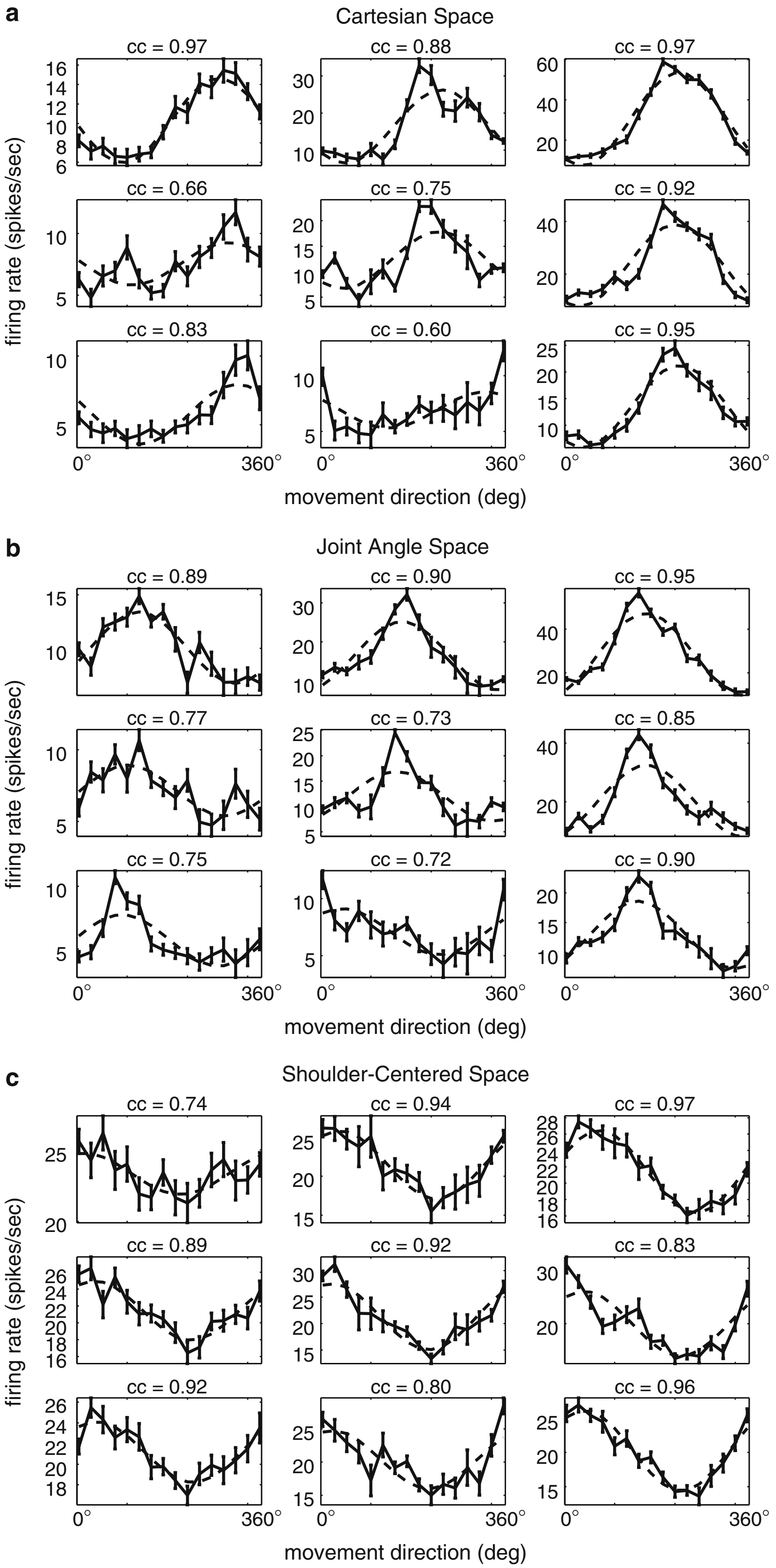
where • denotes the inner product.

Results

Directional tuning of motor cortical neurons

In order to measure the directional tuning of each neuron over the workspace, a standard cosine tuning

Fig. 4 Cosine-fitting of direction in all nine sub-regions in CA, JA, and SC coordinate systems. **a** The mean firing rate (*solid line*) of one neuron as a function of movement direction (16 directions) measured in a CA coordinate system as well as the best fit cosine function (*dashed line*) over all nine sub-regions. The *error bar* denotes the standard error of the mean firing rate. **b** and **c** are the same neuron and cosine fit as (**a**) except that direction is measured in the JA and SC coordinate systems. Here *CC* denotes the correlation coefficient between the neuron's firing rate and the cosine estimation



function (Georgopoulos et al. 1982; Scott and Kalaska 1997) was fit to the neural data to estimate the neuron's PDs at each of nine sub-regions of the workspace in all the CA, JA, and SC coordinate systems (Fig. 4). To ensure accurate estimation of PDs, we only considered neurons that were task-related (ANOVA, $p < 0.05$) and well-fit to a cosine function over at least two of the nine sub-regions in each of the three coordinate systems. We required the correlation coefficient between the neural data and the cosine function to be larger than 0.5 ($p < 0.05$, t-test). This requirement resulted in our examining 88% (585 neuron samples: 334 from monkey one, 251 from monkey two) out of a total of 664 task-related MI neuron samples.

Invariance of preferred directions under the three coordinate systems

We then examined whether the PDs remained spatially invariant over different sub-regions under each coordinate system. We found a minority of neurons that exhibited highly invariant directional encoding in each of the three coordinate systems (Fig. 5). For each neuron, we examined the degree of spatial invariance of PDs by measuring the PD standard deviation (Eq. 6) over different sub-regions of the workspace. The PD standard deviations over the entire neuronal population possessed a broad distribution ranging from highly invariant (less than 10°) to highly variable tuning (around 90°) (Fig. 6) in each coordinate system. Only 13% (26, 25, and 26 neuron samples for CA, JA, and SC coordinate systems, respectively) of the population exhibited highly invariant tuning in only one (i.e. uniquely invariant) of the three coordinate systems. This indicated that invariant directional encoding was observed in each coordinate system for small sub-populations of cells in MI and that none of the three coordinate systems dominated in terms of spatial invariance of directional tuning.

We then compared the PD invariance in the three systems by computing the difference in PD standard deviations between any two coordinate systems. The distribution of PD standard deviation differences over the entire neuronal population (585 neuron samples) indicated a larger degree of invariance in the SC coordinate as compared to either the CA or JA coordinate systems ($p < 0.01$, paired t-test) (Fig. 7a). Though significant, the difference in directional variability between the CA and JA coordinate system was weaker ($0.01 < p < 0.05$, paired t-test). By counting the number of neuron samples with smaller PD standard deviation in one coordinate system versus another (Fig. 7b), we also observed a significantly larger population of samples with smaller directional variability in the SC as compared to either CA ($p < 0.01$, sign test) or JA coordinate systems ($p < 0.01$, sign test). There was no difference in population size when comparing CA and JA coordinate systems ($p = 0.51$, sign test). Similar results were obtained if we restricted our analysis to only those neuron samples (175 samples) that exhibited cosine-tuning over all nine sub-regions (Fig. 7c,d). Furthermore, the results among those 175 samples were consistent over each of the six data sets. That is, there were more neurons with smaller variability in the SC as compared to either CA or JA coordinate systems for each of the six data sets across two monkeys.

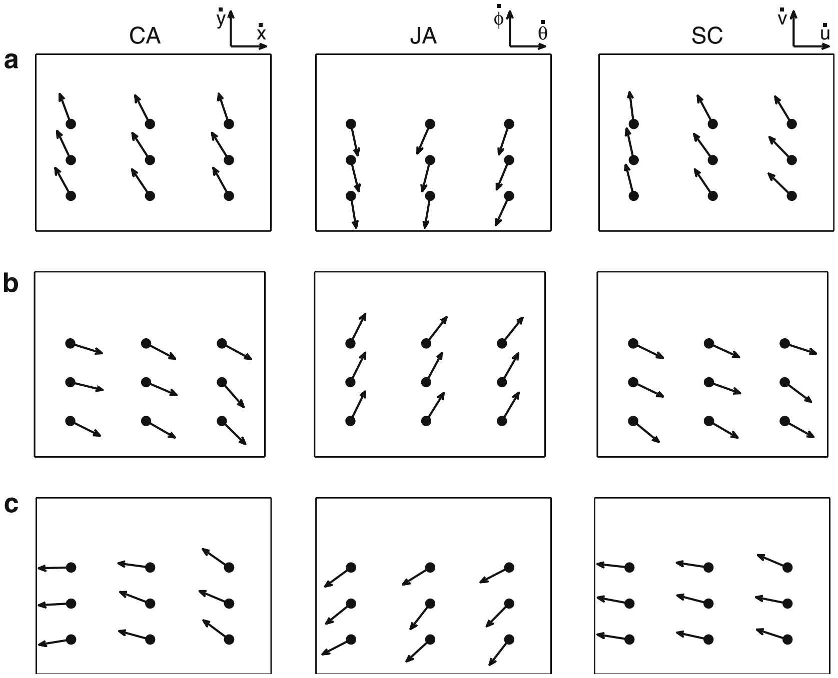


Fig. 5 Spatial invariance of directional encoding in CA, JA, and SC coordinate systems. **a** A neuron whose PDs (*arrows*) measured in the CA coordinate system remain relatively invariant over the workspace. The standard deviations of its PDs in the CA, JA, and SC coordinate systems are 5, 15, and 13°, respectively. **b** A second neuron whose PDs (*arrows*) measured in the JA coordinate system remain relatively invariant over the workspace. The PD standard deviations in the three systems are 7, 4, and 11°. **c** A third neuron whose PDs (*arrows*) measured in the SC coordinate system remain relatively invariant over the workspace. The PD standard deviations in the three systems are 16, 9, and 5°

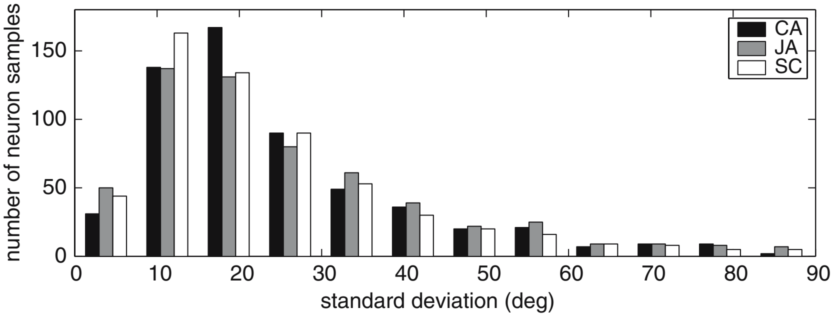


Fig. 6 Spatial variations in directional tuning over the neuronal population. The distribution of standard deviations of PDs measured in the CA coordinate system (*black bars*), the JA coordinate system (*gray bars*), and SC coordinate system (*white Bars*) for all 585 neuron samples. The standard deviation is broadly distributed from 0 to 90° in each system

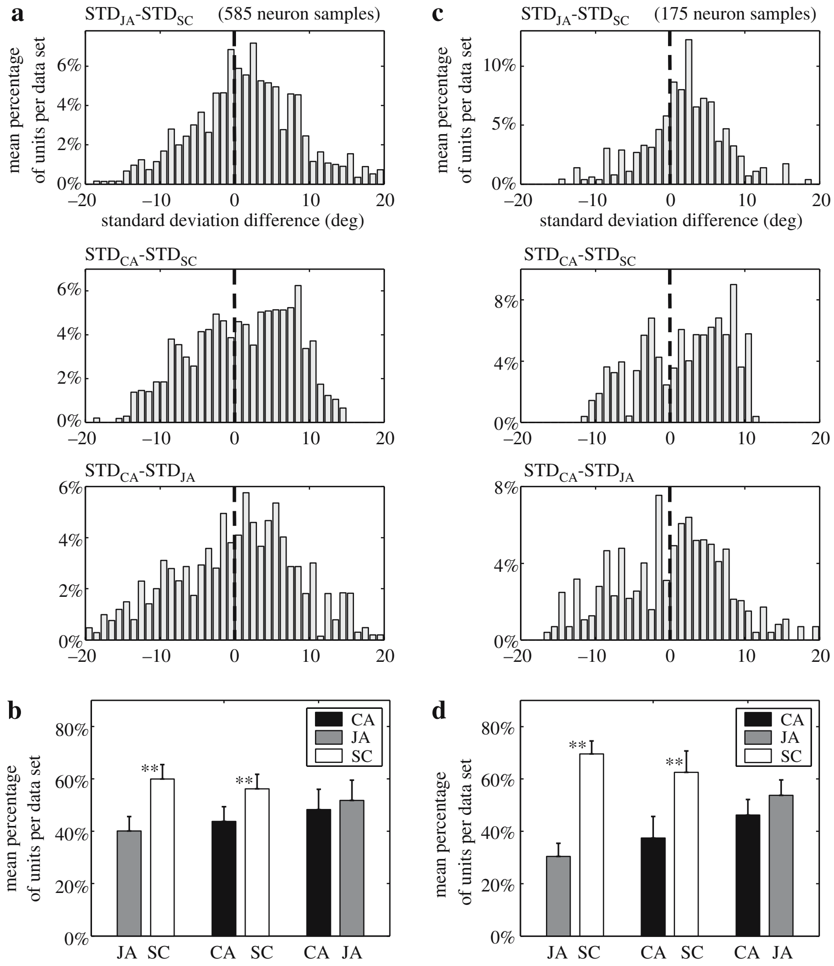


Fig. 7 A comparison of PD standard deviations in the CA, JA, and SC coordinate systems. **a** The average (over all six recording sessions or data sets) distribution of differences in PD standard deviations between JA and SC (*top panel*), between CA and SC (*middle panel*) and between CA and JA (*bottom panel*) coordinate systems for all 585 neuron samples. The *y-axis* denotes the average percentage of neurons per data set at each bin. **b** The average (over all six sessions) percentage of neurons per data set with larger directional invariance (i.e. smaller PD standard deviation) within pairs of coordinate systems. *Black, gray*, and *white bars* denote population sizes in CA, JA, and SC systems, respectively. *Error bars* denote the standard deviations over the six data sets and *double star* denotes a significance p-value < 0.01. **c, d** Same as (**a, b**) except for the subset of 175 samples that had directional cosine tuning over all nine sub-regions

Spatial shifts in preferred direction

Having found sub-populations of neurons that exhibited spatially invariant PDs in one coordinate system, we compared the observed shifts in PDs in another coordinate system with the systematic shifts that would be predicted based on the coordinate system transformation (Eqs. 3, 4). For example, neurons with spatially invariant PDs in a JA or SC coordinate system should result in systematic shifts in PD over the workspace in the CA coordinate system. Theoretically, PDs in half of the direction domain that are invariant in the JA or SC coordinate system will result in a clockwise shift in PDs over the workspace in the CA coordinate system, while the other half direction domain will result in a counterclockwise shift. This can be quantified by computing the theoretic curl of the vector field measured at each of the nine sub-regions in the workspace and counting the number of positive curl values (i.e. the theoretical *POS* value) (Fig. 8a). These two direction domains will vary with the arm lengths of the monkey and exact locations of the nine sub-regions.

We then computed the actual *POS* values from the PD vector field measured in CA coordinate system. A

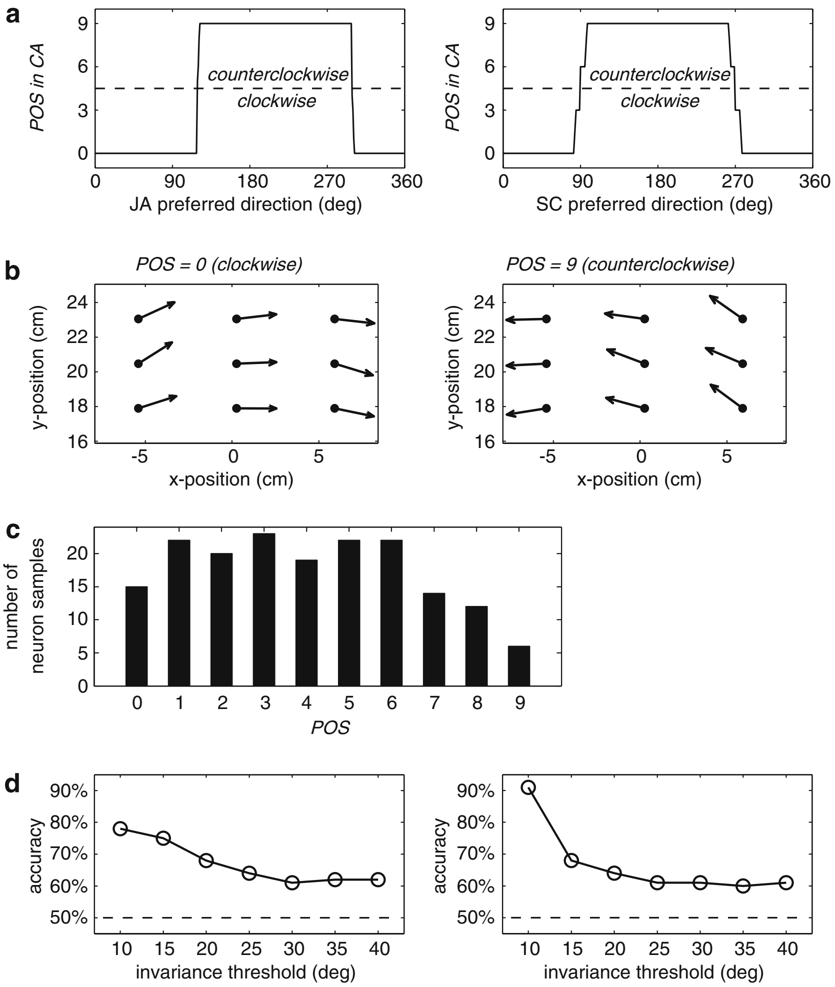


Fig. 8 Predicting shifts in preferred direction across coordinate systems. **a** Theoretical shifts in PD (*clockwise* and *counter-clockwise*) in the CA coordinate system as quantified by the number of *POS* at the nine sub-regions in one data set as a function of the invariant PD in the JA (*left panel*) and SC (*right panel*) coordinate systems. The *dashed line* marks the threshold between a clockwise shift (*POS* ≤ 4) and a counter-clockwise shift (*POS* ≥ 5). *Left panel*: One half ([130, 310°]) of the JA domain maps to a counter-clockwise shift in the CA coordinate system, while the other half ([0, 130°] ∪ [310, 360°]) maps to a clockwise shift; *Right panel*: The SC direction domain ([90, 270°]) maps to a counter-clockwise shift in the CA coordinate system while the other half domain ([0, 90°]∪[270, 360°]) maps to a clockwise shift. **b** Observed clockwise (*left panel*) and counter-clockwise (*right panel*) shifts in preferred direction in the CA coordinate system for two recorded neurons. **c** Histogram of *POS* values over the subset of 175 neuron samples with cosine tuning across all nine sub-regions. **d** Rotational shift prediction accuracy in the CA coordinate frame as a function of invariance PD thresholds in the JA (*left panel*) and SC (*right panel*) coordinate systems

POS value of zero indicated a vector field with a "highly clockwise" shifting trend (Fig. 8b, left panel) while a *POS* value of nine described a vector field with a "highly counter-clockwise" trend (Fig. 8b, right panel). The actual *POS* values over the subset of 175 neuron samples with cosine-tuning in all nine sub-regions were broadly distributed over the {0, ..., 9} range (see Fig. 8c).

Due to experimental noise, variability in neuronal firing rate, and lack of precise cosine tuning, a neuron will likely not exhibit perfect invariance in either JA or SC coordinate system. By selecting a threshold on the variation of PDs, we found a subset of neurons that were considered "invariant" if their PD standard deviation across the nine sub-regions were less than the threshold. Using the average of the small variations of PD in the "invariant" coordinate system, we predicted either a clockwise or counter-clockwise shift in the CA coordinate system. Using a conservative threshold of 10°, we found that we could accurately predict the systematic shifts in PD in the CA coordinate system in 78% (18/23) and 91% (32/35) of neurons with "invariant" PDs in JA and SC coordinate systems, respectively. As expected, the prediction accuracy dropped as the threshold value increased but remained significantly higher than 50% ($p < 0.01$, sign test) even at a 40° threshold (Fig. 8d).

Mutual information between firing rate and direction

Neurons that encode direction in a spatially invariant manner in one coordinate system should provide more directional information in that coordinate frame as compared to one in which directional tuning was more variable. To test this hypothesis, we used information theory to compute the mutual information between firing rate and movement direction over the entire workspace in each of the three coordinate systems. The distribution of mutual information differences over all 585 neuron samples revealed significantly higher information values in the SC coordinate system as compared to the JA and CA coordinate systems ($p < 0.01$, paired *t*-test) (Fig. 9a). Though significant, the difference in mutual information between the CA and JA coordinate system was relatively weaker ($0.01 < p < 0.05$, paired *t*-test). Likewise, there were significantly more neuron samples with higher mutual information values in the SC coordinate system as compared to the JA ($p < 0.01$, sign test) and CA coordinate systems ($p < 0.01$, sign test). There was no difference in population sizes between JA and CA coordinate systems ($p = 0.19$, sign test) (Fig. 9b). Consistent results were also observed over the subset of 175 neuron samples that exhibited cosine directional tuning over all nine sub-regions (Fig. 9c,d). The nearly identical results observed in the directional invariance and mutual information analyses can be better understood if one considers the relationship between directional tuning variability and mutual information. As expected, the standard deviation of PDs and mutual information between firing rate and direction are statistically anti-correlated (correlation coefficient = -0.25) over the neuronal population (Fig. 9e).

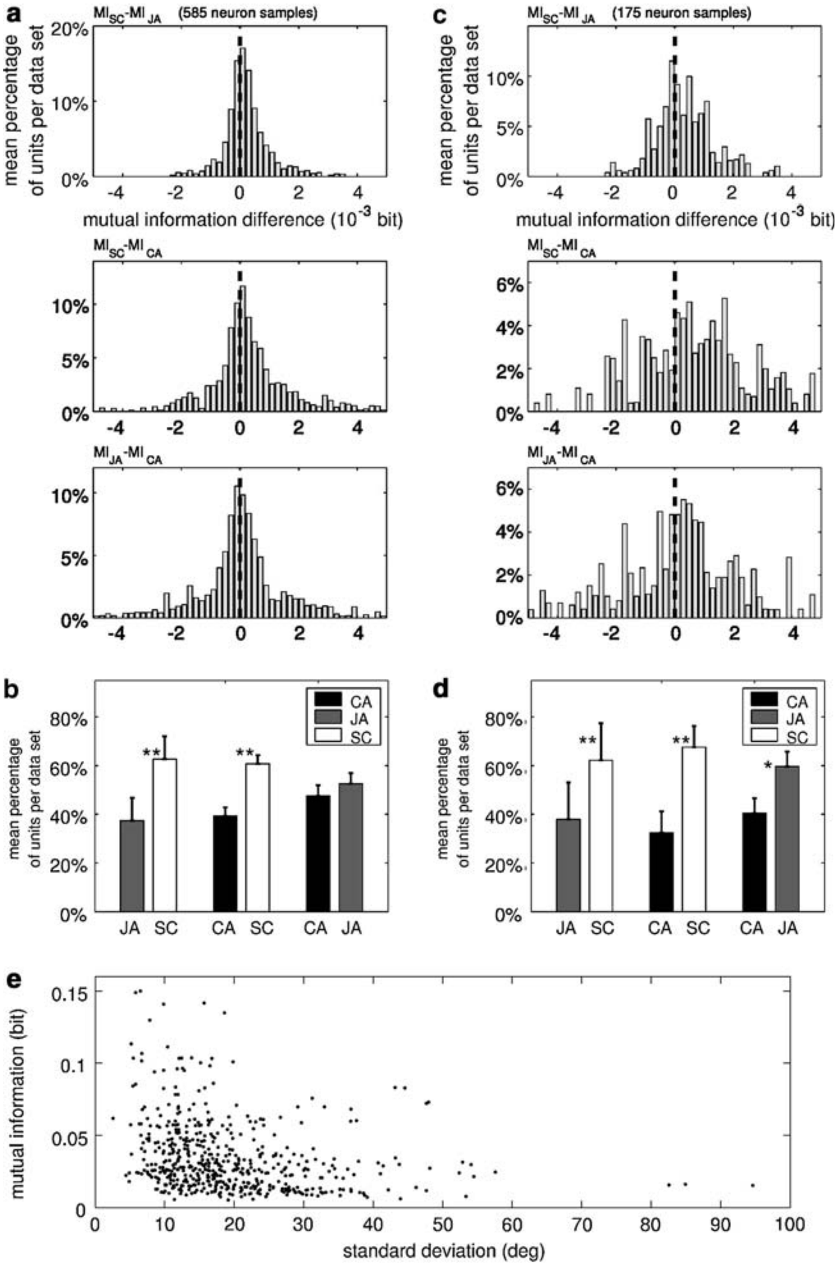


Fig. 9 The comparison of mutual information between firing rate and movement direction in the CA, JA, and SC coordinate systems. **a** The average (over all six recording sessions) distribution of the mutual information differences between SC and JA (*top panel*), between SC and CA (*middle panel*), and between JA and CA (*bottom panel*) coordinate systems for all 585 neuron samples. The *y-axis* denotes the average percentage of neurons per data set at each bin. **b** The average (over all six sessions) percentage of neurons per data set with larger directional mutual information values within pairs of coordinate systems. *Black, gray*, and *white bars* denote population sizes in CA, JA, and SC systems, respectively. *Error bar denotes* the standard deviation over the six data sets and *double star* denotes a significance *p*-value < 0.01. **c, d** Same as (**a, b**) except for the subset of 175 samples that had directional cosine tuning over all nine sub-regions. *Single star* denotes a significance *p*-value < 0.05. **e** A scatter plot relating the PD standard deviation and the mutual information over the 175 samples in all three coordinate systems

Population vector decoding

If a neuron encodes a movement parameter such as direction more accurately and with less variability in one coordinate system, then it would seem plausible that decoding this movement parameter from its response would likewise be more accurate in that coordinate system. Since we measured the directional tuning of the neurons using a standard cosine function, we used the population vector decoding algorithm (Moran and Schwartz 1999) to predict movement direction from an ensemble of simultaneously recorded MI neurons under each of the three coordinate systems.

By computing the absolute directional error over successive 50 ms time points during the performance of the task, we measured an average decoding error (averaged over time and data sets) of 52.82, 52.43, and 51.98° in the CA, JA, and SC coordinate systems. Although the SC coordinate system had a significantly larger portion (53.1 and 51.5%) of total time steps with lower decoding error than the CA (46.9%, $p = 2.2\times 10^{-98}$, sign test) and JA (48.5%, $p = 2.2 \times 10^{-24}$, sign test) coordinate systems, the average improvement in decoding in the SC coordinate system was extremely small ($< 1°$).

To examine the effect of PD invariance on decoding in each coordinate system separately, we partitioned the neurons in each data set into two equal-sized subsets based their PD invariance. That is, all neurons in one subset had more invariant PDs than the ones in the other. We measured an average decoding error of 58.1, 57.3, and 56.2° in the CA, JA, and SC coordinate systems, respectively, in the more invariant PD subset as compared to an average error of 65.2, 64.5, and 65.7° in the less invariant PD subset. This analysis indicates that by carefully selecting a subset of neurons with stronger PD invariance, it would be possible to improve directional decoding accuracy by at least 7°.

Comparisons in the kinetic domain

We compared directional encoding in the kinetic domain in each of the three coordinate systems by computing the preferred direction of hand force (in CA and SC coordinate systems) or joint torque direction (see Materials and methods). By measuring the variability in the preferred kinetic direction over all nine sub-regions in each coordinate system, we found a significant difference in PD standard deviation between the SC and CA coordinate systems ($p < 0.01$, sign test) and a marginally significant difference between SC and JA systems ($0.05 < p < 0.1$, sign test) indicating a stronger invariance in the SC coordinate system. There was no significant difference between CA and JA coordinate systems. These results, however, should be considered with some caution. First, after the same pre-selection process (that is, ANOVA and good cosine-fit selection) as in the kinematic domain, only 411 (60% of the total 680) neuron samples were qualified for further study. This is largely due to relatively poor cosine-fits in the kinetic domain. Second, most of the selected cells had fewer numbers of sub-regions (≤ 5) with good cosine-fits (Fig. 10b), while the numbers were much higher in the kinematic domain (Fig. 10a). Therefore, most PD standard deviations were estimated from few sub-regions and are likely to be poor estimates of the variability.

In contrast to the estimates of kinetic directional tuning variability, mutual information estimates between kinetic direction and firing rate were based on all 680 neuron samples and did not require partitioning into different sub-regions and are therefore more reliable. The distribution of mutual information differences indicated significantly higher information values in the SC and CA coordinate systems as compared to the JA system ($p < 0.01$, paired t-test) (Fig. 9a, top and bottom panel). However, there was no significant difference in mutual information between the CA and SC systems ($p = 0.13$, paired t-test) (Fig. 11a, middle panel). Consistent results were obtained when comparing the number of neurons with higher mutual information values in each coordinate system (Fig. 11b). Furthermore, the inferiority of the JA system was highly consistent over all the data sets. There were fewer cells with higher mutual information in the JA as compared to the CA coordinate systems in five of the six data sets, and fewer cells in the JA as compared to the SC coordinate systems in all six data sets.

Although our study focused on the directional encoding in the kinetic domain, a number of studies (Evarts 1968; Smith et al. 1975; Thach 1978; Cheney and Fetz 1980; Taira et al. 1996; Ashe 1997) have shown that force magnitude also influences the firing rate of motor cortical neurons. We, therefore, examined the relationship between the firing rate and kinetic magnitude (force or torque) under each coordinate system, and found that 44% (298 out of 680) of neuron samples exhibited a linear increase in firing rate with magnitude (Cheney and Fetz 1980; Ashe 1997) (Fig. 9c, left panel). The remaining samples exhibited either a linear decrease (11% or 79 out of 680) or no linear trend (45% or 309 out of 680) in firing rate with magnitude (Fig. 11c, middle and right panels). By considering only those ‘‘linear increasing’’ cells, mutual information comparisons also revealed a difference between the SC and CA as compared to the JA coordinate systems (Fig. 11d,e).

Discussion

Our aim in this study was to directly compare the neural representation of movement and force direction in primary motor cortex under three different coordinate systems. Such comparisons are valuable for two reasons: (1) these three systems (particularly the CA) are widely used in current neural coding research, and, therefore, it is important to fully understand their performance

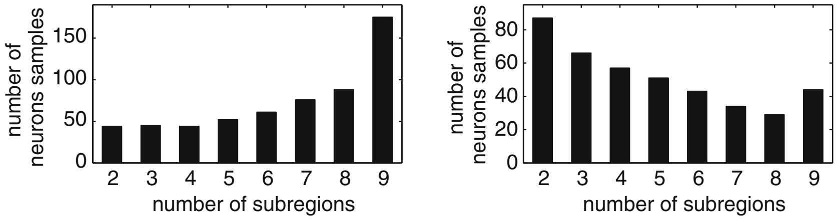


Fig. 10 **a** Distribution of number of sub-regions with good cosine fit among 585 pre-selected neuron samples in the kinematic domain. **b** Distribution of number of sub-regions with good cosine fit among 411 pre-selected neuron samples in the kinetic domain

under the same framework; (2) previous work has not systematically and directly compared encoding in these three coordinate systems in a large population of MI neuronal recordings. Our study investigated whether one coordinate system was more dominantly represented than the others over the neuronal population. Three analytic methods examining the degree of spatial invariance of directional tuning, the magnitude of directional mutual information, and the performance of directional decoding demonstrated a lack of dominance of any of these three coordinate systems although there was a small SC bias.

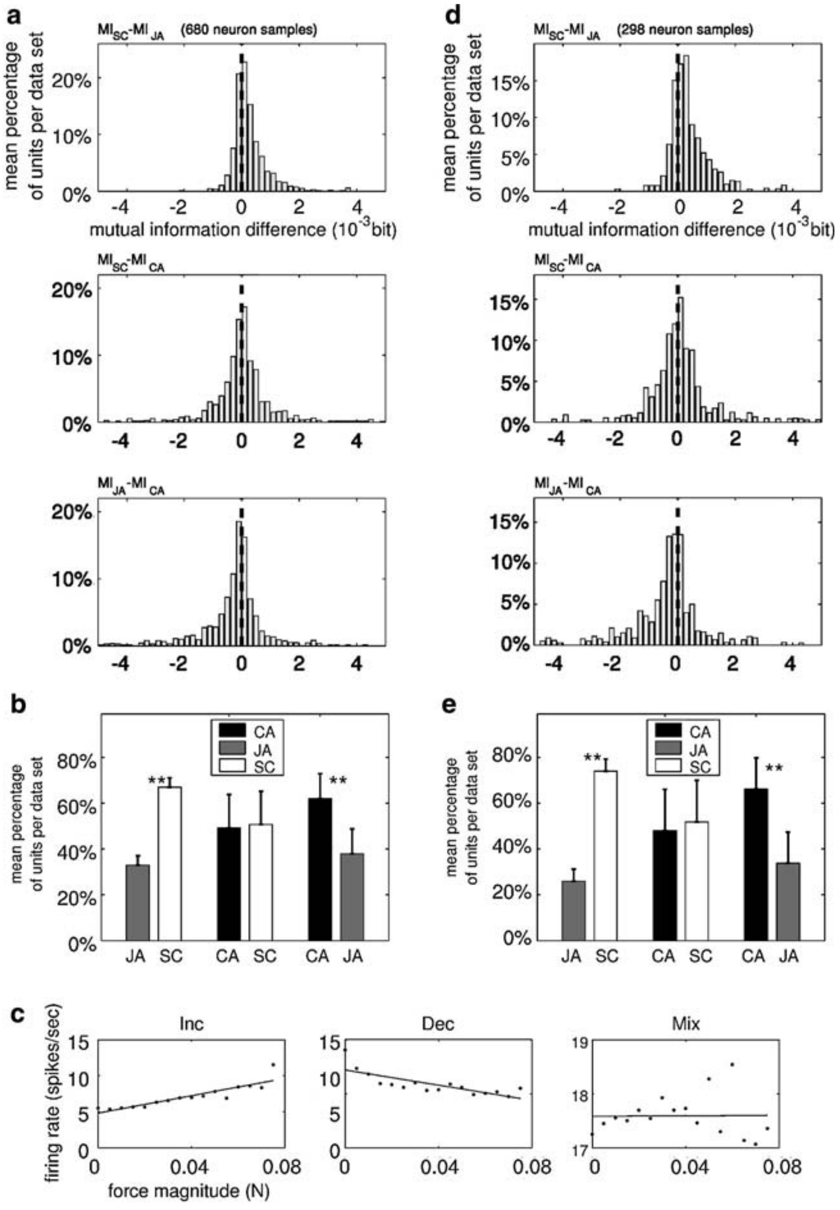


Fig. 11 The comparison of mutual information between firing rate and kinetic direction in the CA, JA, and SC coordinate systems. **a** The average (over all six recording sessions) distribution of the mutual information differences between SC and JA (*top panel*), between SC and CA (*middle panel*), and between JA and CA (*bottom panel*) coordinate systems for all 680 cell samples. The *y-axis* denotes the average percentage of neurons per data set at each bin. **b** The average (over all six sessions) percentage of neurons per data set with larger directional mutual information values within pairs of coordinate systems. *Black, gray*, and *white bars* denote population sizes in CA, JA, and SC systems, respectively. *Error bar denotes* the standard deviation over the six data sets and *double star* denotes a significance p-value < 0.01. **c** Kinetic magnitude tuning functions. The dots denote the measured firing rate as a function of force magnitude, and the solid lines are their optimal linear fit. The *left panel* shows a linear increasing tuning curve; the *middle* one shows a linear decreasing tuning curve; and the *right* one shows no linear trend. **d, e** Same as (**a, b**) except for the subset of 298 samples that exhibited linear increasing magnitude tuning functions in the three systems

It should be noted that our results may not generalize to all regions of motor cortex. First, we recorded from the precentral gyrus and not from within the central sulcus. Neurons recorded from the anterior bank of the central sulcus appear to have physiological properties that may be different from those on the gyrus (Sergio et al. 2005). Second, our chronically implanted electrode arrays have electrodes that are 1 mm long. Histological analyses from previous implants have shown that the arrays can sink up to 600 μm over time. However, the time course of this sinking is unclear. Therefore, the recordings that are presented here may be from cell bodies located either in lower portions of layer 3 or upper portions of layer 5. If we are recording from layer 3 neurons, our results may not necessarily apply to projection neurons in layer 5.

Psychophysical studies examining the errors made during reaching movements have suggested that human subjects employ a SC coordinate to guide the hand (Soechting and Flanders 1989; Soechting et al. 1990; Flanders et al. 1992). Moreover, previous electrophysiological experiments found systematic shifts in directional tuning of MI neurons measured in a body-centered-CA coordinate system when monkeys performed three-dimensional reaching movements from three different initial positions (Caminiti et al. 1990, 1991). Caminiti and colleagues found that the orientation of PDs were more strongly correlated between neighboring parts of the workspace than between left and right parts. Moreover, the authors found the preferred direction orientations shifted predominantly along the *z*-axis. They hypothesized that these shifts could be explained if one assumed that the motor cortex employed a SC coordinate system to represent movement direction. Our results confirmed this hypothesis by directly demonstrating that the systematic shifts in preferred direction that we observed in a body-centered coordinate system could be predicted by the coordinate transformation between SC and body-centered coordinate systems. Our results are similar to the systematic shifts in preferred force directions observed by Sergio and colleagues (Sergio and Kalaska 2003; Sergio et al. 2005) when monkeys were required to generate isometric forces in different directions from nine different starting positions. Although they did not directly compare encoding of force direction in different coordinate systems, the shifts they measured were proportional to the shoulder angle.

Our study demonstrates that there is no dominance toward a joint-centered coordinate system, which is inconsistent with the results of Ajemian et al. (2000). It is unclear why their results were not consistent with ours although our results are based on a direct estimation of PDs under all three coordinate systems.

Our work focuses on the motor cortex; however, it is well known that limb movement is also encoded in other cortical areas, such as the parietal cortex (Lacquaniti et al. 1995). Lacquaniti and colleagues found that parietal cortical neurons are tuned in a body-centered reference frame. The coordinate systems in their study included the CA space, the spherical space, the (SC) spherangular space, and the orientation angles space. They showed that each coordinate tends to be encoded in a different sub-population of parietal cortical neurons. This is basically consistent with our findings in the motor cortex that none of the systems uniquely can fully describe the encoding of movement information.

Note that by the use of the KINARM system, the monkey's hand movements were constrained to two dimensions in the horizontal plane. Such a constraint is necessary for the comparison of the three coordinates as only under this framework is there a one-to-one mapping between them (Eqs. 3, 4). If the movements were unconstrained in three dimensional space, the external, CA coordinate system would have three degrees of freedom (for the hand movement direction), while the intrinsic, JA coordinate system would have at least four degrees of freedom. In that case, we would not have a direct mapping between the coordinate systems. Therefore it would be difficult to do many of the comparisons and impossible to do the analysis in Fig. 8 which is straightforward in the two dimensional situation.

Our results based on kinetic direction encoding were generally consistent with those based on kinematic direction. However, we did observe a strong bias toward stronger mutual information in the CA as compared to the JA coordinate systems, which was not observed when examining movement direction. In fact, we observed a weak bias in the opposite direction such that the mutual information for movement direction was slightly stronger in the JA as compared to the CA coordinate systems. In addition, there was no difference in mutual information estimates between SC and CA coordinates in the kinetic domain whereas there was a strong bias in mutual information for movement direction in SC as compared to CA coordinates. It is unclear why such discrepancies occurred although kinetic direction is quite distinct from movement direction due to interaction and inertial torques that occur during the performance of the task.

The experimental methods we employed in our study offer certain advantages when exploring the question of coordinate system encoding. First, we recorded simultaneously from multiple single units using a multielectrode array while monitoring the behavior of the animal in a given data set. This has the attractive feature that the behavior of the animal was identical for all simultaneously recorded neurons so that differences in coordinate system encoding that we observed cannot be attributable to differences in behavior. Second, the nature of the task was quite different from the more common center-out task used to explore directional tuning. As Fig. 1b demonstrates, our task allowed us to sample a broader range of the movement space. Our estimates of preferred direction, therefore, may better generalize over different behavioral conditions.

Our results demonstrate that none of these three coordinate systems are uniquely represented in motor cortex. Although we observed a bias toward a SC coordinate system representation, it was small and likely not to be functionally significant in terms of decoding on-going motion of the arm. These results lead to at least two implications. First, there may be a coordinate system that is employed by motor cortex that is yet to be discovered. We believe this is unlikely. Second, an intriguing possibility is that motor cortex does not represent movement parameters in any coordinate system. Rather, the motor cortex as a whole may constitute a substrate for various transformations including coordinate and inverse dynamics transformations. Individual motor cortical neurons would represent terms in these transformations which would then be aggregated downstream from the motor cortex to form the necessarily language to control the periphery. Alternatively, the optimal feedback theory proposed by Todorov and Jordan (2002) argues that a particular desired trajectory is not planned in the cortex but rather an optimal control law is realized in the motor cortex which exploits the redundancy of the motor periphery by attempting to minimize the task-relevant errors (e.g. reaching a sequence of targets in our task) at the expense of task-irrelevant errors. Instead of representing spatially invariant directional commands, individual motor cortical neurons would realize control signals that when taken together realize an optimal control law.

Acknowledgments We thank Greg Ojakangas for rederiving and implementing the equations of motion of the exoskeletal robot together with the animal's arm. We also thank S. Francis, D. Paulsen and J. Reimer for training the monkeys and collecting the data. Finally, we thank Z. Haga for helpful discussions regarding the data analyses. This work was supported by a grant from the Whitehall Foundation and grants N01-NS-2-2345 and R01 NS45853-01A2 from the NINDS. N. Hatsopoulos has stock ownership in a company, Cyberkinetics, Inc., that is commercializing neural prostheses for severely motor disabled people.

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