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Update article

Sensorimotor transformations in cortical motor areas

Shinji Kakei [a,b,*], Donna S. Hoffman [d,f], Peter L. Strick [c,d,e,f]

[a] *Systems Neuroscience, Graduate School of Life Science, Tohoku University, 2-1-1 Katahira, Aoba-ku, Sendai 980-8577, Japan*
[b] *PRESTO, Japan Science and Technology Corporation (JST), Japan*
[c] *Research Service, Veterans Affairs Medical Center, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261, USA*
[d] *Department of Neurobiology, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261, USA*
[e] *Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261, USA*
[f] *Center for the Neural Basis of Cognition, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261, USA*

Abstract

A central problem in motor research has been to understand how sensory signals are transformed to generate a goal-directed movement. This problem has been formulated as a set of coordinate transformations that begins with an extrinsic coordinate frame representing the spatial location of a target and ends with an intrinsic coordinate frame describing muscle activation patterns. Insight into this process of sensorimotor transformation can be gained by examining the coordinate frames of neuronal activity in interconnected regions of the brain. We recorded the activity of neurons in primary motor cortex (M1) and ventral premotor cortex (PMv) in a monkey trained to perform a task which dissociates three major coordinate frames of wrist movement: muscle, wrist joint, and an extrinsic coordinate frame. We found three major types of neurons in M1 and PMv. The first type was termed 'extrinsic-like'. The activity of these neurons appeared to encode the direction of movement in space independent of the patterns of wrist muscle activity or joint movement that produced the movements. The second type was termed 'extrinsic-like with gain modulation'. The activity of these neurons appeared to encode the direction of movement in space, but the magnitude (gain) of neuronal activity depended on the posture of the forearm. The third type was termed 'muscle-like' since their activity co-varied with muscle activity. The great majority of the directionally-tuned neurons in the PMv were classified as 'extrinsic-like' (48/59, 81%). A smaller group was classified as 'extrinsic-like with gain modulation' (7/59, 12%). In M1, the three types of neurons were more equally represented. Our results raise the possibility that cortical processing between M1 and PMv may contribute to a sensorimotor transformation between extrinsic and intrinsic coordinate frames. Recent modeling studies have demonstrated the computational plausibility of such a process.
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1. Introduction

To generate a goal-directed movement, the brain must translate the location of a target into a set of muscle activation patterns. A central problem in motor research has been to understand how the process of sensorimotor transformation is accomplished by the central nervous system. The solution is thought to involve a set of transformations between the coordinate frames or reference frames for movement representation. A co-ordinate frame describes the measurement system which encodes specific movement variables (Soechting and Flanders, 1992). Two general types of coordinate frames can be described: extrinsic and intrinsic. An extrinsic coordinate frame is fixed to external space and is independent of body movement. In contrast, an intrinsic coordinate frame is related to and moves with a specific body part such as a joint or muscle. Each type of coordinate frame provides a specialized description of movements and has unique advantages. For instance, an extrinsic coordinate frame is essential to specify the location of a target in space, whereas a joint coordinate frame provides the most concise description of the position of a limb. It is likely that the nervous system

* Corresponding author. Tel.: +81-22-217-5047; fax: +81-22-217-5048.
E-mail address: s-kakei@mail.cc.tohoku.ac.jp (S. Kakei).

uses multiple reference frames to represent a goal-directed movement and to control explicitly or implicitly different physical movement variables (e.g. movement endpoint, movement velocity, force) in a motor task.

Using this framework, the process of generating a goal-directed movement can be re-formulated as involving a set of coordinate transformations. At the very minimum, the spatial location of a target in an extrinsic coordinate frame must be translated into a set of muscle activations in an intrinsic coordinate frame (Hollerbach, 1982; Alexander and Crutcher, 1990; Soechting and Flanders, 1992; Flash and Sejnowski, 2001). The usage of intermediate coordinate frame(s) will depend on the specific algorithm(s) developed by the central nervous system to accomplish the process of sensorimotor transformation. We believe that insight into the process of sensorimotor transformation can be gained by examining the coordinate frames that are represented in various cortical and subcortical areas of the motor system.

2. Dissociation of coordinate frames related to wrist movements

We developed a novel paradigm which dissociates three different coordinate frames related to wrist movements: extrinsic (related to the direction of movement in space), muscle (related to the activity of individual or groups of muscles) and joint (related to the angle of the wrist joint; Kakei et al., 1999). Briefly, a monkey was trained to make rapid step-tracking movements of the right wrist with a 2-degree-of-freedom manipulandum (Hoffman and Strick, 1986, 1999). The monkey faced a computer screen that displayed a 'cursor' and a 'target'. The cursor was a small filled circle that moved in proportion to the animal's wrist movements. The target was a larger open circle with an inside diameter equal to 8° of wrist movement. The target was positioned initially at the center of the screen. A trial began when the monkey placed the cursor in the target for a variable 'Hold' period (0.75–1.5 s). The monkey maintained the cursor in the central target during a variable 'Instruction' period (1–3 s) while a second target appeared at a peripheral location. The Instruction period was terminated when the central target disappeared. This provided a 'Go' signal which told the animal to move from the central to the peripheral target. The animal was allowed 200 ms to complete the initial trajectory of the movement. Target locations required a 20° change in wrist angle.

We required the monkey to move to eight different peripheral target locations that were evenly spaced at 45° intervals and required eight different combinations of wrist flexion–extension and radial–ulnar deviation. The monkey performed the task with the forearm in each of three different postures: pronated (Pro), supinated (Sup) and midway between pronation and supination (Mid; Fig. 1A). The change in forearm posture resulted in a dissociation of the direction of joint movement from the direction of movement in space. For instance, an upward movement in space is produced by wrist extension when the forearm is in the pronated posture (Fig. 1A, Pro) or by wrist flexion when the forearm is rotated 180° clockwise to the supinated posture (Fig. 1A, Sup). Thus, a movement description based on the wrist joint configuration rotates with the forearm (i.e. 180° rotation, Fig. 1D, right, 'Joint'), whereas a movement description fixed to extrinsic space is indifferent to forearm posture (i.e. 0° rotation, Fig. 1D, right, 'Extrinsic').

Of the many muscles in the primate arm, seven forearm muscles were determined to be task-related because they displayed phasic agonist bursts prior to movement onset in all three postures and the bursts varied in amplitude for different directions of movement. In fact, the variation in amplitude for each individual muscle was well fit by a cosine function (Fig. 2A; Hoffman and Strick, 1999; Kakei et al., 1999). We calculated the preferred direction (PD) for each task-related muscle with the limb in each of the three separate postures (Fig. 1B and C). The PDs of the task-related muscles shifted by a mean of 71.1° (range 46–90°; Fig. 1D, right) for a shift in posture from Pro to

Fig. 1. Experimental design: dissociation of extrinsic, joint and muscle coordinate frames with changes in forearm posture. (A) Schematic of the monkey right hand gripping the handle of the manipulandum in three forearm postures. Pro, fully pronated; Sup, fully supinated, Mid, midway between pronation and supination. Ext, extension; Flx, flexion; Rad, radial deviation; Uln, ulnar deviation. Up and Down indicate direction of movements in space. (B, C) PDs of the seven task-related muscles ((B) four wrist muscles and (C) three finger muscles, respectively) when the limb was in the three forearm postures (two to four recordings from each muscle). APL, abductor pollicis longus; ECRB, extensor carpi radialis brevis; ECRL, extensor carpi radialis longus; ECU, extensor carpi ulnaris; ED23, extensor digitorum 2,3; EDC, extensor digitorum communis; FCR, flexor carpi radialis. 'Up', 'Down', 'Left' and 'Right' indicate directions of movements in space. (D) Normalized shifts of PDs of the task-related muscles in the three forearm postures. Left circle, the single vector represents the PDs of the task-related muscles in the Pro position, which were normalized to the Up direction. Middle circle, the unlabeled vectors represent the relative shifts of the PDs of the task-related muscles with forearm rotation from Pro to Mid. Right circle, the unlabeled vectors represent the relative shifts of the PDs of the task-related muscles with forearm rotation from Pro to Sup. The vectors labeled 'Extrinsic' represent the PDs of ideal vectors fixed to an extrinsic coordinate frame. The vectors labeled 'Joint' represent the PDs of ideal vectors fixed to the wrist joint. Note that the unlabeled vectors are clearly separated from the Extrinsic and Joint vectors. Modified from Figure 1 in Kakei et al. (1999).
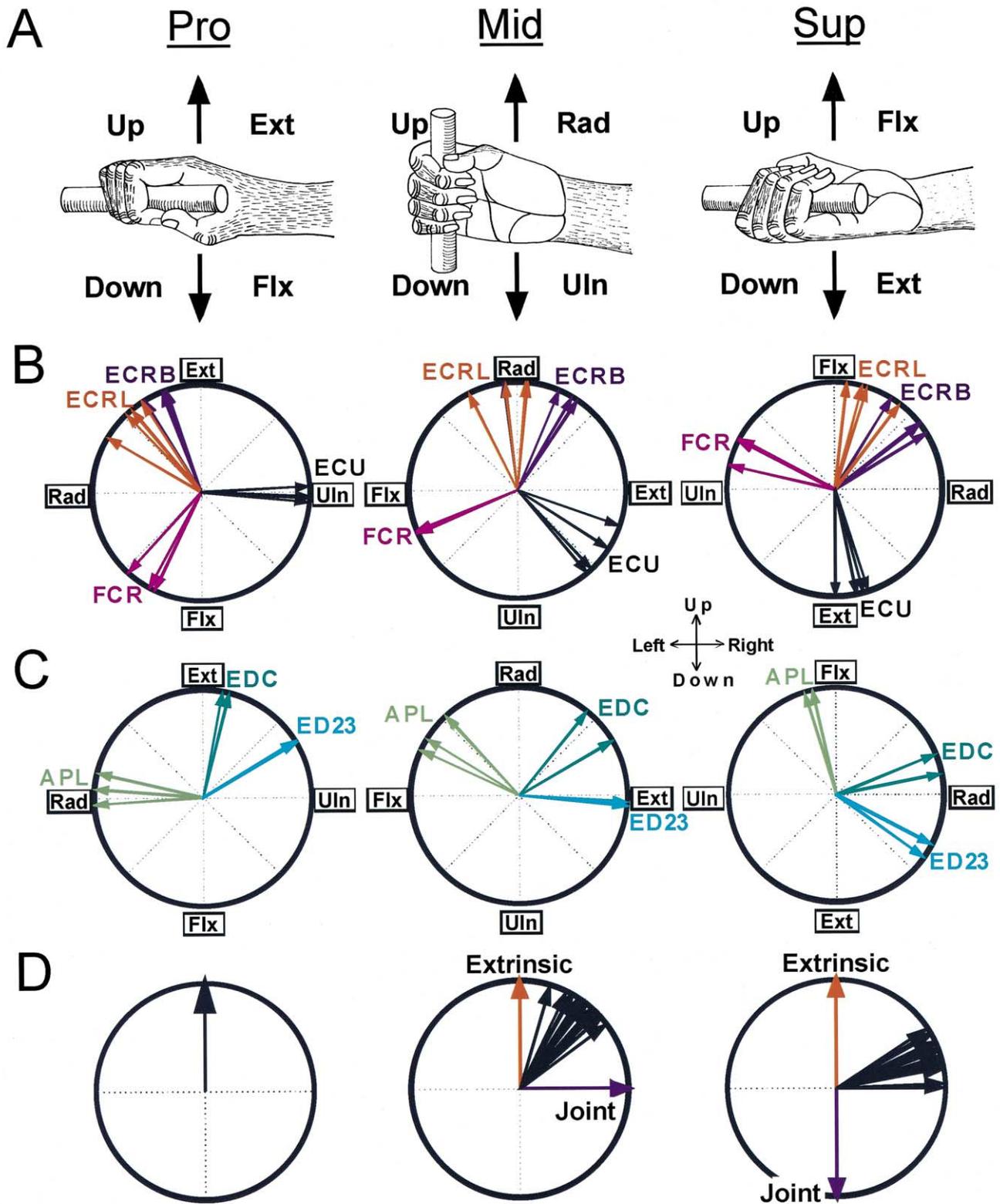
Fig. 1

Sup (i.e. a 180° clockwise rotation of the forearm; Kakei et al., 1999). These shifts in PDs were considerably more than a coordinate frame tied to extrinsic space (0°) and than a coordinate frame tied to the wrist joint (180°). Clearly, a key feature of our step-tracking task is that it dissociates three major variables

of wrist movement: direction of movement in space, direction of movement at the wrist joint and activity of forearm muscles.

On the basis of these observations, we reasoned that neurons signaling information in a muscle- or joint-like coordinate frame will have PDs that shift by 46–90° (muscle) or 180° (joint) when wrist movements are first made with the forelimb in the Pro posture and then, made in the Sup posture. On the other hand, neurons signaling information in an extrinsic-like coordinate frame will have PDs that are relatively stable regardless of posture. Therefore, we used this task to examine coordinate frames of single neurons in the primary motor cortex (M1) and in the ventral premotor cortex (PMv).

3. M1 and PMv

We focused on neurons in M1 because this cortical region is the primary source of cortico-motoneuronal neurons that have direct access to motoneurons (Fetz and Cheney, 1980; Shinoda et al., 1981). In addition, there is a longstanding controversy about what movement variables are encoded in the activity of M1 neurons. Some studies have provided evidence that intrinsic parameters are represented by the activity of M1 neurons (e.g. Evarts, 1968; Smith et al., 1975; Kalaska and Crammond, 1992), whereas other studies have concluded that extrinsic parameters are encoded in M1 (e.g. Georgopoulos et al., 1982). On the other hand, we examined activity in the PMv because this cortical region is adjacent to the forelimb region of M1 and is densely interconnected with it (Matsumura and Kubota, 1979; Muakkassa and Strick, 1979). The PMv also has strong interconnections with regions of posterior parietal cortex (Dum and Strick, 1991; Kurata, 1991; Matelli et al., 1986) and is the one premotor area that is interconnected with area 46 in prefrontal cortex (Lu et al., 1994). Neurons in the PMv receive visual and somatosensory inputs (Kubota and Hamada, 1978; Rizzolatti et al., 1981a,b; Fogassi et al., 1996; Graziano et al., 1997) and are active during the preparation for and execution of visually guided movements (Kubota and Hamada, 1978; Godschalk et al., 1981; Gentilucci et

al., 1988; Boussaoud and Wise, 1993; Kurata, 1993). Lesions involving the PMv disrupt movements directed towards visual targets (Moll and Kuypers, 1977). These and other observations suggest that the M1 and PMv are important members of the cortical network that performs sensorimotor transformations to generate goal-directed movements. Thus, we compared the reference frames of neurons in the M1 and PMv to gain insight into the coordinate transformations that may occur between these areas (Kakei et al., 1999, 2001).

4. Task-related neuron activities in M1 and PMv

We recorded the activity of single neurons in the hand areas of M1 and PMv while a monkey performed step-tracking movements of the wrist with the forearm in each of three postures (Kakei et al., 1999, 2001). We found 117 neurons in PMv and 125 neurons in M1 that displayed task-related activity during either the Instruction period (measured 0–300 ms prior to the Go signal) or the Execution period (measured 0–100 ms prior to movement onset) (ANOVA; $P < 0.05$). The remainder of this article will be focused on the neuronal activity that occurred during the Execution period. We examined in detail the properties of those neurons that were directionally tuned in all three postures. Most of these neurons had a strong phasic change in activity during the Execution period. The amplitude of this activity varied with movement direction in a unimodal manner that was fit by a cosine function (Georgopoulos et al., 1982). We calculated the PD for each neuron in each of the three wrist postures (Fig. 2B–D; for details, see Kakei et al., 1999, 2001). In addition, we compared the amplitudes of the neuronal activity in the three different postures to determine whether the neuron displayed a gain modulation of greater than 30% among the three postures during the Execution period (Fig. 2C, Fig. 4).

5. Coordinate frames of neuron activities in M1

Of the 125 task-related neurons in M1, 72 were directionally-tuned during the Execution period in all three wrist postures. Based on the changes in directional

Fig. 2. Cosine-tuning of activity of muscles and neurons in different forearm postures. (A) Directional tuning of a wrist prime mover, ECRB, in the three forearm postures. The summed activity in a time window of −25 to +25 ms relative to the movement onset was plotted for each direction of movement in each forearm posture. (B) Directional tuning of a neuron in the PMv that was 'extrinsic-like'. (C) Directional tuning of a neuron in M1 that was 'extrinsic-like with gain modulation'. The gain modulation for this neuron was 69% (see legend of Fig. 4 for calculation). (D) Directional tuning of a neuron in M1 that was 'muscle-like'. For graphs B–D, neuron activity was measured in a time window of −100 to 0 ms prior to movement onset. In each graph, black symbols and lines are used for Pro position, blue symbols and lines are used for Mid position, and red symbols and lines are used for Sup position. The tic marks on the data points show 95% confidence intervals. Note that a cosine function provides a good fit to the data points. The vertical lines indicate PDs. The horizontal arrows indicate the average baseline activity during the central-hold period. Up, Down, Left, Right indicate the direction of movements in space, as defined in Fig. 1.
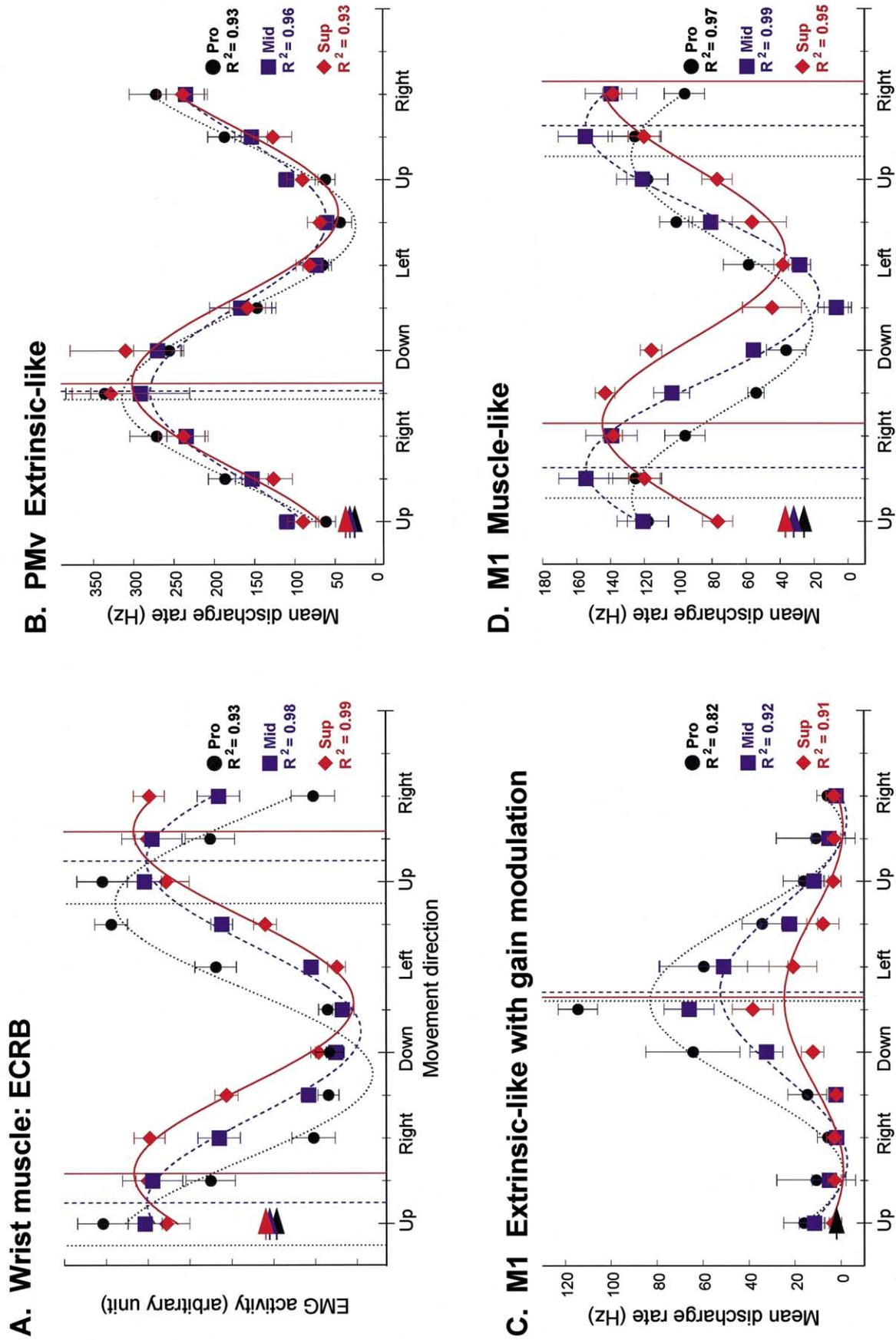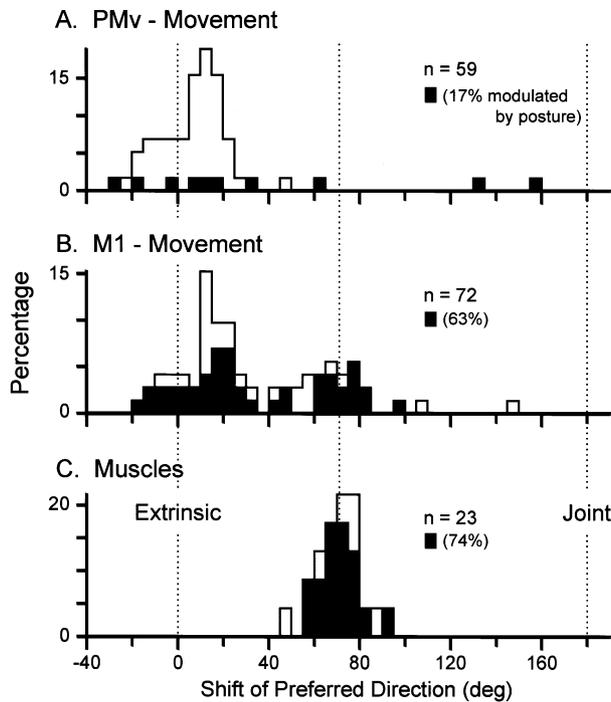
Fig. 2

Fig. 3. Distribution of the shifts in PDs for neurons and forearm muscles. The histograms plot the shifts in PD for a 180° clockwise rotation of forearm posture from Pro to Sup (cf. Fig. 1). Clockwise shifts are positive. The dotted line labeled Extrinsic indicates an ideal extrinsic-like PD that does not shift with changes in posture. The dotted line labeled Joint indicates an ideal PD related to the wrist joint that shifts 180° with a change in posture from Pro to Sup. The unlabeled dotted line in the middle indicates the average shift (71.1°) of activity in the seven task-related muscles. The shaded areas indicate neurons or muscles with gain modulation > 30% in the different forearm postures. (A) Shift in PDs of Execution period activity of PMv neurons. (B) Shift in PDs of Execution period activity of M1 neurons. (C) Shift in PDs for task-related muscles (23 recordings from seven forearm muscles; Kakei et al., 1999). Modified from Figure 4 in Kakei et al. (2001).
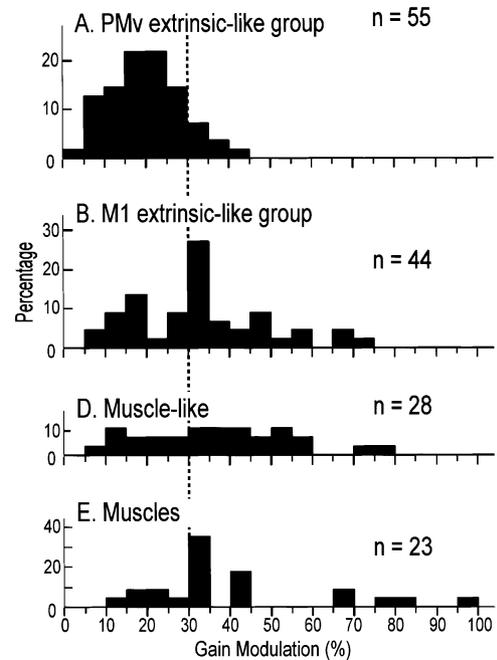

Fig. 4. Distributions of the gain modulations of neurons and forearm muscles. The histograms plot the gain modulation of Execution period activity between the three forearm postures. In each neuron, for each posture, we calculated an average firing rate during the time window of 0–100 ms prior to movement onset. Then we calculated the ratio of the minimum and the maximum values. Gain modulation is plotted as (1-min value/max value) × 100. For muscles, the same calculation was performed during the time window of ±25 ms relative to movement onset. (A) Gain modulation of extrinsic-like neurons in PMv. (B) Gain modulation of extrinsic-like neurons in M1. (C) Gain modulation of muscle-like neurons in M1. (D) Gain modulation of task-related muscles (23 recordings from seven forearm muscles). Those neurons or muscles to the right of the dotted line are defined as having a large gain modulation and those to the left are defined as having small or minimal gain modulation. Note that the distributions of gain modulations are strikingly different between the extrinsic-like neurons in M1 and PMv. Extrinsic-like neurons in PMv have gain modulations that are similar and small, with a peak at 20%. In contrast, extrinsic-like neurons in M1 have gain modulations that are widely distributed, with a large peak at 35% and a smaller separate peak at 20%. Based on the distribution of gain modulations in M1, we used a gain modulation of 30% (the dotted line) to separate 'extrinsic-like with gain modulation' neurons from 'extrinsic-like' neurons (Kakei et al., 1999, 2001).

preference and the gain modulation of neuronal activity, the 72 neurons formed three types: 'muscle-like', 'extrinsic-like' and 'extrinsic-like with gain modulation' (Kakei et al., 1999). The muscle-like neurons ($n = 28/72$, 39%) showed orderly and relatively large (> 40°) shifts in PD (mean ± S.D. = 70.2 ± 21.9°, range = +43 to +147°) when the forearm posture was rotated by 180° from Pro to Sup (Fig. 2D; Kakei et al., 1999). The shifts in PD paralleled those of task-related muscles (compare Fig. 3B and C). Thus, the activity of this type of neuron appears to represent movement in an intrinsic coordinate frame and may encode commands for single or groups of muscles.

In contrast, the other two types of neurons, extrinsic-like and extrinsic-like with gain modulation ($n = 44/72$, 61%), showed little or no change in PD (< 35°) (mean ± S.D. = 12.3 ± 12.5°, range = −15.3 to +32.8°; Fig. 2C, Fig. 3B). The absence of shifts in PD for these neurons

appeared to mirror the stability of an extrinsic coordinate frame.

We examined the 'gain' of neuronal activity in the three forearm postures (Fig. 4B and C). This led us to distinguish two subtypes of extrinsic-like neurons in M1. A minority of the extrinsic-like neurons ($n = 17/72$, 24%; Fig. 4B) was largely uninfluenced by changes in forearm posture. Thus, these neurons appeared to represent the direction of action for wrist movement in space in a manner that is largely independent of the pattern of muscle activity or the specific changes in joint movement. On the other hand, a majority of the extrinsic-like neurons in M1 ($n = 27/72$, 37%) showed a large change (> 30%) in the amplitude of their activity during the

Execution period when forearm posture was altered (Fig. 2C, Fig. 4B). We considered this to be 'gain modulation' and termed this type of neuron, 'extrinsic-like with gain modulation'. The presence of large modulations in gain induced by changes in posture implies that the activity of these neurons is influenced by the state of the motor apparatus in periphery. Thus, we consider that the activity of these neurons is related to both extrinsic-like and intrinsic-like coordinate frames.

6. Coordinate frames of neuron activities in PMv

Among 117 task-related neurons in PMv, 59 were directionally-tuned in all three wrist postures during the Execution period. Our most notable observation is that the activity of most of the directionally-tuned neurons in the PMv was extrinsic-like ($n = 48/59$, 81%). That is, these neurons showed little or no shift in PD, as well as little gain modulation with changes in posture (Fig. 2B, Fig. 3A, Fig. 4A). The lack of a shift in PD and the small gain modulation with a change in posture clearly distinguished this group of neurons from the motor apparatus in the periphery and its associated intrinsic coordinate frame. In other words, the activity of this group of neurons appears to encode commands for the direction of wrist movement in space, independent of the wrist joint configuration or the pattern of muscle activity, which generates the movement. In contrast, we found relatively few neurons with activity that was extrinsic-like with gain modulation ($n = 7/59$, 12%) and even fewer intrinsic-like neurons ($n = 4/59$, 7%) with muscle-like or joint-like shifts in PD.

7. Contrasts in movement representations in M1 and PMv

Clearly, both M1 and PMv contained many neurons that were strongly related to step-tracking movements of the wrist. However, the populations of directionally-tuned neurons in the M1 and PMv showed striking differences in terms of the coordinate frames of their activity (Table 1). In PMv, a great majority (81%, 48/59) of the directionally-tuned neurons were extrinsic-like. This population of neurons appeared to form a rela-

tively homogeneous functional group in which the directional tuning and gain were largely uninfluenced by changes in posture (Fig. 3A, Fig. 4A). Thus, the activity of these neurons was strongly related to a spatial coordinate frame, independent of intrinsic variables of movement. In contrast, the motor representation in M1 was more varied. Some neurons (24%, 17/72) were extrinsic-like (Fig. 3B, Fig. 4B) and were quite similar to their counterparts in PMv. Other neurons (39%, 28/72) were muscle-like (Fig. 3B, Fig. 4C) and coded movement in a muscle-related coordinate frame (Fig. 3C, Fig. 4D). An equally large population (37%, 27/72) appeared to encode movement in a composite coordinate frame in which changes in forearm posture had little effect on their PD, but produced large modulations in gain (Fig. 4B).

Another salient difference between the two motor areas was that, on average, the movement-related activity of extrinsic-like neurons in the PMv occurred earlier than the corresponding activity in M1 (Kakei et al., 2001). All of these observations are consistent with the proposal that the PMv is involved in the spatial guidance of limb movements (Kurata and Hoshi, 1999; Kakei et al., 2001) and that it functions at an earlier stage of sensorimotor processing than M1 (Kakei et al., 2001).

Based on these results and the dense interconnections between the PMv and regions of posterior parietal cortex, and the M1 and PMv (e.g. Dum and Strick, 1991; Kurata, 1991; Matelli et al., 1986; Lu et al., 1994; Luppino et al., 1999), we suggest that the extrinsic-like activity of PMv neurons may be involved in the transformation of target location in a visual frame of reference into the direction of action needed to acquire the target in a motor frame of reference (Kakei et al., 2001). This proposal is similar to a prior suggestion that PMv neurons translate the visual features of an object into a potential motor action (Murata et al., 1997).

8. Sensorimotor transformation with gain modulation: a hypothesis

Recent modeling studies (Salinas and Abbott, 1995; Ajemian et al., 2001; Baraduc et al., 2001) have demonstrated that neurons with gain modulation could

Table 1
Types of directionally-tuned neurons in M1 and PMv

	Extrinsic-like[a]	Extrinsic-like with gain modulation[b]	Muscle-like	Total neurons
M1	17	27	28	72
PMv	48	7	4	59

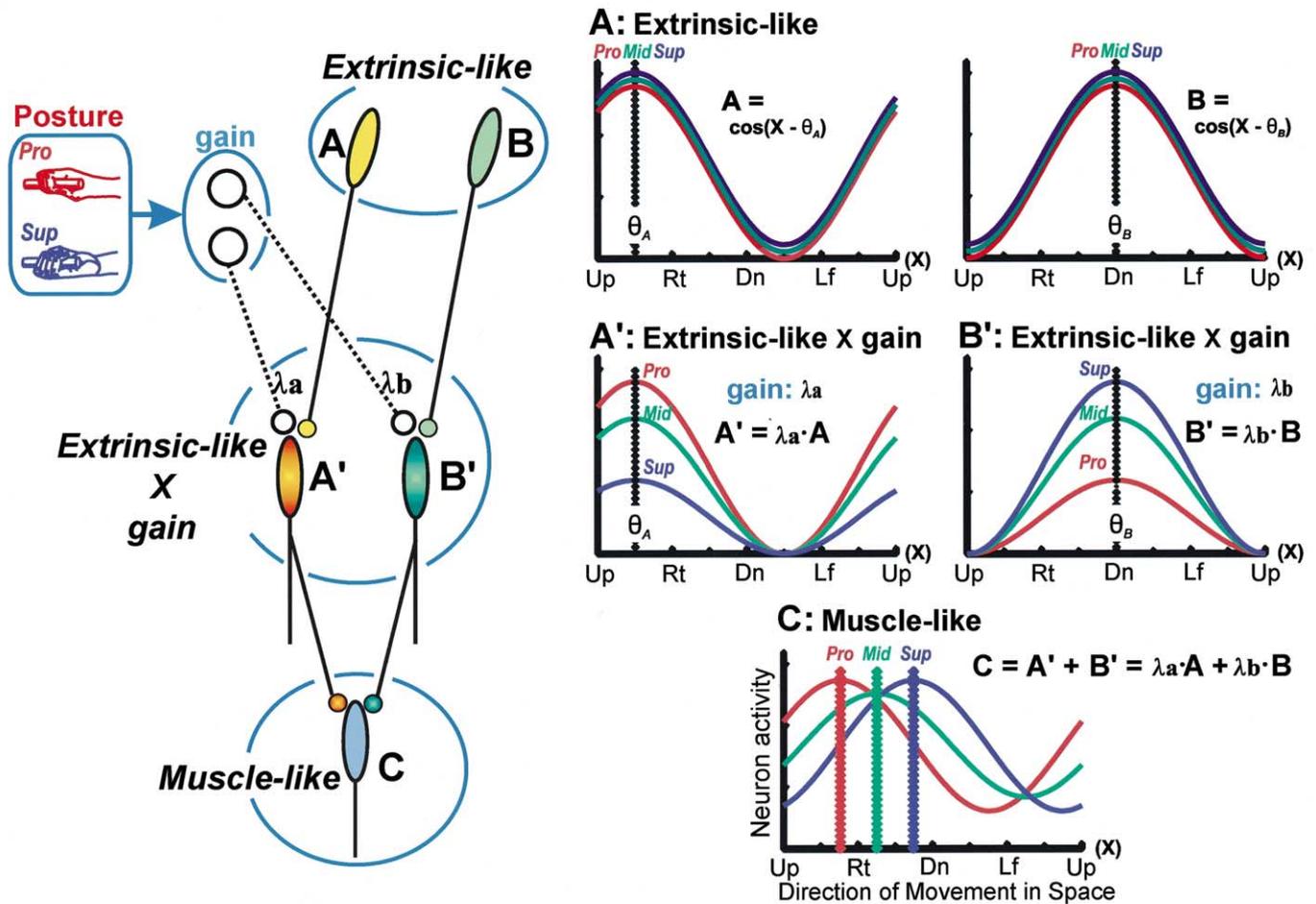[a] Gain modulation $< 30\%$.
[b] Gain modulation $> 30\%$.

Fig. 5. A simple model that derives muscle-like shifts in PD from activity of two types of Extrinsic-like neurons. Left: model of a neuronal circuit that explains a proposed relationship between Extrinsic-like neurons (A and B), Extrinsic-like neurons with gain modulation (A′ and B′) and Muscle-like neurons (C). Right: putative tuning curves of the model neurons. λ_a (the gain of neuron A′) for Pro, Mid and Sup are 1.0, 0.79 and 0.43, while λ_b (the gain of neuron B′) for Pro, Mid and Sup are 0.43, 0.79 and 1.0, respectively. See text for further explanation.

be effective in producing coordinate transformations. These modeling studies suggest that in M1, extrinsic-like neurons with gain modulation could represent a step in a sensorimotor transformation from an extrinsic coordinate frame to an intrinsic coordinate frame. Fig. 5 shows a model of how such a transformation might occur between M1 and PMv. In this model, A and B represent neurons that are 'extrinsic-like' and have different PDs. A′ and B′ represent neurons that are 'extrinsic-like with gain modulation'. Neuron A projects to A′, and these two types of extrinsic-like neurons have identical PDs. The same is true for neurons B and B′. Gain modulation of neurons A′ and B′ arises from separate Gain inputs (λ_a and λ_b, respectively) which change monotonically with forearm posture. In our model, the gain input to neuron A′ has a gradient which is highest in Pro and lowest in Sup. The gain input to neuron B′ has a different gradient, which is highest in Sup and lowest in Pro. The gain input and the extrinsic-

like input are multiplied in neurons A′ and B′ to give these neurons activity that is 'extrinsic-like with gain modulation'. A feasible way of producing multiplication of inputs may be through a recurrently connected network of neurons with additive synaptic inputs (Salinas and Abbott, 1996). Finally, the outputs from neurons A′ and B′ are summed linearly in neuron C. Neuron C shows a 'muscle-like' shift in PD when forearm posture is changed from Pro to Mid and then from Mid to Sup. The shift in PD of neuron C results from the graded contributions of neurons A′ and B′. This hierarchical model takes full advantage of the following points, (1) task-related neurons in M1 and PMv are cosine-tuned for movement direction regardless of their coordinate frames; and (2) the sum of two cosine functions with an identical cycle length (360°) produces another cosine function with the same cycle, although its PD and peak amplitude may vary. It should be noted that Fig. 5 is intended to provide a simple

model of a mechanism for producing a muscle-like shift in PD. By appropriate adjustment of the gains of the neurons that are extrinsic-like with gain modulation, this two-neuron model also can account for gain modulation of the muscle-like neurons. Note that as long as we keep the ratio of the two gains constant, the amount of shift in PD will remain unchanged.

This model suggests a putative relationship among the three types of neurons. A key feature of our model is that neurons with gain modulation are able to generate a transformation of coordinate frames. One way to test this model is to use multi-unit recording techniques to examine correlations in the activity of the different types of neurons. We are currently testing this possibility.

9. Conclusion

The neural mechanisms that produce coordinate transformations in order to generate a goal-directed movement have been a central issue in motor research for decades. Our results suggest that cortical processing between M1 and PMv may be involved in the coordinate transformation between extrinsic and intrinsic representations of wrist movements. Furthermore, an important step of this transformation could include a neuronal process that combines a spatial movement representation with gain factors that are modulated by forearm posture.

Andersen et al. (1985) found that activity of neurons in parietal area 7a is a function of both the retinotopic position of a target and the position of the eye in the orbit. They demonstrated that the retinotopic responses of area 7a neurons are systematically modulated with the eye position, and described the gain fields of individual neurons. Their results suggested that target location in a retinotopic coordinate frame is transformed into target location in a head-centered coordinate frame using modulations in gain that are dependent on eye position signals. Our results suggest that a similar mechanism may play an essential role in M1 and PMv to produce sensorimotor transformations between space based and muscle based coordinate frames.

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