6 Conceptual Frameworks for Interpreting Motor Cortical Function: New Insights from a Planar Multiple-Joint Paradigm

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CONTENTS

6.1   INTRODUCTION

Visually guided reaching is a natural motor task performed regularly by primates in order to reach for and interact with objects of interest in the environment. The well-defined goal, moving the hand to a spatial location, makes it a popular paradigm for exploring sensorimotor function.[1] In general, the problem solved by the brain is how to convert visual information about the target location, initially sensed by receptors in the retina, into motor action generated by temporal and spatial patterns of muscle activities so as to stabilize the body and move the hand to the target. This conversion of sensory to motor signals involves many cortical and subcortical regions of the CNS, and a major focus of research is to identify the role played by each of these regions.
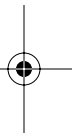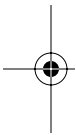
The basic question posed by studies that record neural activity during behavior is this: What type of information is conveyed by the discharge pattern of individual or populations of neurons? While cells are unlikely literally to code any engineering-inspired variable, it is nonetheless valuable (and even necessary) to relate neural activity to some features of behavior reflecting sensory, cognitive, or motor aspects of the task.

How one chooses which variable to correlate depends highly on the conceptual framework used to develop the experiment. This chapter starts with the important issue of how theoretical concepts guide experimental design and data analysis.[2] Such frameworks can be explicitly defined, or in some cases, only implicitly imbedded in the experiment and analysis. I will describe two conceptual frameworks for interpreting neural activity during reaching: sensorimotor transformations and internal models. Both frameworks address the same biological problem: How does the brain control the limb to reach toward a spatial target? The key difference is that each framework focuses attention on a different aspect of the motor task and thus each leads to different experiments. The sensorimotor transformations framework has been used extensively over the past 20 years to guide neurophysiological experiments on reaching, whereas the internal models framework has only recently had an impact on experimental design.

The second half of this chapter illustrates how the notion of internal models can be used to explore the neural basis of movement. A new experimental facility is described that can sense and perturb multiple-joint planar movements and this is followed by a brief description of the mechanics of limb movement. Finally some preliminary observations are presented on neural correlates in the primary motor cortex (M1) of the mechanical properties of the limb and of external mechanical loads.

6.2 CONCEPTUAL FRAMEWORK

6.2.1 SENSORIMOTOR TRANSFORMATIONS

The most common framework for exploring the neural control of reaching has been based on the idea of coordinate frames and sensorimotor transformations.[3–5] The brain is assumed to convert visual information on target location into forelimb muscle activation patterns through intermediary coordinate frames first through various kinematic representations of movement followed by kinetic representations. One putative series of transformations is shown in Figure 6.1A, where spatial target location is sequentially converted into hand kinematics, joint kinematics, joint muscle torques, and, finally, muscle activation patterns. The use of intermediary representations to plan and control movement seems like a reasonable assumption, particularly given the ubiquitous observation that hand trajectories are relatively straight for point-to-point reaching movements.[6,7]

Based on the concept of sensorimotor transformations, it seems obvious that the key neurophysiological question is which coordinate frame is specified by the discharge patterns of individual neurons in each brain region. Over the past 20 years this framework has spawned myriad studies. As described below, some experiments
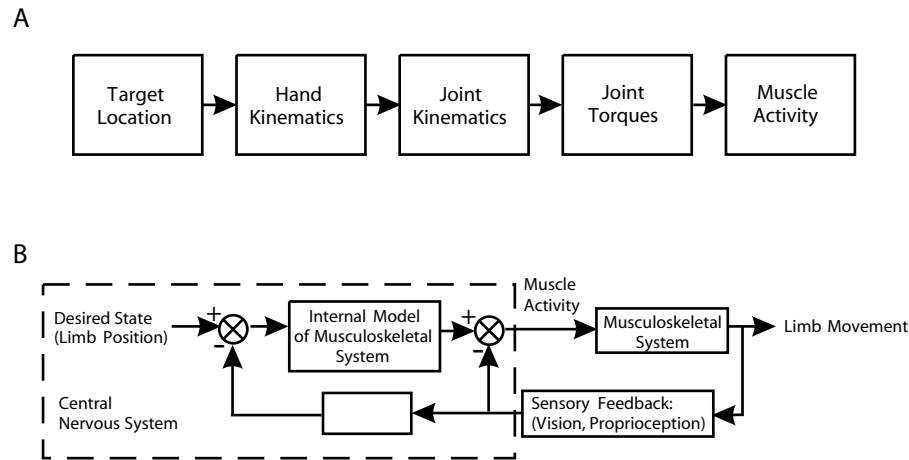
A

B

FIGURE 6.1 Two alternate frameworks for interpreting how the brain performs visually guided movements. (A) The notion of sensorimotor transformations assumes that information on spatial targets is converted into muscle activation patterns through a series of intermediary representations. This framework leads to the scientific problem of identifying how these representations are reflected in the discharge pattern of neurons in different brain regions. (B) The idea of internal models is that neural processes mimic the properties of the musculoskeletal system and physical objects in the environment. This framework leads to the scientific problem of identifying how information related to the motor periphery and physical loads is reflected in the discharge pattern of neurons.

have been designed to dissociate different variables, or levels of representation. In other cases, a specific class of variable has been chosen *a priori*, either based on the results of previous studies or simply for technical reasons.

One of the first studies to record neural activity in the motor cortex during reaching found that cell discharge was broadly tuned to the direction of hand motion.[8] This study showed that the cell discharge rate was maximal for movements in one direction, the preferred direction (PD), and that the cell's activity decreased as the angle between movement direction and the cell's PD increased. Further, the direction of hand motion could be predicted from the discharge pattern of an ensemble of neurons; this was termed the population vector hypothesis.[9,10]

A criticism often levied upon these studies has been that these hand-based correlates could be observed regardless of the type of information conveyed by individual neurons.[11–13] Variables of movement such as hand and joint motion are highly intercorrelated, such that even if neural activity coded muscle velocity, one would find significant correlations between cell discharge and hand motion. Moreover, the population vector will point in the direction of hand motion if three conditions are met: (1) neural activity is symmetrically tuned to the direction of movement; (2) the PDs of neurons are uniformly distributed; and (3) there is no coupling between a cell's PD and the magnitude of modulation during movement.[11] Any population of neurons that satisfies these conditions will predict the direction of hand motion regardless of the underlying information conveyed in its discharge

patterns. A recent theoretical study by Todorov[13] reiterated this point by illustrating how a broad range of observations between hand movement and neural activity, both at the single-cell and at the population level, could be explained if cells were simply coding multidimensional muscle activation patterns. While the correct explanation of the precise details of all hand-based correlations is a matter of debate,[14–17] the article by Todorov illustrates how difficult it is to interpret the discharge of neurons with simple correlation methods.

In spite of these concerns, a school of thought was created around the population vector hypothesis and the notion that neural activity in M1 during reaching should be interpreted using hand-based variables. Studies illustrated that neural activity in M1 and other sensorimotor areas correlates with the direction of hand motion, hand velocity, movement extent, and end position.[18–21] These studies illustrate that neural activity certainly correlates with these hand-based or end-point variables, but in many cases such activity may actually reflect relationships to the sensory and motor periphery such as motor patterns at a single joint or multiple joints.[11,13]

Few believe neural activity in M1 is coding the activity of single muscles, but the hand-based framework makes a substantive leap away from the motor periphery. In the extreme, descending commands are assumed to convey only the direction of hand movement that gets converted into motor output at the spinal level.[22] The shift away from the motor periphery has been extended further to suggest that M1 may be involved in cognitive processing such as mental rotation[23,24] although such interpretations remain controversial.[25–27]

A key feature of many studies has been to dissociate explicitly different features of the task, such as sensory versus motor,[28,29] global variables (hand–target) versus joint–muscle,[30–36] or kinematic versus kinetic variables.[37–39] For example, we performed an experiment where reaching movements were performed to the same target locations but with two different arm postures: first, in a natural arm posture where the elbow tended to remain directly below the hand and shoulder, and second, in an abducted posture with the shoulder abducted and with the elbow almost at the level of the hand and shoulder.[31] This task dissociated global features of the task related to the spatial target and hand motion, which remained constant, from joint-based variables related to joint motion, joint torque, or muscle activity, which varied between arm orientations. We found that most neurons showed changes in activity either by changing their directional tuning or by modulating the overall level of activity, suggesting that neural discharge was related in some way to the motor periphery. Some cells, however, showed no changes in activity when movements were performed with the two arm orientations. Such invariances could reflect that these cells are specifying global features of the task, although it is still possible that such cells could reflect joint-based information. (See Scott and Kalaska.[31])

A cleaner dissociation between muscle- and hand-based features of movement was provided in a study where wrist movements were performed with three different forearm orientations: neutral, supinated, and pronated .[34] They found that some cells varied their directional tuning in a manner that was similar to the variation observed for muscles, whereas others showed no change in directional tuning, as would be expected if neurons reflected the spatial direction of the task. However, most of these
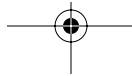
latter spatial/hand cells still showed changes in the magnitude of activity for movements with different forearm orientations.

All these studies illustrate that primary motor cortical activity correlates to almost every imaginable task variable, including spatial target location, hand movement direction and extent, hand velocity, joint velocity, force output, and muscle activity, to name a few.[1,20,40] The obvious conclusion is that there appears to be no single unified coordinate frame in M1. This of course causes considerable problems for the population vector hypothesis, which presupposes that a global signal related to the direction of hand motion is created across the cell population. In M1, cells respond to many different variables, with some cells largely reflecting kinematic features of the task and other neurons reflecting kinetic features. Whenever force but not kinematic motion is modified, these latter cells, which modulate their activity with force output, will alter estimates of hand motion.

While most agree that neural activity in M1 reflects a mixture of different kinematic and kinetic features of movement, the notion that the brain performs a series of sensorimotor transformations to execute reaching movements assumes a certain relationship between these representations. Specifically, cells insensitive to force output are assumed to reflect a higher level representation of movement which gets converted by cortical processing into a lower level representation; cells sensitive to force output are classified as this lower level representation. Are cells that are insensitive to force output necessarily reflecting a higher level representation than cells that are sensitive to force output? This assumption would seem reasonable, if muscle activity (electromylography [EMG]) were the only feature of motor behavior controlled by the brain.

However, descending commands to the spinal cord must consider more than just muscle activity.[1,41,42] Alpha motoneurons, which innervate extrafusal muscle fibers and produce force, represent only one type of motoneuron. In each motoneuron pool, there is a large number of gamma motoneurons that innervate intrafusal fibers in muscle spindles,[43] which may be equal in proportion to alpha motoneurons in some muscles. There are even beta motoneurons innervating both intra- and extrafusal muscle fibers.[44] Another role for descending commands is to modulate and influence sensory feedback.[45] Spinal reflexes can also create various contingency plans for unexpected perturbations or errors,[46] which must also be selected or modified by descending commands. It is quite possible that up to two thirds of descending signals from the cortex to the spinal cord are related to controlling these other features of motor output. However, little is known about cortical discharge related to controlling gamma-motoneuron activity and spinal reflexes during volitional tasks since experimental paradigms, including our own, tend to focus on alpha-motoneuron activity.[47,48] It is quite possible that neurons related to these other features are relatively insensitive to variations in force output during motor behavior. Within the rubric of sensorimotor transformations, such neurons would be assumed to code a higher level representation of movement related to the kinematic features of the task when in fact they were simply involved in controlling relatively low-level but non-EMG features of the task. Furthermore, such discrete segregation between alpha-motoneuron activity and other spinal processing is highly unlikely and descending signals likely reflect a mixture of influences on spinal circuitry.

across a single neural population. A third load condition, where viscous loads were applied to joints simultaneously (viscous both [VB]), allowed us to examine how mechanically dependent loads with common features or characteristics are represented neurally. We found that many cells changed their activity for one, two, and in some cases all three load conditions as compared to their activity during unloaded reaching. The representation of VS and VE loads were not completely independent, but demonstrated at least a partial overlap across the cell population in M1. Of the 51 cells that responded to either loading condition, 27 were sensitive only to VE, 9 were sensitive only to VS, and 15 showed significant changes in discharge for both VS and VE ($p < 0.05$, analysis of variance [ANOVA]). There was a highly consistent relationship between how a cell responds in VS and VE. Cells that increase discharge for VS also tend to increase discharge for VE, while decreases in discharge for VS are likewise associated with discharge decreases in VE.

Perhaps the most important observation was that there was considerable overlap in the representations of VB and either VS or VE. Almost all neurons that changed their activity for VB as compared to unloaded movements, also showed significant changes of activity related to VE or VS. We found that almost all cells showed similar signs of change across all three load conditions. If a neuron increased its discharge for a given loading condition, its response to any other load condition would also be an increase in discharge. If a neuron decreased its discharge for a load condition, responses to other loads would also tend to be a reduction in discharge.

With regard to whether the brain uses a single internal model or multiple internal models for different mechanical contexts, the present results illustrate that neural activity in M1 appears to reflect a single internal model for both these single- and multiple-joint loads. However, other regions of the brain, such as the cerebellum, may use separate internal models for these different contexts. Further, because only velocity-dependent loads were used in this study, it is quite possible that neural representations for different types of mechanical loads (i.e., viscous versus elastic) may be treated separately.[75]

One of the key differences between the present study and previous studies is that loads were applied at different parts of the motor apparatus: shoulder versus elbow. This mechanical segregation allowed us to illustrate that load-related activity for some neurons was limited to loads at only one of the two joints, whereas other neurons responded to loads applied to either joint. These results suggest that there is some separation, but not a complete separation, in neurons responding to loads at different joints, reflecting a course somatotopic map within M1.[76,77] We are presently developing cortical maps of neurons related to the shoulder and elbow joints to observe if there is any variation in their distribution within the cortex.

The present data on neural responses for single- and multiple-joint loads allow us to ask how information related to different joints is integrated together. We tested two possible models, one in which load-related activity related to each joint is linearly summed across all joints. However, we found this model consistently overestimated the response of neurons to multiple-joint loads. We examined a second model that assumed that the response of a neuron reflected vector summation of its response to loads at each joint. This vector summation model assumes that activity

related to each joint can be treated as orthogonal vectors and that multiple-joint loads reflect the vector sum of these single-joint loads. Our data illustrated that the response of neurons tended to follow this simple rule. We are presently assessing whether this integrative feature of multiple-joint loads reflects an inherent feature of cortical processing or simply parallels the activity of shoulder and elbow muscles for these movement-dependent loads.

Another of our recent studies examined the response of neurons to constant-magnitude (bias) loads applied to the shoulder or elbow as the monkey maintained its hand at a central target.[78] The response of many neurons paralleled our results on viscous loads applied during reaching: some neurons responded to loads at only one of the two joints, whereas others responded to loads at both joints. Load-sensitive cells again responded to both multiple-joint loads and at least one of the two single-joint loads so that there was no segregation between neural responses to single- and multiple-joint loading conditions. Further, the response of neurons to multiple-joint loads again could be predicted using a vector summation model from the response of neurons to single-joint loads.

A key feature of both of these studies was that we could load the shoulder and elbow joints independently. It seems reasonable to assume that these single-joint loads would selectively influence the response of muscles that span that joint. We were mistaken. Many muscles that only spanned one of the two joints modified their activity for loads applied to the other joint. For example, brachioradialis, an elbow flexor muscle, increased its activity when the monkey generated either an elbow flexor *or* a shoulder extensor muscular torque (Figure 6.7). The greatest activity level was observed when the monkey generated an elbow flexor and a shoulder extensor torque simultaneously. At first, this seems paradoxical, but it simply reflects the action of biarticular muscles that span both joints. Changes in a biarticular muscle's activity for loads applied at one joint necessarily create torque at the other joint. As a result, the activity of muscles spanning this second joint must change to compensate for the change in activity of the biarticular muscles.[79,80]

This coupling of muscle activity at one joint to the mechanical requirements of another joint obfuscates any simple mapping between torque at a joint and the activity of muscles spanning that joint. This has important implications with regard to the response of neurons during single- and multiple-joint loads. While the response of single-joint muscles was almost always greater for loads applied to the spanned as compared to the nonspanned joint, its effect cannot be discounted. Therefore, one cannot assume that neurons that changed their activity for loads applied to both joints are necessarily related to controlling muscles at both joints.

This example underlines the inherent complexity of the peripheral motor apparatus. Our description earlier illustrated that joint torque does not match joint motion for multiple-joint movements due to intersegmental dynamics. The present observations on EMG activity related to mechanical loads illustrates that muscle activity does not match joint torque at a given joint. Therefore, all three levels of description — motion, torque, and muscle activity — provide unique, complementary information on limb motor function. Our ongoing studies are continuing to explore limb mechanics including using simulations to better understand the relationship between muscle activity and motor performance.
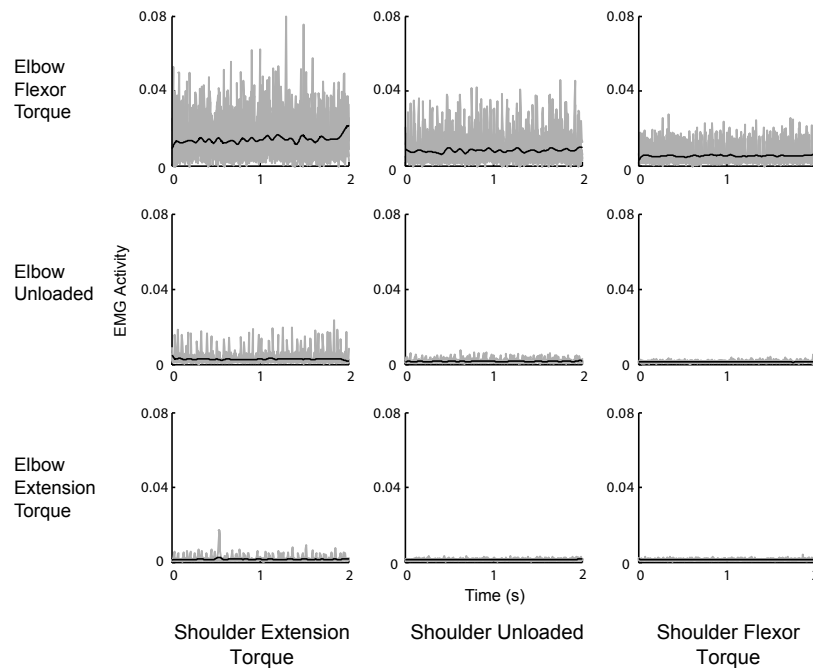
FIGURE 6.7 Activity of brachioradialis, an elbow flexor muscle, when the monkey maintains a constant hand position, but with different constant loads (0.11 Nm) applied to the shoulder or elbow joints. Nine different loading conditions were examined, generating flexor, null, or extensor muscular torque at each joint.[78] The central panel shows the activity of the muscle when no loads were applied to the joints (the solid line is the mean of five repeat trials). Muscle activity increases when the monkey generates an elbow flexor torque. However, its magnitude also varies with shoulder muscle torque such that it increases when the monkey generates a shoulder extensor torque. Therefore, brachioradialis muscle activity varies with shoulder muscle torque even though this muscle does not span the shoulder joint.

6.6 SUMMARY AND CONCLUSIONS

The goal of this chapter was twofold. The first goal was to describe two conceptual frameworks, sensorimotor transformations and internal models, for interpreting how the brain controls visual-guided reaching. This comparison was presented because it helps to explain how conceptual frameworks, whether implicitly or explicitly defined, strongly influence the design, analysis, and interpretation of experimental data. What seems like a logical experiment from one perspective can be irrelevant from another. My recent experiments have been designed and interpreted based on the concept of internal models, where the brain mimics or reflects the physical properties of the limb and the environment. This concept has been very influential for human studies on motor performance and learning and appears to be ideal, at this time, for exploring the neurophysiological basis of movement in nonhuman primates.

The second goal of this chapter was to describe the results from our recent studies using a planar experimental paradigm. Our robotic device can both sense and perturb limb motor function, and our initial studies have illustrated several of the ways in which the mechanics of the limb and of physical loads are represented in M1. It is important to realize that the present results do not disprove the notion of sensorimotor transformations. The present experiments illustrate that both kinematic and kinetic information is reflected in primary motor cortical activity, as shown by other studies. The value of the concept of internal models is that it demonstrates that body motion and its interaction with the physical world must obey the laws of Newtonian physics. In effect, motor control is the study of how biological systems consider and manage these basic laws of physics.

We initially focused on well-learned tasks rather than on the process of learning such tasks. This was largely a pragmatic approach to the question of how stable neural states are represented in the brain. However, M1 is clearly involved in motor learning and adaptive control.[81–84] KINARM can apply loads at the shoulder or elbow joint based on almost any variable imaginable, and our future studies will focus on exploring the role of the motor cortex in adaptive motor control.

The robotic device also appears to be well suited for exploring the role of afferent feedback in motor control. It is known that there is a rough correspondence between sensory and motor representations in M1.[85,86] Along with the motor tasks described above, we regularly record the response of neurons during passive limb movements and to perturbations during postural tasks.[87,88] The long-term goal is to compare and contrast the sensory and motor responses of individual neurons in order to better understand how afferent feedback contributes to motor function.
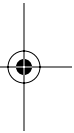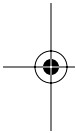
ACKNOWLEDGMENTS

REFERENCES

1. Scott, S.H., The role of primary motor cortex in goal-directed movements: insights from neurophysiological studies on non-human primates. *Curr. Opin. Neurobiol.,* 13, 671, 2003.
2. Kuhn, T.S., *The Structure of Scientific Revolutions*, 2nd edition, University of Chicago Press, Chicago, 1970.
3. Saltzman, E., Levels of sensorimotor representation, *J. Math. Psychol.*, 20, 91, 1979.
4. Soechting, J.F. and Flanders, M., Moving in three-dimensional space: frames of reference, vectors, and coordinate systems*, Annu. Rev. Neurosci.*, 15*,* 167, 1992.
5. Kalaska, J.F. et al., Cortical control of reaching movements, *Curr. Opin. Neurobiol.*, 7*,* 849, 1997.
6. Morasso, P., Spatial control of arm movements, *Exp. Brain Res.*, 42, 223, 1981.
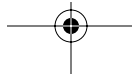
7. Sergio, L.E. and Scott, S.H., Hand and joint paths during reaching movements with and without vision, *Exp. Brain Res.,* 122, 157, 1998.

8. Georgopoulos, A.P. et al., On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex, *J. Neurosci.*, 2, 1527, 1982.

9. Georgopoulos, A.P. et al., Interruption of motor cortical discharge subserving aimed arm movements, *Exp. Brain Res.,* 49, 327, 1983.

10. Georgopoulos, A.P., Kettner, R.E., and Schwartz, A.B., Primate motor cortex and free arm movements to visual targets in three-dimensional space. II. Coding of the direction of movement by a neuronal population, *J. Neurosci.*, 8, 2928, 1988.

11. Mussa-Ivaldi, F.A., Do neurons in the motor cortex encode movement direction? An alternative hypothesis, *Neurosci. Lett.*, 91, 106, 1988.

12. Sanger, T.D., Theoretical considerations for analysis of population coding in motor cortex, *Neural Comp.*, 6, 29, 1994.

13. Todorov, E., Direct cortical control of muscle activation in voluntary arm movements: a model, *Nat. Neurosci.*, 3, 391, 2000.

14. Moran, D.W. and Schwartz, A.B., Letter to the editor: "One motor cortex, two different views," *Nat. Neurosci.*, 3, 964, 2000.

15. Georgopoulos, A.P. and Ashe, J., Letter to the editor: "One motor cortex, two different views," *Nat. Neurosci.*, 3, 963, 2000.

16. Todorov, E., Reply in "One motor cortex, two different views," *Nat. Neurosci.*, 3, 963, 2000.

17. Scott, S.H., Reply in "One motor cortex, two different views," *Nat. Neurosci.*, 3, 964, 2000.

18. Schwartz, A.B., Motor cortical activity during drawing movements: single-unit activity during sinusoid tracing, *J. Neurophysiol.*, 68, 528, 1992.

19. Fu, Q.G. et al., Temporal encoding of movement kinematics in the discharge of primate primary motor and premotor neurons, *J. Neurophysiol.,* 73, 836, 1995.

20. Johnson, M.T., Mason, C.R., and Ebner, T.J., Central processes for the multiparametric control of arm movements in primates, *Curr. Opin. Neurobiol.*, 11, 684, 2001.

21. Poppelle, R. and Bosco G., Sophisticated spinal contributions to motor control, *Trends Neurosci.*, 26, 269, 2003.

22. Georgopoulos, A.P., On the translation of directional motor cortical commands to activation of muscles via spinal interneuronal systems, *Cogn. Brain Res.*, 3, 151, 1996.

23. Georgopoulos, A.P. et al., Mental rotation of the neuronal population vector, *Science*, 243, 234, 1989.

24. Lurito, J.T., Georgakopoulos, T., and Georgopoulos, A.P., Cognitive spatial-motor processes. 7. The making of movements at an angle from a stimulus direction: studies of motor cortical activity at the single cell and population levels, *Exp. Brain Res.*, 87, 562, 1991.

25. Whitney, C.S., Reggia, J., and Cho, S., Does rotation of neuronal population vectors equal mental rotation? *Connection Sci.*, 9, 253, 1997.

26. Cisek, P. and Scott, S.H., An alternative interpretation of population vector rotation in macaque motor cortex, *Neurosci. Lett.*, 272, 1, 1999.

27. Moody, S.L. and Wise, S.P., Connectionist contributions to population coding in the motor cortex, *Progr. Brain Res.*, 130, 245, 2001.

28. Shen, L. and Alexander, G.E., Neural correlates of a spatial sensory-to-motor transformation in primary motor cortex, *J. Neurophysiol.,* 77, 1171, 1997.

29. Zhang, J. et al., Dynamics of single neuron activity in monkey primary motor cortex related to sensorimotor transformation, *J. Neurosci.,* 17, 2227, 1997.

30. Caminiti, R., Johnson, P.B., and Urbano, A., Making arm movements within different parts of space: dynamic aspects in the primate motor cortex, *J. Neurosci.,* 10*,* 2039, 1990.

31. Scott, S.H. and Kalaska, J.F., Reaching movements with similar hand paths but different arm orientations: I. Activity of individual cells in motor cortex, *J. Neurophysiol.*, 77*,* 826, 1997.

32. Sergio, L.E. and Kalaska, J.F., Systematic changes in directional tuning of motor cortex cell activity with hand location while generating static isometric forces in constant spatial directions, *J. Neurophysiol.*, 78, 1170, 1997.

33. Sergio, L.E. and Kalaska, J.F., Systematic changes in motor cortex cell activity with arm posture during directional isometric force generation, *J. Neurophysiol.*, 89, 212, 2003.

34. Kakei, S., Hoffman, D.S., and Strick, P.L., Muscle and movement representations in the primary motor cortex, *Science*, 285, 2136, 1999.

35. Scott, S.H., Sergio, L.E., and Kalaska, J.F., Reaching movements with similar hand paths but different arm orientations. II. Activity of individual cells in dorsal premotor cortex and parietal area 5, *J. Neurophysiol.*, 78, 2413, 1997.

36. Kakei, S., Hoffman, D.S., and Strick, P.L., Direction of action is represented in the ventral premotor cortex, *Nat. Neurosci.*, 4, 1020, 2001.

37. Evarts, E.V., Representation of movements and muscles by pyramidal tract neurons of the precentral motor cortex, in *Neurophysiological Basis of Normal and Abnormal Motor Activities*; Yahr, M.D. and Purpura, D.P., Eds., Raven Press, New York, 1967.

38. Kalaska, J.F. et al., Comparison of movement direction-related versus load direction-related activity in primate motor cortex, using a two-dimensional reaching task, *J. Neurosci.*, 9*,* 2080, 1989.

39. Gribble, P.L. and Scott, S.H., Overlap of internal models in motor cortex for mechanical loads during reaching, *Nature,* 417, 938, 2002.

40. Fetz, E.E., Are movement parameters recognizably coded in the activity of single neurons? *Behav. Brain Sci.*, 15, 679, 1992.

41. Lundberg, A., To what extent are brain commands for movements mediated by spinal interneurons? *Behav. Brain Sci.*, 15, 775, 1992.

42. Loeb, G.E., Brown, I.E., and Cheng, E.J., A hierarchical foundation for models of sensorimotor control, *Exp. Brain Res.*, 126, 1, 1999.

43. Burke, R.E. et al., Anatomy of medial gastrocnemius and soleus motor nuclei in cat spinal cord, *J. Neurophysiol.*, 40, 667, 1977.

44. Barker, E. et al., Types of intra- and extrafusal muscle fibre innervated by dynamic skeletofusimotor axons in cat peroneus brevis and tennissimus muscles as determined by the glycogen depletion method, *J. Physiol. Lond.*, 266, 713, 1977.

45. Seki, K., Perlmutter, S.I., and Fetz, E.E., Sensory input to primate spinal cord is presynaptically inhibited during voluntary movement, *Nat. Neurosci*., 6, 1309–1316, 2003.

46. Cole, K.J. and Abbs, J.H., Kinematic and electromyographic responses to pertubation of a rapid grasp, *J. Neurophysiol.*, 57, 1498, 1987.

47. Conrad, B. et al., Cortical load compensation during voluntary elbow movements, *Brain Res.*, 71, 507, 1974.

48. Evarts, E. and Tanji, J., Reflex and intended responses in motor cortex pyramidal tract neurons of monkey, *J. Neurophysiol.*, 39, 1069, 1976.

49. Harris, C.M. and Wolpert, D.M., Signal dependent noise determines motor planning, *Nature*, 394, 780, 1998.

50. Todorov, E. and Jordan, M.I., Optimal feedback control as a theory of motor coordination, *Nat. Neurosci.*, 5, 1226, 2002.

51. Kawato, M., Furukawa, K., and Suzuki, R.A., Hierarchical neural-network model for control and learning of voluntary movement, *Biol. Cybern.,* 57*,* 169, 1987.

52. Miall, R.C. and Wolpert, D.M., Forward models for physiological motor control, *Neural Netw.*, 9*,* 1265, 1996.

53. Scott, S.H. and Norman, K.E., Computational approaches to motor control and their potential role for interpreting motor dysfunction, *Curr. Opin. Neurol.*, 16, 693, 2003.

54. Shadmehr, R. and Mussa-Ivaldi, F.A., Rapid adaptation to coriolis force perturbations of arm trajectory, *J. Neurosci.*, 14*,* 3208, 1994.

55. Lackner, J.R. and DiZio, P., Rapid adaptation to coriolis force perturbations of arm trajectory, *J. Neurophysiol.*, 72, 299, 1994.

56. Sainburg, R.L., Ghez, C., and Kalakanis, D., Intersegmental dynamics are controlled by sequential anticipatory, error correction, and postural mechanisms, *J. Neurophysiol.*, 81, 1045, 1999.

57. Wolpert, D.M., Ghahramani, Z., and Flangan, J.R., Perspectives and problems in motor learning, *Trends Cogn. Sci.*, 5, 487, 2001.

58. Wolpert, D.M. and Ghahramani, Z., Computational principles of movement neuroscience, *Nat. Neurosci.*, 3, 1212, 2000.

59. Flanagan, J.R. and Wing, A.M., The role of internal models in motion planning and control: evidence from grip force adjustments during movements of hand-held loads, *J. Neurosci.*, 17*,* 1519, 1997.

60. Westling, G. and Johansson, R.S., Factors influencing the force control during precision grip, *Exp. Brain Res.*, 53, 277, 1984.

61. Scott, S.H., Apparatus for measuring and perturbing shoulder and elbow joint positions and torques during reaching, *J. Neurosci. Meth.*, 89, 119, 1999.

62. Porter, R. and Lemon, R., *Corticospinal Function and Voluntary Movement*, Clarendon Press, Oxford, 1993.

63. Graham, K.M. et al., Kinematics and kinetics of multi-joint reaching in non-human primates, *J. Neurophysiol.*, 89, 2667, 2003.

64. Favilla, M. et al., Trajectory control in targeted force impulses. VII. Independent setting of amplitude and direction in response preparation, *Exp. Brain Res.*, 79, 530, 1990.

65. Graham, K.M. and Scott, S.H., Morphometry of macaca mulatta forelimb. III. Moment are of shoulder and elbow muscles, *J. Morphol.*, 255, 301, 2003.

66. Cheng, E.J. and Scott, S.H., Morphometry of *Macaca mulatta* forelimb. I. Shoulder and elbow muscles and segment inertial parameters, *J. Morphol.,* 245*,* 206, 2000.

67. Scott, S.H., Brown, I.E., and Loeb, G.E., Mechanics of feline soleus: I. Effect of fascicle length and velocity on force output, *J. Musc. Res. Cell Motil.*, 17, 207, 1996.

68. Hollerbach, J.M. and Flash, T., Dynamic interactions between limb segments during planar arm movement, *Biol. Cybern.,* 44*,* 67, 1982.

69. Scott, S.H. et al., Dissociation between hand motion and population vectors from neural activity in motor cortex, *Nature*, 413*,* 161, 2001.

70. Georgopoulos, A.P., Cognitive motor control: spatial and temporal aspects, *Curr. Opin. Neurobiol.,* 12, 678, 2002.

71. Amirikian, B. and Georgopoulos, A.P., Directional tuning profiles of motor cortical cells, *Neurosci. Res.*, 36, 73, 2000.

72. Georgopoulos, A.P., Schwartz, A.B., and Kettner, R.E., Neuronal population coding of movement direction, *Science*, 233, 1416, 1986.

73. Schwartz, A.B., Kettner, R.E., and Georgopoulos, A.P., Primate motor cortex and free arm movements to visual targets in three-dimensional space. I. Relations between single cell discharge and direction of movement, *J. Neurosci.*, 8, 2913, 1988.

74. Wolpert, D.M. and Kawato, M., Multiple paired forward and inverse models for motor control, *Neural Netw.,* 11, 1317, 1998.

75. Tong, C., Wolpert, D.M., and Flanagan, J.R., Kinematics and dynamics are not represented independently in motor working memory: evidence from an interference study, *J. Neurosci.* 22, 1108, 2002.

76. Sanes, J.N. and Schieber, M.H., Orderly somatotopy in primary motor cortex: does it exist? *NeuroImage*, 13, 968, 2001.

77. Park, M.C. et al., Consistent features in the forelimb representation of primary motor cortex in rhesus macaques, *J. Neurosci.*, 21, 2784, 2001.

78. Cabel, D.W., Cisek, P., and Scott, S.H., Neural activity in primary motor cortex related to mechanical loads applied to the shoulder and elbow during a postural task, *J. Neurophysiol.*, 86, 2102, 2001.

79. Buchanan, T.S., Rovai, G.P., and Rymer, W.Z., Strategies for muscle activation during isometric torque generation at the human elbow, *J. Neurophysiol.*, 62, 1202, 1989.

80. van Zuylen, E.J. et al., Coordination and inhomogeneous activation of human arm muscles during isometric torques, *J. Neurophysiol.*, 60, 1523, 1988.

81. Classen, J. et al., Rapid plasticity of human cortical movement representation induced by practice, *J. Neurophysiol.*, 79, 1117, 1998.

82. Li, C.S.R., Padoa-Schioppa, C., and Bizzi, E., Neuronal correlates of motor performance and motor learning in the primary motor cortex of monkeys adapting to an external force field, *Neuron*, 30, 593, 2001.

83. Sanes, J.N. and Donoghue, J.P., Plasticity and primary motor cortex, *Annu. Rev. Neurosci.*, 23, 393, 2000.

84. Paz, R. et al., Preparatory activity in motor cortex reflects learning of local visuomotor skills, *Nat. Neurosci.*, 6, 882, 2003.

85. Murphy, J.T., Wong, Y.C., and Kwan, H.C., Sequential activation of neurons in primate motor cortex during unrestrained forelimb movement, *J. Neurophysiol.*, 53, 435, 1985.

86. Scott, S.H., Comparison of onset time and magnitude of activity for proximal arm muscles and motor cortical cells prior to reaching movements, *J. Neurophysiol.*, 77, 1016, 1997.

87. Singh, K. and Scott, S.H., Neural circuitry influences learning and generalization of novel loads during reaching in humans, *Soc. Neurosci. Abstr.*, 28, 269.9, 2002.

88. Korbel, T.K. and Scott, S.H., Neural activity in primary motor cortex related to multi-joint pertubations during a postural task, *Soc. Neurosci. Abstr.,* 28, 61.10, 2002.