

A multi-level approach to understanding upper limb function

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Abstract: Here we describe a multi-level approach to study upper limb control. By using non-human primates we were able to examine several different levels of motor organization within the same individual including their voluntary behavior, musculoskeletal plant, and neural activity. This approach revealed several parallels in the global patterns of activity of upper arm muscles and neurons in primary motor cortex (M1). For example, during postural maintenance both arm muscles and arm-related M1 neurons exhibit a bias in torque-related activity towards whole-limb flexion and whole-limb extension torque. A similar bias could be reproduced with a mathematical model of muscle recruitment that minimized the effects of motor noise suggesting a common constraint for the population activation of muscles and cortical neurons. That said, M1 neurons were not merely “upper motor neurons” as they exhibited substantial context-dependency in torque-related activity compared to arm muscles. This flexible association with low-level processing is consistent with M1 having a pivotal role in an optimal feedback controller.

Keywords: primary motor cortex; posture; reaching; monkey; muscle activity

Introduction

A truism of motor control is that it is highly complex and involves multiple levels of organization (Fig. 1). One basic level of motor organization is the behavioral goal or the target state of our actions. Notably, behavioral goals are often composed of a constellation of more specific subgoals as “driving a car” is subserved by lane and speed control which are likewise subserved by coordinated arm and leg movements. A second level is the neural circuitry that supports behavioral goals.

The neural network underlying voluntary behavioral goals is highly distributed and includes cerebral and subcortical structures. The last basic level is the peripheral apparatus of muscles, tendons, and skeletal structure. Importantly, an animal's peripheral apparatus has evolved to support particular behavioral goals as exemplified by the specialization of the human hand and kangaroo hindlimb for prehension and hopping, respectively. In sum, behavioral goals, neural circuits, the peripheral apparatus are three basic and inter-related levels of motor organization.

A central problem that confronts motor control researchers is how to fruitfully study this multi-leveled complexity (Scott, 2003). We feel it is

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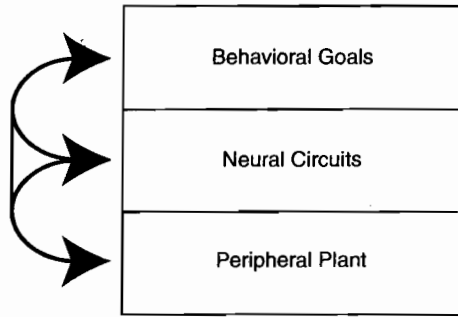


Fig. 1. Framework for examining upper limb function. Cartoon of a putative multi-level organization and the interactions between different levels.

essential to understand each level in order to understand the whole and, consequently, have employed a multi-level approach to study upper limb function. The use of behaving macaque monkeys (in our case, *Macaca mulatta*) is central to this paradigm and allows us to utilize simple behavioral tasks, monitor task-related muscular/neural activity, and examine the musculoskeletal properties in the same individuals. Monkeys are also an invaluable animal-model of human sensori-motor function given their close evolutionary kinship, trainability on arbitrary/complex tasks, dominant use of vision for guiding action, and similar motor repertoire to humans, e.g., ability to reach and grasp objects. Hence, the mechanisms identified from these studies can be readily extended to human studies of motor performance and learning.

Throughout our studies we constrain the upper limb to motion in the horizontal plane as a compromise between single-joint and unconstrained tasks (Fig. 2A) (Scott, 1999). Single-joint studies can be rigorously controlled (Evarts, 1968; Thach, 1978; Cheney and Fetz, 1980) but cannot examine the rich pattern of multi-joint coordination (Hollerbach and Flash, 1982). In contrast, unconstrained tasks involve multiple degrees of freedom but exert far less experimental control (Georgopoulos et al., 1982; Moran and Schwartz, 1999). Our approach limits the limb's motion to flexion and extension at the elbow and shoulder so that we can readily identify the limb's dynamics and examine multi-joint coordination. Although similar paradigms have been extensively used in human studies (Morasso, 1981; Hollerbach and

Flash, 1982; Karst and Hasan, 1991; Gordon et al., 1994; Shadmehr and Mussa-Ivaldi, 1994; Sainburg et al., 1999; Flanagan and Lolley, 2001; Singh and Scott, 2003), they are surprisingly rare in monkey studies. The following three sections summarize our results on musculoskeletal mechanics, task-related activity in muscles, and the parallel/unique aspects of cortical processing related to the primate upper limb.

Section 1: Global features of upper limb mechanics

The non-neural "plant" of the motor system is comprised of a complex musculoskeletal system. Since the intrinsic properties of this plant have co-evolved with a species' behavioral goals, its influence on motor function is undoubtedly deep and qualifies any cross-species comparison of motor function. To address this issue our lab undertook several studies on the segmental dynamics and muscle properties of the macaque upper limb.

Limb dynamics

The relation between joint motion and joint torque is qualitatively different between single- and multi-joint systems. Whereas torque and motion are linearly related in a single-joint system, inter-joint coupling allows single-joint torque to induce multi-joint motion and multi-joint torque to induce single-joint motion. Such multi-joint dynamics can be formally represented by a coupled set of complex non-linear equations (Hollerbach and Flash, 1982) that allows us to recognize important component terms including centripetal forces, the combined mass of both segments, and position-dependencies. A more heuristic understanding can be gained by examining the co-varying patterns of joint torque, joint motion, and hand motion in a familiar behavioral task (Buneo et al., 1995; Gottlieb et al., 1997). Note that movement-dependent torque cannot be directly measured but can be calculated with linked-segment models (Scott, 1999) and morphometric tables to scale the size dimensions of individual segments into inertial estimates (Cheng and Scott, 2000). Applying the following procedures to center-out movements revealed

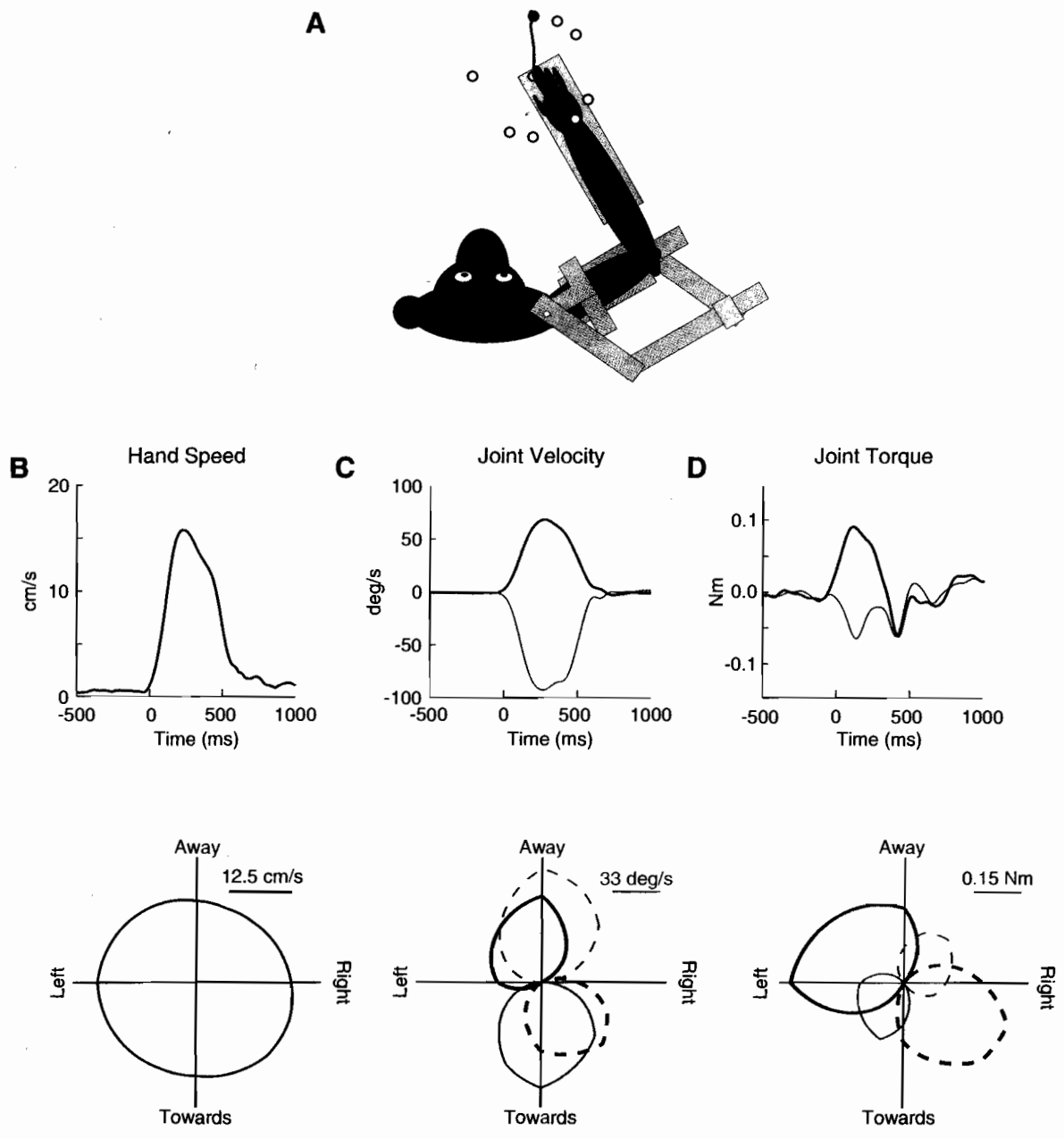


Fig. 2. Limb mechanics during center-out reaching. (A) Schematic of a monkey in the KINARM device to scale and target arrangement during the center-out reaching task. The targets had a non-uniform distribution in hand-space to allow a more uniform distribution in joint space. The thick trace shows an exemplar hand path to the target directly in front of the starting position, filled circle. (B–D) Measured limb mechanics: hand velocity, joint motion, and joint torque. Top panels show kinematics/kinetics from exemplar reach. Bottom panels show data across all targets depicted in polar coordinates of magnitude and angular position; magnitude indicates the average value between movement onset and peak hand velocity whereas angular position indicates the direction of hand motion. Thick and thin lines denote the shoulder and elbow joint, respectively. Flexion and extension are denoted by solid and dashed lines, respectively. All data is from one representative monkey.

several significant patterns in the monkey forelimb (Graham et al., 2003a).

Monkeys were trained to move their hand from a central start position to a peripheral target (Fig. 2A). Since reinforcement depended on endpoint timing and accuracy the monkeys adopted similar peak hand speeds and movement times across target direction (Fig. 2B). In contrast to the hand-based kinematics, joint motions changed substantially with target direction (Fig. 2C). Maximum joint velocities and joint displacements occurred near the fore-aft axis with elbow velocity being ~50% greater than shoulder velocity. Elbow flexion and extension was greatest towards and away from the body whereas shoulder flexion and extension was greatest away/slightly-left and towards/slightly-right of the body. The combined shoulder-elbow motion is about four times greater for movements towards or away from the body as compared to movements to the left or right. This mapping reflects the "inefficiency" of opposing flexion and extension at the shoulder and elbow to cause a net hand displacement towards or away from the body (Graham et al., 2003a).

The muscular torque generated at the shoulder and elbow also exhibited significant non-uniformities across target direction (Fig. 2D). The combined muscular torque of the two joints is about two times greater for movements to the left or right compared to movements towards or away from the body. The largest shoulder torque occurs for movements away and to the left, and movements towards and to the right. Elbow torque is maximal in the opposite directions (away and to the right, and towards and to the left) at about half of the magnitude observed for the shoulder. And as previously mentioned, joint motion does not necessarily equal joint torque in a multi-joint system. During movements to the left and away from the body, elbow extension occurs from purely shoulder-flexion torque whereas movements directly right involve negligible elbow motion but significant elbow torque, approximately half that of the shoulder.

This task presents several similarities to human studies. First, the monkeys reached with gently curved hand paths and single-peaked velocity profiles as observed in human studies (Morasso,

1981). Second, their small movement amplitudes (6 cm) were appropriate for the monkeys' smaller size (shoulder-elbow length ~30 cm) (Cheng and Scott, 2000) when compared to the movement amplitudes in human studies (between 4 and 30 cm); a typical length for the shoulder and elbow in the adult human is ~55 cm (Diffrient et al., 1978). Moreover, the similar arm geometry of monkeys led to comparable patterns of kinematics and kinetics to those in human studies (Buneo et al., 1995; Gottlieb et al., 1997). The main difference in limb dynamics is the smaller mass of the monkey's arm (~1/7th of human) leading to a much lower moment of inertia, ~1/40th of humans!

Muscle morphometry

All mammalian skeletal muscle exhibits dynamic properties that constrain the efficacy of motor commands. These include a time-dependent transformation of neural excitation into activation of the molecular motors (activation dynamics) and from the molecular motors into muscle force (contraction dynamics) (Zajac, 1989). Muscle force also reflects a complex function of the muscle's length and velocity (Rack and Westbury, 1969; Scott et al., 1996). In brief, the peak active force of a muscle occurs at a single length whereas shortening and lengthening velocities result in decreases and increases in muscle force, respectively.

The close evolutionary kinship of humans and old-world monkeys ensures several additional similarities in their proximal arm musculature (Graham and Scott, 2003b). Both possess the same 14 arm muscles for flexion-extension at the elbow-shoulder, excepting a biarticular (dors-oeipitrochlearis) that non-human primates use for arboreal ambulation. Also, the tendons of both monkey and human arm muscles are relatively short precluding significant energy storage as in the kangaroo hindlimb (Zajac, 1989).

When comparing between human and monkey muscles the most significant difference is their relative strength. Monkey muscles have a much larger physiological cross-sectional area (PSCA) when scaled to body-weight than humans, between 8 and 10 times larger (Graham and Scott, 2003b).

These muscles are also composed of a large percentage of fast fibers (50%) (Singh et al., 2002), which allows efficient force production at high shortening velocities. The greater relative strength and lower limb inertia of monkeys allows them to generate much faster and more powerful movements than humans.

We observed several broad patterns across the monkey's upper limb muscles (Graham and Scott, 2003b; Graham et al., 2003a). The passive torques of the elbow and shoulder (which includes moment arms, tendon slack length, and optimum fascicle length of all spanning muscles) are well described by simple cubic functions. Second, the zero torque-intercept of these cubic functions — approximately 90° elbow angle and 30° shoulder angle — is near the muscles' optimum fascicle angle — approximately 100° elbow angle and 0° shoulder angle. A third general pattern is that the maximum torque that can be produced at the shoulder and elbow varies systematically and symmetrically with its joint angle: greater flexion/extension elbow torque occurs with greater flexion, and greater flexion/extension shoulder torque occurs with greater extension.

The broad patterns just described strongly contrast with the significant diversity among the individual arm muscles (Graham and Scott, 2003b). Biceps brachii longus and triceps brachii longus both span the shoulder and elbow joint but closer examination reveals that biceps has a greater effect on the elbow (~3:1) whereas triceps has far greater affect on the shoulder (~3:1). The moment arms of the limb's muscles also include increases, decreases, minimal change, and even non-monotonic changes with elbow and/or shoulder angle. Finally, the diverse properties of muscles can even lead to similar effects through reciprocal contributions that balance each other out. Brachioradialis and brachialis (both elbow flexors) have significant differences in their PSCA and moment arm but possess a similar torque capability since these differences are reciprocal, small cross-section/large moment arm and large cross-section/small moment arm.

In sum, the upper arms of monkeys and humans possess similar mechanical and muscular properties. The following section will describe how the

most salient properties of the peripheral plant (including the non-uniform joint mechanics and muscle dynamics) shape the patterns of muscle activity during voluntary motor tasks.

Section 2: Task-related activity of upper limb muscles

A thorough understanding of an organism's peripheral apparatus is insufficient for predicting its pattern of motor behavior. This gap reflects, in part, the well-known “degrees of freedom” problem (Bernstein, 1967). A single motor task such as “reaching for a cup” can be achieved by many different joint trajectories. The fact that multiple muscles have a similar mechanical action also ensures that a particular joint torque can be achieved by many different patterns of muscle activity. To address this issue we examined muscle activation of the monkey upper limb during two basic tasks: postural maintenance and point-to-point reaching. Importantly, we applied loads to the shoulder and elbow joints via a custom robotic exo-skeleton (KINARM, BKIN Technologies, Kingston) allowing us to examine muscular (and neural) activity associated with load compensation at each joint and during multi-joint loads.

Posture task

During the postural task the animal maintained a fixed hand position while countering flexion and extension loading of their shoulder and/or elbow joints (Cabel et al., 2001; Herter et al., 2007). Since the limb kinematics were effectively fixed changes in muscular activity could be related specifically to the change in joint torque. The most significant finding was that a muscle's activation pattern could differ from its anatomical action (Kurtzer et al., 2006b). For example, brachioradialis varied its activity with torque at the shoulder even though it lacked any direct mechanical action at that joint (Fig. 3A). This anatomical elbow flexor was maximally activated by a combination of elbow flexor and shoulder extensor torque. A similar bias in preferred torque direction (PTD) was observed for the entire sample of monoarticulars — shoulder

extensors and elbow flexors were maximally active with shoulder-extension/elbow-flexion and shoulder flexors and elbow extensors were maximally active with shoulder-flexion/elbow-extension torque.

Moreover, the PTDs of biarticular extensor and flexor muscles were not directed to extension-extension and flexion-flexion torques (as one might expect from their moment arms) but towards

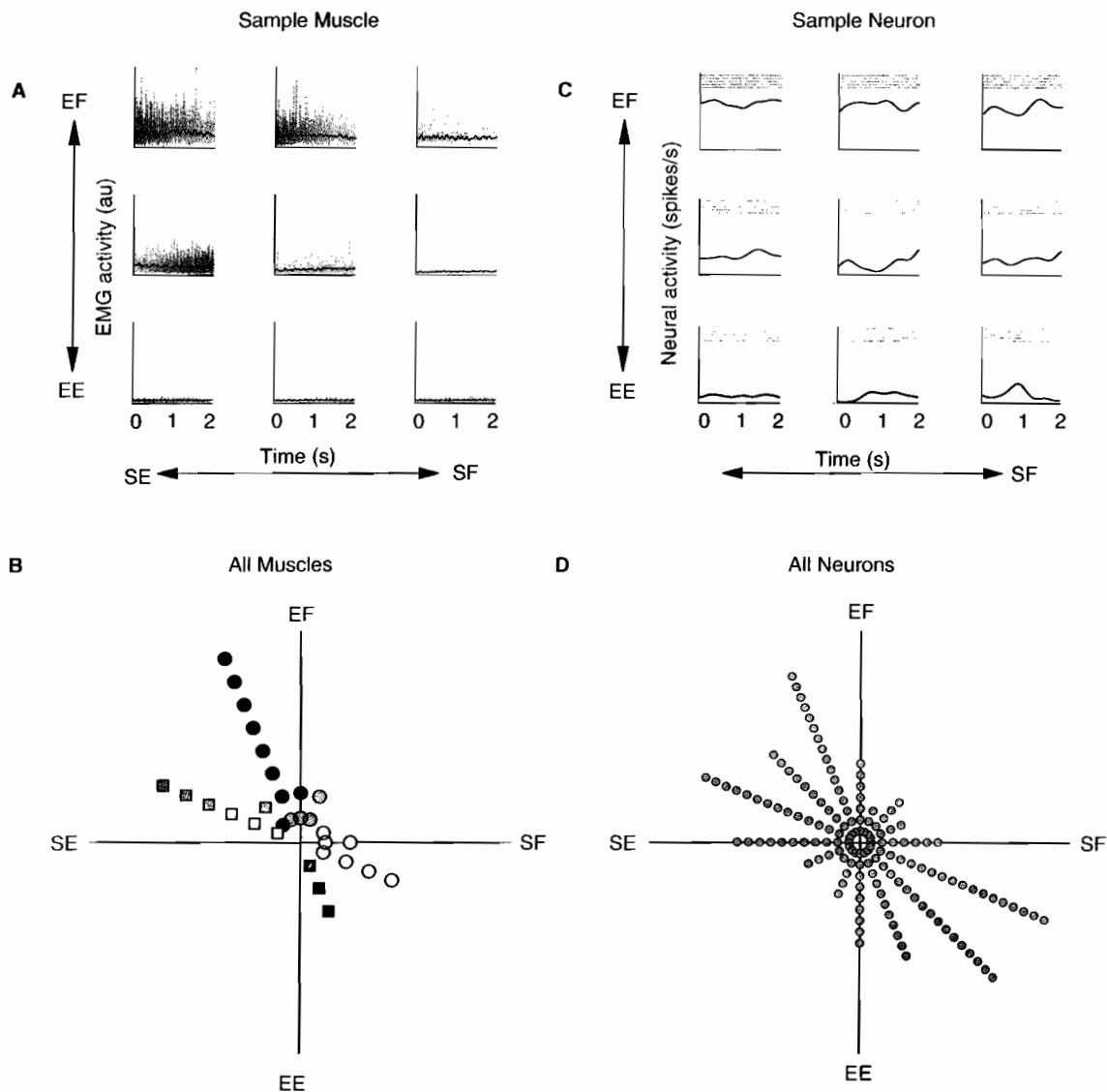


Fig. 3. Torque-related activity during the posture task. (A) Activity of a sample muscle (elbow flexor/brachioradialis) during the nine load conditions of shoulder-elbow torque. The load conditions are presented in a particular coordinate system: shoulder flexion is 0° , elbow flexion is 90° , shoulder extension is 180° , and elbow extension is 270° . Note that the muscle's maximal activity is directed towards elbow-flexion and shoulder-extension. (B) Polar histogram summarizes the preferred torque direction (PTD) from all sampled muscles during the posture task. Each muscle's PTD is represented by a single icon within an angular bin (16 bins of 22.5° used throughout figures). White, black, and gray symbols indicate shoulder monoarticulars, elbow monoarticulars, and biarticulars; circles and squares indicate flexors and extensors. (C) Sample neuron during the posture task. Same format as A. (D) Polar histogram summarizes the PTDs from all sampled neurons during the posture task. Same format as B. Gray circle denote neurons. (Panels A, B adapted from Kurtzer et al., 2006b; Panel C adapted with permission from Kurtzer et al., 2005.)

shoulder-extension/elbow-flexion torques. The resulting global pattern of upper limb muscle activity was a bimodal distribution of PTDs to shoulder-extension/elbow-flexion and shoulder-flexion/elbow-extension torque (Fig. 3B).

Our results are consistent with earlier dissociations of muscle function and action in the monkey wrist (Hoffman and Strick, 1999), human leg (Nozaki et al., 2005), and human arm (van Zuylen et al., 1988; Buchanan et al., 1989). Several of these previous studies (such as Fagg et al., 2002; Nozaki et al., 2005) have suggested that this dissociation reflects an optimization process for muscle coordination. We tested whether a similar process could account for our results. In brief, a lumped representation for the six muscle groups — shoulder extensor, shoulder flexor, elbow extensor, elbow flexor, biarticular flexor, biarticular extensor — was employed using known values for the monkey moment arms, fascicle length and PCSA (Cheng and Scott, 2000; Graham and Scott, 2003b). The model was further constrained so that conditions were isometric and muscles could only pull. Finally, an iterative procedure scaled each muscle group's activity to achieve a target torque with the minimal muscle noise $\sum(\text{force}_i^*/\text{PCSA}_i)^2$ (JHarris and Wolpert, 1998; van Bolhuis and Gielen, 1999; Hamilton et al., 2004) also equivalent to muscle stress (van Bolhuis and Gielen, 1999).

The optimization model successfully predicted PTD rotations towards shoulder-flexion/elbow-extension and shoulder-extension/elbow-flexion torque (Fig. 4). In fact, a similar PTD bias will result from minimizing any number of different variables related to muscle activity such as metabolic energy and muscle force (Kurtzer et al., 2006b). Consider if several muscles can contribute to a particular agonist torque then each can be activated at relatively low levels. But if fewer muscles can contribute then each must have a higher relative activity. And since biarticular muscles in the primate proximal forelimb generate extension–extension and flexion–flexion torques this leads to a PTD bias towards the “gaps” in torque space, i.e., shoulder-extension/elbow-flexion and shoulder-flexion/elbow-extension torque. It should be noted that although the model qualitatively accounts for

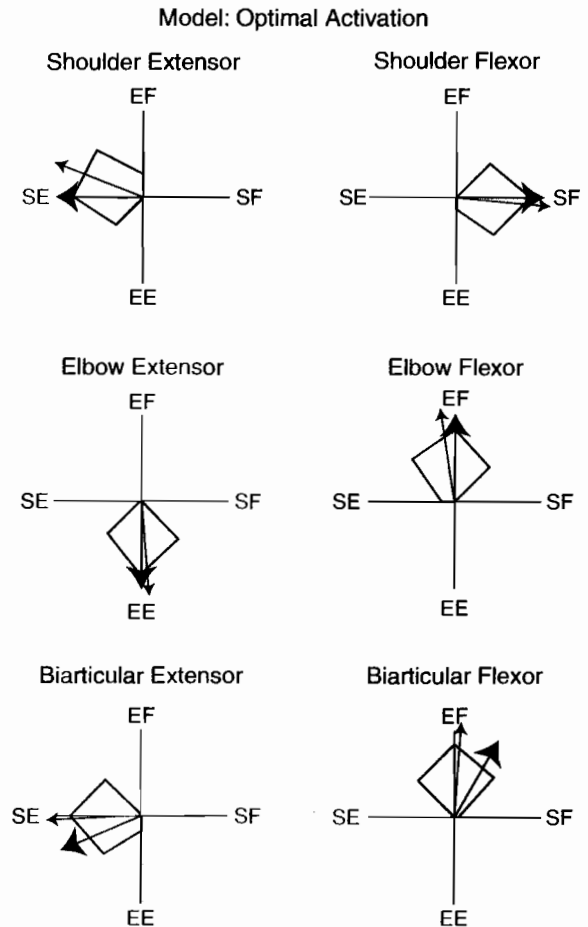


Fig. 4. Modeled activation of muscles during posture task. (Adapted with permission from Kurtzer, 2006b.) Panels illustrate the predicted activation when minimizing net muscle noise. Large and small arrows indicate anatomical action and PTD of each “muscle group”: shoulder flexors/extensors, elbow flexors/extensors, and biarticular flexors/extensors.

PTD rotations, (in our hands) it underestimated the magnitude of rotation and did not predict the relative amount of rotation on a muscle group by muscle group basis.

Reaching task

Inferring the function of muscular activity during multi-joint movement is complicated by inter-segmental and muscular dynamics (Zajac and Gordon, 1989). However, one can “factor out”

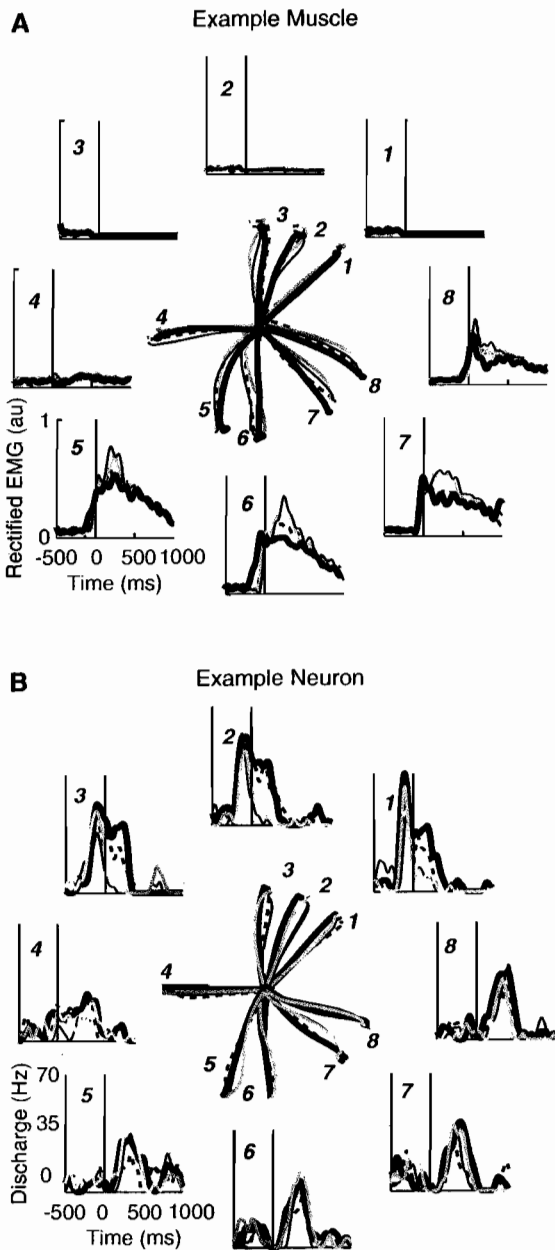


Fig. 5. Activity during the reaching task. (A) Center panel shows the hand path during reaching movements to the eight targets depicted in Fig. 2A. Different lines denote the different load conditions: unloaded (thick black), viscous shoulder (dashed), viscous elbow (gray), and viscous both (thin black). Peripheral panels show associated activity of a sample muscle (elbow flexor/brachioradialis). Here the greatest activity during unloaded reaching occurs towards the body whereas the different load conditions lead to further increases in activation near this

the complex transformation of muscle activity to joint torque by enforcing similar movement patterns under different load conditions. Any change in activity between conditions can then be related specifically to the changes in load across conditions (Gribble and Scott, 2002). This novel paradigm revealed that upper arm muscles often exhibited changes in activity across the different load conditions during a reaching task. An example muscle is shown in Fig. 5A. Moreover, comparing the change in activity versus the change in joint torque revealed that the muscles' PTDs deviated from their anatomical action towards shoulder-flexion/elbow-extension and shoulder-extension/elbow-flexion torques (Fig. 6A) (Kurtzer et al., 2006a). Hence, the muscles exhibited the same torque bias during reaching as seen during in the posture task (Fig. 3B).

Another striking result was that during unloaded reaching the monoarticular and biarticular arm muscles were mostly active for movements towards or away from the body (Kurtzer et al., 2006a). Single-joint elbow flexors and extensors had preferred hand directions (PHDs) towards and away from the body, respectively (Figs. 5A and 7A). In contrast, the single-joint shoulder flexors and extensors had PHDs away/slightly-left and towards/slightly-right, respectively. Importantly, the muscles' PHDs better mirrored the fore-aft orientation of joint motion than the left-right orientation of the joint torque (Fig. 2B, C). Without knowing that these responses reflected the activity of force generators one could wrongly conclude that muscles were encoding joint velocity!

So how did the muscles' PHDs come to match joint velocity better than joint torque? This bias likely reflects the impact of several factors already identified. Reaching movements in the fore-aft axis require the fastest joint velocities and largest joint displacements. Since greater activity is necessary to

preferred hand direction. (B) Center panel shows the hand path from a different session. Peripheral panels show associated activity of a sample neuron. Its greatest (initial) activity during unloaded reaching occurs away from the body and the different load conditions lead to decreased activation to targets near the PHD. (Panel A adapted with permission from Kurtzer et al., 2006a.)

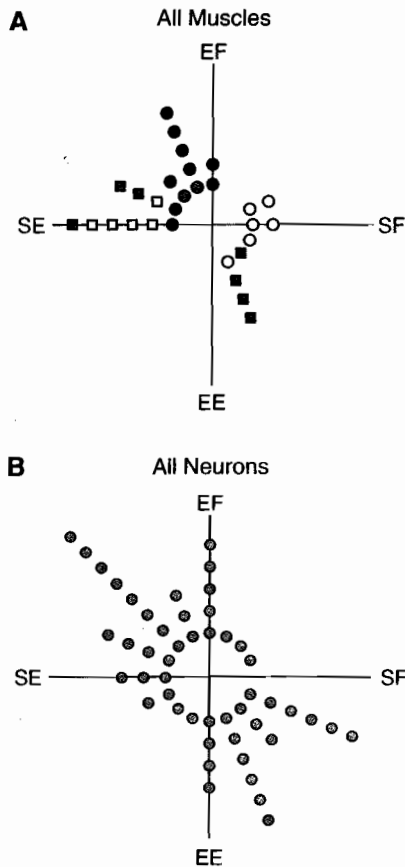


Fig. 6. Summary of observed and simulated preferred torque directions during reaching. Polar histograms of preferred torque directions determined by comparing change in activity to change in torque between unloaded and load reaching movements. (A, B) PTDs from sampled muscles and sampled neurons. Same icons and format as Fig. 3B. (Panel A adapted with permission from Kurtzer et al., 2006a.)

compensate the velocity-dependent drop in force and length-dependent resistance to center-out displacements, the additional activity in these directions is measured as a PHD bias to the fore-aft axis. Another likely factor for the fore-aft bias of muscles' PHDs is their bias in load-related activity towards shoulder-flexion/elbow-extension and shoulder-extension/elbow-flexion torques. Since these torque combinations occur with movements towards and away from the body (Fig. 2B, C), then the torque bias again induces a spatial bias to the fore-aft axis.

In fact, we could reproduce the fore-aft bias of PHDs (Fig. 7C) with a model of muscle activation that included length- and velocity-dependent properties and a recruitment strategy that minimizes the total muscular activity (Kurtzer et al., 2006a), i.e., an expansion of the model used for the posture task. Without accounting for the known muscle properties or interactions among muscles the PHDs simply mirror the left-right bias of the joint torque (Fig. 7D).

In sum, we observed that the salient features of the peripheral plant — included non-uniformities in joint mechanics, muscle dynamics, and muscle redundancy — shaped the activity of muscle during voluntary tasks. The following section will compare and contrast these patterns of activity with those of primary motor cortex.

Section 3: Relation to motor cortical processing

Over a century of research has established a significant role for primary motor cortex in voluntary motor control (Hepp-Reymond, 1988; Porter and Lemon, 1993; Scott, 2003). Anatomically, M1 possesses an intimate link with the motor periphery including somatosensory inputs (Wong et al., 1978; Asanuma et al., 1979) and a dense output to intermediate spinal lamina and a small direct input to motor neurons (Fetz and Cheney, 1987; Dum and Strick, 1991; Lemon and Griffiths, 2005). The specific functional role of M1 is less apparent due to feedback effects, the complexity of the musculoskeletal properties, and the many roles for spinal processing. However, many M1 neurons clearly exhibit muscle-related activity. Cortico-muscular associations include frequency coherence between EMG and cortical oscillations (Baker et al., 1999), steady-state activity in M1 linked to static load requirements (Evarts, 1968; Smith et al., 1975; Thach, 1978; Fromm, 1983), and time-varying activation linked to the dynamic load requirements and muscle activity (Morrow and Miller, 2003; Sergio and Kalaska, 2005). Here we add to this rich story by demonstrating parallels and contrasts in their global patterns of reach- and torque-related activity.

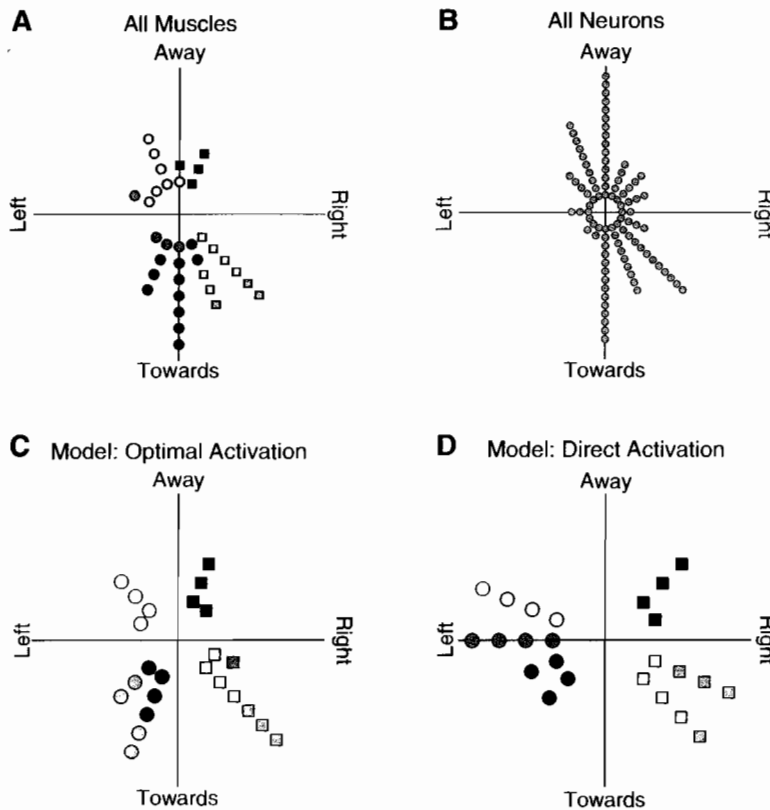


Fig. 7. Summary of preferred hand directions during reaching. Polar histograms of preferred hand directions during unloaded reaching movements. (A, B) PHDs from sampled muscles and sampled neurons. Same icons as Fig. 3B (Panel A adapted with permission from Kurtzer et al., 2006a). (C, D) PHDs of simulated muscles when including both muscle properties and a minimization criterion (Optimal Activation) or directly matching the required torque (Direct Activation).

Similarities in global activity

As described in the previous section, arm muscles exhibited several distinctive patterns of activity during postural maintenance and reaching tasks. Upper arm muscles were maximally activated with shoulder-flexion/elbow-extension and shoulder-extension/elbow-flexion torques while countering joint loads in a fixed limb posture (Kurtzer et al., 2006b). This pattern was recapitulated in the population activity of M1 neurons (Fig. 3C, D) from the same animals (Cabel et al., 2001; Herter et al., 2007). It should be emphasized that this similarity was not an entirely foregone conclusion. In principle, the complex connectivity inherent in M1 could allow it to preferentially represent single-joint torques, or equally represent all torque

combinations, or offset the whole-limb extensor bias of brainstem structures controlling quadrupedal stance.

Further parallels were observed during visually guided reaching. In the unloaded condition, M1 neurons typically had a preferred hand direction near the fore-aft axis (Figs. 5B and 7B) (Scott et al., 2001) as previously shown for arm muscles (Figs. 5A and 7A) (Kurtzer et al., 2006a). Moreover, many of these M1 neurons exhibited changes in activity when reaching across different load conditions with an overall trend of PTD biased to shoulder-flexion/elbow-extension and shoulder-extension/elbow-flexion torques (Kurtzer et al., 2006a). Hence, the global pattern of reach- and torque-related activity was similar for M1 neurons and arm muscles.

Note that this mirroring relation during posture and movement tasks does not imply a point-to-point mapping where M1 neurons are merely upper motor neurons. Rather, it suggests that there are similar constraints on the activation of muscles and cortical neurons — such as minimizing the effects of motor noise, the motion-dependent aspects of muscle force, and the mechanics of multi-joint movements.

Context-dependent cortical activity

While several parallels exist between muscular and (some) M1 activity it should be emphasized that M1 neurons express a diverse range of activity patterns and there is no ideal M1 neuron (Scott, 2003). Some, but not all, M1 neurons receive strong somatosensory inputs. Some, but not all, are modulated with muscle force. And some M1 neurons are sensitive to events at a single joint whereas others reflect events across multiple joints. This diversity likely reflects the many possible roles for M1 in spinal processing — an afferent template to fusimotor neurons, gating of sensory input, and setting muscle tone — in addition to providing patterned input to alpha motor neurons. In addition, M1 neurons show an impressive degree of plasticity not present in limb muscles (Sanes and Donoghue, 2000; Li et al., 2001; Scott, 2003; Paz et al., 2004); short-term adaptation paradigms (~5–15 min) can focally alter a neuron's tuning orientation and shape whereas long-term practice or trauma (days to months) can even affect how much cortical area subserves a particular effector.

Our studies have extended this diverse range in M1 processing to include how neurons process torque-related information across different behavioral tasks. A direct comparison of different behavioral tasks is typically compromised because of the intrinsic differences in kinematics such as between posture and movement. We addressed this issue by examining how neurons express torque-related activity, a salient non-movement feature. Interestingly, we observed a broad range of responses. Some neurons showed significant torque-related activity in both tasks (Fig. 8, left column). Other neurons only showed torque-related activity

during the reaching task and were wholly irresponsive to loads during posture (Fig. 8, center column). And still others only expressed torque-related activity during the posture task; their reach-related activity was unaffected by loads (Fig. 8, right column). In all, ~20% of M1 neurons were unaffected by load conditions (even though they expressed strong reach-related activity) whereas ~30% had torque-related activity in both tasks. The arm muscles showed a much more uniform pattern with almost all having load effects (97%) in at least one task and most in both tasks (64%). Further, neurons expressed torque-related decreases in activity during reaching equally often as increases whereas the muscular responses were dominated by increases in torque-related activity (Fig. 5A, B).

Another across-task comparison involved comparing different aspects of torque-related activity (Kurtzer et al., 2005). One aspect is the PTD, an index of the relative sensitivity to shoulder and elbow loads. Interestingly, PTDs of neurons and muscles were conserved across tasks with a mean absolute difference of 52° and 28°, respectively; a random pairing would have a mean of ~90°. [Note that larger inter-task correlations were observed when the animals countered a constant load during both posture and movement tasks (Kurtzer et al., 2005).] This implies that both neurons and muscles had a consistent relative effect at the motor periphery (Fig. 9A, C). In contrast, the absolute sensitivity to torque magnitude, or torque gain, was completely unpredictable across tasks for M1 neurons ($r = 0.13$) but highly similar for muscles ($r = 0.81$) (Fig. 9B, D); the greater load-sensitivity of muscles during reaching presumably reflects the force-velocity relation.

Summary and interpretation

The previous three sections elaborated on a multi-level approach to motor function whereby we could examine the peripheral apparatus, muscular activation patterns, and cortical processing within the same organism. This approach allowed us to compare and contrast the global properties of each level. Briefly, the limb's dynamics during unloaded reaching involved a significant non-uniformity at

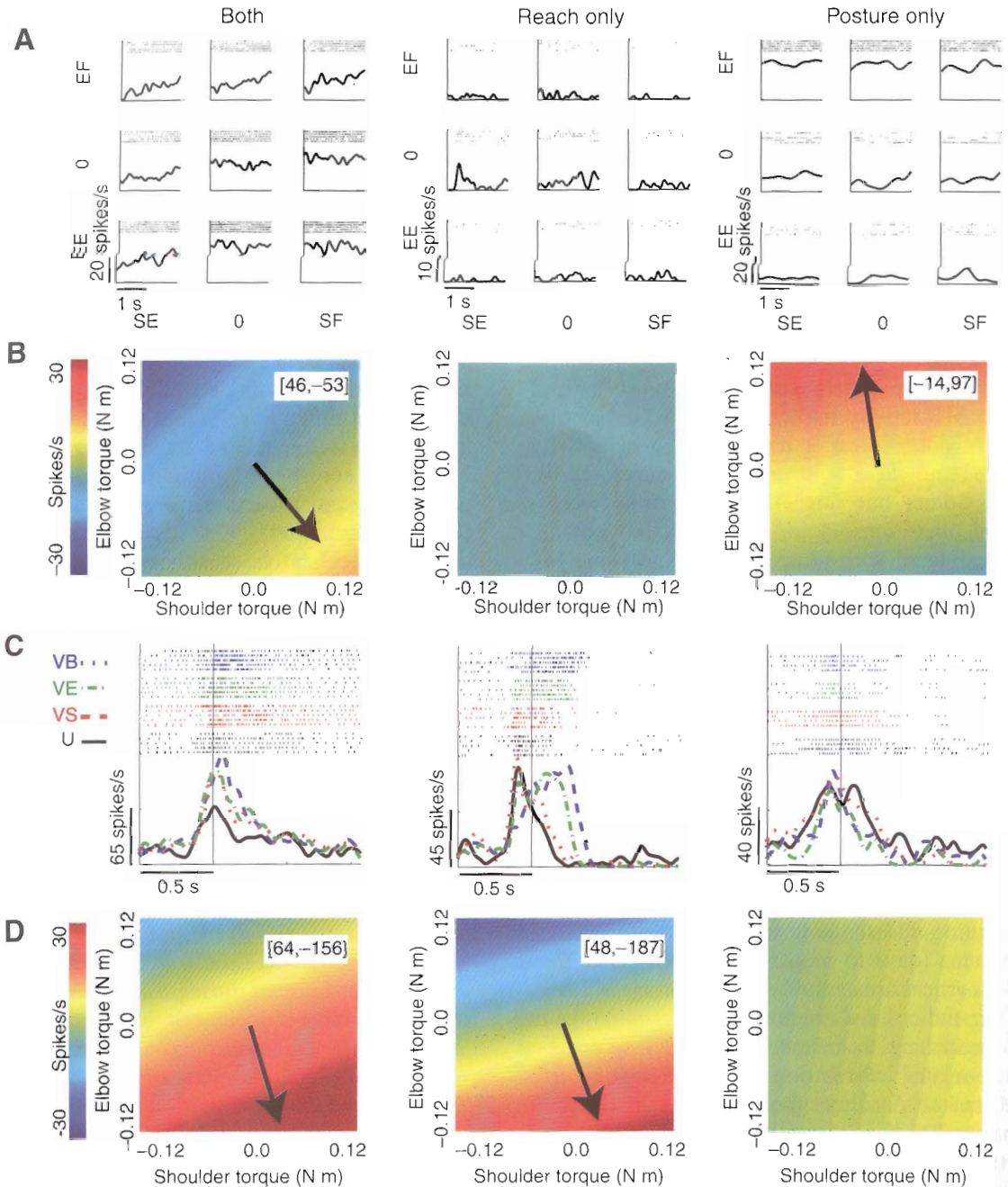


Fig. 8. Exemplar neurons exhibiting torque-related activity. Three sample neurons showing torque-related activity during both the posture and movement tasks (left column), only the movement task (center column), and only during the posture task (right column). (A) Activity during the posture task. (B) Planar regressions of torque-related activity during the posture task indicated by gradient. Arrows denote the PTD for significant torque-related activity. Numerical inset shows the change in activity versus the change in torque, large numbers indicate a high sensitivity to torque magnitude. (C) Activity during the reaching task to the target nearest the neuron's PHD during the viscous shoulder (VS), viscous elbow (VE), viscous both (VB), and unloaded (U) conditions. (D) Planar regressions of torque-related activity during the reaching task. (Adapted with permission from Kurtzer et al., 2005.)

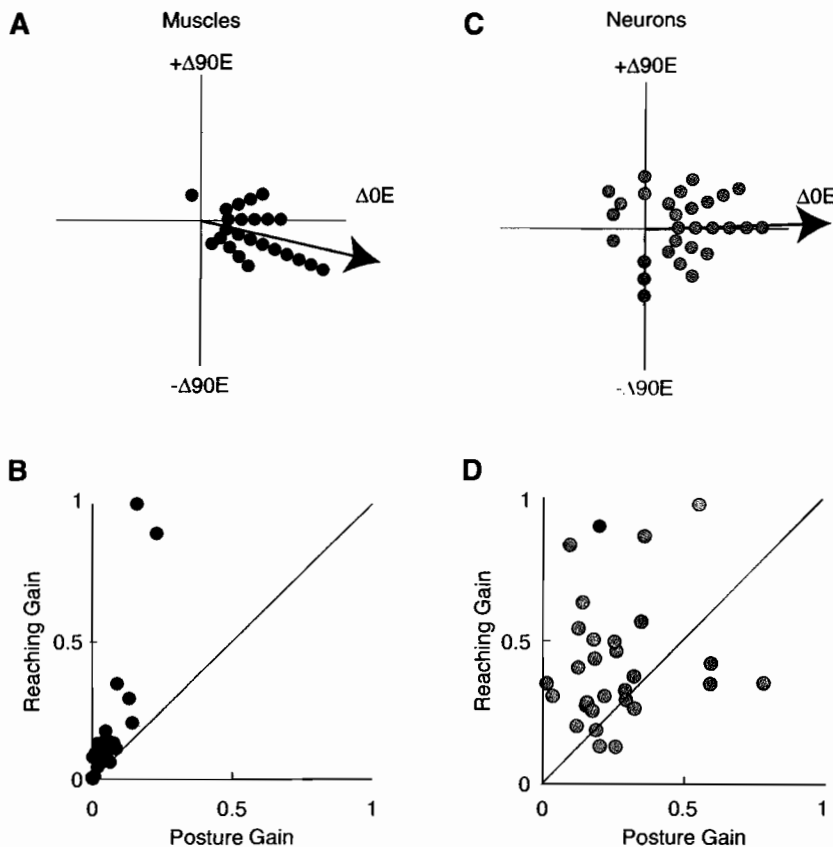


Fig. 9. Comparing torque-related activity across posture and reaching tasks. (A, B) Polar histogram of angular difference in preferred torque direction across tasks. Identical PTDs would be aligned to the right at $\Delta 0^\circ$. Data are shown separately for muscles and neurons (Panel B is adapted with permission from Kurtzer et al., 2005). (C, D) Linear regression of torque gain across tasks; unity line indicates an identical torque gain. Torque gain is the sensitivity to absolute magnitude of torque. Data is shown separately for muscles and neurons and is normalized to the peak gain. (Panel D is adapted with permission from Kurtzer et al., 2005.)

the joint level with larger combined joint torque with movement towards/right and away/left and larger joint motion in the fore-aft axis. This pattern was mirrored in the global pattern of both muscular and M1 activity. Second, the torque-related activity of muscles and M1 neurons tasks had an overall bias towards whole-limb flexor and whole-limb extensor torques which could be modeled as an optimization of muscle activity. And finally, M1 neurons (but not muscles) exhibited substantial changes in their torque-related activity between posture and movement contexts including specificity to a particular task.

On a more cautionary note, without adopting a multi-level approach to study the motor system

one is simply unable to identify (and experimentally control) the potential co-variations among these levels. For example, Georgopoulos and colleagues recently confirmed our observation of a fore-aft bias of preferred reaching directions by using an unconstrained 3D task though this only emerged when a very large number of neurons were sampled ($n > 1000$) (Naselaris et al., 2006). Without knowing how the limb behaves in its generative details, the authors could only interpret these findings as an augmented representation or “hyperacuity” of particular spatial directions. We suspect that limb mechanics remains an important factor regardless of whether movements are performed in the plane or throughout 3D space and

that the factors we have identified provide a simpler explanation for their observation. However, unraveling the link between neural processing and limb mechanics for 3D movements is fraught with many caveats and pitfalls due to the rapid escalation in mechanical complexity.

While our observations elaborate the significant parallels between multiple levels of motor organization, they do not provide a theoretic framework. Such a theory would have to comfortably address several (apparently) disparate features. Why would M1 reflect the global features of the motor periphery? Why would M1 represent such a diverse range of "low-level" features? Why would these representations exhibit plasticity on so many time scales from behavioral context to long-term changes? And how do M1's substantial (and generally neglected) somatosensory inputs figure into this organization?

We are currently exploring the merits of optimal feedback control as theory of motor function (Scott, 2004). In broad strokes, optimal feedback control involves a modifiable sensory-motor mapping (or feedback law) that is tailor-made for the task at hand by balancing multiple conflicting demands such as speed, accuracy, and effort (Todorov and Jordan, 2002). The sensory inputs to this controller can also include multiple sources of information that are flexibly integrated with motor commands for predictive estimates. Thereby, optimal control can provide rapid "intelligent" responses that reflect "higher-level" goals using "low-level" representations. These aspects are broadly consistent with the known anatomy and physiology of M1 including the observations we've described throughout this chapter. Determining whether optimal feedback control is a heuristic framework requires careful experimentation and is the focus of our current research.

Abbreviations

M1	primary motor cortex
PHD	preferred hand direction
PSCA	physiological cross-sectional area
PTD	preferred torque direction

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References

- Asanuma, H., Larsen, K.D. and Zarzecki, P. (1979) Peripheral input pathways projecting to the motor cortex in the cat. *Brain Res.*, 172: 197-208.
- Baker, S.N., Kilner, J.M., Pinches, E.M. and Lemon, R.N. (1999) The role of synchrony and oscillations in the motor output. *Exp. Brain Res.*, 128: 109-117.
- Bernstein, N.A. (1967) *The Coordination and Regulation of Movements*. Pergamon Press, Oxford.
- van Bolhuis, B.M. and Gielen, C.C. (1999) A comparison of models explaining muscle activation patterns for isometric contractions. *Biol. Cybern.*, 81: 249-261.
- Buchanan, T.S., Rovai, G.P. and Rymer, W.Z. (1989) Strategies for muscle activation during isometric torque generation at the human elbow. *J. Neurophysiol.*, 62: 1201-1212.
- Bunco, C.A., Bolino, J., Soechting, J.F. and Poppele, R.E. (1995) On the form of the internal model for reaching. *Exp. Brain Res.*, 104: 467-479.
- Cabel, D.W., Cisek, P. and Scott, S.H. (2001) Neural activity in primary motor cortex related to mechanical loads applied to the shoulder and elbow during a postural task. *J. Neurophysiol.*, 86: 2102-2108.
- Cheney, P.D. and Fetz, E.E. (1980) Functional classes of primate corticomotoneuronal cells and their relation to active force. *J. Neurophysiol.*, 44: 773-791.
- Cheng, E.J. and Scott, S.H. (2000) Morphometry of *Macaca mulatta* forelimb. I. Shoulder and elbow muscles and segment inertial parameters. *J. Morphol.*, 245: 206-224.
- Diffrient, N., Tillery, A.R. and Bardagjy, J.C. (1978) *Human-scale*. MIT Press, Cambridge, MA.
- Dum, R.P. and Strick, P.L. (1991) The origin of corticospinal projections from the premotor areas in the frontal lobe. *J. Neurosci.*, 11: 667-689.
- Evarts, E.V. (1968) Relation of pyramidal tract activity to force exerted during voluntary movement. *J. Neurophysiol.*, 31: 14-27.
- Fagg, A.H., Shah, A. and Barto, A.G. (2002) A computational model of muscle recruitment for wrist movements. *J. Neurophysiol.*, 88: 3348-3358.
- Fetz, E.E. and Cheney, P.D. (1987) Functional relations between primate motor cortex cells and muscles: fixed and flexible. *Ciba. Found. Symp.*, 132: 98-117.

- Flanagan, J.R. and Lolley, S. (2001) The inertial anisotropy of the arm is accurately predicted during movement planning. *J. Neurosci.*, 21: 1361–1369.
- Fromm, C. (1983) Changes of steady state activity in motor cortex consistent with the length-tension relation of muscle. *Pflügers Arch.*, 398: 318–323.
- Georgopoulos, A.P., Kalaska, J.F., Caminiti, R. and Massey, J.T. (1982) On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *J. Neurosci.*, 2: 1527–1537.
- Gordon, J., Ghilardi, M.F. and Ghez, C. (1994) Accuracy of planar reaching movements. I. Independence of direction and extent variability. *Exp. Brain Res.*, 99: 97–111.
- Gottlieb, G.L., Song, Q., Almeida, G.L., Hong, D.A. and Corcos, D. (1997) Directional control of planar human arm movement. *J. Neurophysiol.*, 78: 2985–2998.
- Graham, K.M., Moore, K.D., Cabel, D.W., Gribble, P.L., Cisek, P. and Scott, S.H. (2003a) Kinematics and kinetics of multijoint reaching in nonhuman primates. *J. Neurophysiol.*, 89: 2667–2677.
- Graham, K.M. and Scott, S.H. (2003b) Morphometry of *Macaca mulatta* forelimb. III. Moment arm of shoulder and elbow muscles. *J. Morphol.*, 255: 301–314.
- Gribble, P.L. and Scott, S.H. (2002) Overlap of internal models in motor cortex for mechanical loads during reaching. *Nature*, 417: 938–941.
- Hamilton, A.F., Jones, K.E. and Wolpert, D.M. (2004) The scaling of motor noise with muscle strength and motor unit number in humans. *Exp. Brain Res.*, 157: 417–430.
- Harris, C.M. and Wolpert, D.M. (1998) Signal-dependent noise determines motor planning. *Nature*, 394: 780–784.
- Hepp-Reymond, M. (1988) Functional organization of motor cortex and its participation in voluntary movements. In: Alan R. (Ed.), *Comparative Primate Biology*. Liss, New York, pp. 501–624.
- Herter, T.M., Kurtzer, I., Cabel, D.W., Haunts, K.A. and Scott, S.H. (2007) Characterization of torque-related activity in primary motor cortex during a multijoint postural task. *J. Neurophysiol.*, 97: 2887–2899.
- Hoffman, D.S. and Strick, P.L. (1999) Step-tracking movements of the wrist. IV. Muscle activity associated with movements in different directions. *J. Neurophysiol.*, 81: 319–333.
- Hollerbach, J.M. and Flash, T. (1982) Dynamic interactions between limb segments during planar arm movement. *Biol. Cybern.*, 44: 67–77.
- Karst, G.M. and Hasan, Z. (1991) Initiation rules for planar, two-joint arm movements: agonist selection for movements throughout the work space. *J. Neurophysiol.*, 66: 1579–1593.
- Kurtzer, I., Herter, T.M. and Scott, S.H. (2005) Random change in cortical load representation suggests distinct control of posture and movement. *Nat. Neurosci.*, 8: 498–504.
- Kurtzer, I., Herter, T.M. and Scott, S.H. (2006a) Non-uniform distribution of reach-related and torque-related activity in upper arm muscles and neurons of primary motor cortex. *J. Neurophysiol.*, 96: 3220–3230.
- Kurtzer, I., Pruszynski, J.A., Herter, T.M. and Scott, S.H. (2006b) Primate upper limb muscles exhibit activity patterns that differ from their anatomical action during a postural task. *J. Neurophysiol.*, 95: 493–504.
- Lemon, R.N. and Griffiths, J. (2005) Comparing the function of the corticospinal system in different species: organizational differences for motor specialization? *Muscle Nerve.*, 32: 261–279.
- Li, C.S., Padoa-Schioppa, C. and Bizzi, E. (2001) Neuronal correlates of motor performance and motor learning in the primary motor cortex of monkeys adapting to an external force field. *Neuron*, 30: 593–607.
- Moran, D.W. and Schwartz, A.B. (1999) Motor cortical representation of speed and direction during reaching. *J. Neurophysiol.*, 82: 2676–2692.
- Morasso, P. (1981) Spatial control of arm movements. *Exp. Brain Res.*, 42: 223–227.
- Morrow, M.M. and Miller, L.E. (2003) Prediction of muscle activity by populations of sequentially recorded primary motor cortex neurons. *J. Neurophysiol.*, 89: 2279–2288.
- Naselaris, T., Merchant, H., Amirikian, B. and Georgopoulos, A.P. (2006) Large-scale organization of preferred directions in the motor cortex. I. Motor cortical hyperacuity for forward reaching. *J. Neurophysiol.*, 96: 3231–3236.
- Nozaki, D., Nakazawa, K. and Akai, M. (2005) Muscle activity determined by cosine tuning with a nontrivial preferred direction during isometric force exertion by lower limb. *J. Neurophysiol.*, 93: 2614–2624.
- Paz, R., Wise, S.P. and Vaadia, E. (2004) Viewing and doing: similar cortical mechanisms for perceptual and motor learning. *Trends Neurosci.*, 27: 496–503.
- Porter, R. and Lemon, R.N. (1993) *Corticospinal Function and Voluntary Movement*. Oxford University Press, New York.
- Rack, P.M. and Westbury, D.R. (1969) The effects of length and stimulus rate on tension in the isometric cat soleus muscle. *J. Physiol.*, 204: 443–460.
- Sainburg, R.L., Ghez, C. and Kalakanis, D. (1999) Intersegmental dynamics are controlled by sequential anticipatory, error correction, and postural mechanisms. *J. Neurophysiol.*, 81: 1045–1056.
- Sanes, J.N. and Donoghue, J.P. (2000) Plasticity and primary motor cortex. *Annu. Rev. Neurosci.*, 23: 393–415.
- Scott, S.H. (1999) Apparatus for measuring and perturbing shoulder and elbow joint positions and torques during reaching. *J. Neurosci. Methods*, 89: 119–127.
- Scott, S.H. (2003) The role of primary motor cortex in goal-directed movements: insights from neurophysiological studies on non-human primates. *Curr. Opin. Neurobiol.*, 13: 671–677.
- Scott, S.H. (2004) Optimal feedback control and the neural basis of volitional motor control. *Nat. Rev. Neurosci.*, 5: 532–546.
- Scott, S.H., Brown, I.E. and Loeb, G.E. (1996) Mechanics of feline soleus: I. Effect of fascicle length and velocity on force output. *J. Muscle Res. Cell Motil.*, 17: 207–219.

- Scott, S.H., Gribble, P.L., Graham, K.M. and Cabel, D.W. (2001) Dissociation between hand motion and population vectors from neural activity in motor cortex. *Nature*, 413: 161-165.
- Sergio, L.E. and Kalaska, J.F. (2005) Motor cortex neural correlates of output kinematics and kinetics during isometric force and arm-reaching tasks. *J. Neurophysiol.*, 94: 2353-2378.
- Shadmehr, R. and Mussa-Ivaldi, F.A. (1994) Adaptive representation of dynamics during learning of a motor task. *J. Neurosci.*, 14: 3208-3224.
- Singh, K., Melis, E.H., Richmond, F.J. and Scott, S.H. (2002) Morphometry of *Macaca mulatta* forelimb. II. Fiber-type composition in shoulder and elbow muscles. *J. Morphol.*, 251: 323-332.
- Singh, K. and Scott, S.H. (2003) A motor learning strategy reflects neural circuitry for limb control. *Nat. Neurosci.*, 6: 399-403.
- Smith, A.M., Hepp-Reymond, M.C. and Wyss, U.R. (1975) Relation of activity in precentral cortical neurons to force and rate of force change during isometric contractions of finger muscles. *Exp. Brain Res.*, 23: 315-332.
- Thach, W.T. (1978) Correlation of neural discharge with pattern and force of muscular activity, joint position, and direction of intended next movement in motor cortex and cerebellum. *J. Neurophysiol.*, 41: 654-676.
- Todorov, E. and Jordan, M.I. (2002) Optimal feedback control as a theory of motor coordination. *Nat. Neurosci.*, 5: 1226-1235.
- Wong, Y.C., Kwan, H.C., MacKay, W.A. and Murphy, J.T. (1978) Spatial organization of precentral cortex in awake primates. I. Somatosensory inputs. *J. Neurophysiol.*, 41: 1107-1119.
- Zajac, F.E. (1989) Muscle and tendon: properties, models, scaling, and application to biomechanics and motor control. *Crit. Rev. Biomed. Eng.*, 17: 359-411.
- Zajac, F.E. and Gordon, M.E. (1989) Determining muscle's force and action in multi-articular movement. *Exerc. Sport Sci. Rev.*, 17: 187-230.
- van Zuylen, E.J., Gielen, C.C. and Denier van der Gon, J.J. (1988) Coordination and inhomogeneous activation of human arm muscles during isometric torques. *J. Neurophysiol.*, 60: 1523-1548.