

32 Motor Cortex and Cognitive Processing

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ABSTRACT This chapter summarizes key observations and concepts concerning the involvement of the motor cortex in motor cognitive processes operating on the direction of movement in space. Large populations of neurons in motor cortex are engaged with reaching movements. Single cells are directionally broadly tuned, but the neuronal population carries an unambiguous directional signal. The outcome of this population code can be visualized as a vector that points in the direction of the upcoming movement during the reaction time, during an instructed delay period, and during a memorized delay period. Moreover, when a mental transformation is required for the generation of a reaching movement in a direction different from a reference direction, the population vector provides a direct insight into the nature of the cognitive process by which the required transformation is achieved.

Most of the brain deals with motor function. A number of areas of the cerebral cortex and a number of subcortical structures, including the cerebellum and large portions of the basal ganglia, brain stem and spinal cord, are concerned with the specification, control, and ongoing modification of self-initiated or stimulus-elicited movements. The variety and complexity of the structures involved and the intricacy of the aspects of motor function controlled can be appreciated by considering the large variety of motor syndromes produced by disease processes affecting motor structures. These motor deficits range, in two extremes, from paralysis, which is loss of voluntary movement, to apraxia, which is loss of particular motor skills in the absence of paralysis.

A crucial node in brain control of motor function is occupied by the motor cortex, a strip of cerebral cortex located just in front of the central sulcus, in the precentral gyrus. The motor cortex provides major out-

puts to the spinal cord and brain stem and is heavily interconnected with other cortical areas and with the major subcortical structures, the cerebellum and the basal ganglia. The question of how the motor cortex performs its function has been intensely investigated in the past century, but it is only during the last 25 years that major advances have been made as a result of the availability of a direct technique by which the ongoing activity of cells in the motor cortex could be recorded in awake, behaving animals performing various motor tasks (Lemon, 1984). Several studies showed that changes in motor cortical cell activity precede the development of the motor output and relate quantitatively to its intensity and spatial characteristics (for reviews, see Evarts, 1981; Georgopoulos, 1990). Specifically, when reaching in space, cell activity relates primarily to the direction of the movement and less to its extent (see Georgopoulos, 1990). Under isometric conditions, when a static force is exerted, cell activity relates to the magnitude (see Evarts, 1981) and direction (Kalaska et al., 1989) of force, and when a force pulse is developed, cell activity relates to the incremental dynamic force exerted but not to the total force output (Georgopoulos et al., 1992).

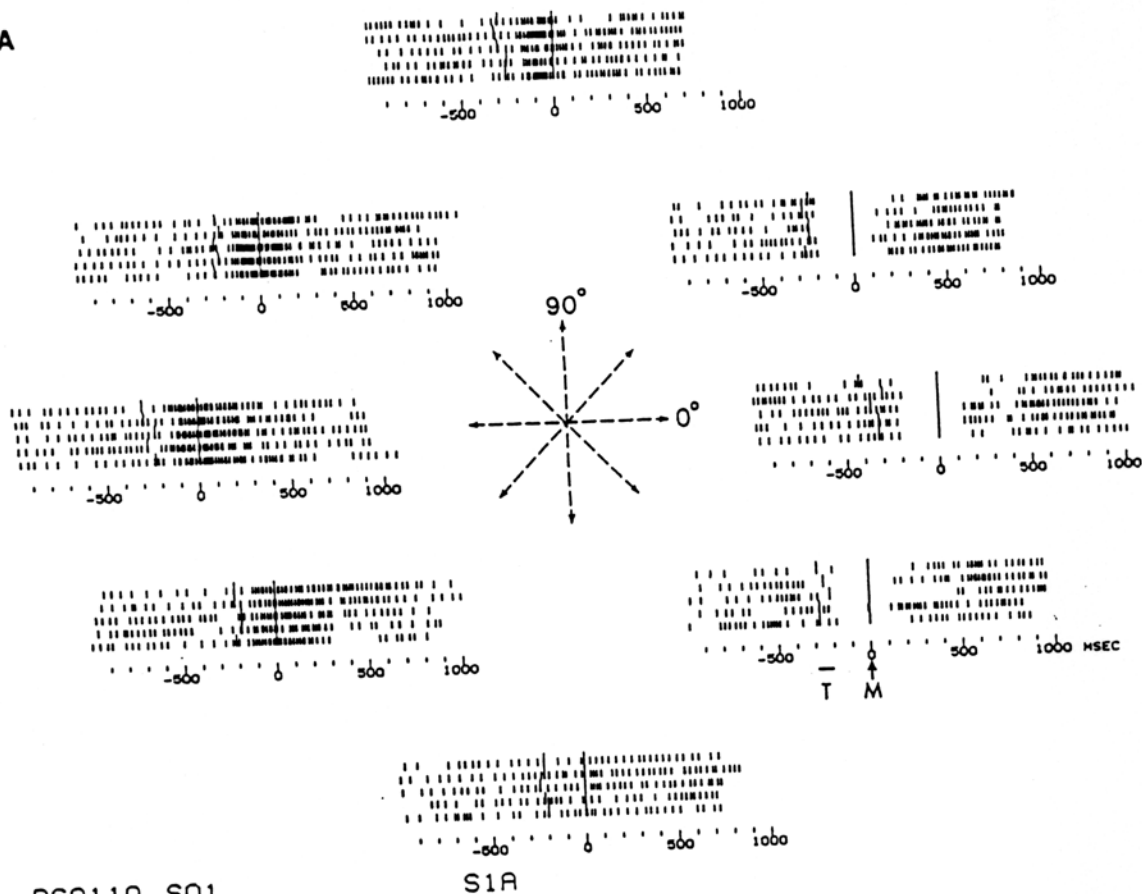
Coding of motor direction by single cells and neuronal populations

A major aspect of the spatial characteristics of the motor output, be it movement or isometric force, is its direction in space. Cells in the motor cortex (Georgopoulos et al., 1982; Georgopoulos, Schwartz, and Kettner, 1986; Schwartz, Kettner, and Georgopoulos, 1988; Kalaska et al., 1989; Caminiti, Johnson, and Urbano, 1990; Schwartz, 1993), as well as in other structures (Kalaska, Caminiti, and Georgopoulos, 1983; Fortier, Kalaska, and Smith, 1989; Caminiti et al., 1991), are broadly tuned to the direction of movement. This means that the cell activity is highest

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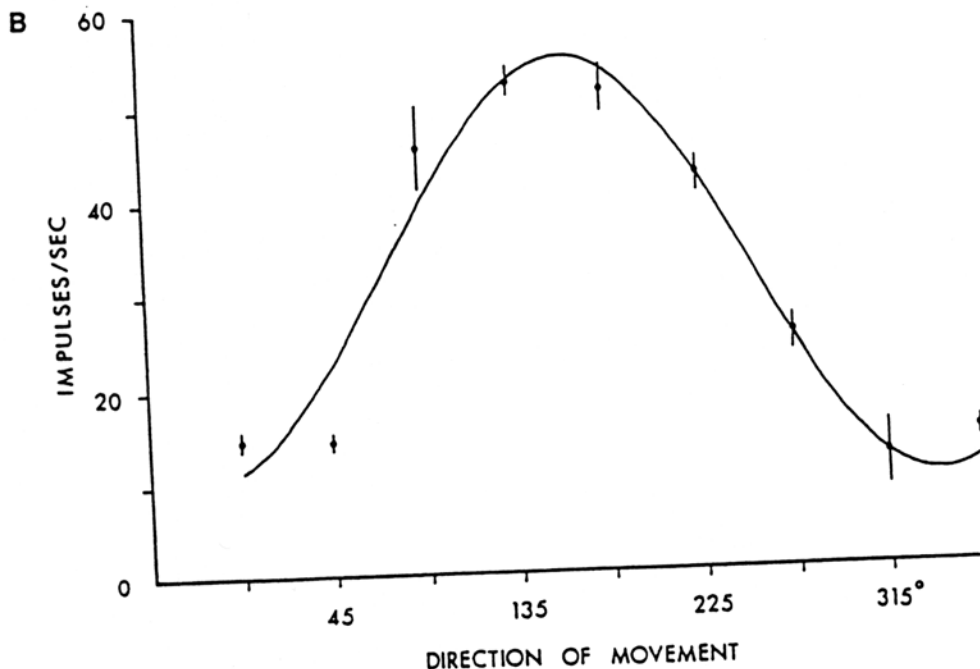
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for a movement in a particular direction (the cell's preferred direction) and decreases progressively with movements farther away from this direction. The changes in cell activity relate to the direction and not the endpoint of the reaching movement (Georgopoulos, Kalaska, and Caminiti, 1985). Quantitatively, the crucial variable on which cell activity depends is the angle formed between the direction of the movement and the cell's preferred direction: The intensity of cell activity is a linear function of the cosine of this angle (Georgopoulos et al., 1982; Schwartz, Kettner, and Georgopoulos, 1988). An example is shown in figure 32.1. The preferred directions of single cells range throughout the three-dimensional directional continuum (Schwartz, Kettner, and Georgopoulos, 1988) (see color plate 12, top panel).

The broad directional tuning indicates that a given cell participates in movements of various directions and that a movement in a particular direction will involve activation of a whole population of cells. Given that single cells are directionally tuned, we proposed a vectorial neural code for the direction of reaching by the neuronal ensemble (Georgopoulos et al., 1983; Georgopoulos, Schwartz, and Kettner, 1986; Georgopoulos, Kettner, and Schwartz, 1988): (1) A particular vector represents the contribution of a directionally tuned cell and points in the cell's preferred direction; (2) cell vectors are weighted by the change in cell activity during a particular movement; and (3) the sum of these vectors (i.e., the population vector) provides the unique outcome of the ensemble coding operation. We found that the population vector points in the direction of the movement (Georgopoulos et al., 1983;

Georgopoulos, Schwartz, and Kettner, 1986; Georgopoulos, Kettner, and Schwartz, 1988) (figure 32.2 and color plate 12, middle panel). Ninety-five percent confidence intervals on the direction of the population vector can be generated using statistical bootstrapping techniques (Georgopoulos, Kettner, and Schwartz, 1988) (color plate 12, lower panel). The population vector approach has proved useful not only in studies of motor cortex (Georgopoulos et al., 1983; Georgopoulos, Schwartz, and Kettner, 1986; Georgopoulos, Kettner, and Schwartz, 1988; Kalaska et al., 1989; Caminiti, Johnson, and Urbano, 1990) but also in studies of other motor areas, including the cerebellum (Fortier, Kalaska, and Smith, 1989), the premotor cortex (Caminiti et al., 1991), and areas 5 (Kalaska, Caminiti, and Georgopoulos, 1983; Kalaska, 1988) and 7 (Steinmetz et al., 1987) of the parietal cortex.

SOME GENERAL PROPERTIES OF THE NEURONAL POPULATION VECTOR *The neuronal population vector predicts the direction of reaching for movements of different origin.* In these experiments, monkeys made movements that were begun from different points and were in the same direction but described parallel trajectories in three-dimensional space. Under these conditions, the population vector in the motor cortex predicted well the direction of the reaching movement (Kettner, Schwartz, and Georgopoulos, 1988; Caminiti et al., 1991), even if the preferred directions of individual cells shifted systematically in the horizontal plane with different movement origins (Caminiti, Johnson, and Urbano, 1990).

The direction of reaching is predicted well by neuronal population vectors in different cortical layers. The average absolute angle between the population vector calculated from cells in the upper layers (II and III) and the direction of movement was $4.31^\circ \pm 2.98^\circ$ (mean \pm standard deviation, $n = 8$ movement directions), compared to $2.32^\circ \pm 2.06^\circ$ for the lower layers (V and VI) (Georgopoulos, 1990). This finding suggests that the ensemble operation of the population vector can be realized separately in the upper and lower layers, which is important, for that information can then be distributed to different structures according to the differential projections from the upper and lower layers (Jones and Wise, 1977).

The neuronal population coding of the direction of reaching is resistant to loss of cells. The population coding just described is a distributed code and, as such, does not

FIGURE 32.1 Directional tuning of a cell recorded in the arm area of the motor cortex during two-dimensional reaching. (Top) Impulse activity during five trials of reaching in the directions indicated in the drawing at the center. Short vertical bars indicate the occurrence of an action potential. Rasters are aligned to the onset of movement (M). Longer vertical bars preceding the onset of movement indicate the onset of the target (T); those following the movement indicate, successively, the entrance to the target zone and the delivery of reward. (Bottom) Average frequency of discharge (\pm standard error of the mean) from the onset of the stimulus until the entry to the target zone is plotted against the direction of movement. Continuous curve is a cosine function fitted to the data using multiple regression analysis. (Reprinted from Georgopoulos et al., 1982, by permission. Copyright by Society for Neuroscience.)

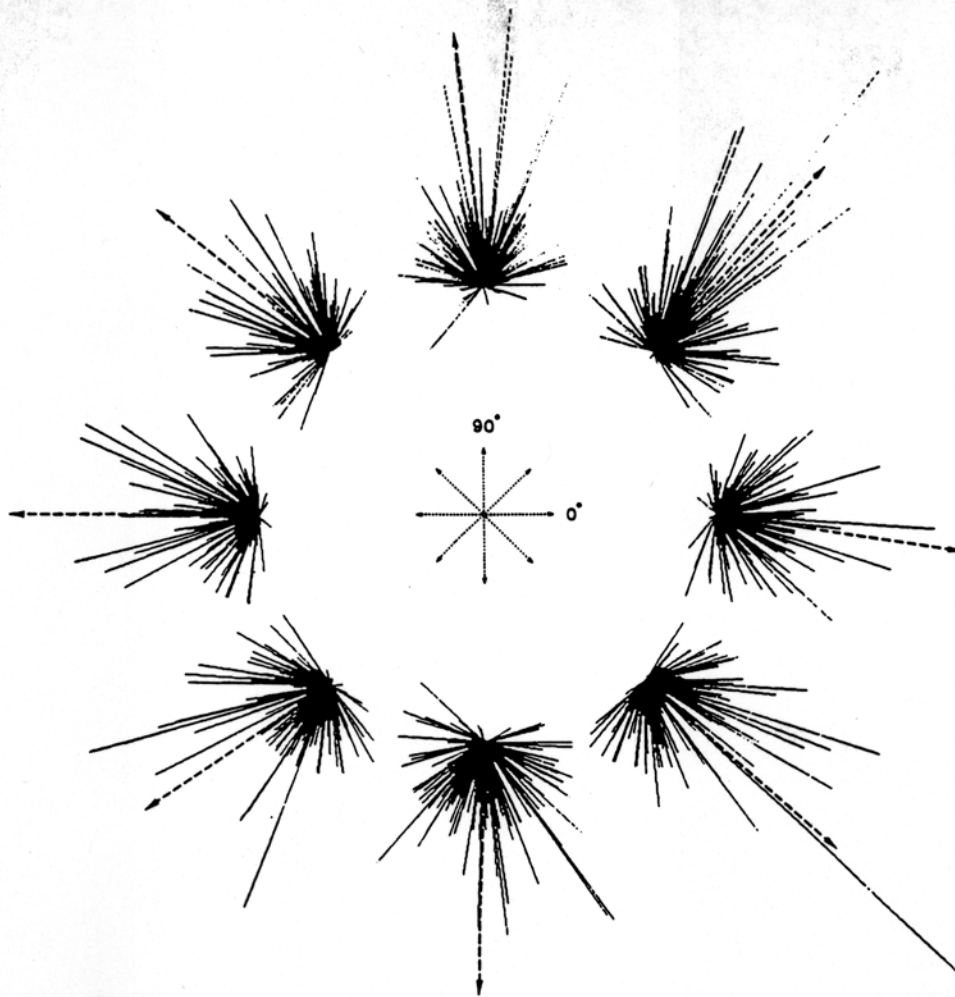


FIGURE 32.2 Population vector analysis applied to eight movement directions in two-dimensional space. Each cluster represents the same population; the movement directions are shown in the diagram at the center. The population vector

(interrupted arrow) points in or near the direction of movement. (Reprinted from Georgopoulos et al., 1983, by permission of the publisher.)

depend exclusively on any particular cell. This robustness was evaluated by calculating the population vector from progressively smaller samples of cells randomly selected from the original population (Georgopoulos, Kettner, and Schwartz, 1988). Indeed, the direction of the population vector can be reliably estimated from as few as 100–150 cells.

The neuronal population vector transmits directional information comparable to that transmitted by the direction of movement. In the standard task used in our studies, monkeys (Georgopoulos et al., 1982) or human subjects (Georgopoulos and Massey, 1988) moved a manipulandum from the center of a planar working surface to a target on a circle. In this case, the direction of the target is the ideal direction: If the subject's movements were

straight lines from the center to the target, the subject's performance would be perfect and we could say that the movement transmitted the maximum possible information. However, movements rarely end dead on target and, therefore, the information transmitted is rarely maximal: The more the dispersion of the movement endpoint around the target, the less information is transmitted. Now, this dispersion can be parcellated into errors in the amplitude of movement and errors in the direction of movement; accordingly, the information transmitted by the amplitude and the direction of movement can be studied separately. Because my colleagues and I were interested in the control of the direction of movement, we asked subjects to "move in the direction of the target" without imposing restrictions

on the amplitude or the endpoint of the movement: This provided a purely directional task (Georgopoulos and Massey, 1988). The calculation of the information transmitted by the direction of movement involves the construction of a performance matrix, in which the ideal and actual directions are tabulated and from which the information transmitted can be computed (Georgopoulos and Massey, 1988). Essentially, the same technique can be used to calculate the information transmitted by the direction of the population vector. Because the population vector is the vectorial sum of weighted contributions of individual cells, and because these weights can vary from trial to trial due to intertrial variability in neuronal discharge, then the direction of the population vector can vary somewhat from trial to trial: This variation can be treated in exactly the same way as the direction of movement, and the information transmitted can be calculated.

Indeed, we calculated the information transmitted by the direction of movement and the direction of the population vector (Georgopoulos and Massey, 1988) and found the following: First, the information transmitted by both of these measures increases with input information but more slowly than the maximum possible, and it tends to saturate at high levels of input information. This loss of information is probably due to noise generated during the initial (perceptual) and successive (perceptual-motor) processing stages. Second, the information transmitted by the population vector was consistently higher than that transmitted by the movement by approximately 0.5 bits. This means that an additional loss of information is incurred between the motor cortex and the movement. However, this loss differs from the previous one, for it does not increase with increasing stimulus information but remains constant at approximately 0.5 bits at all levels of input information. Such a loss could be suffered during processing in other motor structures or at the stage of biomechanical implementation of the movement.

The neuronal population vector predicts the direction of dynamic isometric force (Georgopoulos et al., 1992). This finding established the fact that the coding of directional information applies to the motor output in general, even in the absence of joint motion. Moreover, it showed that the direction specified by the motor cortex is not that of the total force exerted by the subject but that of the dynamic component of the force—that is, the component of the force remaining after a constant, static force is subtracted.

TIME-VARYING PROPERTIES OF THE NEURONAL POPULATION VECTOR *The neuronal population vector predicts the movement trajectory in continuous, tracing movements* (Schwartz, 1993). Monkeys were trained to trace smoothly with their index finger sinusoids displayed on a screen, from one end to the other. The direction of the population vectors, calculated successively in time along the trajectory, changed throughout the sinusoidal movement, closely matching the smoothly changing direction of the finger path. Moreover, a neural “image” of the sinusoidal trajectory of the movement was obtained by connecting successive population vectors tip to tail. This finding suggests that the length of the population vector carries information concerning the instantaneous velocity of the movement.

The neuronal population vector predicts the direction of reaching during the reaction time. This is the simplest case of predicting the direction of an upcoming movement. Given that the changes in cell activity in the motor cortex precede the onset of movement by approximately 160–180 ms, on average (Georgopoulos et al., 1982), it is an important finding that the population vector predicts the direction of the upcoming movement during that period during which the movement is being planned (Georgopoulos et al., 1984; Georgopoulos, Kettner, and Schwartz, 1988). An example is shown in figure 32.3.

The neuronal population vector predicts the direction of reaching during an instructed delay period. Experiments were conducted in which monkeys were trained to withhold the movement for a period of time after the onset of a visual cue signal and to move later in response to a go signal. During this instructed delay period, the population vector in the motor cortex, computed every 20 ms, gave a reliable signal concerning the direction of the movement that was triggered later for execution (Georgopoulos, Crutcher, and Schwartz, 1989).

Neural mechanisms of cognitive processing: neuronal populations as keys for understanding

The results summarized in the preceding sections underscore the operational usefulness of the neuronal population vector for monitoring in time the directional tendency of the neuronal ensemble. We took advantage of this property and used the population vector as a probe to decipher the neural processing of directional information during two cognitive opera-

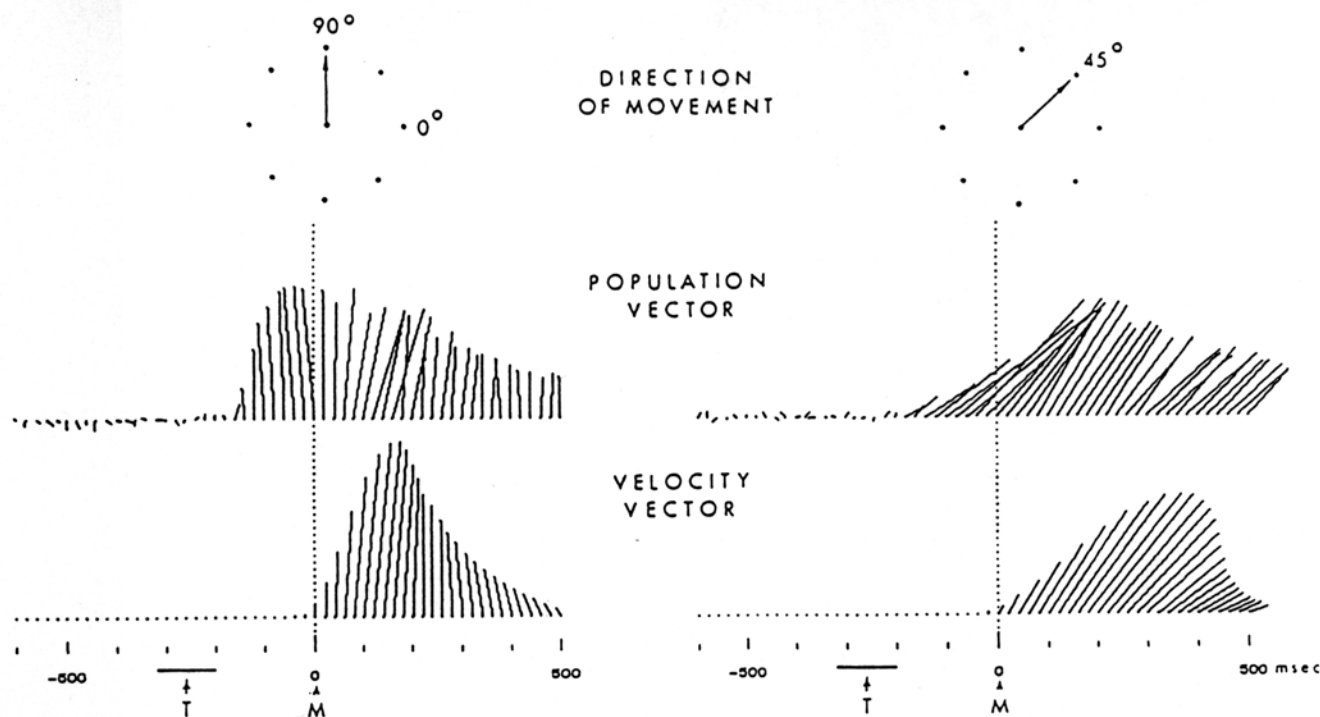


FIGURE 32.3 The population vector points in the direction of movement well before the movement begins. The results for two movement directions in two-dimensional space are illustrated (top). The population vector was calculated every 20 ms (middle). The average instantaneous (20-ms bin) velocity of the movement also is shown (bottom). Before the target onset (T), the population vector is very short and its

direction varies from moment to moment. Well before the onset of movement (M), it increases in length and its direction points to the direction of the upcoming movement. This finding suggests that even the earliest inputs to the motor cortex are relevant to the direction of the upcoming movement. (Reprinted from Georgopoulos et al., 1984, by permission of the publisher.)

tions, one involving memory holding and the other mental rotation.

MEMORY HOLDING In these experiments (Smyrnis et al., 1992), two rhesus monkeys were trained to move a handle on a two-dimensional working surface in directions specified by a light on the plane. They first captured with the handle a light on the center of the plane and then moved the handle in the direction indicated by a peripheral light (*cue* signal). The signal to move (*go* signal) was given by turning off the center light. The following tasks were used: In the *nondelay* task, the peripheral light was turned on at the same time as the center light went off. In the *memorized delay* task, the peripheral light stayed on for 300 ms (cue period) and the center light was turned off 450–750 ms later (delay period). Finally, in the *nonmemorized-delay* task, the peripheral light stayed on continuously, whereas the center light went off 750–1050 ms after the peripheral light came on. Recordings in the arm area of the motor

cortex ($N = 171$ cells) showed changes in single-cell activity in all tasks. The population vector was calculated every 20 ms following the onset of the peripheral light. We were interested in two aspects of the information carried by the population vector. One concerns its direction, which can be interpreted as the directional information carried by the directional signal. The other concerns the length of the population vector, which can be regarded as the strength of the directional signal carried. The direction of the population vector during the memorized delay period was close to the direction of the target (figure 32.4). It is interesting that the population vector length was similar in the cue period, but it was longer during the memorized versus the nonmemorized part of the delay. This is demonstrated in figure 32.5, which illustrates the time course of the length of the population vector in the two delay tasks. Three phases can be distinguished in this time course. First, there is an initial increase of vector length during the 300 ms of the delay period; this increase is

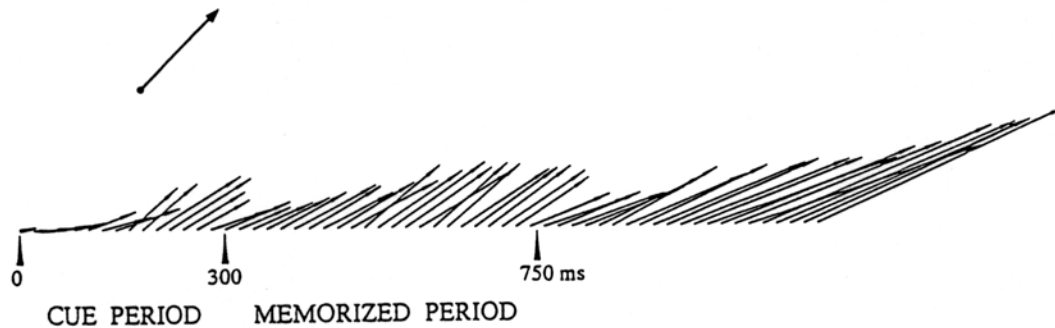


FIGURE 32.4 Population vectors in the memorized delay task for the direction indicated are plotted every 20 ms. The arrow on top indicates the direction of the cue signal present

during the first 300 ms of the delay period. (Reprinted from Smyrnis et al., 1992, by permission.)

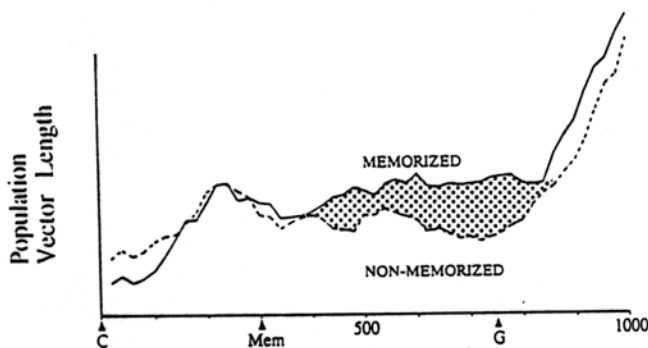


FIGURE 32.5 Length of mean result of the population vector is plotted against time for the two delay tasks. G, minimum time of onset of the go signal. (Reprinted from Smyrnis et al., 1992, by permission.)

similar for both tasks. Second, this increase subsides during the rest of the nonmemorized delay period but continues at a somewhat higher level during the memorized delay period; the latter difference is indicated by stippling in figure 32.5. Finally, there is a steep increase in the population vector length following the go signal at the end of the delay period. Thus, the memorized task is distinguished from the nonmemorized one by the higher population signal in that part of the delay period during which the instructed direction had to be held in memory.

The directional information carried by the population vector in the memorized task identified the memorized information in a direct fashion. Moreover, this analysis provided an insight concerning the time course of encoding and holding directional information. For that purpose, we used the length of the population vector, which can be regarded as reflecting the

strength of the directional signal in the neuronal ensemble. The population vector length showed an initial increase that started approximately 100 ms after the cue onset and peaked at 250 ms. This increase was very similar in both the memorized and the nonmemorized delay tasks (see figure 32.5). We interpret this initial peak as reflecting an *encoding* process. A second phase ensued that differed in the memorized and nonmemorized tasks in that a higher, sustained signal was present during the memorized delay period but not during the nonmemorized delay (see stippled area in figure 32.5). We interpret this as reflecting a *holding-in-memory* process. After onset of the go signal, the population vector length increased similarly in all tasks used. These findings are interesting because the increase in the signal during the memorized delay period was observed *in the absence* of the target, though one would expect that the signal would be stronger in the presence rather than the absence of the visual stimulus. This finding strengthens our interpretation of this increase as a memory signal, in contrast to a sensory one, and raises the more general possibility that the motor cortex may be particularly involved when only part of the visual information about an upcoming movement is provided.

MENTAL ROTATION The second cognitive process my colleagues and I chose to study involved a transformation of an intended movement direction. In these studies, we first carried out psychological experiments in human subjects. Then we trained monkeys to perform the same task and recorded the activity of single cells in the brain of each of these animals during performance of the task. Finally, we tried to connect the

neural results with those of the human studies and interpret the latter on the basis of the former, the objective being to get as close as possible in relating neurophysiology and cognitive psychology. The following is a description of these steps as they were applied to a particular problem of a mental transformation of movement direction.

The task required subjects to move a handle at an angle from a reference direction defined by a visual stimulus on a plane. Because the reference direction changed from trial to trial, the task required that in a given trial, the direction of movement be specified according to this reference direction. In the *psychological studies* (Georgopoulos and Massey, 1987) human subjects performed blocks of 20 trials in which the angle above and its departure (counterclockwise or clockwise) were fixed, although the reference direction varied. Seven angles (5° – 140°) were used. The basic finding was that the time to initiate a movement (reaction time) increased in a linear fashion with the angle. The most parsimonious hypothesis to explain these results is that subjects arrive at the correct direction of movement by shifting their motor intention from the reference direction to the movement direction, traveling through the intermediate angular space. This idea is very similar to the mental rotation hypothesis proposed by Shepard and Cooper (1982) to explain the monotonic increase of the reaction time with orientation angle when a judgment must be made regarding whether a visual image is normal or mirror-image: In both cases, a mental rotation is postulated. In fact, the mean rates of rotation and their range among subjects were very similar in the perceptual (Shepard and Cooper, 1982) and motor (Georgopoulos and Massey, 1987) studies. Moreover, when the same subjects performed both perceptual and motor rotation tasks, their processing rates were positively correlated (Pellizzer and Georgopoulos, 1993), which indicates similar processing constraints for both tasks.

In the *neurophysiological studies* (Georgopoulos et al., 1989; Lurito, Georgakopoulos, and Georgopoulos, 1991), two rhesus monkeys were trained to move the handle 90° and counterclockwise from the reference direction; these trials were intermixed with others in which the animals moved in the direction of the target. When the time-varying neuronal population vector was calculated during the reaction time, it was found that it rotated from the stimulus (reference) to the movement direction through the counterclockwise angle when the

animal had to move away from the stimulus, or in the direction of the stimulus when the animal had to move toward it (figure 32.6). It is remarkable that the population vector rotated at all, but especially that it rotated through the smaller, 90° counterclockwise angle. These results showed clearly that the cognitive process in this task involved rotation of an analog signal. The occurrence of a true rotation was further documented by showing that there was a transient increase during the middle of the reaction time in the recruitment of cells with preferred directions between the stimulus and movement directions: This indicated that rotation of the population vector was not the result of varying activation of just two cell groups, one with preferred directions centered on the stimulus and another in the movement direction. Therefore, this rotation process, sweeping through the directionally tuned ensemble, provided for the first time a direct visualization of a dynamic cognitive process. In this respect, it is noteworthy that the population vector is, in essence, a measure that can take continuous values in direction.

In summary, the results of these studies provide the neural correlates of a dynamic cognitive representation (Freyd, 1987). The essential contribution of this work is in the neural identification and visualization of the time-varying, dynamic representation of direction in the motor cortex when a transformation of this direction is required and achieved. Interestingly, the mean rotation rate and the range of rates observed for different reference directions were very similar to those obtained in the human studies.

Functional imaging of the human motor cortex

Although the single-cell recording technique has contributed significantly to our knowledge of cortical function, it is limited in that it can usually be applied only to a restricted brain area at one time. Other techniques, including positron emission tomography, can provide the greater picture of areas of activation in the brain during performance of a task. A new major tool is the blood oxygenation level-dependent (BOLD) contrast imaging of the brain using nuclear magnetic resonance (Ogawa et al., 1990). The technique is non-invasive and sensitive, does not require averaging of data from more than one subject, and possesses adequate resolution. It has already produced scans with both high spatial resolution and functional, task-dependent activation of the human motor cortex (Ban-

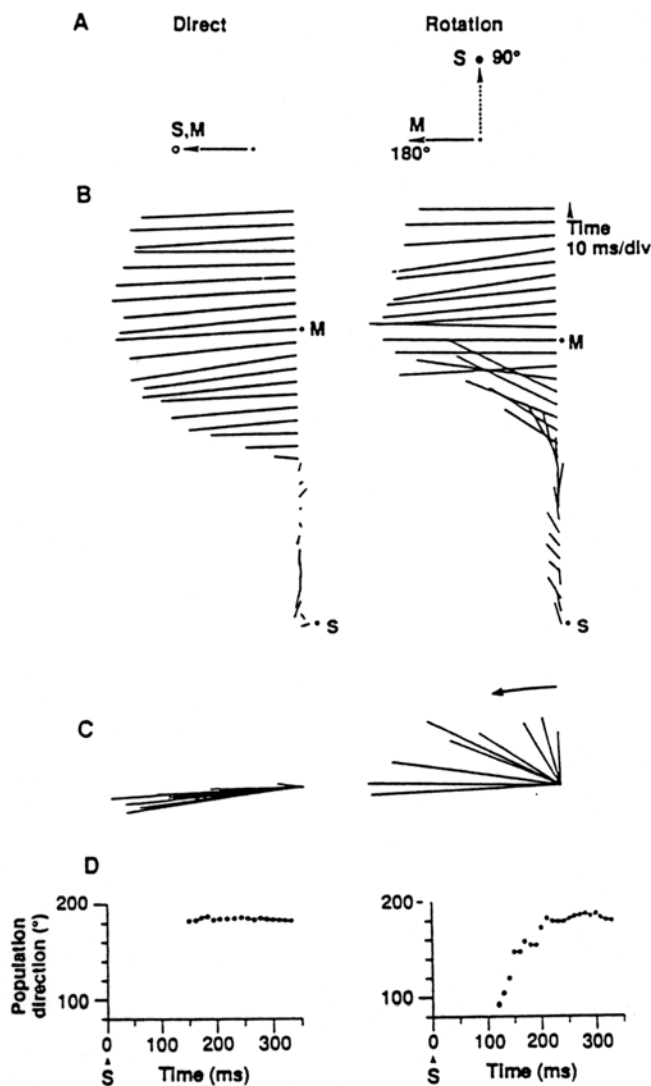


FIGURE 32.6 Results from a direct (left) and rotation (right) movement. (A) Task. Unfilled and filled circles indicate dim and bright light, respectively. Interrupted and continuous lines with arrows indicate stimulus (S) and movement (M) direction, respectively. (B) Neuronal population vectors calculated every 10 ms from the onset of S, at positions shown in (A), until after the onset of 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 counterclockwise (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. Note the counterclockwise 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 following stimulus onset. For the direct case (left panel), the direction of the population vector is in the direction of the movement ($\sim 180^\circ$); for the rotation case (right panel), the direction of the population vector rotates counterclockwise from the direction of the stimulus ($\sim 90^\circ$) to the direction of the movement ($\sim 180^\circ$).

dettini et al., 1992; Kim et al., 1993). Especially at high magnetic fields (4 tesla), functional images of high contrast and spatial resolution (e.g., less than 0.7 mm in image plane) depicting activated gray-matter areas can be obtained. An example of such imaging of the human motor cortex during a finger task is shown in color plate 13. This method holds great promise for understanding the cooperation among various brain regions in motor processing.

Neural modeling of the motor cortex

The motor cortex can be essentially regarded as a neural network. The elements of the network are directionally tuned, and one possible operation of the network is the computation of the neuronal population

vector. The broad directional tuning of single cells seems to be a general aspect of the population operation, as this property appeared in the hidden layer of a three-layer network trained to calculate the population vector (Lukashin, 1990). Another question concerns the interactions among cells. It is known that there are extensive local interconnections (Huntley and Jones, 1991) as well as functional neuronal interactions (Stefanis and Jasper, 1964; Asanuma and Brooks, 1965; for a review see Fetz, Toyama, and Smith, 1991). A three-part objective then is to (1) identify these interactions among the directionally tuned cells in the motor cortex and discover the rules that govern their presence, (2) study an artificial neural network made of directionally tuned elements with massive interconnections, and (3) compare the results obtained in the real (i.e., motor cortical) and artificial networks.

We found the following (Georgopoulos, Taira, and Lukashin, in press): First, interactions between cells in the motor cortex relate to the directional tuning of the cells in a pair: Interactions are more than twice as frequent when the cells are tuned than when they are not and, for directionally tuned cells, the interaction ranges from strongly positive (i.e., excitatory) to strongly negative (i.e., inhibitory) as the angle between the preferred directions of the cells in a pair varies from

0° (i.e., same preferred direction) to 180° (i.e., opposite preferred directions). Second, the same trend was observed between the directionally tuned elements in a massively interconnected, dynamic artificial network during a stable period of computation of the neuronal population vector. Third, it was found that for the network to be stable, the strength of the synaptic interactions must be low: In the best (i.e., most stable) case, the mean synaptic strength tends to $2/N$, where N is the number of elements in the network. This is in keeping with the fact that cortical cells in an area are extensively but weakly interconnected (Martin, 1988). These findings validate the correspondence between the motor cortical and the artificial neural network and open the possibility of using this network in the temporal domain to explore the mechanisms of the cognitive operations described in the preceding section.

Conclusion

Single-cell recording, imaging, and dynamic computer modeling techniques are powerful tools that will continue to advance our knowledge. There is already a good database from the most painstaking and time-consuming studies of single-cell recordings in behaving monkeys, as reviewed previously; the imaging and modeling studies should proceed at a faster pace. Then, we should arrive at a much better understanding of the mechanisms by which the motor cortex and other brain areas process motor and cognitive information.

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