Neuron, Vol. 13, 257–268, August, 1994, Copyright © 1994 by Cell Press

New Concepts in Generation of Movement

Review

Apostolos P. Georgopoulos
Brain Sciences Center
Veterans Affairs Medical Center
Minneapolis, Minnesota 55417
and Departments of Physiology and Neurology
University of Minnesota Medical School
Minneapolis, Minnesota 55455

The motor cortex has long been regarded as a key node in the generation of motor output, based on observations of patients with motor seizures (Jackson, 1889) as well as results from various kinds of studies employing lesions and electrical stimulation (Porter and Lemon, 1993). Evarts (1966, 1968, 1969) recorded the impulse activity of single cells in the motor cortex of behaving monkeys. He showed that cells typically changed activity before the first changes in muscle activity and that the frequency of discharge varied during movement or production of isometric force. These studies initiated research into the role of the motor cortex in the specification and control of motor output, a subject that has been hotly debated and widely speculated upon and that remains under active investigation. Simplistic notions of motor cortical function have been exemplified by the view that motor cortical cells are simply "upper motoneurons." This view is clearly untenable. Early observations from patients with motor seizures had already pointed to the complexity of motor cortical function (Jackson, 1889), as had the variable effects of electrical stimulation (Leyton and Sherrington, 1917). More recently, the technique of recording the activity of single cells during behavior (Lemon, 1984) provided a powerful tool by which to study the activity of motor cortical cells within the full-blown behavioral context of voluntary movement. This was an important advance and the only appropriate way to study the neural mechanisms of the initiation of voluntary movement. Indeed, a wealth of information has accumulated during the past 30 years concerning the involvement of the motor cortex in simple motor functions as well as in more complex aspects of motor behavior (see Georgopoulos, 1991, for a review).

It seems that whether the motor cortex is regarded as "simple" or "complex" depends to a great extent on the richness of the experimental paradigm and the aspects of motor function selected for study. In general, the rich variety of neural processing can be revealed only when appropriate tasks are used and cannot be appreciated if restricted and impoverished paradigms are employed. For example, a task that involves only flexion–extension movements about a single joint cannot, by definition, provide information concerning the neural control of multi-joint movements; a task that involves alternating movements between two mechanical stops cannot provide information concerning accurately aimed movements, nor about movements that are the result of considerable visuomotor processing; and a task that involves steady holding against a constant load cannot provide information concerning dynamic changes in force output.

In general, the choice of the experimental task and design reflects underlying a priori viewpoints of motor cortical function. For example, the use of single-joint, agonist–antagonist paradigms reflected the widespread belief in the 1960s and '70s that control of single joints was the key building block of motor control; in contrast, the use, from the mid '70s on, of tasks involving multi-muscle precision grip, or multi-joint, multi-muscle reaching movements reflected the changing viewpoints that the motor cortex might be involved in the specification and control of complex motor output. Furthermore, the use of tasks involving memorized movements and spatial transformations tested the hypothesis that the motor cortex could also be involved in more complex aspects of sensorimotor processing, under appropriate conditions. The general outcome of these studies has been the insight that changes in activity of motor cortical cells can reflect, at varying degrees, almost the whole gradation of motor and behavioral complexity present in a given task. The picture that has emerged, then, is one of meaningful complexity in motor cortical discharge rather than one of a simplistic upper motoneuron. This has been accompanied by gradual changes in the way in which motor variables are manipulated in a task and of the way in which neural data are analyzed and interpreted within the context of neuronal populations. The main results of this research are discussed briefly below and exemplified with specific examples.

Motor Parameters as Experimental Tools: A Trend Toward Increasing Complexity

A crucial aspect of studies of the neural mechanisms of motor function is the choice of motor parameters to be varied. In early studies, these parameters were relatively simple; for example, they involved the production of one-dimensional (1D) motor output at a single joint, such as alternating, flexion–extension movements at the wrist, or steady holding against flexor or extensor loads. Since then, the trend has been toward increasing spatio-temporal complexity of the motor output tested, which now include multi-joint, multi-dimensional reaching movements, multi-dimensional isometric forces, and dynamic force pulses. This extended appreciably the scope of investigation and has resulted in a wealth of novel information and new insights concerning the role of motor structures in initiation and control of motor output.

Isometric Force

Reciprocal Static Forces

In the original and later work of Evarts and his colleagues (Evarts, 1968; Evarts et al., 1983) and in subsequent work by others (e.g., Thach, 1978; Cheney and Fetz, 1980) the force exerted by the animal was restricted to one joint and to the activation of reciprocal groups of muscles. In these experiments the steady-state activity of motor cortical cells varied with the level of force exerted, especially for those cells that produced postspike facilitation in, and therefore seemed to have monosynaptic connections to, motoneurons innervating distal muscles (Cheney and Fetz, 1980). In contrast, these relations are not prominent for cells projecting to the striatum (Bauswein et al., 1989).

Two-Dimensional Static Forces

The neural relations to static force were recently extended to the direction of multi-joint, two-dimensional (2D) static forces (Kalaska et al., 1989). Here cell activity in the motor cortex varies with, and is broadly tuned to, the direction of force. This effect is more pronounced for cells in the lower than the upper layers of the motor cortex.

Precision Grip

The use of the precision grip as an experimental tool (Smith et al., 1975; Hepp-Reymond et al., 1978; Hepp-Reymond and Diener, 1983) was in accord with the idea that the motor cortex may be particularly involved in the control of precise forces. The precision grip involves the simultaneous activation of a large number of muscles (Smith, 1981; Maier et al., 1990, Eur. J. Neurosci., abstract) and yet requires accurate control of force levels as an output motor parameter. Although earlier results on the relations between motor cortical cell activity and isometric force in a single joint could be interpreted in a simple fashion (Fromm, 1983), in the case of the precision grip these relations cannot be as easily interpreted, given that desired force levels can be attained by various combinations of muscle activation and that the amount of activation of a particular muscle may not vary in a simple fashion with the amount of force exerted (Maier et al., 1990, Eur. J. Neurosci., abstract). Moreover, motor cortical cells with postspike facilitation effects on hand muscles may show both positive and negative correlations with precision grip force (Maier et al., 1993), and the strength of the postspike facilitation can be dissociated from the relation to force (Maier et al. , 1993).

Co-Contraction

A different level of complexity in the use of isometric force as a motor parameter was added by varying the flexion–extension force at the wrist over time, in a sinusoidal fashion and at different frequencies (Humphrey and Reed, 1983). At low frequencies of force change, flexor and extensor muscles contracted reciprocally, but at high frequencies, the joint was stabilized by the co-contraction of flexors and extensors, which increased the mechanical stiffness of the joint. This paradigm revealed the existence of a subset of cells in the motor cortex that became active only at higher frequencies of force change. This finding suggested that these cells might form a separate population controlling joint stiffness.

Dynamic Pulses

The dynamic relations of cell activity in the motor cortex to the direction of 2D isometric force were investigated recently (Georgopoulos et al., 1992). The following experimental arrangement allowed the dissociation between dynamic and static components of the force exerted. Monkeys produced pure force pulses on an isometric handle in the presence of a constant force bias so that the net force (i.e., the vector sum of the monkey's force and the bias force) was in a visually specified direction. The net force developed over time had to stay in the specified direction and to increase in magnitude in order to exceed a required intensity threshold. Now consider the case in which the directions of the net and bias forces differ, by being, for example, orthogonal. For the task to be performed successfully under these conditions, the animal's force has to change continuously in direction and magnitude, so that, at any moment during force development, the vector sum of this force and the bias force is in the visually specified direction. Thus this experimental arrangement effectively dissociated the animal's force vector, the direction of which changed continuously in a trial, from the net force vector, the direction of which remained invariant. Eight net force directions and eight bias force directions were employed. Recordings of neuronal activity in the motor cortex revealed that the activity of single cells was directionally tuned in the absence of bias force and that this tuning remained invariant when the same net forces were produced in the presence of different directions of bias force. These results demonstrated that cell activity does not relate to the direction of the animal's total force. Since the net force is equivalent to the dynamic component of the force exerted by the animal, after a static component vector (equal and opposite to the force bias) is subtracted, these findings suggest that the motor cortex provides the dynamic force signal during force development. Other, possibly subcortical, structures could provide the static compensatory signal. This latter signal could be furnished by antigravity neural systems, given that most static loads encountered are gravitational in nature. According to this general view, the force exerted by the subject consists of dynamic and static components, each of which is controlled by different neural systems. These signals would converge in the spinal cord and provide an ongoing integrated signal to the motoneuronal pools.

In summary, the main insight stemming from these studies is that relations of cell activity to force are complex and should be interpreted within the context of additional information that pertains to the dimensions of the force space (e.g., one- or multi-dimen-

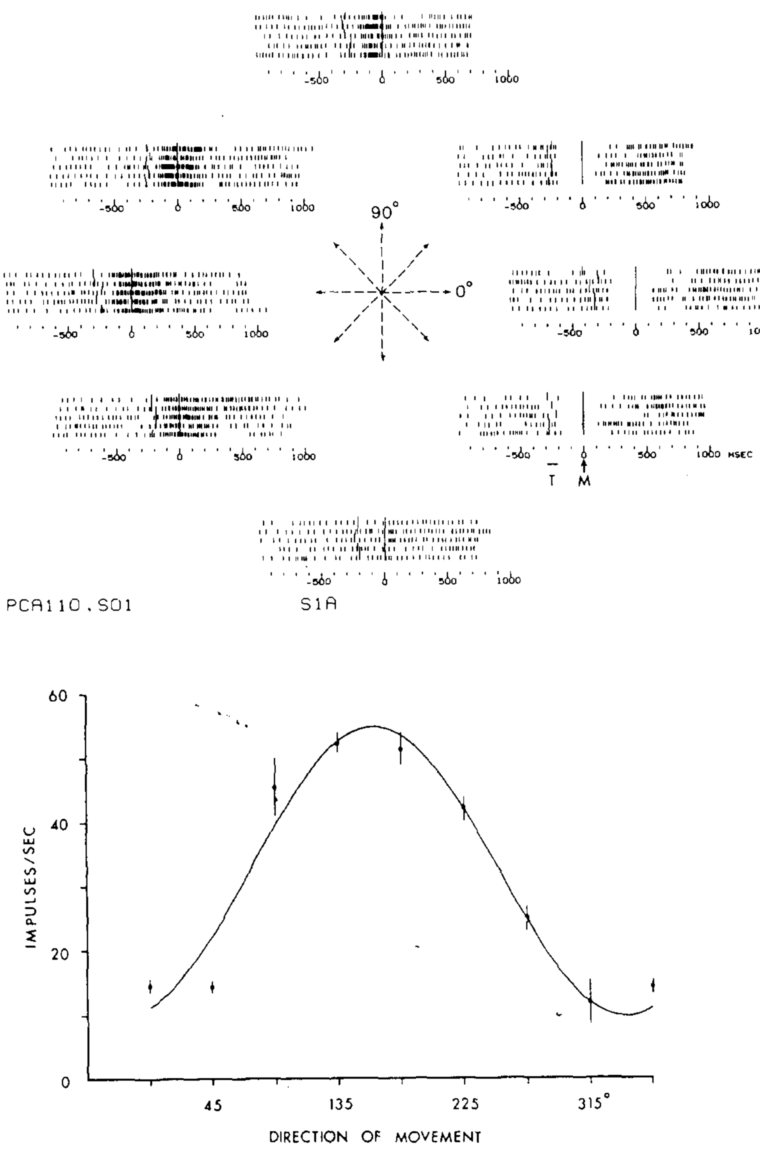

Figure 1. Directional Tuning in 2D Space

(A) Impulse activity during five trials in which equal amplitude movements were made in eight directions from the center of the working surface toward peripheral targets, as indicated by the diagram in the center. The rasters are aligned to the onset of movement (M). Longer vertical bars preceding movement onset denote the time of stimulus onset (target) onset (T).

(B) The average frequency of discharge during the time interval from the onset of the target to the end of the movement is plotted against the direction of the movement. Points are means of five trials ± SEM; the curve is a fitted sinusoidal function. (From Georgopoulos et al., 1982; reproduced with permission of the publisher; copyright by the Society for Neuroscience.)

sional), the static or dynamic nature of the task, the overall objective of the task (e.g., resist force, generate force, stabilize joint, etc.), and the projections of the cells under study (e.g., whether they project to the spinal cord, striatum, etc.). These questions provide the basis for further work.

Movement

Single-Joint Movements

Several studies used 1D movements about a single joint (e.g., Evarts, 1968; Thach, 1978; Alexander and Crutcher, 1990a, 1990b). In some studies monkeys made flexion-extension movements in the presence of constant loads opposing flexion or extension; in this way, the same movements were made using different muscles and were thus dissociated from them. Under these conditions, approximately one-third of motor cortical cells seemed to follow the patterns of muscle activity (Thach, 1978; Alexander and Crutcher, 1990a). Other variables, dissociated from the muscle pattern, were also important in determining motor cortical cell activity, including movement direction (Thach, 1978; Alexander and Crutcher, 1990a, 1990b) and joint angle (Thach, 1978). Therefore, it seems reasonable to suppose that during movements in which direction, position, and muscle activity covary, the activity of cells in the motor cortex relates to all of these parameters with variable strength.

Reaching, Multi-Joint Movements

Recordings in the motor cortex during 2D and three-dimensional (3D) arm movements revealed orderly relations of cell activity to spatial aspects of movements, especially to the direction of movement in space (Georgopoulos et al., 1982; Schwartz et al., 1988). Cell activity is directionally tuned: it is highest with movements in a particular direction (the cell's "preferred direction") and decreases gradually with movements in directions farther and farther away from the preferred one. Typically, the relation of cell activity to the direction of movement is a broad, cosine tuning

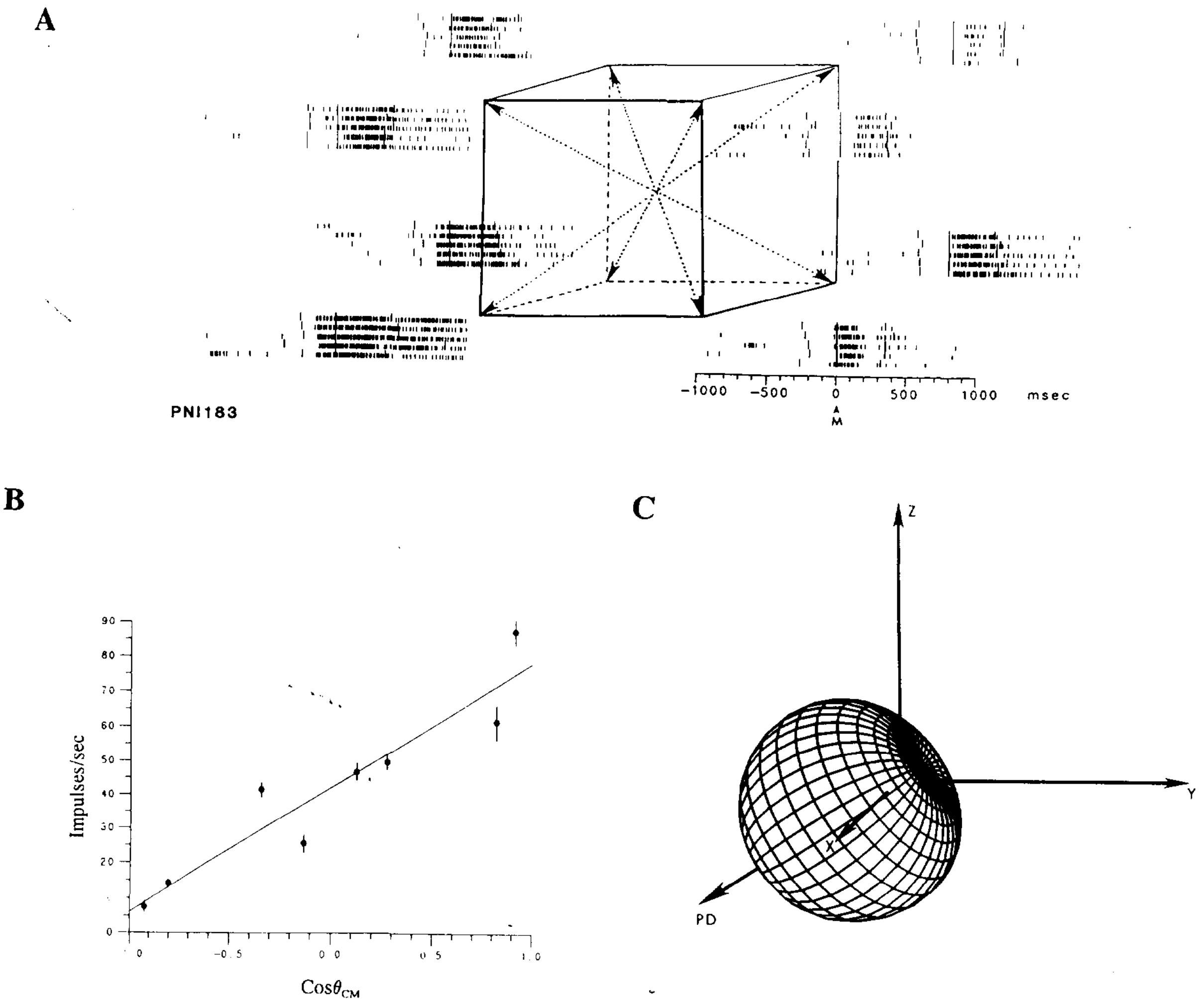

Figure 2. Directional Tuning in 3D Space

All data are for one motor cortical cell.

(A) Impulse activity (short bars) during movements in different directions (arrows). Rasters of five repeated trials for every movement direction are aligned with the onset of movement (M). Longer bars preceding and following the movement onset indicate the onset of the target and the end of the movement, respectively.

(B) Mean discharge rate (±SD) from onset of target to end of movement is plotted against the cosine of the angle θ formed between the direction of the movement and the cell's preferred direction.

(C) Predicted tuning volume based on cosine tuning function. PD, preferred direction. (From Schwartz et al., 1988; reproduced with permission of the publisher; copyright by the Society for Neuroscience.)

function, the peak of which denotes the preferred direction of the cell. Figures 1 and 2 illustrate directional tuning for 2D and 3D movements, respectively. Preferred directions tend to be arranged in vertical columns and are multiply represented in the motor cortex (Georgopoulos et al., 1984). For a population of cells, preferred directions are not clustered in particular directions, but range throughout the directional continuum (Figure 3) (Schwartz et al., 1988).

Analysis and Interpretation of Neural Activity: Neuronal Populations

Single cells provide only the building elements of the neural construct underlying movement generation and control; this construct invariably involves populations of neurons. The idea and use of neuronal populations in this context differ from common statistical measures of populations, such as averages, variances, and frequency distributions of functional cell properties. Instead, the idea is that a single neuron carries only partial information about a movement parameter, which is therefore uniquely represented in the whole neuronal ensemble. This idea was applied to the coding of the direction of movement, as follows. The broad directional tuning indicates that a given cell participates in movements of many directions. From this result and from the fact that preferred directions range widely, it follows that a movement in a particular direction will engage a whole population of cells. A unique code for the direction of movement was proposed (Georgopoulos et al., 1983, 1986, 1988),

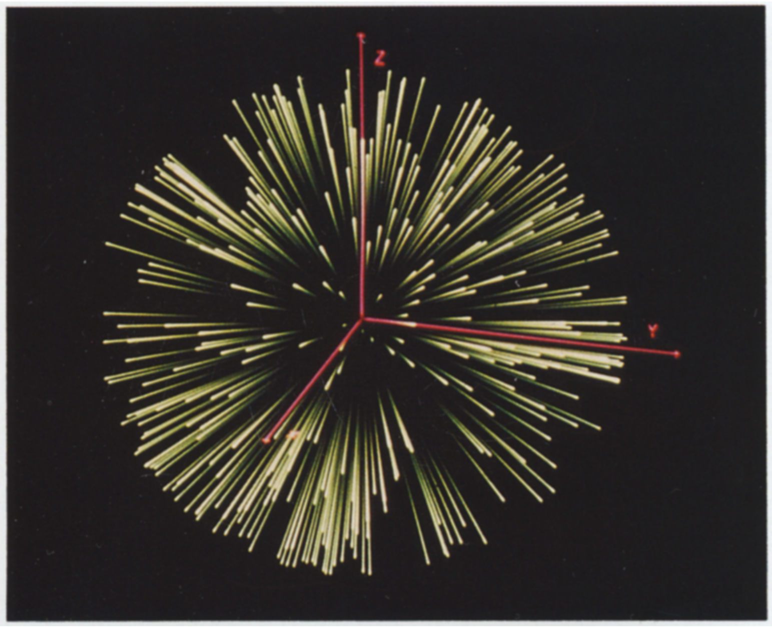

Figure 3. Preferred Directions (Unit Vectors) of 475 Motor Cortical Cells in 3D Space

(From Schwartz et al., 1988; reproduced with permission of the publisher; copyright by the Society for Neuroscience.)

which regarded this population as an ensemble of vectors. Each vector represents the contribution of a directionally tuned cell; it points in the cell's preferred direction and is weighted (i.e., has length) according to the change in cell activity associated with a particular movement direction. The weighted vector sum of these neuronal contributions is the "neuronal population vector" (Figure 4). The population vector points in the direction of reaching (Georgopoulos et al., 1983, 1986, 1988; Kalaska et al., 1983, 1989; Fortier et al., 1989; Caminiti et al., 1990, 1991). Although preferred directions tend to change in the horizontal plane as the origin of the movement changes, the population vector remains an unbiased predictor of the direction of the movement (Caminiti et al., 1991).

The length of the population vector is proportional to the instantaneous speed of a drawing movement (Schwartz, 1993), so that when successive population vectors are added tip to tail, the resulting "neural" trajectory predicts well the ensuing trajectory of the actual movement by an average time lead of approximately 120 ms. Therefore, for drawing movements, the population vector carries information concerning the unfolding movement trajectory.

Thinking along population lines in general is now supported by the results of studies concerning the interaction of the motor cortex with input (e.g., thalamus and other cortical areas) and output (e.g., spinal cord) structures and by the representation of muscles and/or joints in the motor cortex. Concerning the first

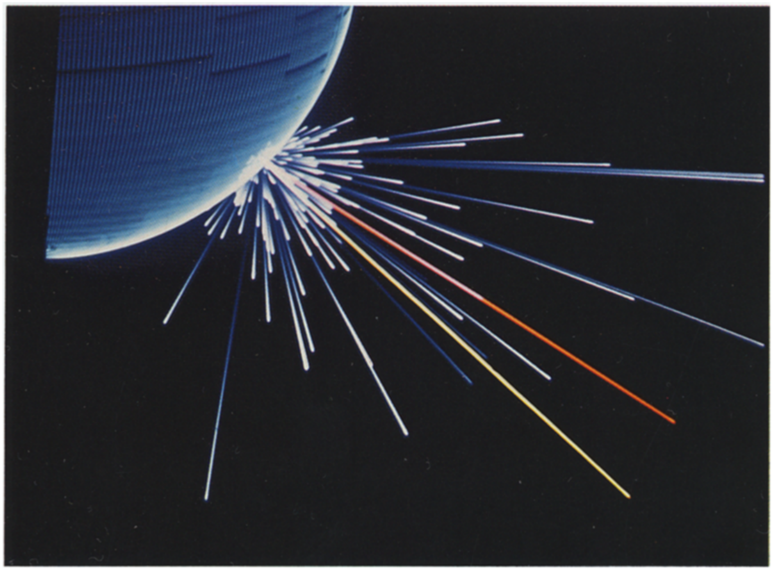

Figure 4. Population Coding of Movement Direction

The blue lines represent the vectorial contributions of individual cells in the population (N = 475). The movement direction is in yellow and the direction of the population vector in red. (From Schwartz et al., 1988; reproduced with permission of the publisher; copyright by the Society for Neuroscience.)

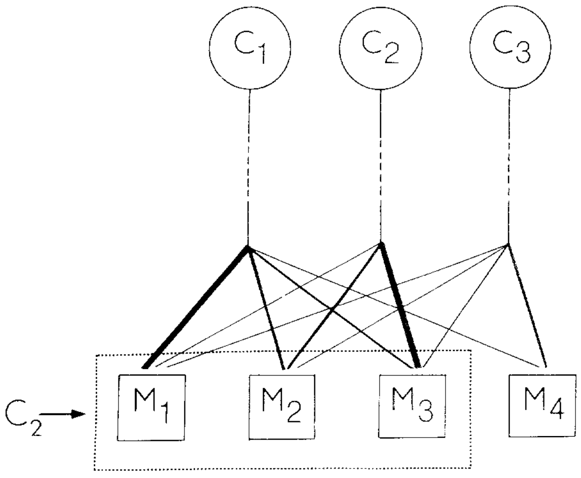

Figure 5. Schematic Diagram Illustrating the Postulated Pattern of Weighted Divergent and Convergent Influences Exerted on Motoneuronal Pools by Single Motor Cortical Cells

The dashed lines indicate intercalated neurons (e.g., C3-C4 propriospinal neurons, force field generators, etc.). The line thickness indicates the weighted influence. Motor cortical cell C2 influences a weighted combination of motoneuronal pools (M1, M2, M3), enclosed within the interrupted parallelogram.

point, studies over the past two decades using anatomical techniques (intra-axonal injections of single fibers) and/or physiological recordings (spike-triggered averaging) have shown a substantial divergence of the inputs to the motor cortex from the thalamus (Shinoda and Kakei, 1989) and somatosensory cortex (DeFelipe et al., 1986) and of the outputs from the motor cortex to the spinal cord (Shinoda et al., 1981; Cheney and Fetz, 1980; Lemon et al., 1986). Concerning the second point, electrical stimulation studies have shown that muscles are multiply represented in the motor cortex in a weighted fashion (Donoghue et al., 1992), as are joints (Humphrey and Mitz, 1989, Symp. Honoring V. B. Montcastle, abstract). Therefore, motor cortical activity should be considered along the lines of distributed population systems both within the motor cortex itself and in its interactions with its inputs and outputs. The fact that input structures to the motor cortex, such as the cerebellum (Fortier et al., 1989), premotor cortex (Caminiti et al., 1991), and area 5 (Kalaska et al., 1983; Kalaska, 1988), follow the distributed population coding and that the reaching movements themselves involve the activation of several muscles and therefore activity in the spinal cord spread over several segments underscore the importance of population coding in the planning and execution of these movements.

Spinal Mechanisms

In general, the neural signals from the motor cortex do not activate motoneurons directly, but ultimately influence the activity of motoneurons through interneurons of the spinal cord. In certain cases, the corticospinal axons terminate within the motor nuclei, as is the case for the motoneurons innervating distal muscles of the limb in adult primates (Porter and Lemon, 1993), but in the vast majority of cases the influence on the motoneuronal pools is exerted through intercalated interneurons, resulting in diverging and converging patterns of influences (Figure 5). These interneurons are found at the segmental level as well as at the upper cervical (C3-C4) level. The latter system has been investigated extensively in the cat, and its intricate inputs from central and peripheral sources have been partially elucidated (Lundberg, 1979).

A detailed analysis of how spinal interneuronal systems influence the spinal motor output in space has been carried out recently in the spinal frog (Bizzi et al., 1991; Giszter et al., 1993). In these studies, the technique of microstimulation was used to determine the effects of interneuronal populations on the direction and magnitude of the force in space developed by the limb of the spinalized frog. There were three major findings of these studies. First, microstimulation at a particular interneuronal zone in the spinal cord elicited the development of force by the limb, the direction and magnitude of which differed depending on the position of the limb in space. The set of these forces define a "force field." In the absence of microstimulation, there were passive forces due to the resistance to stretch of the limb tissues. During microstimulation, active forces were developed, which when added to the passive ones resulted in the total force exerted by the limb. In the experiment, the total and the passive forces were measured, and the passive forces were subtracted from the total to obtain the "active" force field. It was found that microstimulation in a given area resulted in an active force field in which the force vectors converged on a particular point in space at which the force developed was zero. This was called the "equilibrium point" of that field. In many cases, the force field predicted the limb motion when the limb was allowed to move; therefore, these fields can be regarded as underlying movement primitives (Giszter et al., 1993). The second finding was that only a few (3-4) clusters of equilibrium points were found by a detailed and systematic microstimulation of extensive areas of the spinal cord; each equilibrium point was represented at different locations in the spinal cord. Finally, concomitant microstimulation at any two sites produced a new force field that was the result of a point by point linear summation of the force field produced at each of the two stimulation sites; thus new equilibrium points were created.

These findings suggest possible mechanisms by which supraspinal commands could be translated into motor action as follows. First, these intrinsic spinal motor mechanisms involve populations of neurons and summation of influences from potentially separate neuronal ensembles, given that microstimulation will activate an appreciable number of neurons (Phillips and Porter, 1977). Second, it is likely that these ensembles are the targets of supraspinal influences.

For example, a common characteristic of pyramidal tract axons is their appreciable divergence in the spinal cord with collaterals to various spinal segments. Although spinal microstimulation studies have not been performed in primates, it is reasonable to hypothesize a similar plan of spinal organization. Then this divergence of the pyramidal tract axons would enable central motor commands to address concomitantly a number of the spinal populations associated with different force fields, that is, with different movement primitives. Third, this organization could provide the background for the translation of the motor cortical command, as understood at the single-cell and neuronal population level, to motoneuronal activation.

The results of the studies reviewed above suggest that spinal and supraspinal motor structures regard the limb as a functional whole. Recent studies (Bosco and Poppele, 1993) indicate that afferent systems may do the same. In these experiments single-cell activity was recorded in the Clarke's column, the nucleus of origin of the dorsal spinocerebellar tract. Cells were antidromically identified as projecting to the cerebellum, and their activity was recorded during peripheral stimulation of the hindlimb in anesthetized cats. Although single cells received mono- and polysynaptic convergent inputs from various kinds of receptors and parts of the limb, their activity varied in an orderly fashion with the orientation of the limb in space and with the direction of limb movement in space, when the limb was moved passively. This shows that the converging information onto single cells can meaningfully reflect spatial aspects of the status of the limb as a whole. Convergence of peripheral inputs on spinal interneurons has been described in several cases, including the C3–C4 propriospinal interneurons mediating central commands to proximal motoneurons (Illert et al., 1978). It would be interesting to know whether the activity of these neurons similarly reflects spatial aspects of limb posture and/or movement.

Additional support for the idea that the limb may be controlled as a multi-joint unit comes from the results of recent studies in which microstimulation or ablation of central nervous system structures was used. First, microstimulation of the motor cortex in the monkey elicited concomitant activation of various muscles (Donoghue et al., 1992) and a weighted motion of various joints (Humphrey and Mitz, 1989, Symp. Honoring V. B. Montcastle, abstract). Second, reversible inactivation of the motor cortex in the cat affected multi-joint reaching movements of the limb but not single-joint movements about the elbow (Martin and Ghez, 1993). And third, lesion of the dentate nucleus in the monkey also differentially affected reaching but not single-joint movements (Kane et al., 1989, Soc. Neurosci., abstract). These findings are in accord with the suggestion of the original single-cell recording studies (Georgopoulos et al., 1982) that the motor cortex controls reaching movements. The close interaction between the motor cortex and the cerebellum (Asanuma et al., 1986) suggests that both of these structures may share this common feature of whole-limb motor control.

Neural Events Signaling Preparation for Movement

A common example of preparing to move is when a movement is produced in response to a visual stimulus: a period of time intervenes between the occurrence of the stimulus and the beginning of the movement, which is the traditional reaction time. In other cases a delay can be imposed so that the movement will be initiated after a period of waiting, while the stimulus is still present. These instructed delay paradigms probe a step further the representation of planned movements, in the sense that there is not an immediate motor output while the representation is being kept active. Finally, a specific case of delayed tasks involves movements that have to be produced on the basis of information kept in memory. The difference from the instructed delay task is that now the stimulus defining the direction of the movement is turned off after a short period of presentation and the movement is triggered after a delay by a separate "go" signal. Thus information concerning the intended movement has to be retained during the memorized delay.

In all three cases above, the representation of information about the intended movement can be studied under different conditions that impose different constraints on the system. It would interesting to know whether this representation could be identified and visualized during the reaction time, the instructed delay, and the memorized delay periods. Since the information assumed to be represented is about direction, the neuronal population vector could be a useful tool by which to identify this representation. For that purpose, the population vector was computed every 10 or 20 ms during the reaction time (Georgopoulos et al., 1984, 1988), during an instructed delay period (Georgopoulos et al., 1989a), and during a memorized delay period (Smyrnis et al., 1992). The results were clear: in all these cases the population vector pointed in the direction of the planned movement during the above time periods. These findings underscore the usefulness of the population vector analysis as a tool for visualizing representations of the planned movement and show that in the presence or absence of an immediate motor output, as well as when the directional information has to be kept in memory, the direction of the intended movement is represented in a dynamic form at the ensemble level. These results also document the involvement of the motor cortex in the representation of intended movements under various behavioral conditions.

These results illustrate the point that neural events in central motor structures, including the motor cortex, frequently reflect the complexity of the behavioral paradigm. Indeed, changes in motor cortical activity have been observed during performance of memorized, curved movement trajectories (Hocherman and Wise, 1991), when the direction of the movement was dissociated from the direction of its target (Alexander and Crutcher, 1990b), and when monkeys discriminated between two frequencies of mechanical sinusoids delivered to the glabrous skin of their hands (Mountcastle et al., 1992). Another example comes from recent studies of motor cortical activity during a task that required the performance of a memorized movement trajectory with an orthogonal directional bend (Ashe et al., 1993). In these experiments, monkeys were trained to make an arm movement with an orthogonal bend, first up and then to the left, following a waiting period. They held a 2D manipulandum over a spot of light at the center of a planar working surface. When this light went off, the animals were required to hold the manipulandum there for 600–700 ms and then move the handle up and to the left to receive a liquid reward. There were no external signals concerning the "go" time or the trajectory of the movement. It was hypothesized that during that period, signs of directional processing relating to the upcoming movement would be identified in the motor cortex. During the waiting period, the population vector began to grow approximately 130 ms after the center light was turned off; it pointed first in the direction of the second part of the memorized movement and then rotated clockwise toward the direction of the initial part of the movement. These findings indicate processing of directional information during the waiting period preceding the memorized movement. Moreover, we found a few cells whose activity changed during the performance of the memorized movement but not during the visually triggered movements, and others whose activity changed during the visually triggered movement, but not during the memorized movement. Interestingly, the cells activated during the memorized movement were inactive during the waiting period; therefore, it seems that these cells were involved in the *execution* of the memorized movement but not in its *planning* or mental rehearsal.

The Problem of Cognition: Neural Operations Subserving Motor Cognitive Transformations

In the delayed tasks described above the movement to be made was unequivocally defined in the sense that its direction was determined by the location of a stimulus relative to the starting point. In that situation the visual information concerning direction is used to generate the appropriate motor command to implement a movement in that direction; truly, this movement direction has to be generated and kept available during the delay period, but it is defined from the beginning. Therefore, the direction of the movement is the same throughout the various times considered above. A very different situation was created in an experiment (Georgopoulos and Massey, 1987) in which the direction of the movement to be made had to be determined freshly at every trial according to a certain rule, namely that the movement direction be at an angle (counterclockwise [CCW] or clockwise [CW]) from the stimulus direction. This experiment takes us away from the case of a *fixed* motor intention; instead, this intention must now be derived as the solution to the problem. In fact, there are many ways by which this problem can be solved (discussed in Georgopoulos and Massey, 1987). An obvious way would be to form a look-up table that contains the movement directions that correspond to the stimulus directions. Using this strategy, one would simply memorize the corresponding directions in the table, and given a stimulus direction, one would search the table to select the movement direction corresponding to the particular stimulus direction. Of course, one would not have to use numbers, simply imagined directed radii in a unit circle.

A different strategy would be to rotate mentally the stimulus direction in the instructed departure (CCW or CW) by an amount equal to the required angular shift. The look-up table and mental rotation hypotheses lead to different predictions concerning how the reaction time would change, and on this basis they can be distinguished. If the look-up table strategy is followed, the reaction time would increase owing to the time taken for the search, but this increase should not be greater for larger angles because there is no reason to suppose that searching the table in the case of a large angle should take more time than searching the table in the case of a small angle. In contrast, the mental rotation hypothesis predicts an increase of the reaction time with the angle because the time needed to rotate a radius through an angle should be proportional to the angle itself. Indeed, the results of the experiments in human subjects (Georgopoulos and Massey, 1987) showed an increase in the reaction time with the angle and therefore supported the mental rotation hypothesis. The average rate of the hypothesized rotation was approximately 400°/s. Remarkably, this is very close to the value obtained by Shepard and Cooper (1982) in experiments on mental rotation of visual images. Another similarity between the motor rotation (Georgopoulos and Massey, 1987) and visual rotation (Shepard and Cooper, 1982) studies is that there is appreciable diversity in the rotation rates obtained among different subjects. In fact, we used this feature to test the idea that motor and visual mental rotation processes may be associated. Indeed, a significant correlation was found between the two rotation rates in a group of subjects who performed both tasks (Pellizzer and Georopoulos, 1993). This suggests that the two processes might share a common processing stage, or that both processes involve constraints that result in the relation obtained.

The neural mechanisms underlying the process of mental rotation in the movement domain were investigated by training monkeys to perform a task in which they made a movement in a direction 90° CCW from a stimulus direction. We supposed that if a mental rotation of an imagined vector was taking place, it

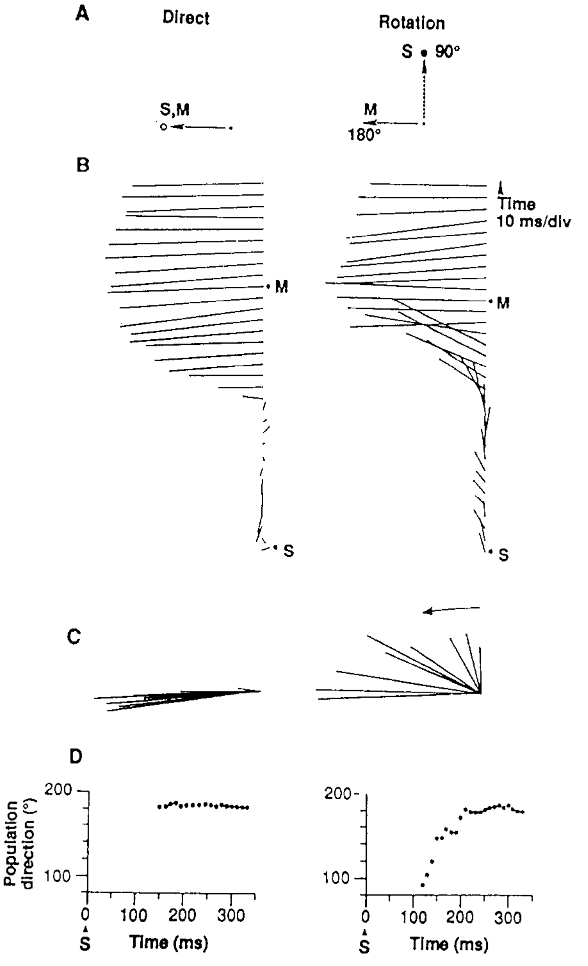

Figure 6. Time Evolution of the Neuronal Population Vector When the Movement Is in the Direction of a Stimulus or 90° CCW from It

(A) Task: open and closed circles indicate dim and bright light, respectively. Interrupted and continuous lines with arrows indicate stimulus (S) and movement (M) directions, respectively.

(B) Neuronal population vectors calculated every 10 ms from the onset of the stimulus (S) at positions shown at (A) until after the onset of the movement (M). When the population vector lengthens, for the direct case (left) it points in the direction of the movement, whereas for the rotation case it points initially in the direction of the stimulus and then rotates CCW (from 12 o'clock to 9 o'clock) and points in the direction of the movement.

(C) Ten successive population vectors from (B) are shown in a spatial plot, starting from the first population vector that increased significantly in length. Notice the CCW rotation of the population vector (right panel).

(D) Scatter plots of the direction of the population vector as a function of time, starting from the first population vector that increased significantly in length after stimulus onset (S). For the direct case (left panel), the direction of the population vector is in the direction of the movement (~180°); for the rotation case (right panel) the direction of the population vector rotates CCW from the direction of the stimulus (~90°) to the direction of the movement (~180°).

could be revealed using the population vector analysis. Indeed, the population vector rotated during the reaction time from the stimulus to the movement direction through the 90° CCW angle (Figure 6) (Georgopoulos et al., 1989b; Lurito et al., 1991). Interestingly, the rotation rates (direction of population vector versus time) observed (Lurito et al., 1991) were very similar to the rates (increase in reaction time versus angle) observed in the human studies (Georgopoulos and Massey, 1987). Thus, the dynamic processing of a directional transformation was successfully visualized using the neuronal population vector analysis.

Concluding Remarks

The results of the experiments discussed above raise several points concerning the representation of movement in the motor cortex.

The first point is that this representation is not obligatorily connected with the production of movement, that is, its presence does not necessarily lead to motor output. This has been shown by the results of previous studies (Tanji and Evarts, 1976) and of the instructed and/or memorized delay studies summarized above. This is in accord with findings of psychophysical studies that movement planning and movement triggering are different processes (Hening et al., 1988). It is interesting that when a delay is introduced, at least two different subsets of cells seem to be involved: one that is active during the delay and becomes further active following the movement triggering signal, and another that is not active during the delay but becomes engaged after the "go" signal (Georgopoulos et al., 1989a). Therefore, it seems that both the planning and the triggering processes involve the motor cortex. It is possible that motor cortical activity could be gated at segmental and propriospinal (Lundberg, 1979) levels in the spinal cord, given the extensive convergence of several supraspinal inputs on these interneuronal systems. Therefore, engagement of the motor cortex is not a sufficient condition for triggering the movement. On the other hand, motor cortical activation seems to be necessary for appropriate planning of the movement, as suggested by the disturbed reaching movements produced by reversible inactivation of the motor cortex (Martin and Ghez, 1993).

The second point concerns the nature of the information that is represented. It may not be appropriate to assign all of this information to the upcoming movement, for it may very well reflect processes subserving the translation of visual or memorized information to motor output. The complexity of potential explanatory factors for motor cortical activity in behavioral tasks is suggested by the results of studies in which such factors were dissociated (Thach, 1978; Alexander and Crutcher, 1990a, 1990b) and by the results of the directional transformation study (Georgopoulos et al., 1989b) discussed above, which showed that motor cortical activity does reflect a process involved in mental rotation. A different aspect of task condition shown to be important for motor cortical cell activity is the independent use of fingers. In particular, it was shown that single cells in the motor cortex can be active during a precision grip but not during a power grip, even when the two grips involve similar amounts of muscle activity (Muir and Lemon, 1983). This shows clearly that the intensity of muscle activation is not the sole, and probably not the most important, determinant of cell activity in the motor cortex.

The third point concerns the place of the motor cortex among other motor structures. In this context, it is important to realize that unlike primary sensory cortices, the motor cortex is the site of convergence from a large number of other areas, both cortical and subcortical. For example, the large extent of the convergence on the motor cortex, in contrast to that on the somatosensory cortex, can be appreciated from the results of recent studies of the thalamocortical projections to small motor cortical areas (Darian-Smith et al., 1990). Therefore, the discharge patterns of motor cortical cells are generated through this convergence rather than being the outcome of a faithful transmission through sensory lines. It seems then that although both primary somatosensory and motor cortices are near the somatic periphery, their proposed close similarity (Fetz, 1984) is misleading. On the other hand, the motor cortex is not the "final" motor path from the cerebral cortex. It has now been shown conclusively that several premotor areas possess direct and dense projections to the spinal cord (Dum and Strick, 1991). It seems that the motor cortex and premotor areas might be concerned with different but overlapping aspects of motor control (Tanji and Kurata, 1985; Alexander and Crutcher, 1990a, 1990b; Chen et al., 1991) in that a particular movement might be the result of this parallel processing. These findings have an important implication, among others, which is that the spinal motor mechanisms involved in the production of voluntary movement can be properly understood only if one takes into account the convergent pattern of influences from the motor and premotor cortical areas, the influences from subcortical structures such as the red nucleus and the reticular formation, and the organization and dynamic interplay of spinal interneuronal circuits involved in the transmission of central commands (Lundberg, 1979), the generation of stereotypic motor patterns (Grillner et al., 1988; Gelfand et al., 1988), and the control of afferent input from the moving limb (Rudomin, 1990). The intricacy of the latter can be appreciated from the elucidation of the mechanisms involved in presynaptic inhibition (Rudomin 1990) and its differential control by supraspinal structures (Rudomin et al., 1986), including the motor cortex (Eguibar et al., 1991, Soc. Neurosci., abstract).

Finally, the patterns of activity of precentral corticospinal neurons will have to be understood in light of their influences on the spinal mechanisms. In that respect, most of the attention in behaving primates has been focused on those motor cortical neurons that are presumably monosynaptically projecting onto motoneurons, and practically no attention has been paid to the cortical influences on spinal interneuronal mechanisms, in spite of the fact that it is through the latter that a major, and indeed exclusive in some species (e.g., the cat), cortical effect is exerted. There is little doubt that understanding the interactions among the various motor areas, and in particular those between the motor cortex and the spinal cord (Georgopoulos and Grillner, 1989), is now the biggest challenge in deciphering the "natural intelligence" of the motor system. In that respect, the results of the recent studies of Bizzi et al. (1991) provide an important advance in understanding the motor spinal mechanisms at the ensemble level and form a base for studying the interactions between central motor areas and spinal interneuronal systems intercalated in the translation of central commands to muscle output.

Acknowledgments

This work was supported by United States Public Health Service grants NS17413 and PSMH48185 and by an Office of Naval Research contract.

References

Alexander, G. E., and Crutcher, M. D. (1990a). Preparation for movement: neural representations of intended direction in three motor areas of the monkey. J. Neurophysiol. *64*, 133–149.

Alexander, G. E., and Crutcher, M. D. (1990b). Neural representations of the target (goal) of visually guided arm movements in three motor areas of the monkey. J. Neurophysiol. *64*, 164–177.

Asanuma, H., Mackel, R., and Bornschlegl, M. (1986). Effect of disuse of hand for recovery of motor function following dorsal column section in the monkey. Neurosci. Res. *3*, 666–771.

Ashe, J., Taira, M., Smyrnis, N., Pellizzer, G., Georgakopoulos, T., Lurito, J. T., and Georgopoulos, A. P. (1993). Motor cortical activity preceding a memorized movement trajectory with an orthogonal bend. Exp. Brain Res. *95*, 118–130.

Bauswein, E., Fromm, C., and Preuss, A. (1989). Corticostriatal cells in comparison with pyramidal tract neurons: contrasting properties in the behaving monkey. Brain Res. *493*, 198–203.

Bizzi, E., Mussa-Ivaldi, F. A., and Giszter, S. (1991). Computations underlying the execution of movement: a biological perspective. Science *253*, 287–291.

Bosco, G., and Poppele, R. E. (1993). Broad directional tuning in spinal projections to the cerebellum. J. Neurophysiol. *70*, 863–866.

Caminiti, R., Johnson, P. B., Burnod, Y., Galli, C., and Ferraina, S. (1990). Shift of preferred directions of premotor cortical cells with arm movements performed across the workspace. Exp. Brain Res. *83*, 228–232.

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

Chen, D. F., Hyland, B., Maier, V., Palmeri, A., and Wiesendanger, M. (1991). Comparison of neural activity in the supplementary motor area and in the primary motor cortex in monkeys. Somatosens. Motor Res. *8*, 27–44.

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.

Darian-Smith, C., Darian-Smith, I., and Cheema, S. S. (1990). Thalamic projections to sensorimotor cortex in the macaque monkey: use of multiple retrograde fluorescent tracers. J. Comp. Neurol. *299*, 17–46.

DeFelipe, J., Conley, M., and Jones, E. G. (1986). Long-range focal collateralization of axons arising from corticocortical cells in monkey sensory-motor cortex. J. Neurosci. *6*, 3749–3766.

Donoghue, J. P., Leibovic, S., and Sanes, J. N. (1992). Organization of the forelimb area in squirrel monkey motor cortex: representation of digit, wrist, and elbow muscles. Exp. Brain Res. *89*, 1–19.

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. (1966). Pyramidal tract activity associated with a conditioned hand movement in the monkey. J. Neurophysiol. *29*, 1011–1027.

Evarts, E. V. (1968). Relation of pyramidal tract activity to force exerted during voluntary movements. J. Neurophysiol. *31*, 14–27.

Evarts, E. V. (1969). Activity of pyramidal tract neurons during postural fixation. J. Neurophysiol. *32*, 375–385.

Evarts, E. V., Fromm, C., Kroller, J., and Jennings, V. A. (1983). Motor cortex control of finely graded forces. J. Neurophysiol. *49*, 1199–1215.

Fetz, E. E. (1984). Functional organization of motor and sensory cortex: symmetries and parallels. In Dynamic Aspects of Neocortical Function, G. M. Edelman, W. E. Gall, and W. M. Cowan, eds. (New York: John Wiley & Sons), pp. 453–473.

Fortier, P. A., Kalaska, J. F., and Smith, A. M. (1989). Cerebellar neuronal activity related to whole-arm reaching movements in the monkey. J. Neurophysiol. 62, 198–211.

Fromm, C. (1983). Changes of steady state activity in motor cortex consistent with the length-tension relation of the muscle. Pflugers Arch. *398*, 318–323.

Gelfand, I. M., Orlovsky, G. N., and Shik, M. L. (1988). Locomotion and scratching in tetrapods. In Neural Control of Rhythmic Movements in Vertebrates, A. H. Cohen, S. Rossignol, and S. Grillner, eds. (New York: John Wiley & Sons), pp. 1–40.

Georgopoulos, A. P. (1991). Higher order motor control. Annu. Rev. Neurosci. *14*, 361–377.

Georgopoulos, A. P., and Grillner, S. (1989). Visuomotor coordination in reaching and locomotion. Science *245*, 1209–1210.

Georgopoulos, A. P., and Massey, J. T. (1987). Cognitive spatial-motor processes. 1. The making of movements at various angles from a stimulus direction. Exp. Brain Res. *65*, 361–370.

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.

Georgopoulos, A. P., Caminiti, R., Kalaska, J. F., and Massey, J. T. (1983). Spatial coding of movement: a hypothesis concerning the coding of movement direction by motor cortical populations. Exp. Brain Res. (Suppl.) *7*, 327–336.

Georgopoulos, A. P., Kalaska, J. F., Crutcher, M. D., Caminiti, R., and Massey, J. T. (1984). The representation of movement direction in the motor cortex: single cell and population studies. In Dynamic Aspects of Neocortical Function, G. M. Edelman, W. E. Gall, and W. M. Cowan, eds. (New York: John Wiley & Sons), pp. 501–524.

Georgopoulos, A. P., Schwartz, A. B., and Kettner, R. E. (1986). Neuronal population coding of movement direction. Science *233*, 1416–1419.

Georgopoulos, A. P., Kettner, R. E., and Schwartz, A. B. (1988). 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*, 2928–2937.

Georgopoulos, A. P., Crutcher, M. D., and Schwartz, A. B. (1989a). Cognitive spatial-motor processes. 3. Motor cortical prediction of movement direction during an instructed delay period. Exp. Brain Res. *75*, 183–194.

Georgopoulos, A. P., Lurito, J. T., Petrides, M., Schwartz, A. B., and Massey, J. T. (1989b). Mental rotation of the neuronal population vector. Science *243*, 234–236.

Georgopoulos, A. P., Ashe, J., Smyrnis, N., and Taira, M. (1992). Motor cortex and the coding of force. Science *256*, 1692–1695.

Giszter, S. F., Mussa-Ivaldi, F. A., and Bizzi, E. (1993). Convergent force fields organized in the frog's spinal cord. J. Neurosci. *13*, 467–491.

Grillner, S., Buchanan, J. T., Wallen, P., and Brodin, L. (1988). Neural control of locomotion in lower vertebrates. In Neural Control of Rhythmic Movements in Vertebrates, A. Cohen, S. Rossignol, and S. Grillner, eds. (New York: John Wiley & Sons), pp. 1–40.

Hening, W., Favilla, M., and Ghez, C. (1988). Trajectory control in targeted force impulses. V. Gradual specification of response amplitude. Exp. Brain Res. *71*, 116–128.

Hepp-Reymond, M.-C., and Diener, R. (1983). Neural coding of force and rate of force change in the precentral finger region of the monkey. Exp. Brain Res. (Suppl.) *7*, 315–326.

Hepp-Reymond, M.-C., Wyss, U. R., and Anner, R. (1978). Neuronal coding of static force in the primate motor cortex. J. Physiol. (Paris) *74*, 287–291.

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

Humphrey, D. R., and Reed, D. J. (1983). Separate cortical systems for control of joint movement and joint stiffness: reciprocal activation and coactivation of antagonist muscles. Adv. Neurol. *39*, 347–372.

Illert, M., Lundberg, A., Padel, Y., and Tanaka, R. (1978). Integration in descending motor pathways controlling the forelimb in the cat. 5. Properties of and monosynaptic excitatory convergence on C3-C4 propriospinal neurones. Exp. Brain Res. *33*, 101–130.

Jackson, J. H. (1889). On the comparative study of diseases of the nervous system. Br. Med. J. *ii*, 355–362.

Kalaska, J. F. (1988). The representation of arm movements in postcentral and parietal cortex. Can. J. Physiol. Pharmacol. *66*, 455–463.

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

Kalaska, J. F., Cohen, D. A. D., Hyde, M. L., and Prud'homme, M. (1989). A comparison of movement direction-related versus load direction-related activity in primate motor cortex, using a two-dimensional reaching task. J. Neurosci. *9*, 2080–2102.

Lemon, R. N. (1984). Methods for Neuronal Recording in Conscious Animals (Chisester: John Wiley & Sons).

Lemon, R. N., Mantel, G. W. H., and Muir, R. B. (1986). Corticospinal facilitation of hand muscles during voluntary movement in the conscious monkey. J. Physiol. *381*, 497–527.

Leyton, A. S. F., and Sherrington, C. S. (1917). Observations on the excitable cortex of the chimpanzee, orang-otan, and gorilla. Quart. J. Exp. Physiol. *11*, 135–222.

Lundberg, A. (1979). Integration in a propriospinal motor centre controlling the forelimb in the cat. In Integration in the Nervous System, H. Asanuma and V. J. Wilson, eds. (Tokyo: Igaku-Shoin), pp. 47–64.

Lurito, J. L., Georgakopoulos, T., and Georgopoulos, A. P. (1991). 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*, 562–580.

Maier, M. A., Bennett, K. M. B., Hepp-Reymond, M.-C., and Lemon, R. N. (1993). Contribution of the monkey corticomotoneuronal system to the control of force in precision grip. J. Neurophysiol. *69*, 772–785.

Martin, J. H., and Ghez, C. (1993). Differential impairments in reaching and grasping produced by local inactivation within the forelimb representation of the motor cortex of the cat. Exp. Brain Res. *94*, 429–443.

Mountcastle, V. B., Atluri, P. P., and Romo, R. (1992). Selective output-discriminative signals in the motor cortex of waking monkeys. Cerebral Cortex *2,* 277–294.

Muir, R. B., and Lemon, R. N. (1983). Corticospinal neurons with a special role in precision grip. Brain Res. *261,* 312–316.

Pellizzer, G., and Georgopoulos, A. P. (1993). Common processing constraints for visuomotor and visual mental rotations. Exp. Brain Res. *93,* 165–172.

Phillips, C. G., and Porter, R. (1977). Corticospinal Neurones (London: Academic Press, Inc.).

Porter, R., and Lemon, R. (1993). Corticospinal Function and Voluntary Movement (Oxford: Clarendon Press).

Rudomin, P. (1990). Presynaptic inhibition of muscle spindle and tendon organ afferents in the mammalian spinal cord. Trends Neurosci. *13,* 499–505.

Rudomin, P., Solodkin, M., and Jiménez, I. (1986). PAD and PAH response patterns of group Ia- and Ib-fibers to cutaneous and descending inputs in the cat spinal cord. J. Neurophysiol. *56,* 987–1006.

Schwartz, A. B. (1993). Motor cortical activity during drawing movements: population representation during sinusoid tracing. J. Neurophysiol. *70,* 28–36.

Schwartz, A. B., Kettner, R. E., and Georgopoulos, A. P. (1988). 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,* 2913–2927.

Shepard, R. N., and Cooper, L. A. (1982). Mental Images and Their Transformations (Cambridge, Massachusetts: MIT Press).

Shinoda, Y., and Kakei, S. (1989). Distribution of terminals of thalamocortical fibers originating from the ventrolateral nucleus of the cat thalamus. Neurosci. Lett. *96,* 163–167.

Shinoda, Y., Yokota, J. I., and Futami, T. (1981). Divergent projections of individual corticospinal axons to motoneurons of multiple muscles in the monkey. Neurosci. Lett. *23,* 7–12.

Smith, A. M. (1981). The coactivation of antagonist muscles. Can. J. Physiol. Pharmacol. *59,* 733–747.

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.

Smyrnis, N., Taira, M., Ashe, J., and Georgopoulos, A. P. (1992). Motor cortical activity in a memorized delay task. Exp. Brain Res. *92,* 139–151.

Tanji, J., and Evarts, E. V. (1976). Anticipatory activity of motor cortex neurons in relation to direction of an intended movement. J. Neurophysiol. *39,* 1062–1068.

Tanji, J., and Kurata, K. (1985). Contrasting neuronal activity in supplementary and precentral motor cortex of monkeys. I. Responses to instructions determining motor responses to forthcoming signals of different modalities. J. Neurophysiol. *53,* 129–141.

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.