Neural Networks and Motor Control

APOSTOLOS P. GEORGOPOULOS
Brain Sciences Center
Veterans Affairs Medical Center
Departments of Physiology, Neurology and Psychiatry
University of Minnesota Medical School
Minneapolis, Minnesota

Motor control is accomplished by the cooperative interaction of many brain networks, among which the motor cortex holds a central place. This article reviews some of the structural and functional properties of neurons of the motor cortical network, some principles of connectivity with other motor networks, the handling of spatial information regarding reaching movements, and some ideas on how motor cortical commands could be translated to muscle activations by spinal motor networks. Finally, I review recent neural network modeling studies of motor cortical ensemble operations. NEUROSCIENTIST 3:52–60, 1997

KEY WORDS *Motor control, Networks, Cortex*

The specification and control of arm movements involve many brain areas, including the cerebral cortex, cerebellum, and large portions of the basal ganglia, brainstem, and spinal cord. Among these areas, the motor cortex occupies a central post. The effects of its lesions can vary in severity, depending on the extent of the lesion. Total disconnection of the motor cortex from subcortical structures, as happens in a stroke at the level of the internal capsule, leads to a devastating hemiplegia, but localized destruction of the motor cortex usually leads to weakness or paresis of a specific body part, depending on the location of the lesion within the motor cortex. The production of movements by electrical stimulation of the surface of the motor cortex of dogs (1) and monkeys (2) established the motor function of the precentral gyrus and led to a series of detailed experiments by which the somatotopic organization of the motor cortex was revealed. Electrical stimulation of the motor cortex of awake humans during neurosurgical operations (3–4) confirmed that electrical stimulation of the motor cortex elicits movements of contralateral body parts and that movements of different body parts are represented in a somatotopic fashion in the mediolateral dimension. In fact, the motor function of the precentral gyrus and an initial suggestion for a topographic organization were postulated by Hughlings Jackson in the nineteenth century on the basis of observations of the spread of Jacksonian seizures (5). Jackson speculated about the functional organization of the motor areas and postulated three levels of ''motor centres:'' ''(1) the anterior spinal horns and their homologues higher up (nuclei of motor cranial nerves) are the lowest motor centres (both of the cerebral and cerebellar systems). These lowest motor centres, with the corresponding sensory centres, make up the lowest level of evolution of the central nervous system. (2) The convolutions of the Rolandic region are the middle motor centres. With the corresponding sensory centres, they make up the second or middle level of the central nervous system. (3) The praefrontal lobes are the highest motor centres of the cerebral system. With the corresponding sensory centers, they make up the third or highest level of the central nervous system, that is, the 'organ of mind'....'' (5). He based the distinction among these levels on the degree of combinatorial representation of muscles to form complicated motor acts. He stated that ''To speak figuratively, the central nervous system knows nothing of muscles, it only knows movements.... There are, we shall say, thirty muscles of the hand; these are represented in the nervous centres in thousands of different combinations—that is, as very many movements; it is just as many chords, musical expressions and tunes can be made out of a few notes. I now speak of the representation of the muscles of the hand in the three orders of motor centres just spoken of. (1) In some lowest motor centres...these muscles are represented in numerous different combinations, as simple and very general movements. (2) In the middle motor centres...the same muscles are represented (re-represented) in still more numerous different combinations, as complex and special movements. (3) In the highest motor centres...the same muscles are represented (re-re-represented) in innumerable different combinations, as most complex and most special movements.'' (5).

The Problem of Representation

This formulation of the basic problem of motor control is still valid today, and indeed quite modern. For ex-

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This work was supported by USPHS grant NS17413, the American Legion Brain Sciences Chair, and the US Department of Veterans Affairs.

Address reprint requests to: Apostolos P. Georgopoulos, M.D., Brain Sciences Center, VAMC (11B), One Veterans Drive, Minneapolis, MN 55417.

ample, it is obvious that movements are produced by the coordinated contraction of muscles and that different movements (e.g., arm movements in different directions) involve weighted re-combinations of these muscles (6). It is also obvious that brain motor structures are somehow involved with muscle function, given the altered state of the muscles encountered following lesions of these structures, resulting, for example, in spasticity (lesions of motor cortex), rigidity (Parkinson's disease), and hypotonia (lesions of cerebellar hemispheres). Not obvious, however, is what is represented in an area, and this is where Jackson made the provocative proposal that what is represented is the combination of muscle activations—namely, a rich variety of movements. Indeed, his ideas have received strong support from three lines of recent studies of the motor cortex.

First, with respect to muscles, it has been shown, using postspike facilitation, that individual motor cortical cells apparently relate to more than one muscle (7). Indeed, these muscles need not be few or spatially contiguous (e.g., act on the same joint). For example, postspike facilitation was observed recently in extensive groups of muscles spanning two or more joints (8). Monkeys were trained to reach to visual targets while EMG activity was recorded from 22 muscles of the digits, hand, forearm, upper arm, and shoulder. It was found that in 33% of cells, the postspike facilitation was effected on muscles at two or more joints across the whole forelimb. These findings show that even single motor cortical cells deal with combinations of muscles from the outset.

Second, motion about a joint is effected by the action of muscles (which is inherently directional), and thus, it is important to determine whether cell activity relates to the direction of joint movement or the muscle activity because, under most conditions, the two are closely related. Indeed, this dissociation can be achieved by applying external loads such that movement in the same direction is performed with different muscle activations. It has been an important finding that whenever such a dissociation was tried, a good proportion of cells was found to relate to the direction of the movement irrespective of the muscle pattern used to implement the movement. This has been observed in the motor cortex (9–11), the supplementary motor area (10–11), the putamen (10–12), the globus pallidus (13), and the dentate and interpositus nuclei (9).

Finally, with respect to the multijoint, reaching movements, it has been shown that the activity of individual motor cortical cells varies in an orderly fashion with spatial aspects of movement. This addresses the issue of representation directly, much along the lines proposed by Jackson in the quotation above. Studies on the neural coding of spatial parameters (i.e., direction and amplitude) of reaching movements were initiated in the early 1980s (14). In 1982, the first systematic study of the relations of motor cortical cell activity to the direction of reaching was published (15). This study was complemented, 11 years later, by a comprehensive investigation of the relations of cell activity to the amplitude of movement (16). The motor cortex, then, can be regarded as a neural network that processes information concerning movement parameters, according to desired specifications, and codes it in a way that is then translated by spinal networks to appropriate multimuscle activations. I discuss below some aspects of these network operations.

Motor Cortical Network

Neural Elements and Connections

The ''nuts and bolts'' of the motor cortex are cells arranged in six layers (Fig. 1), of which layer IV is very thin. The number of cells contained within a strip of tissue through the depth of the cortex is ~110 (17–18), of which approximately two-thirds are pyramidal cells and one-third are non-pyramidal, large and small stellate cells (18). The pyramidal cells send their axons to various brain areas and back to the motor cortex itself through recurrent collaterals, whereas the axons of the stellate cells remain within the cortex. The synaptic action of spiny neurons (pyramidal and stellate) on the postsynaptic cell is thought to be excitatory, whereas that of smooth (i.e. aspiny) stellate cells is inhibitory.

The afferent inputs to the motor cortex come from other cortical areas, located anterior (frontal) and posterior (parietal) to the motor cortex, from the thalamus (reflecting influences from the cerebellum and the basal ganglia), and from subcortical nuclei, the cells of which use monoamines as neurotransmitters, including serotonin, norepinephrine, and acetylcholine. The monoaminergic projections seem to be part of more generalized projections to the cerebral cortex, whereas the corticocortical and thalamocortical inputs reflect more specific interactions from other motor areas. A major principle of organization of these inputs is their substantial divergence, in that a single afferent axon can distribute arborizations for linear distances of several millimeters (19). From this, it follows that any given motor cortical cell receives converging inputs from many input cells. This is also true for the recurrent collaterals of pyramidal axons (20–21), an important aspect of cortical organization. Finally, afferent fibers terminate in all layers and affect both pyramidal and stellate cells (18).

The motor cortex is interconnected with all premotor areas, as well as with parietal areas of the ipsilateral hemisphere, and with areas of the contralateral hemisphere. Recent studies (22) have shown an orderly arrangement in the connectivity pattern, such that frontal areas, from anterior to posterior (e.g., dorsal premotor cortex, motor cortex), connect with parietal areas, from posterior to anterior (e.g., medial intraparietal area, area 5), respectively. This pattern of anatomical connectivity is reflected in similar functional properties of cells (22–23) and is interpreted to mean that these interconnected

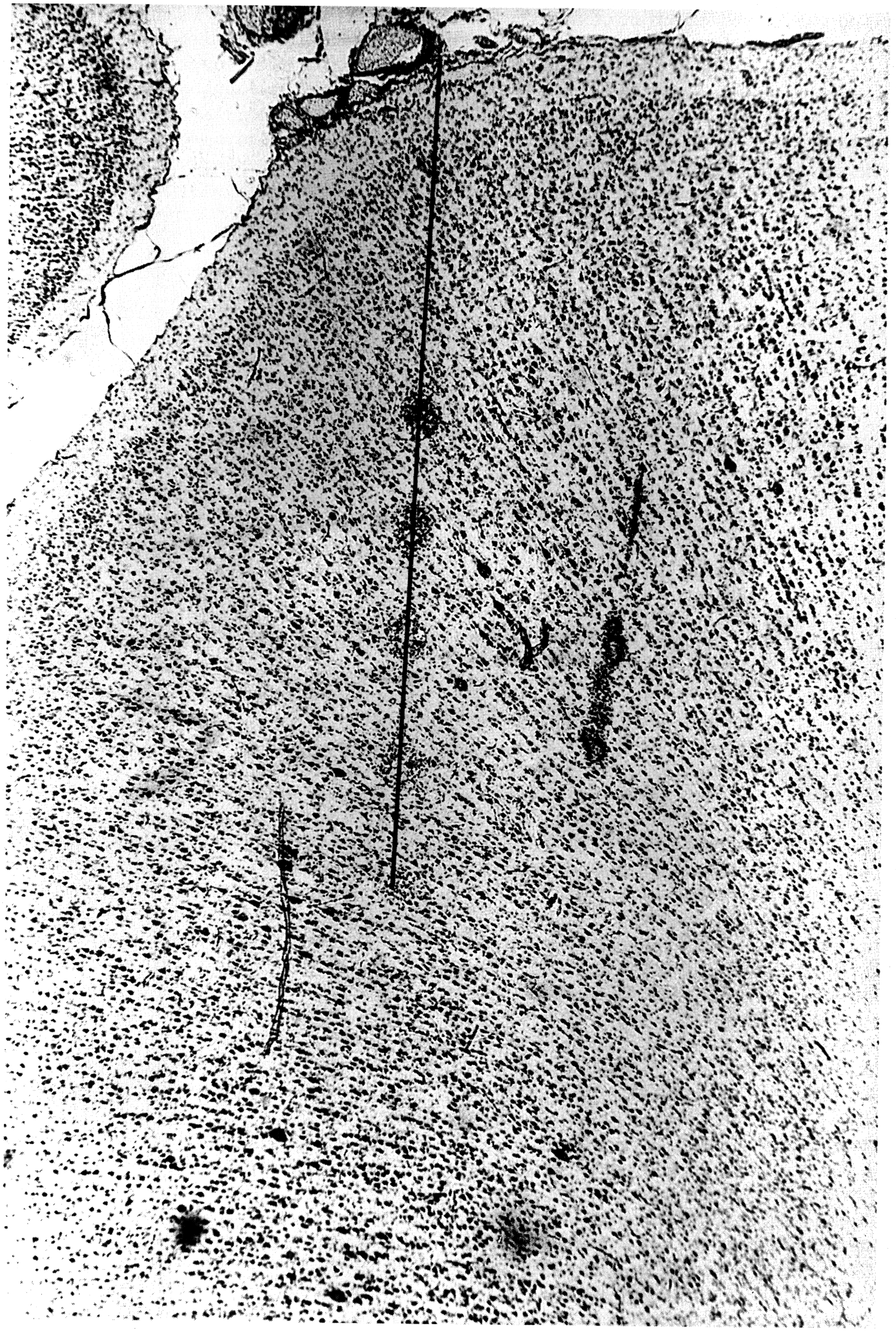

Fig. 1. Section illustrating the motor cortex in the anterior bank and crown of the central sulcus of a brain of a rhesus monkey. The line shows a reconstructed track of a microelectrode penetration passing through four circular gliotic areas, which were the site of small lesions created by passing current through the tip of the microelectrode. (A.P. Georgopoulos, J.F. Kalska, and R. Caminiti, unpublished.)

areas process similar information with respect to arm movements. For example, changes in cell activity during imposed delays in the execution of movement are observed more frequently as one moves forward from the central sulcus, i.e. from posterior (primary motor cortex) to anterior (dorsal premotor cortex). The same gradient is observed in the parietal cortex, as one moves from anterior (Brodmann's area 2) to posterior (down the intraparietal sulcus). Now, these gradients are reflected in the anatomical connectivity: more anterior parietal areas (areas 2 and 5) are connected to the primary motor cortex, whereas more posterior parietal areas (i.e., within the anterior bank of the intraparietal sulcus) are connected to the dorsal premotor area.

Regarding the projections from the thalamus, three general issues are noteworthy—namely, 1) the pattern of termination of thalamocortical fibers, 2) the nuclei of origin of the thalamic projections and the associated convergence-divergence patterns, and 3) the relation of the site of origin of thalamocortical projections to the basal ganglia and the cerebellum. Single thalamocortical axons in the cat terminate in the motor cortex in a multifocal pattern (19). Terminal plexuses are of about 0.5 mm diameter, are separated by terminal-free gaps, and are distributed mainly in the rostrocaudal direction for a distance of up to 6 mm. A similar pattern has been observed for the projections from postcentral to precentral areas in the monkey (20). These findings demonstrate the extensive divergence of the thalamocortical projections. Conversely, there is substantial convergence of these projections, as well. This question was investigated by injecting small areas of the motor cortex with different fluorescent dyes and mapping the resulting retrogradely labeled neurons in the thalamus (24). It was found that projections from several nuclei converged on each small cortical area. Therefore, the information conveyed to a small area in the motor cortex comes from diverse sources and underscores the highly integrative nature of motor cortical processing.

The third issue mentioned above concerns the differential projections of the basal ganglia and cerebellum to different precentral motor areas. Recent studies have shown that motor and premotor areas receive partially overlapping input from the thalamus and that the bulk of the projections from thalamic nuclei receiving from the globus pallidus are directed to premotor areas (25–27). Cerebellar influences to the motor cortex are well established (19).

Directional Tuning of Single Cells

The activity of single cells in the motor cortex is directionally tuned with respect to movement (15) or dynamic isometric force (28), in that cell activity is highest for a given direction ("preferred direction") of movement (or isometric force) and decreases gradually with directions farther and farther away from the preferred one (Fig. 2, top). The tuning is broad and usually unimodal. Typically, the frequency of cell discharge is a linear function of the cosine of the angle formed between the direction of a particular movement (or force) and the cell's preferred direction. Quantitatively, cell activity can be expressed as a linear function of the cosine of the angle between the preferred direction of the cell and the direction of a particular movement, as follows:

$$d_i(\boldsymbol{M}_k) = b_i + a_i \cos\theta_{C_iM_k} \qquad (1)$$

where $d_i(\boldsymbol{M}_k)$ is the discharge rate of the i$^{\text{th}}$ cell with movement in direction $\boldsymbol{M}_k$, b_i and a_i are regression coefficients, and θ is the angle formed between the cell's preferred direction $\boldsymbol{C}_i$ and the direction of movement $\boldsymbol{M}_k$. An example is shown in Figure 2 (bottom). Equation 1 holds both for 2D reaching movements performed on a plane (15) and for free 3D reaching movements (29). The preferred directions differ for different cells, are distributed in the whole 3D directional continuum (29), and remain very similar for movements of different amplitudes (16) but tend to change depending on the posture of the arm (30). Pairs of cells with similar preferred directions tend to show excitatory synaptic interactions, whereas pairs of cells with opposite preferred directions tend to show inhibitory synaptic interactions (31). Finally, the effects of movement direction on cell activity are evident from early on, during the reaction time. By contrast, the effects of the amplitude of movement do not appear until later, toward the end of the movement (32).

It is obvious that the directional tuning is the result of orderly and delicate interplay of excitatory and inhibitory effects, as can be appreciated by inspecting published records (Fig. 2, top). Given that single cortical neurons do not seem to receive more than a small percentage of their inputs from any single source (33), it is also obvious that the directional tuning cannot be explained as the *exclusive* effect of any single input. The fact that probably any motor cortical cell receives convergent inputs from many sources, as mentioned above, attests to the diversity of these factors. Functionally, this is attested by the rich variety of factors that influence motor cortical activity, including memory signals (10, 34, 35) and contextual, task-specific information (36).

Directional Coding by Neuronal Populations

The neural command for the direction of movement in space can be conceptualized as consisting of directionally tuned cells, which, as a neuronal population, provide a unique and unambiguous directional signal. Given a particular direction of movement, this population can be considered, formally, as an ensemble of cell vectors, as follows (Fig. 3): a) a cell is represented as a vector that points in the cell's preferred direction; b) the length of a cell's vector, for a given arm movement, represents the change in the cell's activity during that particular movement; and c) the sum of these vectors (i.e., the population vector) provides the unique outcome of the

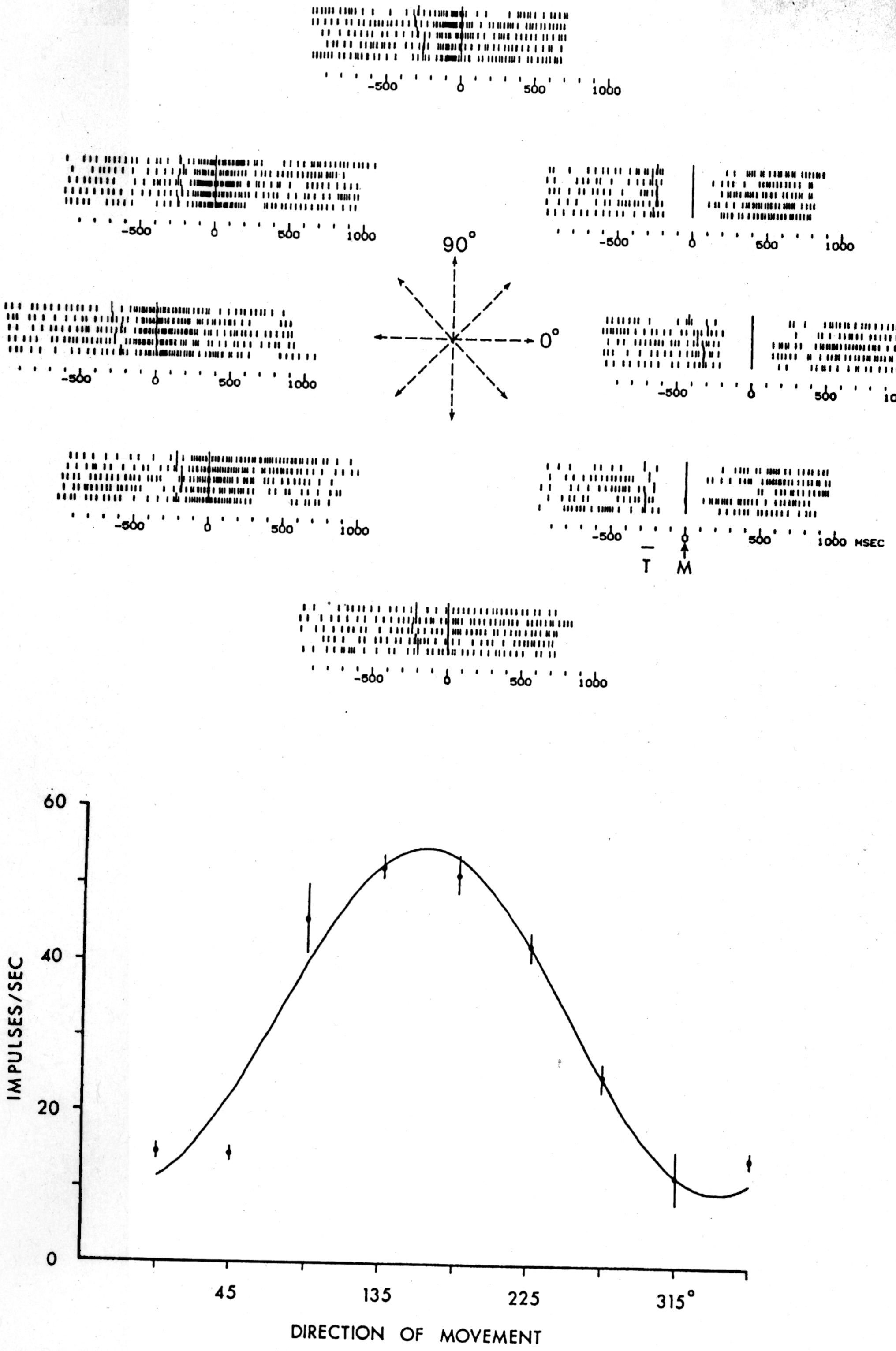

Fig. 2. Directional tuning of a cell recorded in the arm area of the motor cortex during 2-D reaching. *A*, impulse activity during five trials of reaching in the directions indicated in the drawing at the center. Short vertical bars indicate the occurrence of an action potential. Rasters are aligned 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. *B*, average frequency of discharge (± SEM) from the onset of the stimulus until the entry to the target zone is plotted against the direction of movement. The continuous curve is a cosine function fitted to the data using multiple regression analysis. Reproduced with permission from (15).

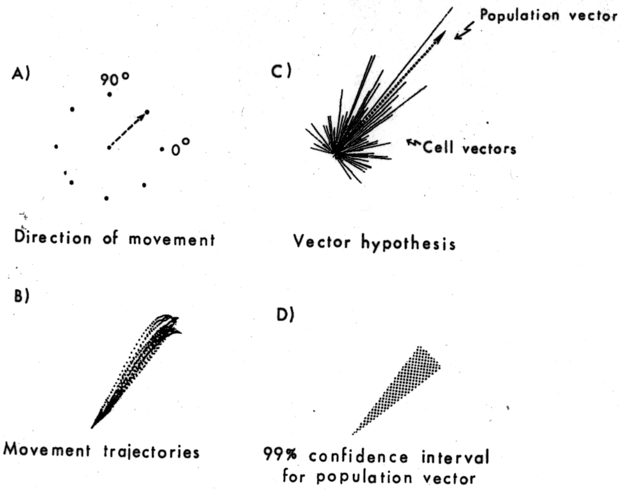

Fig. 3. Neuronal population coding of movement direction illustrated for a motor cortical population (n = 241 cells). *A*, movement direction; *B*, family of trajectories made by a well trained monkey; *C*, vectorial contributions of single cells (*continuous lines*) add to yield the population vector (*interrupted line*), which is in the direction of the movement; *D*, 99% confidence interval for the population vector. Reproduced with permission from (6).

ensemble coding operation and was called the "neuronal population vector" (37–39). This ensemble operation can be expressed as follows:

$$P_k = \sum_{i}^{N} w_{ik} \, C_i \qquad (2)$$

where P_k is the population vector for movement direction l, w_{ik} is the weight for the i^{th} cell and movement in direction k, and C_i is the preferred direction of the i^{th} cell. The population vector has been found to point in the direction of movement (37–39) and dynamic isometric force (28).

Three aspects of the population vector analysis are remarkable—namely, its *simplicity*, its *robustness*, and its *spatial outcome*. With respect to *simplicity*, the calculation of the population vector is a simple procedure, for it 1) rests on the directional selectivity of single cells, which is apparent; 2) involves weighting of vectorial contributions by single cells on the basis of the change in cell activity, which is reasonable, and 3) relies on the vectorial summation of these contributions, which is practically the simplest procedure to obtain a unique outcome. In fact, an important aspect of the population vector analysis is that it relies on the directional tuning as defined operationally by the procedures above; no special assumptions are made or required as to how this tuning comes about.

With respect to *robustness*, the population vector is a distributed code, and as such, it does not depend exclusively on any particular cell. Its robustness is evidenced by the fact that it can convey a good directional signal with only a small number of cells. For example, using the original method (39), ~100 cells were needed, but new, optimal methods have reduced this number to <10 cells (40). It also remains an unbiased predictor of the direction of movement when the posture of the arm changes (41–42). Finally, the population vector is a *spatial* measure, isomorphic to the direction of movement in space. Indeed, the population analysis transforms aggregates of purely temporal spike trains into a directional signal.

The population vector approach has proved useful not only in studies of motor cortex (Fig. 4) (37–39,42–43), but also in studies of other brain areas, including the cerebellum (44), the premotor cortex (42), area 5 (23), and area 7 (45) of the posterior parietal cortex. In addition, the population vector has been a useful tool by which the directional information being processed by a neuronal population in time has been identified and monitored during complex operations, including memory holding (34), mental rotation (46), memory-scanning (47), and nonstandard motor mapping (48). Some of these applications of the time-varying population vector analysis have been discussed elsewhere (49).

Spinal Motor Networks

Spinal Cord Studies of Isometric Force Production

In general, the neural signals from the motor cortex do not activate muscles directly but ultimately influence the activity of motoneurons through the spinal cord. In certain cases, the corticospinal axons terminate within the motor nuclei, as is the case, for example, for the motoneurons innervating distal muscles of the limb in adult primates (7), but in the vast majority of cases, the influence on the motoneuronal pools is exerted through intercalated interneurons. These interneurons are found at the segmental level, as well as at upper cervical (C3-C4) levels. The latter system has been investigated extensively in the cat, and its intricate inputs from central and peripheral sources have been partially elucidated (51).

A detailed analysis of how spinal interneuronal systems can influence the spinal motor output in space has been performed recently in the spinal frog (52–54). 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" (Fig. 5). In the absence of microstimulation, there were passive forces because of the resistance of limb tissues to stretch; during microstimulation, active forces were developed which, 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 subtracted

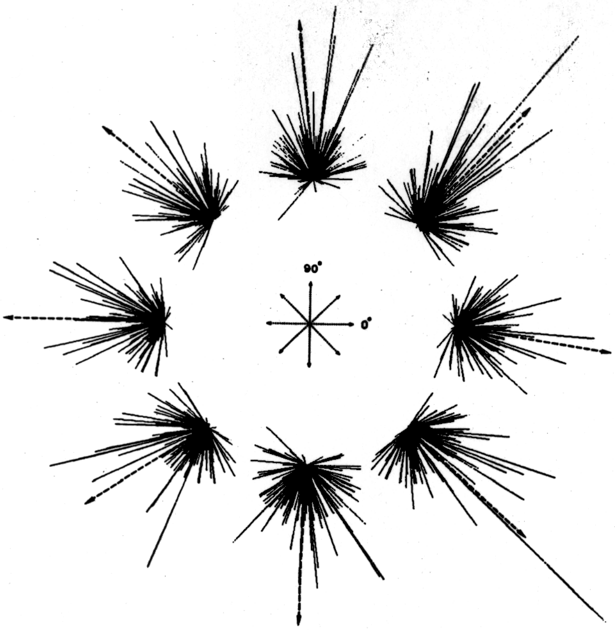

Fig. 4. Neuronal population coding of the direction of reaching illustrated for a motor cortical population (n = 241 cells) and 8 movement directions towards in a 2-D working surface. Vectorial contributions of single cells (*continuous lines*) add to yield the population vector (*interrupted line*). Each cluster represents the same population; the movement directions are shown in the diagram at the center. The population vector points in or near the direction of the movement. Reproduced with permission from (37).

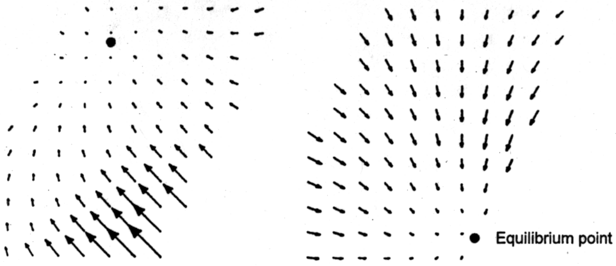

Fig. 5. Examples of two force fields resulting from microstimulation at two different sites in interneuronal areas of the lumbar spinal cord of the spinalized frog. Each vector represents the direction and magnitude of the 2-D isometric force developed at the ankle during microstimulation when the limb was positioned at the point of origin of the vector. *Filled circles* indicate the equilibrium points. Adapted from (51).

from the total to obtain the "active" force field (Fig. 5). It was found that microstimulation in a given area resulted in an active force field where 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 (52). The second finding was that only a few (e.g., 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 (53). These findings suggest possible mechanisms by which supraspinal commands could be translated into motor action as follows: first, because microstimulation will activate an appreciable number of neurons, these intrinsic spinal motor mechanisms involve populations of neurons and summation of influences from potentially separate neuronal ensembles; and 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. 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—with different movement primitives. Finally, 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 (54–56).

Neural Network Modeling of the Motor Cortical Network

The time-varying directional operations discussed in the preceding sections have been modeled recently using a massively interconnected artificial neural network that consists of directionally tuned neurons and produces as an outcome the neuronal population vector (57–58). This network has reproduced well many of the experimental findings and has led to a novel hypothesis on how memorized trajectories of complex movements could be stored in the synaptic connections of overlapping neural networks (59). The idea is that there is a general purpose network involved in all kinds of movements, memorized or not, but that it carries no information about memorized trajectories of specific shapes (e.g., circles, ellipses, scribbles, etc.) and that, if activated alone, would produce straight line trajectories. It is now hypothesized that there are also networks highly specific for a particular trajectory (e.g., clockwise circle), which are interconnected with the general purpose network: when a specific trajectory needs to be performed, the appropriate specific network fuses with the general purpose network and, now as one network, produces the desired trajectory (Fig. 6). It is remarkable that the size of the specific network need only be <5% of the size of the general purpose network for the desired trajectory to be effectively stored and reproduced (59). It is noteworthy that such very specific cells have been observed at low proportions in neurophysiological recordings during performance of memorized trajectories (35).

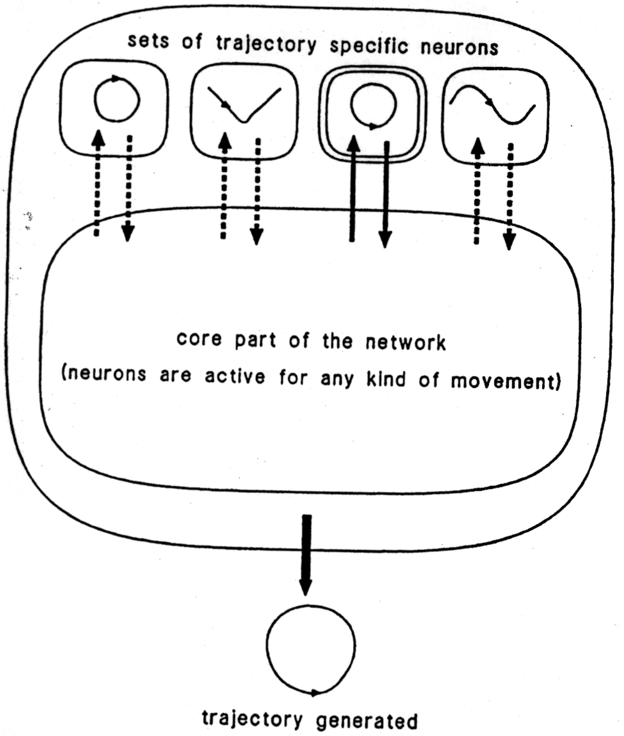

Fig. 6. The neural network for generation of four different types of neural-vector trajectories. All units in the core part are interconnected with each other and with all units in the trajectory-specific sets. All units in each trajectory-specific set are interconnected with one another and with all units in the core part. There are no connections between different trajectory-specific sets. Both kinds of *heavy arrows, solid and dashed*, indicate that this is a feedback network, and that the connections between the core part and the trajectory-specific parts are adjusted during the training of the network to generate different types of trajectories. The *double drawn ovoid* indicates that this particular set is currently activated, and connections between the core part and this set (*solid arrows*) determine the shape of generated neural-vector trajectory. *Single drawn ovoids* indicate that the other three trajectory-specific parts of the network are inhibited, and that the connections between the core part and these sets (*dashed lines*) do not interfere with the dynamics of the network. Reproduced with permission from (59).

Breaking the Directional Code

Voluntary movement is still an evolving ''hot'' topic in behavioral, neural and modeling research. The problems involved are very challenging and not easily amenable to simple solutions. Although *simplistic* solutions are abundant, true advancements are hard to come by. A major question is: how do such diverse brain structures as the cerebral cortex, basal ganglia, and cerebellum cooperate to produce graceful, accurate, and seemingly effortless reaching movements? The neuronal population vector analysis is a first step in ''breaking'' the code by which individual brain areas process directional information. The fact that this code applies to several areas involved in motor control suggests that the interactions among areas could be expressed within a common, population-vectorial framework. In addition, the fact that the *time-varying* population vector can provide crucial information on how directional information is being processed in different tasks opens the possibility that the dynamic interplay of the involved areas could also be expressed and elucidated within this population-vectorial framework. For this purpose, simultaneous recordings from various areas will be needed—a technically difficult but not insurmountable task. Modern functional brain imaging techniques (e.g., fMRI) could provide useful guidance as to which areas are involved in a task, and, therefore, which areas to record from simultaneously. This combination of approaches should lead to an efficient and effective approach to understanding the real-time, dynamic cooperation of diverse brain areas in planning, initiating, and controlling voluntary movements.

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