Are movement parameters recognizably coded in the activity of single neurons?

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Abstract: To investigate neural mechanisms of movement, physiologists have analyzed the activity of task-related neurons in behaving animals. The relative onset latencies of neural activity have been scrutinized for evidence of a functional hierarchy of sequentially recruited centers, but experiments reveal that activity changes occur largely in parallel. Neurons whose activity covaries with movement parameters have been sought for evidence of explicit coding of parameters such as active force, limb displacement, and behavioral set. Neurons with recognizable relations to the task are typically selected from a larger population, ignoring those cells with complex relations to the task and unmodulated cells. Selective interpretations are also used to support the notion that different motor regions perform different motor functions; again, current evidence suggests that units with similar properties are distributed over widely different regions.

These coding issues are reexamined for premotoneuronal (PreM) cells, whose correlational links with motoneurons are revealed by spike-triggered averages. PreM cells are recruited over long times relative to their target muscles; they show diverse response patterns, relative to the muscle force they produce, functionally disparate PreM cells such as afferent fibers and descending corticomotoneuronal and rubromotoneuronal cells can exhibit similar patterns. Neural mechanisms have been further elucidated by neural network simulations of sensorimotor behavior; the pre-output hidden units typically show diverse response patterns in relation to their target units. Thus, studies in which both the activity and the connectivity of the same units are known reveal that units with both simple and complex relations to the task contribute significantly to the output. This suggests that the search for explicit coding may be diverting us from understanding distributed neural mechanisms that operate without literal representations.

Keywords: chronic recording; motor cortex; movement parameters; neural computation; neural networks; parallel distributed processing; premotoneuronal cells; representation; spike-triggered averages

1. Introduction

Many systems neurophysiologists record the activity of single units in behaving animals in the hope of understanding the neural mechanisms generating motor behavior. Such “chronic unit recording” experiments are typically designed to test a plausible hypothesis about the function of neurons at some recording site: The animal is trained to perform a behavioral task involving that function and the experimenter searches out relevant task-related cells. Over the last three decades this formula has generated numerous papers illustrating neurons whose activity appears to code (i.e., to covary with) various movement parameters or representations of higher-order sensorimotor functions. Initially, such studies seemed to provide supportive evidence for plausible notions, for example, that motor cortex cells code muscle force and that premotor cortex cells are related to programming movements. With an increasing number of more sophisticated studies it has become clear that the accumulating experimental evidence undermines many of our simplistic notions about neural coding. Moreover, the search for neural correlates of motor parameters may actually distract us from recognizing the operation of radically different neural mechanisms of sensorimotor control.

This article begins with a review of experiments designed to show how various movement parameters may be represented in neural activity. This includes attempts to delineate a functional hierarchy of cells on the basis of their response latencies. We then consider studies of explicit coding of simple movement parameters such as active force and limb displacement and preparation to move. We discuss functional specialization in different cortical regions as well as the possibility that parameters are coded in populations of neurons. Since synaptic connections are an important determinant of the functional consequences of neural activity, we reexamine these coding questions for premotoneuronal cells, which have direct links with motoneurons. Finally, we reconsider these issues in light of results from neural network modeling studies.
2. Representation of movement parameters in neural activity

2.1. Relative timing of cell activity. To obtain evidence for a causal hierarchy of cells in different motor centers that mediate the programming and execution of movement, it first seemed reasonable to determine the sequential recruitment order of cells in different areas. A particularly useful behavioral paradigm for this purpose is the simple reaction-time response, in which an animal makes a repeatable movement in response to a stimulus such as light. The successive activation of neurons in different regions would then define a causal sequence of neurons mediating the transform between stimulus and response. For a visually triggered key release, for example, the sequence would begin with stimulation of retinal cells followed by propagation of activity to diverse cortical and subcortical centers, which might code the sensory aspects of the stimulus. The conversion of the stimulus-evoked activity into the preparation for movement might occur at intermediate times in cortical association areas. Finally, the neural activity involved in execution would converge in proper combination to activate agonist motoneurons that generate the movement. The peripheral links at the input and output stages of such a sequential scenario have been elucidated, but the central stages have consistently eluded temporal resolution.

The timing of motor cortex cells relative to movement was first studied by Evarts (1968), who showed that pyramidal tract neurons (PTNs) began to change their activity up to 100 msec before the onset of activity in agonist muscles. To determine the relative onset times of other cells that might precede activation of motor cortex neurons, Thach (1978) recorded neural activity in cerebellar nuclei, motor cortex, and muscles during the same responses. The onset times of activity changes of units in cerebellar nuclei were found to largely overlap those of precentral motor cortex cells (Figure 1). The onset times of different neurons in two cerebellar nuclei and motor cortex were distributed over hundreds of milliseconds, with a relatively slight difference in their mean onset times. Comparable overlap in recruitment times has been found in many subsequent experiments. Neurons in the supplementary motor area and primary motor cortex are recruited almost simultaneously in a reaction-time task (Chen et al. 1991) and during a stepping task (Alexander & Crutcher 1990c).

The basic problem in attempting to demonstrate serial activation of cells in different motor centers is that each region contains neurons that are recruited over diverse times. The extensive overlap in onset times makes it difficult to assign a sequential order of activation to different regions. Moreover, the duration of most movements as well as the duration of task-related activity greatly exceeds the conduction time between centers, so that recurrent loops could be "traversed" repeatedly during a single response. It is also relevant to note that the focus on the first change in neuronal activity puts undue emphasis on a subtle shift in firing rate that requires statistical determination. Functionally, the initial onset of a change has less to do with the cell's contribution to movement than its maximal activity. In any case, the appealing notion that initiation of movement involves the sequential activation of cells in hierarchically related centers is quite difficult to prove experimentally. In fact, the experimental results suggest that cells in diverse regions are activated more or less in parallel.

2.2. Coding of movement parameters. Although a cell's onset time provides equivocal evidence for its role in a causal hierarchy, its discharge pattern could provide a more robust indication of its contribution to movement. The hypothesis that parameters of movement are recognizably coded in the activity of motor system cells seems so reasonable that many experiments have been launched on the basis of this assumption. Neural coding, in the sense of covariation, has been amply investigated for a variety of movement parameters (reviewed in Evarts 1981; Fetz 1981; Fuster 1985). Since muscles are ultimately the generators of active force, it seems plausible that central cells controlling muscles could be coding the
force exerted during a movement. On the other hand, since we normally think in terms of moving a limb to particular target positions, it also seems reasonable that cortical cells could code the displacement or position of the limb. Evarts's first experiments to determine whether motor cortex neurons code force or displacement provide an excellent example of a behavioral paradigm designed to dissociate these variables. Evarts trained monkeys to make the same movements against different loads and, in some cases, to generate isometric activity without any displacement. In these studies, the activity of selected PTNs was related more to the active force or to the change of force than to displacement (Evarts 1968).

Yet a third variable to which cells could be related was found in monkeys prepared to make a movement: Some cortical cells changed activity long before an intended movement, suggesting that these cells may be involved in the preparation to make a movement, as contrasted with its execution, that is, with a behavioral set. Experiments designed to reveal set-related activity typically involve behavioral trials beginning with a sensory cue that indicates the correct movement, followed by a delay period and then a go signal to execute the cued motor response. During the delay between the cue and go signal, the monkey is prepared to initiate the movement and neurons in many cortical and subcortical regions exhibit associated changes in discharge.

Numerous other movement parameters have been suggested to be coded in neural activity, such as limb velocity (Gibson et al. 1985), direction of movement (Fortier et al. 1989; Georgopoulos et al. 1984; Schmidt et al. 1978), and target position (Alexander & Crutcher 1990c; Martin & Chez 1985). The issue of neural coding can be discussed in relation to three parameters: active force, displacement, and behavioral set. Thach (1978) was the first to investigate all three variables systematically for motor cortex and cerebellar cells. He used a task (shown schematically in Figure 2, top) that involved each of these three parameters: The monkey moved the wrist through a sequence of successive hold positions against different loads. The lower trajectories schematized the expected activity patterns of cells primarily related to patterns of muscle force (MPAT), position of the wrist joint (JPOS), and preparation or set for the next direction of movement (DSET). Thach calculated the degree of correlation between these idealized patterns and the recorded activity of cells in motor cortex, cerebellum, and muscles and found that the degree of correlation for different cells was continuously distributed from weak to strong. As expected, many motor cortex cells showed the best correlation with the MPAT sequence. Many other cells in the motor cortex correlated more strongly with joint position and still others correlated with set. Perhaps the most remarkable finding was the relative numbers of cells in each category; as described by Thach, "In summary of the rather astonishing results on neural discharge patterns in motor cortex during holding, all the types of neuron that were looked for were found, in nearly equal numbers" (1978, p. 665). Proponents of coding of movement parameters can only interpret this result as indicating that the motor cortex contains a variety of cells, each coding a different parameter of the movement.

However, such a conclusion would have to be tempered by another remarkable finding in this study: A slight change in response conditions could change the parameter that correlated best with a particular neuron. For example, the motor cortex cell illustrated in Figure 17 of Thach's paper had a strong relation to muscle patterns under condition of external load but was better related to joint position when the load was removed. Consistent relations between the activity of motor cortex cells and isometric muscle force have also been dissociated by changing the rewarded response patterns (Fetz & Finocchio 1975). Diehard proponents of coding would have to conclude that such flexible relationships that the same cells can "code" different parameters under different response conditions.

One basic problem with many attempts to relate neural activity to movement parameters is that the data are usually skewed by two types of experimental bias. One is the "task-induced bias" introduced by recording neural activity under particular behavioral conditions. In these experiments animals are performing a specific task designed to test the experimenter's hypothesis, and the activity of the modulated cells is interpreted in relation to that task. The data are further skewed by what could be called a "selection bias." The analysis of neural activity is typically confined to the subclass of neurons that show an interpretable relation to the task. Those cells that best
support the hypothesis are illustrated in the figures, and those that are statistically consistent are tabulated. However, in such studies two other groups of cells are invariably encountered: Many neurons are modulated with the task, but in complex ways that seem paradoxical or uninterpretable. In addition, many more neurons are simply unmodulated with the task. Although the latter two classes outnumber the interpretable task-modulated group, they are typically ignored. The paradoxical cells are rarely illustrated in papers, since they would detract from the main hypothesis, provoking the reviewers and confusing the readers. Instead, the interpretable and unmodulated cells are usually neglected in the final account of neural coding. Of course, many cells would in fact be marginally relevant to the ongoing task; however, by ignoring all the neurons with complex patterns we risk misunderstanding the real neural mechanisms in favor of dealing only with idealized and simplistic correlates.

This strong selection bias clearly undermines the contention that the functionally interpretable group of task-related cells provides convincing evidence for coding. Observations consistent with a given hypothesis can always be selected from a sufficiently large random data set. A rarely acknowledged fact of life in the neurophysiology laboratory is that neurons in many regions, including the motor cortex, exhibit an enormous variety of responses, a fact that provides an opportunity to find cells related to any given functional hypothesis. Thach (1978) eliminated this bias by objectively correlating the activity of the same population with three different, dissociable parameters. His finding that cells related to all three functions existed in nearly equal numbers suggests that something else may be going on besides preferential coding of particular movement parameters.

2.3. Localization of function. A common notion that is closely related to coding and also turns out to be simplistic in retrospect is the idea that different cortical areas are devoted to computing different motor functions. For example, it is commonly thought that the role of the motor cortex is to execute movement whereas motor association areas, such as the premotor and supplementary motor areas, are supposed to be concerned with motor programming or preparation to move under particular circumstances. Experiments designed to record neural activity in these regions under the appropriate behavioral conditions did indeed discover cells with the appropriate sorts of relationships. However, experiments in which neural activity in different regions was obtained under similar behavioral conditions have revealed that cells of the same type are found widely distributed over many areas. For example, neurons related to activation of muscles are found not only in the motor cortex but in the supplementary motor area (Chen et al. 1991; Crutcher & Alexander 1990c), premotor cortex (Godschalk et al. 1985; Weinrich & Wise 1982), prefrontal cortex (Fuster 1985; Niki & Watanabe 1976), and posterior parietal cortex (Mountcastle et al. 1975). Similarly, experiments involving delayed movements reveal set-related activity in the motor cortex (Tanji & Evarts 1976), premotor areas (Godschalk et al. 1985; Weinrich & Wise 1982), and prefrontal cortex (Fuster 1985; Niki & Watanabe 1976), as well as in the thalamus (Alexander & Fuster 1973) and basal ganglia (Alexander & Crutcher 1990c). Taken together, these studies suggest a very broadly distributed representation of these motor functions.

An extreme example of cortical specialization, which still remains almost axiomatic, is the presumed dichotomy between the functions of somatosensory and motor cortex. In this view, all precentral cells are thought to be involved in the execution of movement, whereas all postcentral cortex cells are assumed to be involved in somatosensory function. This view was challenged by Woolsey (1958), who noted that the maps of sensory input and motor output are similar and overlapping, in both precentral and postcentral gyri. Chronic unit recordings under active and passive conditions show that cells with similar response types can be found in both areas (e.g., Fetz et al. 1980; Soso & Fetz 1980). If this functional dichotomy is considered to be absolute rather than relative, identical response properties of single units must be interpreted in totally different functional terms. The responses of postcentral cells to passive stimulation are naturally interpreted as subserving somatic sensation, but the equally clear responses of precentral cells to passive joint movement and cutaneous stimulation are thought to subserve unconscious reflex functions. Similarly, the early responses of precentral cells preceding active limb movement are naturally thought to be involved in generating the movement, whereas identical early responses in postcentral cells are interpreted as subserving some sensory "corollary discharge."

The rationale for these diverse interpretations of identical response properties rests on functional presuppositions derived from the effects of cortical stimulation. Stimulation thresholds for evoking movements are clearly lower in precentral than postcentral cortex (Woolsey 1958). And in conscious humans, cortical stimulation evokes somatic sensations from a larger number of postcentral than precentral sites (Penfield & Boldrey 1937); however, these differences are a matter of degree rather than absolute. In fact, similar effects can be evoked from both gyri, albeit at different thresholds. Nevertheless, the conceptual dichotomy between "sensory" and "motor" cortex is again preserved by applying a double standard to this experimental evidence. The somatic sensations evoked by stimulating precentral "motor" cortex in conscious humans are ascribed to a spread of activity to postcentral sites. The movements evoked by stimulating postcentral cortex are similarly ascribed to mediation via precentral cortex; reports that movements can be evoked from postcentral sites after ablating precentral cortex (Woolsey 1958) are even taken as evidence that the lesions were incomplete.

The assumed functional dichotomy of sensory and motor cortex is further based on their differing output projections. In the macaque the corticospinal axons from postcentral cortex terminate more dorsally in the spinal cord than axons of the precentral PTNs, although there is a good deal of overlap (Coulter & Jones 1977). The postcentral PTNs are undoubtedly more likely than precentral PTNs to affect afferently driven spinal cells, but their target region also contains cells involved in reflex circuitry, as well as dendrites of motoneurons. Perhaps more relevant to the function of individual cortical neurons than the output projections of the descending cells are the strong interconnections between pre- and postcentral cortex. These massive corticocortical connections allow the reorganization of functional outputs of neurons not found in the sensorimotor cortex.

Thus, the cortex has been divided into different functionally independent units, often seemingly unrelated to one another. It is usually assumed that each such functional unit corresponds to a discrete cortical area, and that a single cortical area is composed of a single functional module (the idea that corticocortical connections are too diffuse to be of any functional significance is explicitly rejected by the experimental data). This extreme view has led to a number of oversimplified interpretations of the results of the experiments. For example, when a specific corticospinal projection is identified (e.g., Fetz et al. 1980; Soso & Fetz 1980), it is often assumed that all the cells in that region have the same functional role as the projection. This is not only an oversimplification of the results, but also an oversimplification of the functional role of the region.
allow the cells in each region to participate in the functions of the other; indeed, these reciprocal connections would explain the similar response properties of neurons found in these areas.

Thus, the notion that cortical functions are segregated into different cortical areas can be preserved only by imposing different interpretations on similar experimental evidence. Units with the same response properties are imagined to code either sensory or motor parameters, depending on the presumed function of their recording sites. A plausible alternative is to consider the similar response properties of cells in different cortical regions as evidence that they are involved in performing similar functions; the neural substrate for these functions is then distributed correspondingly. This means that a given cortical region would be involved in diverse functions, consistent with the diverse cell types observed. This view provides a basis for distributed interactions between the functionally related sets of cells and helps explain the recovery of function after lesions. Note that this view does not claim equal involvement of all regions in all functions, since cortical areas are undoubtedly specialized. The point is that a region's specialized function need not be its only function, and certainly should not be the only standard for interpreting what each of the cells in this region is coding.

2.4. Population coding. Investigators have recently found that the activities of populations of cells can provide functions that match movement parameters more closely than the firing pattern of any single neuron. The fact that movements are ultimately produced by activity in large ensembles of neurons provides a clear rationale for population coding. Humphrey et al. (1970) first showed that the activities of multiple motor cortex neurons could be added together in the right proportion to match different parameters of wrist movement in an isometric task. Weighted sums of the cells' firing rates could match the force trajectories and the wrist displacements, as well as their temporal derivatives, if the weighting factors for each cell could be optimally chosen for each parameter. Moreover, the match between the cells' weighted activities and the mechanical parameters improved with the number of cells included. The ability to freely optimize the weighting coefficients, of course, helped to ensure convergence on the movement trajectories; closer matches were obtained with larger populations because each additional nonredundant cell could serve to further reduce the remaining difference.

More recently, Georgopoulos et al. (1984) showed that populations of motor cortex cells could be used to match the direction of limb movement by invoking the "vector hypothesis" to sum the activity of directionally tuned cells. For a given movement direction, each cell was assumed to make a vector contribution pointing in the direction of its maximal activity, and by an amount proportional to the change in its overall mean rate during the given movement. The vector sum of all the unit vectors then approximated the direction of hand displacement. Again, the match improved as more cells with diverse directional preferences were included. This match with movement direction could be taken to suggest that the direction of hand displacement by the arm rather than muscle force is coded in motor cortex populations. The direct match between the population function and arm displacement is appealing because it conveniently avoids the intervening complexities of synaptic connections and limb mechanics, which present formidable obstacles to a causal explanation. Moreover, the vector hypothesis is virtually guaranteed to work, given a sufficient distribution of cells. For a particular movement the cells whose best direction coincides with the movement will make the largest direct contribution; cells whose vectors point in the opposite direction will make a negative vector contribution, since average rates are subtracted, and therefore also contribute positively to the movement direction. The other cells have off-axis vector components that would tend to cancel with a sufficiently large population. Thus, the vector hypothesis will produce a match with movement direction whether the directionally "tuned" cells have any output effects on muscles or not. The same sorts of matches have been demonstrated for populations of posterior parietal area 5 neurons (Kalaska et al. 1983) as well as cerebellar cortical and nuclear cells (Fortier et al. 1989) and globus pallidus (Turner 1991).

Musia-Ivaldi (1988) showed that the findings of Georgopoulos et al. (1984) would also result from a population of cells that code muscle shortening, and thus reconciled the apparent coding of limb displacement with the fact that many precentral cells do have effects on muscles. Recent studies by Kalaska et al. (1989) have shown that when the required force is varied independently of movement direction, the population vector of certain motor cortex cells shifts in the direction of active force. This result is consistent with a role in activating the agonist muscles. However, there are other motor cortex neurons whose population vector remains in the direction of movement, independent of force, much like posterior parietal cells (Kalaska et al. 1983). In this case, a key ingredient in making the matches with force or displacement is the ability to select the appropriate cells for each population.

Although one can find good descriptive matches between functions derived from the activity of neuronal populations and particular movement parameters, this correspondence is no proof of neural coding in the causal sense. To demonstrate that the candidate cells actually make a causal contribution requires additional evidence that they have appropriate output effects. Such a direct link is obviously difficult, and often impossible, for many central neurons. Still, a coding theory based merely on a descriptive match with a parameter provides no further basis for dealing with the neural interactions that would mediate the control of that parameter. A useful coding theory should provide some framework for understanding how the observed activity could contribute to the movement. For example, it would be helpful to know how the activity of the population whose "vector" points in the direction of movement is actually transformed into the movement. Descriptive correlates alone do not provide a causal framework for dealing with the underlying neural computation.

2.5. The coding problem. In retrospect, experiments designed to demonstrate coding of movement parameters have provided data that can be interpreted in either of two ways. Proponents of neural coding can point to the slight differences in mean onset latencies in different
regions as evidence of a sequential hierarchy of cells; they can point to examples of covariation of neural discharge with movement parameters as evidence of coding and they can ignore the complex and unrelated cells as unlikely to be involved; finally, they can consider different proportions of cell types in different areas as evidence of functional segregation. Alternatively, one could now argue that the accumulating experimental results have largely undermined these simplistic notions. The extensive overlap of activation times in different regions speaks more for parallel than for serial activation. Neural correlates of movement parameters in a particular task can always be selected from what is invariably a much larger variety of response types, but cells with more complex discharge could be just as involved in generating the movement, albeit in more complex ways. The distribution of similar cell types over diverse cortical fields speaks more for distributed representation than for functional segregation.

These issues cannot be resolved by more chronic unit recording data, because observing the activity of single and even multiple units is inherently insufficient to determine the mechanisms that generate movements. These studies usually lack another essential ingredient required to make causal inferences, namely, the connectivity between cells. In addition to the activation patterns generated during task performance, one must also know the output connections of the recorded cells in order to determine the consequences of that activity. The possible output connections are often inferred from independent anatomical evidence on major projections. However, such indirect inference is misleading for many neurons, since the cells encountered at a given recording site typically have diverse projections. If the cells' response properties are correlated with their projections, the functional distinctions described above could have been blurred by lumping them all together.

3. Response coding in premotorneuronal cells

To determine whether the variety of relationships observed in previous studies could be reduced by dealing with cells that directly affect motoneurons, some investigators have focused on those cells that have correlational linkages to motoneurons, as determined by spike-triggered averaging. These premotorneuronal (PreM) cells include the so-called corticomotoneuronal (CM) cells in precentral motor cortex (Buys et al. 1986; Cheney & Fetz 1980; Fetz and Cheney 1980; Lemon et al. 1986), the rubromotoneuronal (RM) cells in red nucleus (Cheney et al. 1988; Mewes 1988), and peripheral afferent fibers recorded in cervical dorsal root ganglia (DRG) (Flament et al. 1992). These PreM cells all produce short-latency postspike facilitation of EMG activity and have been documented in relation to comparable ramp-and-hold wrist movements—a response designed to elucidate the relation of cellular activity to changes in force and sustained force. It is interesting to consider the properties of PreM cells in the context of the four issues discussed above with regard to neural coding.

3.1. Timing. Although previous studies had shown that unidentified motor cortex cells exhibit a broad range of onset times relative to movement, it seemed possible that CM cells would show a more restricted range of recruitment times relative to onset of activity in their target muscles. This turned out to be only partly true, as shown in Figure 1. The surprising result was that CM cells began to fire up to several hundred milliseconds before the onset of activity in their target muscles. Similar broad distributions of onset latencies have been observed for RM cells (Mewes 1988) and for afferent fibers in DRG (Flament et al. 1992). Since these PreM cells produce postspike facilitation of their target muscles in about 10 msec, the much earlier onset times are presumably related to bringing the motoneurons to threshold; those cells with reciprocal inhibitory linkages to antagonists of their target muscles would also contribute to turning the antagonist muscles off.

The inescapable conclusion is that even connected PreM-motoneuronal pairs are recruited relative to each other over times that straddle hundreds of milliseconds. Thus, connectivity is not a critical factor in restricting relative recruitment times; instead, there may be other relevant variables (if indeed there are any systematic explanations). Even within the same motoneuron pool, motoneurons are recruited in sequential order over extended periods of time. One variable that may be more relevant to recruitment order than the spatial location or the output connections of a neuron is its relative size. An increasing synaptic drive on motoneurons recruits the smallest motoneurons first and then successively larger ones with higher thresholds. Similar size relations may explain the timing of early and late recruited cells in the PreM population, a subject for future investigation. In any case, the distribution of onset times of PreM cells relative to their target muscles is almost two orders of magnitude broader than the latency of their postspike effects.

3.2. Coding of muscle force. The activity of PreM cells clearly has a direct output effect in facilitating their target muscles, which in turn generate active force. In this sense the PreM cells can be said to causally affect force. The relation of CM and RM cell discharge to active force has been confirmed by having monkeys generate different levels of isometric force. The tonic discharge rates of these cells during the static hold period are indeed proportional to active force over a range of torques, as shown in Figure 3 (Cheney & Fetz 1980; Cheney et al. 1985; Mewes 1988). In addition, many of these PreM cells show a phasic discharge at the onset of movement, which is preferentially related to change of force.

These observations pertain to the major subsets of the PreM cells, namely, those that show phasic-tonic or tonic discharge patterns during the ramp-and-hold movement. Figure 4 illustrates the basic response patterns of the three groups of PreM cells and single motor units during the ramp-and-hold movements. Of these patterns, only the tonic pattern is strictly proportional to the ramp-and-hold force trajectory. Other PreM cells show patterns that differ significantly from the active force and from the activation patterns of their target muscles. For example, the phasic-ramp CM cells show a strong burst of discharge at the onset of movement and a gradually increasing discharge during the static hold period. This pattern is totally different from the discharge of its target muscles.

There are also many PreM cells that show more com-
Thus, PreM cells show three different relationships to their target muscles (as well as to force): Some PreM cells are simply coactivated with target muscles, others exhibit more complex and counterintuitive patterns, and still others are unmodulated. Despite these various relationships in discharge patterns, the correlational evidence confirms that they are all causally involved in activating their target muscles.

Furthermore, just as central cells can change their discharge patterns in relation to motor parameters under different conditions, single CM cells also can fire differently relative to their target muscles and force for different types of movements. When a monkey performed a finely controlled ramp-and-hold tracking task, the CM cells were strongly modulated with their agonist target muscles. When the monkey made rapidly alternating ballistic movements, however, the same cells were relatively inactive, even though their target muscles were more strongly activated (Cheney & Fetz 1980). Similarly, Muir and Lemon (1983) found that CM cells were preferentially active during a precision grip of a force transducer between thumb and forefinger, but the same CM cells were paradoxically inactive during a power grip, which involved even more intense activity in their target muscles. These results indicate an unexpected variability in the relation between even PreM cells and their target muscles under different movement conditions.

3.3. Localization of function. To determine whether supraspinal cells in motor cortex and red nucleus may have functional specializations that are different from those offferent cells providing feedback from the periphery, one can compare the CM and RM populations with PreM cells recorded in the DRG. Surprisingly, the response patterns of the DRG cells fell into the same categories as the most common supraspinal cells (tonic, phasic-tonic, and phasic; see Figure 4). Moreover, the relative onset times of many afferent cells also preceded the onset of their target muscle activity. This suggests that many PreM cells in radically different locations are recruited in similar ways. A similar result was obtained by Schieber and Thach (1985): During a slow ramp-and-hold tracking task they found similar classes of cells in DRG, motor cortex, and cerebellum.

In addition to PreM cells with similar response properties in all three locations, the supraspinal populations each included some unique types. As indicated in Figure 4, the ramp cells were observed only among cortical cells and the unmodulated neurons were found only in the RM group. This suggests that the three groups of PreM cells are not entirely equivalent but contain subsets of cells whose unique properties suggest some functional distinctions.

3.4. Population coding. Although individual PreM cells exhibited a variety of distinct discharge patterns, the net contribution of all the PreM cells to a target motoneuron would be more relevant to assessing their total effect. The response patterns of the PreM cells can be synthesized into a population average (Fetz et al. 1989). Since the cells were recorded under similar behavioral conditions, the average activity of the population can be obtained by summing the response histograms of individual cells (as well as their target muscles) aligned with the onsets of the
movements. This was done in stages, by first compiling subaverages for each response type and then adding these in proportion to the number of cells of each type. The resulting net ensemble averages of the discharge patterns of both the CM and RM population exhibited a phasic-tonic pattern. However, the motor cortex population showed a greater difference in the depth of modulation between opposite directions of active wrist force than the rubral cells, whose population histogram showed tonic activity during both directions of movement.

The net synaptic drive of the PreM cells on their target motoneurons would be proportional to these population histograms. The population histograms could also be used to infer the quantitative effect of the cells on their target muscles; the population activity can be multiplied by the correlational consequences of the postsynaptic potentials evoked from cortex and red nucleus (Fetz et al. 1989). The results provide a causal picture of the population influence on target motoneurons that is based on physiological measures of the synaptic linkages.

It is interesting to note that coding of muscle force in motor units requires a population average. Under normal conditions, single motor units code muscle force in a highly nonlinear manner, since motor unit firing rates are limited at the lower end by their recruitment threshold and at the upper end by saturation (Figure 3 and Palmer & Fetz 1985). Moreover, the net force generated by the twitch tensions of a motor unit is a nonlinear function of its firing rate. This nonlinear behavior of the individual motor units is resolved by the population sum, which includes the successive recruitment of motor units with larger twitch tensions.

3.5. Implications of PreM cell properties for neural coding.

The properties of PreM cells have significant implications for the coding issue, insofar as their activity is causally related to generating muscle force, but this activity comes in a remarkable variety of discharge patterns. The connectivity of PreM cells to motoneurons is confirmed by cross-correlation methods, yet the response patterns of these PreM cells include all three types of relation observed between central cell activity and movement parameters. Many PreM cells clearly covary with the muscles that they facilitate, as one would intuitively expect. Others, such as the phasic-ramp CM cells and the bidirectionally activated RM cells, show counterintuitive discharge patterns that are distinctly different from the activity of their facilitated target muscles. Moreover, some cortical cells are paradoxically coactivated with arm muscles that they inhibit. In addition, a large group of unmodulated RM cells is tonically active during both phases of movement. This would indicate that the response patterns of neurons alone are not a reliable guide to their causal role in the task and that neural interactions between connected cells involve some highly nonlinear relationships. If the activities of connected PreM neurons and their target motoneurons can show such diverse relations, the chance of finding meaningful correlates of movement parameters would seem even more remote.

The same considerations apply to the relation of PreM cell discharge and the mechanical parameter of force, on which they clearly have a causal effect. Only the activity of the tonic PreM cells is directly proportional to force in this task. Indeed, the entire population of cortical and rubral PreM cells exhibits a net phasic-tonic pattern, suggesting that force is coded in a nonlinear way even in the output cells that generate this force.


4.1. Holographic coding mechanisms. The basic reason that movement parameters need not be explicitly coded in the activity of single neurons is that movement is the consequence of large populations of interacting cells, which can generate an output without requiring any one cell to fire in proportion to the resultant movement parameters. Instead, the activity that is appropriate for a given cell is determined largely by its connections with the rest of the network rather than by any need to code an output parameter explicitly. This point can be illustrated by an apt analogy: the storage of images by holographic mechanisms. Holographic storage is based on a distributed representation of phase relations between wavefronts rather than a literal representation of the stored image. Recall that a holographic plate is constructed by exposing a photographic plate to the interference patterns between two coherent light beams — a reference beam obtained directly from the coherent source and an object beam reflected from the object whose image is to be stored. The spots on a holographic plate record the points of constructive interference, where the two light beams are in phase. These spots are distributed in a pattern that has no recognizable relation to the image. However, when the plate is illuminated with the reference beam, this distribution of spots forms a diffraction grating that reconstructs the object wavefront by the interference patterns in the transmitted beams.

The idea that neural networks may store and process information through holographic mechanisms is based on many salient analogies between the two systems. A small lesion in a holographic plate does not destroy any specific portion of the image but rather degrades the overall image quality; similarly, small lesions in the nervous system typically produce subtle behavioral deficits at most. The association between images of two spatially adjacent objects can be readily demonstrated by creating a hologram from the light reflected from the two objects; illuminating the developed plate with the light reflected from only one of the objects will reproduce a ghost image of the missing one. In this case the light from the remaining object essentially acts as the reference beam for reconstructing the other. This mechanism provides an analogue of associative memory and a model of content-addressable memory (Hinton & Anderson 1981; Pribram et al. 1974). Such a mechanism is likely to be involved in perceptual processes such as figure completion. The ability to execute a skilled movement sequence in a particular context may well involve similar associations between changing sensory inputs and central programs.

The basis for these analogous properties is the distributed representation of the information, using constructive interference between activity propagated in parallel pathways. Activity in a neural network is also propagated by the coincident arrival of sufficient synaptic input to activate the relaying neurons. With regard to coding mechanisms, the relevant point is that the spots on the hologram do not form a literal pictorial representation of the encoded images.
of the image; instead, the "meaning" of each spot depends on its relation to the rest of the hologram – each point diffracts light in such a way that the net interaction with adjacent points reconstructs the wavefront of the stored image. Similarly, in the nervous system, the activity of a cell need not form a literal representation of a movement parameter; instead, its contribution to movement depends on its diverse connections and interaction with the rest of the network.

Optical holograms clearly represent highly simplified examples of this type of distributed nonlinear coding mechanism, insofar as they store only static images. Nevertheless, the same principles apply to storage and retrieval of dynamic information in neural networks (see papers in Hinton & Anderson 1981). Such analogies between neural and holographic mechanisms have been largely speculative until now. With the advent of neural network modeling, it has become possible to demonstrate these same properties in simulated populations of cells.

4.2. Neural network models. Model networks can be used to simulate the mechanisms operating in populations of cells; they also have unique heuristic value in elucidating the principles of neural computation. The behavior of ensembles of neurons is difficult if not impossible to synthesize by "bottom-up" inferences from single-unit recordings alone, mainly because the relevant connections between the recorded neurons are typically unknown. In contrast, model networks that simulate a particular behavior can be obtained by "top-down" derivations based on examples of the behavior, using training algorithms such as back-propagated error correction (Rumelhart et al. 1986b) or trial-and-error learning (Kuperstein 1988). The resulting dynamic networks can simulate motor activity without explicitly representing movement parameters in the activity of particular units.

For example, to determine what sort of neural network might be able to transform the step change in target position that a monkey sees into the response patterns generated by his agonist motor units, we used back propagation to derive the appropriate dynamic recurrent networks (Fetz & Shupe 1990; Fetz et al. 1990). The input and output layers were connected to intervening excitatory and inhibitory hidden units, as shown by the schematic diagram in Figure 5; an example of a specific weight matrix is shown in Figure 6. Initially, the synaptic weights were assigned randomly; presenting the input produced an initial output that deviated drastically from the desired target output. The difference between the actual output and the desired output was used to change the weights appropriately to reduce the error between actual and target outputs. Successive training iterations produced a network that transformed the temporal input patterns (step and transient inputs for flexion and extension) to the desired output patterns (eight motor unit patterns: tonic, phasic-tonic, decrementing, and phasic, for both flexion and extension). One resulting network is shown in Figure 6; the size of each square represents the strength of connection from the unit identified at the left to the unit at the top. The activation patterns for a flexion-extension cycle are illustrated for each unit. This result represents a complete neural network solution for this simplified sensorimotor transform in that the activity patterns of the somotor transform that the activity patterns of the intervening hidden cells, as well as their connectivity, are completely specified.

These network solutions can be analyzed systematically to determine how the output patterns are derived. Relevant to the issue of "coding" we can examine how the response patterns of the output units are represented in the activity of the hidden units. For example, to see how the network in Figure 6 produced activity of the phasic flexor output unit (fp), one can examine its synaptic inputs (represented by the vertical column of weights under fp). The strongest weights indicate that phasic flexion was derived by two different means. As proponents of explicit coding might predict, the phasic output cell had strong excitatory connections from phasically active hidden units (e.g., a1, a8). A second contribution, however, came from excitatory units with tonic activity (a11), in conjunction with a delayed tonic input from inhibitory hidden units (b1). The difference between these two also contributes to the phasic output. Yet a third mechanism has been observed in other network simulations, which were allowed to have tonic biases on the cells. In those cases, the phasic output could also be derived from the sum of excitatory input from a phasic-tonic hidden unit in combination with a negative bias that essentially subtracted the tonic component. Thus, a pertinent lesson from these simulations is that many combinations of hidden unit activity can and do contribute to the same output response pattern.

It is interesting to note that many properties of the hidden units in these networks are analogous to those found in cells in the nervous system. For example, a hidden unit (e.g., a11) may have divergent excitatory connections to many different types of output cells, just as CM cells facilitate motor units of different response types. Conversely, a given output unit typically receives convergent input from many hidden units, with different activations. Nevertheless, the connections are not equally distributed; this simulation produced preferen-
Figure 6. Neural network transforming step and transient inputs to firing patterns of motor units at output. Unit activations during a flexion-extension cycle are shown at left and along the top. The weight matrix gives the strength of connections from the row to the column units (weight scale at top). The rows represent, from top to bottom, the bias (which was eliminated for this simulation), the inputs (fs to eb), the excitatory hidden units (a's), inhibitory hidden units (b's), and the output flexor and extensor motor units (ft to ep). The target output patterns for both flexion and extension are tonic (ft & et), phasic-tonic (ftp & ept), decrementing (fd & ed), and phasic (fp & ep). To better visualize the relationships between units, the hidden units were sorted in order of the strength of their contribution to the phasic-tonic output units (from Fetz & Shupe 1990).
The response patterns of hidden units that contribute to the output also show all three types of relation to the output. Some hidden units simply covary with the output unit that they excite, as might be expected intuitively (e.g., a1 and fp). Many other units show activity patterns that differ significantly from their target outputs (e.g., a11 and a10 compared with fp). In some simulations of reciprocal movement, many hidden units have bidirectional responses during both flexion and extension; the inappropriate portion of their activity is simply eliminated by inhibitory units. In addition, the inhibitory hidden units frequently show counterintuitive coactivation with cells that inhibit (e.g., b10), as has been seen in some cortical neurons. Finally, the tonic bias units used by many of these networks are clearly analogous to the unmodulated activity seen in many RM cells. Thus, the activity of output units is not necessarily coded recognizably in the activity of hidden units, even those that provide direct input. Not only do the network simulations reveal all three types of relations between hidden units and output units, but experiments with network lesions (Fetz & Shupe 1990) confirm that each type makes a significant contribution to the output.

The issue of localization of function can also be seen in a new light with network simulations. The functional consequence of the activity of any particular hidden unit is determined by its connectivity in the network; its physical location would be entirely arbitrary. Thus, if the hidden units were physically implemented, they could be reorganized in space without affecting the network computations, so long as their connectivity remained intact.

Relevant to functional localization, a common property of representation in cortical fields is the tendency to form topographic maps of the peripheral receptors or muscles. This feature of cortical organization has been simulated in neural network models; using local Hebbian rules to change synaptic strengths will lead to topologically organized feature maps (Kohonen 1982). This type of topographical organization within a cortical field should be distinguished from the segregation of functional computations among different fields. As demonstrated by network models, topographic organization can result from local synaptic interactions; in biological networks this may also have some wiring convenience. In contrast, functional segregation in the form of explicit separation of computational stages does not appear in network simulations.

The issue of population coding is also illuminated by these network simulations. The response pattern of any particular output unit is simply derived from the computed sum of all its inputs, weighted by the connection strengths. There is no need for explicit coding of any other sort. One could imagine taking the activity of a population of hidden units and matching some movement parameter by an appropriately weighted sum of their activities. Despite the success of such a mathematical exercise, the weights that are actually significant for the neural calculations are the synaptic links between units, not the mathematical coefficients required to calculate an optimal match. Put another way, the ability to obtain a population function that matches a parameter is quite irrelevant to the neural mechanisms that generate the output.

Clearly, these initial network simulations are still too simplistic in their connectivity and cell properties to be
taken as realistic models; nevertheless, they serve to illustrate some of the mechanisms at work in large populations of units interacting in ways analogous to neuronal interaction. Thus, network models provide a useful heuristic tool for investigating network mechanisms and can help to bridge the impasse between single-unit data and behavior. In the future, these network simulations can be improved to provide more realistic models of biological networks by incorporating the activity of more cells recorded in behavioral experiments and by making the connections more appropriate.

5. Concluding comments

We have taken the devil's advocate position on the notion that movement parameters are explicitly "coded" in neural activity. If "coding" is defined simply as covariation with movement parameters, the nervous system will provide ample opportunities to search out cells whose activity correlates with this or that parameter. Given the variety of neural discharge patterns and the ability to select the best examples, one can anticipate further examples of cells that could code some hypothesized variable. Like reading tea leaves, this approach can be used to create an impression, by projecting conceptual schemes onto suggestive patterns. This selective approach ignores two major groups of neurons: those with a complex or paradoxical relation to the task and those that are not modulated. It seems significant that studies in which both the activity and the connectivity of the same neurons are known — namely, physiological studies using spike-triggered averaging and modeling studies with neural network simulations — reveal that all three classes of units can and do contribute significantly to the output. Thus, the search for explicit coding may actually be misleading, and may divert our understanding of distributed neural mechanisms that operate without literal representations.

If virtually any neuron can potentially contribute to generation of movement, how can we ever hope to understand the underlying mechanisms? Ultimately, systems neurophysiologists can profitably use a combination of single-unit recording techniques and neural modeling to investigate the network mechanisms generating motor behavior. Unit recordings can provide important constraints on the activity of related neurons, but the network models can provide working examples of complete solutions to sensorimotor behavior. To the extent that models can incorporate anatomical and physiological constraints, they can provide plausible explanations of the mechanisms of neural computation.

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6. References


Neurophysiology of motor systems: Coming to grips with connectionism

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[EEF, DAR] In their respective target articles, Fetz and Robinson argue persuasively that insights derived from neural network modeling indicate that we are unlikely to learn how information is processed in biological motor systems through neurophysiological studies alone. They point out that conventional attempts to explain brain-based movement control in terms of the response properties of individual central neurons (considered analogous to the hidden units of artificial neural networks) are predicated on a variety of unwarranted assumptions, including: (a) individual central neurons may make substantial contributions to the generation of motor behavior; (b) in the absence of detailed information about its connections with other units of the network a neuron’s ultimate influence upon motor behavior can be inferred from its response properties alone; and (c) only those neurons with simple, readily interpretable response properties need to be taken into account in explaining how a particular brain region contributes to movement control.

Arguing from what might be termed a connectionist heuristic (one that assumes that neural network – i.e., connectionist – models, crude though they may be at this early stage in their development, represent the most promising approaches yet devised for modeling biological nervous systems), both target articles provide compelling and incisive critiques of the naive belief that it is possible to learn how biological networks control movement simply by recording the movement-correlated activity of a sufficiently large sample of each network’s neurons. In this respect, both offer useful and sobering reappraisals of the limitations of our conventional neurophysiological methods for studying the neural substrates of motor behavior.

Robinson’s critique is moderately pessimistic about the prospects of our ever learning in detail how brains manage to control movement. He could be right. We certainly know little enough now about how signals are processed in central motor networks, even after two and a half decades of recording neuronal activity throughout the brain’s motor fields. Nevertheless, a case could be made for guarded optimism about the future of systems research on the neural substrates of motor processing. It is precisely the advent of more realistic, neural-network models of the motor system that should make it possible eventually for neurophysiologists to conduct experiments that will not simply correlate neuronal activity with various motor behaviors, but will serve instead to test detailed connectionist theories of how motor networks process information.

As Robinson points out, the complexity of biological networks is such that it may be futile to attempt to explain how any of them processes information on a cell-by-cell basis. Were it possible, however, to devise connectionist models that solved the same problems and were structured in much the same way as their biological counterparts, and if the model networks were found after training to contain hidden units with the same types and distributions of response properties as the neurons in the networks that had been modeled, would it not be reasonable to at least hypothesize that the models and their biological counterparts were processing information in the same fashion? Such a hypothesis could be detailed and mechanistic, and would be testable in that any of the specific features of the model (e.g., observed changes in the types and distributions of hidden unit response properties after the network had been trained to perform a different task) could be compared with those of the biological network.

This would obviously be an indirect approach to the problem of discovering how biological networks process information. (The direct approach would be ruled out by the impracticality of characterizing all the connection strengths and activation values of the myriad elements within even the simplest of the brain’s networks.) But indirect though it might be, such a strategy has the potential of permitting us to learn in some detail how information is actually processed in the brain’s various networks. In fact, this approach is already beginning to yield useful insights, as is well illustrated in both Fetz’s and Robinson’s target articles. It might be argued, then, that the conclusions we should draw from Robinson’s critique is not that information processing in central motor networks is inherently unanalyzable, but rather that we will need better, more realistic models to understand such processing, and that to be taken seriously, those models will need to make detailed, testable predictions about the behavior of neurons in the networks that are modeled.

The development of such models has barely begun, and thus far there have been few attempts to incorporate meaningful biological constraints. This is caused in part by a lack of information concerning some of the relevant neurobiological details (such as the strengths and distributions of local circuit connections, the electrotonic summary functions of complex postsynaptic elements, and the types and distributions of synaptic learning rules). And, as Robinson points out, neural network
neurons can be considered directly analogous to those of the hidden units of an artificial neural network. Moreover, the responsiveness of both types of elements is usually gauged in a similar manner, by measuring the neuron's or the hidden unit's differential responses to a variety of system-level input/output conditions. This is the hallmark of the single-unit recording method, which can be very useful in this regard, provided sufficient care is taken to dissociate the relevant behavioral conditions (e.g., sensory inputs, motor outputs, behavioral sets) that are being used to define each neuron's response profile.

Even without knowing the connection strengths between functional layers of processing elements, it is possible in some multilayer networks — of both the biological and the artificial varieties — to detect distinctive changes in the types of hidden unit response properties encountered from layer to layer (see, for example: Linsker 1990; Maunsell & Newsome 1987). The strategy of comparing hidden-unit response properties of artificial networks to those of the biological networks being modeled may well suffice therefore as a reasonable test of the modeler's accuracy. Still better, however, would be comparisons that also included some gauge of the strengths and distributions of connections between layers. Perhaps this will some day be possible, if the spike-triggered averaging technique used so effectively by Fetz and his colleagues to assess connections between premotoneurons and motoneurons can eventually be adapted to the study of more centrally located connections.

Nonetheless, it does not follow from this that the response properties of central neurons are meaningless or uninterpretable. Fetz goes on to assert that "if the activities of connected Prem [premotor] neurons and their target motoneurons can show such diverse relations, the chance of finding meaningful correlates of movement parameters would seem even more remote." The implication here seems to be that neural correlates of movement parameters (i.e., the response profiles of central neurons) are only meaningful if they covary with the activity of the muscles with which that neuron is ultimately connected. On the contrary, the fact that a particular neuron discharges exclusively in relation to a specific movement parameter (e.g., direction of movement, irrespective of force or amplitude) seems to me to be a meaningful observation, whether or not that same neuron happens to have a net excitatory influence on the agonist muscles that generate the movement. To conclude otherwise would be to conflate a neuron's response properties with its connections to downstream structures. In the analysis of artificial neural networks it has proven essential to distinguish carefully between these two features of the hidden processing units. It would seem to be equally important to keep these two issues (response properties vs. connection strengths) separate if there is to be any hope of using neurophysiological experiments to test connectionist models.

It is a fortunate consequence of the fact that connectionist models are neurally inspired that the response profiles of central
Taking distributed coding seriously

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EEF] Extending distributed coding to the motor system applies a set of principles that has been accumulating support in sensory systems for some years. Distributed coding is an alternative to the detector cells of the sensory systems, or of the equivalent command cells of motor systems. Distributed codes are revealing a previously unsuspected flexibility of organization. Together with the lateral connectivity and efferent control that are its corollaries, however, distributed coding has even greater consequences than those reviewed by Fetz.

Efferent control magnifies the effects of distributed coding. If a neuron at level n feeds its signals back to a receptor, for example, that receptor combines peripheral information with level n information to create a new level n + 1. A higher-level signal moves through the afferent channels of the sensory pathway right from the start. The concept of successive recordings in successive layers breaks down as the logical level of an anatomical structure can no longer be defined.

Along with distributed coding, then, comes the necessity for distributed stages. In the motor system, sensory feedback from the muscles can have analogous effects on control. This new idea contrasts with the classical conception of discrete stages, in which all the neurons at one stage do about the same things on different parts of the input and a transfer function can be written to describe what that stage does to the signals flowing through it.

The idea of distributed stages complements Fetz's finding that even neighboring neurons may show widely different responses in a given situation. In discussing localization of function, he might have added that many more neurons participate in motor activity than are found in the classical precentral motor cortex, for about 1/3 of the pyramidal tract axons originate not in the motor cortex but elsewhere in the cortex. As a psychologist, I am generally happy to be able to explain 1/3 of anything. Thus, to a psychologist's approximation, the pyramidal tract arises from locations other than precentral motor cortex. The neurons and their types of discharge from these other areas are even more varied than those of the precentral motor cortex.

Fetz's observation that neurons in a given region can display nearly every imaginable response pattern is important but too little investigated. It recalls similar evidence that D. N. Spindell, R. W. Phelps, and I collected in the laboratory of Karl H. Pribram in 1970. We were interested in the problem of distance constancy, the ability of the visual system to recognize an object as having a certain size regardless of its distance from the observer or the size of its retinal projection. To look at how the striate cortex of the cat contributed to distance constancy we isolated the various distance cues and presented them separately and in combination while recording from single neurons. Our automated receptive field mapping apparatus swept a small spot or bar in a raster pattern across a square area. We could vary the size of the square, the sweep speed, the display distance, and the bar size independently. We could also record monocularly or binocularly, of course.

After factorially varying the parameters of stimulation and recording receptive field properties in a few dozen neurons, we attempted to sort the data into a small number of discrete receptive field types, as was the fashion at the time. We failed miserably — it seemed that every neuron responded in a different way, showing constancy when some parameters were varied and no constancy when others were manipulated. The only consistent finding was that if recording was monocular and if every parameter was varied in a way that kept the retinal image the same, we could change the target distance without changing a neuron's responses. Except for that, no two neurons followed the same rules. The number of receptive field types would have been as large as the number of neurons. We abandoned the study, and we never published the data.

In light of Fetz's target article, it seems we gave up prematurely. Our results, in hindsight, demonstrate a parallel between the organization of the sensory and the motor systems, with each neuron adding a unique signature to the composite population code; groups of neurons with similar receptive fields are found only when incomplete or relatively trivial questions are asked of the neurons.

In subsequent neurophysiological work, aimed at elucidating the processing of a stimulus rather than at the responses of single neurons, a similar pattern has emerged. Working in cat and monkey striate cortex, I attempted to find out how each neuron would respond to a stimulus that had a meaning in a discrimination task. Recording from neurons occurred while the awake animal performed a discrimination for a liquid reward. Rather than trying to find the optimal stimulus for each neuron, and thus driving it far beyond its normal physiological rate, we recorded every neuron with the same stimulus. Single-cell responses were meager compared to those customary in optimal-stimulus studies, and were widely different for each neuron. Only the composite responses, analogous to the population vectors of Georgopoulos et al. (1984), began to look like reasonable codes for the stimulus. The same population of neurons also carried information about the correctness of the response in the behavioral trials (Artim & Bridgeman 1989; Bridgeman 1980; 1982; Bridgeman & Artim 1983).

Finally, a historical note: Although the neural hologram hypothesis originated with Pribram (1971; Pribram et al. 1974) in a sensory context, its recent use has been mostly in models of memory (Eich 1982; Murdoch 1982). Fetz makes an important contribution in expanding the idea to coding in motor regions as well.
Network simulations and single-neuron behavior: The case for keeping the bath water

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[EEF, DAR] David Robinson has been a guiding force in shaping the direction of oculomotor research for the past two decades. From his control-systems-engineering vantage point, he has formalized vague concepts into testable models that have provided the motivation for many studies of the oculomotor system. Those early models were based on the discharge patterns of actual neurons that were then just being discovered. He gave us such important concepts as the local feedback burst generator for saccadic eye movements and the neuronal integrator for eye position. Many of our colleagues who are interested in the control of somatic movement have noticed the general applicability of his ideas and have incorporated them into their thinking. It is disappointing, therefore, that the pop of eye movements is now worshiping at the altar of a lesser god.

Robinson’s target article seems a bit schizoid. On the one hand, he says that unit recording is useless because we cannot see signals in the behavior of single neurons and because the CNS has a variety of solutions to any given problem anyway. On the other hand, he uses published discharge patterns (but only his own) to legitimize his models. For example, the myriad of cell types he and his colleagues found throughout the vestibular nuclei all turn up in the hidden neurons of his network simulation of the vestibulo-ocular reflex (VOR). In particular, he points out that his model predicts the existence of hidden units whose discharge pattern “seems contrary to an engineering mentality.” Indeed, such “rogue cells” are occasionally found in the vestibular nuclei.

While decrying unit recording in favor of modeling, Robinson fails to point out two important facts. First, in his VOR model the weighting coefficients of the rogue cells are always very small, so those cells contribute little to the resulting network output. Second, only certain neuron types in the vestibular nuclei in fact project to motoneurons and are therefore interneurons of the VOR; that is, the hidden neurons of his network. It is clear that none of those identified interneurons behave like rogue cells. The network simulation therefore suggests a signal processing solution that we already know the CNS does not employ. It suggests this solution because it is not constrained by the anatomy and neurophysiology that is known to underlie the VOR. Therefore, it simply is incorrect that the actual neural “network disassembles the input signals, scatters them over the hidden units, and then reassembles them.” Until it includes the appropriate neurophysiological constraints, this type of network model will only be an interesting laboratory exercise to “amuse the applied engineer,” who is not concerned with explaining an existing system but only in creating a new one. Indeed, if this were all there was to it, the brain would be easy to build because it would solve all of its problems with a rather simple learning algorithm.

There is a similar myopia in Robinson’s arguments concerning the neural integrator. For almost two decades, Robinson has enthralled the oculomotor community with the possible existence of a black box whose function is to integrate the prenuclear eye velocity signals present in the various oculomotor subsystems and thereby produce the eye-position signal required by extracocular motoneurons. According to Robinson, few neurons in the pons and medulla have the pure eye-position signal expected at the output of such a neuronal integrator. Instead, brainstem neurons with a position signal often carry velocity information as well. The hidden neurons that emerge in Robinson’s simulated network integrator also have various combinations of eye-position and velocity information; he therefore concludes that the network performs integration as the brain does. His basic tenet is that biology is messy and that intermediate stages that have position and velocity signals distributed “thoroughly” over all of the interneurones are to be expected. “This property imparts a biological flavor to simulations” and “it is hard not to believe that similar features also shape the real networks.” But wait a minute; were we not told in the Introduction that “the study of single neurons or neuron ensembles is unlikely to reveal the task in which [the units] are participating or the contribution they are making to it?”

As with the VOR, Robinson’s network model of the neural integrator ignores some fundamental neurophysiological data. First, lesions of the cerebellum impair gaze-holding ability, suggesting that the integration process is distributed in the brain, not just confined to hidden neurons in the nucleus prepositus hypoglossi (NPH), the site of the putative integrator. Second, some neurons in the simian NPH have pure eye-position signals, whereas probably none have only pure eye-velocity signals. Indeed, the neurons that exhibit a relatively pure eye-velocity sensitivity also have a signal related to head velocity, whereas none of the cells with any eye-position sensitivity do. Consequently, it is again incorrect that there is a “thorough” distribution of signals among actual neurons in the NPH.

In sum, unlike Robinson, we believe that there is considerable evidence of order in the processing of neuronal signals in the oculomotor system if one considers all of the available neurophysiological data. Furthermore, we believe that black-box models constrained by the rigorous application of available data will continue to be invaluable conceptual tools that will serve to guide oculomotor research. Surely the alternative of network models with no real physiological constraints is merely an intellectual exercise at best. Indeed, whenever the neurophysiology of an oculomotor subsystem is taken into account, the network model is shown to be hopelessly naive. To paraphrase Robinson, perhaps it would be wiser to keep the neurophysiological bath water and just throw out the network babies.

Fetz’s approach to network modeling appears to have more promise than that of Robinson and his colleagues. First, the connectivity of Fetz’s model is constrained by known anatomical connections for, as he says, “the cells encountered at a given recording site typically have diverse projections.” It follows that a network such as Robinson’s, which finds a use for all of the neurons in a structure, represents no great breakthrough and is probably simply wrong. Second, Fetz’s model produces the temporal discharge patterns of its elements, whereas Robinson’s networks can deal only with the coefficients that specify each hidden unit’s sensitivities to eye or head movement variables. Fetz’s simulation therefore has the potential to allow optimization of the temporal characteristics of discharge patterns.

We do take issue, however, with Fetz’s contention that movement parameters are not reliably encoded in the discharge properties of even those neurons connected monosynaptically to motoneurons. This generalization comes from his observations that some cortical cells, identified by spike-triggered-averaging (STA) as connected to certain muscles, exhibit counterintuitive discharge patterns that are distinctly different from the activity of their facilitated target muscles. Moreover, some cortical cells are paradoxically coactivated with arm muscles that [STA says] they inhibit. . . . This would indicate that the response patterns
of neurons alone are not a reliable guide to their causal role in the task.
A similarly "counterintuitive discharge pattern" occurs in the oculomotor system where there is a logical explanation for it. The so-called position-vestibular-pause (PVP) neuron in the vestibular nuclei projects directly to oculomotor neurons and during suppression of the VOR it continues to provide an unwanted signal related to head velocity. Fortunately, Robinson has made us feel comfortable with such rogue cells! Recent work by Cullen et al. (1992) shows that the motoneuron eventually receives at least two additional inputs, which either cancel or inhibit the PVP drive during VOR suppression depending on the behavior being generated. By Fetz's standards, the PVP discharge during suppression is "paradoxical," but it is easily interpretable when there is a more complete understanding of the system. We suggest that Fetz think of such "paradoxical" responses as enriching the repertoire of his cells' behaviors rather than as presenting irreconcilable problems.

Fetz is also concerned that "neural computation between connected cells involves some highly nonlinear relationships." Nonlinear input/output relations are characteristic of most neurons in most neural systems. In the vestibular nuclei, for example, many neurons have relatively low resting rates, so they are driven to cutoff during part of a sinusoidal cycle of head rotation. Despite this obvious nonlinearity, the resulting eye movements are complete sinusoids because the motoneurons are driven by "push-pull" signals. Therefore, even though a prominent input may have a nonlinear relation to some movement parameter, it may be linearized by some other input to produce a net linear response. The only disadvantage of nonlinear relations is that they tax the mathematical capabilities of the modelers; they are not difficult for the investigators to interpret.

Indeed, many neuron types in the oculomotor system do have firing rates that are linear functions of some movement parameter. This is obviously true for most vestibular nerve afferents and for oculomotor motoneurons operating above their thresholds for steady firing. For most brainstem neurons that discharge a burst of spikes with saccades, the number of spikes increases linearly with saccade size, as does burst duration. Many of these neurons drive motoneurons directly. Another example is the floccular Purkinje cell, which exhibits a monotonic increase of firing rate with eye velocity. Because the discharge characteristics of all of these neuronal populations are relatively homogeneous, one gets an accurate impression of the salient discharge features of the entire population by evaluating the discharge of a single cell. For these examples, it has been possible to use the behavior of archetypical cells in black-box models that produce reasonable replicas of eye movement. As one progresses inward to the dark regions of the brain where the sensorimotor interface and other exotic transformations occur, the relations between firing rate and sensory or motor events may become more obscure. But at least in the oculomotor system, a robust relation seems to exist several synapses from the motoneuron, even as distant as the superior colliculus.

In conclusion, perhaps the complexities resulting from the many muscles and feedback loops controlling the limbs tend to dissociate the relations of "descending" neuronal signals from specific motor parameters. The oculomotor plant, with its constant load and its apparent immunity to signals from muscle receptors, presents a simpler control problem. The eye movement system is therefore more manageable and the signals carried by its individual neurons at all levels are easier to recognize. We find it just as likely, however, that when the somatic motor system is as well understood as several of the oculomotor subsystems, the paradoxes will disappear and the nonlinearities will become transparent.

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How complex is a simple arm movement?

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[EEF] Fetz has pointed out neatly some conceptual limitations to recordings from cells in the motor cortex and other putative motor areas of the brain. In particular, there is difficulty in interpreting the discharge of cells that appear unmodulated by the task and the discharge of cells that show a complex and “counterintuitive” relationship to the task in their timing or pattern of discharge. Hence, a model neural network that produces an array of discharge profiles similar to those observed in vivo is obviously attractive.

The complexity of the motor tasks must be considered before one reconsiders one’s credence in the messages contained in actually observed neural discharges. Although a number of studies have required subhuman primates to produce torque around a particular joint, commonly the wrist (e.g., Fetz & Cheney 1980; Thach 1978), the total “movement” may require much more than simply generating say, flexor torque by the two prime wrist flexor muscles (flexor carpi ulnaris and flexor carpi radialis). In some studies, the hand is also required to grip a manipulandum so that contraction must occur in finger flexor and thenar muscles (for example, see Fig. 2 in Fetz’s target article). Should one regard as “rather astonishing” the observation that motor cortical cells correlated for force, position, and next movement direction occurred in equal proportions (Thach 1978)? This would require one to accept either that gripping the manipulandum had no effect on the motor cortical cells or that its effect was constant under the different experimental conditions. Given that corticospinal axons diverge to several muscles and that cutaneous and muscle afferent inputs from the hand can rapidly influence the discharge of motor cortical cells (e.g., Lemon 1981; Lemon et al. 1976; Wannier et al. 1991), the observation may not be so surprising. Small changes in contact between the digits, and between them and the handle, could change the afferent input so much that finding altered correlations between one parameter of the wrist movement and the cell’s discharge may be expected rather than “remarkable.” Similarly, in studies requiring a precise grip by the digits (e.g., Buys et al. 1986; Muir & Lemon 1983), activity in many intrinsic and extrinsic muscles of the hand must occur. Given the number of intrinsic and extrinsic muscles acting on a digit, the torque generated by its tip is not specified uniquely by only one pattern of muscle activities. This provides an additional source of variation between the discharge of central cells and mechanical movement. Furthermore, when studies require movements of more proximal parts of the limb, contraction of shoulder and trunk muscles occurs, perhaps with “stabilizing” contractions in eg muscles.

Thus, in what seems to the animal (and possibly the experimenters) to be a simple mechanical task, there is potential activation of a multiplicity of muscles. The variable spatial and temporal activations of many muscles represent suboptimal conditions for examining causal relationships between a single neuron’s discharge and force production. The size of this problem can of course be controlled by appropriate electromyographic recordings of seemingly remote and uninvolved muscles (e.g., Tanji et al. 1988), but it may increase when, as is the current trend, the experimental animals make movements of increasing biomechanical complexity, including multijoint movements with the upper limb to a range of positions in threedimensional space (e.g., Schwartz et al. 1988). One possible experimental strategy would be to examine smaller, more discrete movements such as isolated recruitment of only a few motor units in an intrinsic hand muscle as the initial task. This task could then be drafted onto tasks needing active movement (or just postural stabilization) at the wrist and elbow, while the properties of neuronal discharge were re-examined. Such a strategy may also reveal the importance of cells whose discharge is unmodulated in the initial task, but which are recruited as the “spatial” requirements of the task increase.

Observations reported very briefly for dorsal root ganglion cells are difficult to fit into Fetz’s scheme without much more information. Since the cells have an excitatory projection to motoneurons, they are most likely to come from muscle spindle endings, but their parent muscle is not indicated. The discharge of spindle afferents is a complex function of changes in muscle length, location of the spindle within the muscle, fusimotor drives, and intrinsic spindle properties (see Gandevia & Burke, this issue). Although it should be easier to understand the role of proprioceptive afferents than that of cells in the motor cortex and other “motor” areas, it remains necessary to know which muscles are contracting and how their lengths are changing.

Finally, it will ultimately be necessary to overlay the knowledge about the discharge of “upper” motoneurons with the properties not just of motoneurons but also of spinal interneurons. For example, some propriospinal neurons activated by descending motor “commands” play a crucial role in forelimb grasping in the cat (Alstermark et al. 1981). Of course, simple linear correlations between cellular discharge and movement parameters may not be sufficiently sensitive for judging how such interneuronal circuits are turned on, switched, and modulated by descending and afferent activity.

NOTE

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Information processing styles and strategies: Directed movement, neural networks, space and individuality

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[GEA, EEF, DAR, JFS] 1. Neural networks, brain function and what's in between: Let's indeed have a new baby... and not throw out the old ones. Having myself dared to say in print that the neuron is no longer the centerpiece of neuroscience (Grobstein 1987; see also Grobstein 1986; 1988a; 1988b), I can't argue with Robinson (or Alexander et al., Fetz, or Stein) on that score. "Discomfort, if not always openly acknowledged, has been increasingly expressed by neurobiologists of almost every sort... While diagnoses of the problem vary in detail, a common theme is that characterization of functional populations is not only "difficult to construct from individual elements' but frequently impossible" (Grobstein 1990). It's been a bit lonely out here, and so I welcome with open arms Robinson's decision (and anyone else's) to come out of the closet and join the community of skeptics.

Mild irony aside, there are real issues to be addressed by those who understand the limitations of not only "bottom-up" approaches to the brain, but "top-down" approaches as well. "Beginning with the computational task is fine if one is dealing with an engineering problem; it can be highly misleading if one is concerned with a preexisting complex information-processing device whose computational tasks, styles, and constraints are in fact part of what needs to be discovered" (Grobstein 1990). Robinson's thoughts are particularly welcome, given his leadership with top-down approaches. I gladly accept his correction to my remark: Not even all engineering problems are necessarily best solved with top-down approaches. Robinson's target article, and those of Alexander et al., Fetz, and Stein, are important contributions to the requisite discussion of the obvious question: Beyond bottom-up and top-down, what approaches to the analysis of complex information-processing devices are available? I have written elsewhere, in the context of sensorimotor integration (Grobstein 1988c), neuroscience as a whole (Grobstein 1990), and biological systems more broadly (Grobstein 1988b), about an "intermediate level approach" that proceeds from the middle outward. Here I want to test some of those ideas against the insights of my colleagues (and theirs, in turn, against my own) in the specific arena they have defined: Sensorimotor processing and the new insights into it that have been, and will be, gained from the use of artificial neural networks.

My first point is one of whole-hearted agreement with Robinson and the others: artificial neural networks have much to offer. Among the things they have to teach is that solutions to information processing problems may have a highly distributed character, which in turn could account both for difficulties in making
sense of neuronal behavior that has troubled those using a bottom-up approach and the failure to find particular algorithms in particular neurons or brain regions that has frustrated those using a top-down approach. My second point, however, is that none of this necessarily follows; artificial networks have much more to teach us, including this caveat itself. My third point is that, as always, the brain is cleverer than the clever ways we think up to try and understand it. If we forget that again, we’ll be galloping off in the wrong direction. Again.

Many investigators, ourselves included (Carr et al. 1991), have been impressed by the finding that artificial neural networks tend to come up with distributed solutions to input/output problems. This has helped to alter expectations of what one should be looking for in the brain, in both new ways and old (Grobstein 1988a; 1990). What has not been generally appreciated, however, is the reality that artificial neural networks do not always come up with distributed solutions (Carr et al. 1991). Even for simple sensorimotor tasks, artificial networks come up with more or less distributed solutions depending on exactly how the task is defined (what investigators think is the important part of the task the brain is doing, and hence how the task is translated into network terms). And even for exactly the same task description, more or less distributed solutions are found depending on details of network structure (the number of hidden units, mentioned by Robinson, is one, but only one, example). And even for exactly the same task description and network structure, more or less distributed solutions are found depending on exactly where one starts on the solution landscape (the initial random synaptic weight distribution) and how one searches the landscape from that location (Fetz calls attention to solution variability in relation to a different but also important point; see my discussion of Stein, below).

Clearly, investigators using artificial neural networks need to be as skeptical about the feeling that everything fits, as do other investigators, and some indication of the ways in which solutions were sought, as well as the frequency with which different kinds of solutions were observed, should become a standard part of any report of artificial network findings. That artificial networks are capable of generating a variety of different kinds of solutions, however, has a more exciting implication (and an aspect of unpredictability and playfulness that needs wider recognition as fundamental both to the nervous system [Grobstein 1992] and to scientific inquiry [Grobstein 1988c]; see Alexander et al., Fetz, and discussion of Stein, below). The issue of why artificial neural networks come up with particular kinds of solutions raises questions that are both intriguing and experimentally approachable in their own right, precisely by exploration of the variations in solution character with deliberate modifications of the variables mentioned above. We have begun such a research program, aimed at providing new insights into general information-processing rules (Grobstein 1988c) and at testing hypotheses about why the nervous system uses particular forms of organization in particular cases (do artificial networks indeed come up with similar solutions under the hypothetically expected set of circumstances and not under others?). If this is the sense of Robinson’s cryptic concluding remark that future work on artificial networks may yield “a bridge between system function and hidden-unit behavior,” I couldn’t agree more.

An equally important implication of the reality that artificial networks may generate different kinds of solutions (in particular, more distributed and less so) is that available information does not at the moment provide any basis to believe that all of the difficulties in understanding neuronal behavior can be comfortably swept under the blanket of distributed processing (see Grobstein 1988a; 1988c; 1990 for additional reasons for the difficulties). Nor does it give a solid foundation for expectations “as we move centrally,” as Robinson puts it (and others imply). It’s a good thing it doesn’t, because whatever the single unit data in particular cases, it is abundantly clear from other methods of investigation, methods more appropriate to the detection of order at levels of organization above that of the neuron (Grobstein 1990), that one is not in general dealing with a fully distributed system but rather with one possessing discrete “information processing blocks.” Lesions in appropriate locations in the frog brain do not yield “graceful degradation” of directed movement; they instead reveal distinct information-processing steps, including an abstract central representation of space itself composed of dissociable, discrete elements (Grobstein 1988b; 1989; 1991; and see below). The same is true of many aspects of brain organization, including neocortical function. There is no argument whatsoever that different neocortical regions do different things. The only question is how to characterize what the distinctive things are that each cortical region does.

In short, let’s not, in the enthusiasm over the appearance of distributed solutions in artificial neural networks, give up the idea of “boxes” in the nervous system. Particular boxes, presumed to exist from particular top-down perspectives, may or may not exist, but boxes there certainly are. No, let’s not throw out the baby with the bath water. Robinson’s integrator is real, rigorously demonstrable, and localizable with appropriate techniques. So too are maps, and central pattern generating circuitry, and corollary discharge signals (these two constituting at least part of Alexander et al.’s “motor programs”), and an abstract central representation of spatial location. It is the blocks, and not distributed circuits, that are the real intermediaries between neurons and global behavior. If artificial neural networks come to be equated with distributed processing, they will hinder rather than help in the primary task for better understanding the brain: the rigorous identification and characterization of information processing blocks. On the other hand, given identification and characterization of such blocks by more “classical” methods (Grobstein 1990), an exploration of the circumstances under which artificial networks do and do not develop solutions that display similar “blockiness” should indeed provide both new insights into how and why the brain does what it does (see below) and new broader principles for complex information processing in general.

2. Egocentric, corticocentric and noncorticocentric views of spatial representation: Respect for diversity, or learning about space and individuality from differences. Stein dismisses the notion of a master topographic representation for a variety of reasons, including the fact that there are reports of “space seotomata” following small brain lesions. He also cogently argues that saccadic eye movements do not require any explicit representation of egocentric space: Retinal and oculomotor vectors would suffice, with no intermediate coding in egocentric coordinates. However, Stein’s general hypothesis—that signals in different sensorimotor reference frames need never be converted into a common coordinate system, and that the basic representation of space is instead a distributed lookup table in the parietal cortex which directly transforms signals between particular sensory and motor coordinate frames—seems to me off the mark. Stein may be right in his analysis of what the parietal cortex is doing and how, but I think he is wrong in his suggestion that the most fundamental form of spatial representation is a highly distributed, task-oriented one in the parietal cortex. What is at issue is not only how space is represented in the brain and why it is represented that way, but also what the parietal cortex (and neocortex in general) does and why it does that way. Some points made by Fetz, by Alexander et al., and by Robinson are relevant.

I work with an animal that precludes getting distracted by the admittedly elegant but clearly overgrown and unnecessary neocortex. The frog simply doesn’t have one, and, like many other vertebrates, it performs admirably on a wide variety of behavioral tasks despite its absence. Included are directed movements, which vary with object location in all three spatial dimensions. Subcortical circuitry is clearly adequate for such behavior. The frog might seem a prime candidate for accom-
lishing directed movements "reflexively," by a direct coupling of sensory and motor cortex (as Stein has in mind) rather than via an intervening abstract spatial representation (Grobstein et al. 1983). [See also Berkowitz et al. "Adaptability of Innate Motor Patterns and Motor Control Mechanisms" BBS 9(4) 1986.] This has proven wrong, however (Grobstein 1988a; 1989; 1991; 1992). Multidimensional input signals representing at least two different sensory modalities converge in the frog's midbrain tegmentum to yield a three-dimensional signal that represents object location in a head- or body-centered coordinate frame experimentally distinguishable from both sensory and motor coordinate frames. It is, for at least some behaviors, a true bottleneck (Grobstein 1991; 1992) of precisely the kind that Stein suggested probably did not exist ("Having laboriously translated all coordinate systems into a common reference frame . . . the common coordinate system would then have to be transformed into that of the recipient system all over again" Introduction, para. 5). This bottleneck also corresponds to what Alexander et al. (and others) have characterized as an "ill posed" problem, since it means that a number of different movements can be associated with a given location signal. What appears a problem to particular sorts of top-down theorists seems to me an advantage to organisms, endowing them with the basis for "choice" (Grobstein 1992).

As Stein expects, the abstract spatial representation in the frog tegmentum is not topographically organized (Grobstein 1991). There are certainly two, and probably three, physically distinct structures on each side of the brain that code independently for stimulus location relative to each of three perpendicular axes (Alexander et al.'s and Fetz's distributed processing). Within each structure, the value of the relevant variable is represented not by the location of neural activity but rather by something like the total amount of neural activity. The upshot of this arrangement, and one of the initial and still strongest lines of evidence for its existence, is that appropriately located brain lesions in the frog do not produce "space scotoma," but do produce hemifield disturbances, with at least some similarities to those following unilateral parietal cortex lesions. Unilateral destruction of one component of the representation, coding horizontal eccentricity of stimuli to one side of the midsagittal plane, abolishes a sense of horizontal location on one side of the body, causing stimuli (either visual or tactile) throughout one hemifield to be referred to the midsagittal plane.

Several points follow from this. The first is that if there is a primordial and basic abstract spatial representation it is more likely to be in the midbrain tegmentum than in the parietal cortex. Neocortex is elegant and attractive, so much so that it must be doing something very special for organisms that have it. In efforts to understand this, it seems to me useful to know what subcortical circuitry is capable of, and hence to avoid becoming distracted by things that are not sufficiently special to warrant adding a neocortex. "Seeing" is not adequately special, whereas knowing that one has seen may be (Weiskrantz 1980). [See also Campion et al.: "Is Blindsight an Effect of Scattered Light, Spared Cortex, and Near-Threshold Vision?" BBS 6(3) 1983.]

Knowing where things are relative to oneself is not sufficiently special, whereas feeling that one knows where they are relative to oneself may be (see Grobstein, 1992, for a likely comparable distinction between choosing and feeling one is making a choice).

My second point is that Stein's arguments for the advantages of a highly distributed processing system to deal with problems of space are apparently wrong. Frogs succeed with a more organized system of identifiable "information processing blocks," and there is increasing evidence that most other vertebrates, including humans (and perhaps even invertebrates) do it that way too (Grobstein 1989; 1991; Flanders et al. 1992, and my accompanying commentary on that article). This raises the obvious question of why space is not in general represented in a highly distributed fashion. Although studies of artificial neural networks have generally impressed people with the capabilities of distributed networks, they can also be used to explore the question of why under particular circumstances less distributed processing is more common (see above). Such explorations are underway (Carr et al. 1991).

These points notwithstanding, it is still possible that Stein is right in his interpretation of parietal cortex as a distributed processing system concerned specifically with egocentric spatial location, that is, the ability to feel oneself where other things are. If so, then there may be something about this particular kind of information processing that favors distributed networks, and perhaps their creation by something akin to what sometimes goes on in artificial learning networks. Such networks are capable of exploring for solutions to a given problem and of creating a number of different solutions to the same problem (see earlier discussion on Robinson, and also the target article by Fetz; see also Grobstein, 1988c, on "bounded variance" of which the possible outputs of artificial neural nets are an example). Alexander et al.'s distinction between supervised and "unsupervised" learning, with the suggestion that the latter provides even greater exploratory ability, is relevant in this context. True self-organization, however, is independent of any external information. "Unsupervised" seems to me a misleading term for an important intermediate case in which circuits get information about whether they are or are not achieving the task, but none about what direction to go in if they are not. Regardless, if subcortical circuitry is already built to deal adequately with most immediate challenges of life, neocortex may provide the luxury of additional parallel circuitry that can be used to play, to generate and explore alternate solutions to the same problems (see Grobstein, 1988c, for a discussion in a broader biological context). A sense of onself feeling or acting, together with a sense of one's own individuality, may emerge from the interplay of such a parallel cortical system interacting with subcortical circuitry (Grobstein 1992).

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Converging approaches to the problem of single-cell recording

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[EEF] Fetz is to be congratulated for a very informative and critical appraisal of single-cell recording techniques. Any experimenter who has been involved in single-cell recording will understand the dilemmas and methodological problems outlined in this target article. It is a timely criticism of this method, which makes one stop and think about the meaning and interpretation of information obtained from single-cell recording.

A major problem with single-cell recording is that it does not take into account population effects on behaviour. How do we assess the output of a population of cells that differ in discharge patterns yet are directed towards a similar goal or connection? In Fetz's target article the possible role of neural network modelling is detailed in a clear and informative manner. Numerous examples are given of the power of this technique to explain neuronal population function in regulating specific parameters of movement. However, despite all the deficiencies of the single-cell recording technique it is suggested that future research should use neural network modelling, though based on the results of single-cell recorded information. It is hard to reconcile this conclusion given the detailed deficiencies of the single-cell recording technique outlined in the target article. After all is not the quality of the information provided by the neural network dependent on the quality of information put into it? If that information is wanting, then surely we should question the result.

We welcome new ideas as to how the brain might control movement as long as they can assist in the clarification of the problem at hand. We find that a combination of single-cell recording and clinical observations is beneficial (Brothie et al. 1991a; 1991b). The concept of the motor plan as suggested by Marsden (1987) has provided our best explanation of the possible interaction between the supplemental motor area (SMA) and the basal ganglia to date. The concept of a motor plan was based on astute clinical observations. It is the clinical data that have provided us with the best clue as to the role of structures such as the basal ganglia in movement control, and this should not be overlooked.

We have interpreted our findings from single-cell recordings (Brothie et al. 1991a; 1991b) in the context of such algorithmic control mechanisms as the motor plan. We have suggested, with experimental evidence, that pallidal phasic activity may signal the end of a movement in a movement sequence. This internal cue might be used by cortical structures such as the SMA to terminate set-related activity and to trigger the execution of previously prepared movements. One can further hypothesise a sequential domino effect that would allow a movement sequence to run once initiated by the SMA.

In addition we have used neural networks to generate possible neural discharge patterns in the basal ganglia and test whether this was indeed its role (Brothie et al. 1991c). Results suggest that there should be both set sustained premovement-related activity and phasic movement-related activity in the basal ganglia. The patterns predicted by this model fit our findings of neural discharge patterns in the globus pallidus. Our concept of the interaction between the basal ganglia and SMA suggests that a movement sequence is initiated in the cortex. As the first movement in the sequence is executed, a phasic burst is generated in the basal ganglia. This burst is appropriately timed to turn off the set-related activity in the cortex concerning the next movement in the sequence. The next movement then executes, during which time a phasic burst is generated in the basal ganglia and this turns off set-related cortical activity for the third movement. Again, as the third movement is executed, a phasic burst is generated in the basal ganglia to turn off set-related activity for the fourth movement. This hypothesis would allow the sequence to run until it terminated.

Our point here is that a number of converging approaches are useful in elucidating the underlying neuronal mechanisms. Researchers do not yet understand how the brain controls movement. In that context, any models and paradigms that help explain the evidence we have so far should be fostered.
The necessity of a complex approach in studying brain mechanisms of movement

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[EEF] The question posed in Fetz's target article title is very timely. The relativity of movement parameters "coding" in single-neuron activity is very well demonstrated. The question seems to be a much broader one, however. Any attempt to correlate neuronal activity recorded in different brain structures with parameters of movement is a way to analyse the functions of these structures in the organization and performance of movement. In analysing neuronal activity related to movement one can draw conclusions mainly on the level of structures or large populations of neurons. This is also true of Fetz's approach: Three points are discussed in each section, namely, timing, population coding, and localization of function. The general problem can be formulated at a macrostructural level: That is, what brain structures are involved in performance of different kinds of movements and what is the sequence of their activation?

Two main features seem to be important in studying localization of function. First, the specificity of some structures in the control of different kinds of movement, and second, the plasticity of functions that can be changed by learning. These two features appear controversial; however, they are both essential in motor control. Specificity of function can be seen, for example, in lateral and ventromedial descending systems (Lawrence & Kuypers 1968). The lateral system, including the corticospinal and rubrospinal pathways, controls mainly distal muscles, whereas the ventromedial system, including the reticulospinal and vestibulospinal pathways, is responsible for the control of axial and proximal musculature.

The other example of functional specificity concerns the motor cortex. This structure is well known to control fine discrete movements (see Phillips & Porter 1977). In addition, during the elaboration of new movements through learning, some innate synergies interfering with the new movement have to be suppressed. It has been shown (Ioffe 1973; 1991) that the motor cortex is responsible for generating a command that descends via the pyramidal pathway and inhibits coordinations that interfere with a learned movement. After motor cortical ablation the interfering innate motor patterns become disinhibited and the performance of the learned movement is disturbed. So the inhibition of interfering patterns in motor learning is one of the specific functions of motor cortex.

On the other hand, functional plasticity is also a feature of different structures. It can be seen in the modification of behavioral patterns by learning. For example, it is possible to obtain eating behavior in response to stimulating the ventromedial hypothalamus, which usually produces aversive behavior (Pavlova 1970). It is also possible to rearrange some innate motor patterns by learning. For example, in a dog the flexor reflex to nociceptive stimulation can be suppressed by learning and once conditioned the dog can perform extension to escape stimulation of a limb (Frolov 1983). To take another example, the "diagonal" pattern of postural displacement usually accompanying limb lifting in quadrupeds can be rearranged by learning into an "ipsilateral" one (Ioffe et al. 1988). [See also Golani: "What are the Building Blocks of the Frog's Wiping Reflex?" BBS9(4):1986.]

As mentioned above, the motor cortex is the structure providing such a rearrangement of motor patterns by suppressing interfering innate reflexes or coordinations. These data come mainly from lesioning the motor cortex and other structures. The role of the motor cortex in motor learning and, in particular, the role of different inputs to the motor cortex has also been closely examined using a combination of lesions and microstimulation (Asanuma 1989). Though neuronal plasticity in learning and, in particular, the instrumentalization of neuronal responses were shown in Fetz's classical works (Fetz & Finocchio 1972; 1975), changes in neuronal activity and interneuronal relation during motor learning and rearrangement of the coordinations have unfortunately not been well enough studied. Only a few works on this point are available (Bures et al. 1988; Kotlyar et al. 1983; Mayorov et al. 1977).

The above data were briefly cited to show that the old methods for functionally investigating the brain, namely, stimulation and lesioning, are still available to study the role of different structures in motor control. Methods like lesioning are not without complications. Nevertheless, they have been successfully used by such neuroscientists as Sherrington, Lashley, Sperry, and many others and have allowed us to obtain basic data concerning brain mechanisms of motor behavior.

The new epoch began when Evarts (1981) popularized the method of recording activity of the identified neurons in behaving animals. Much data obtained by many authors allowed us to analyse the timing of different structures in the control of movement, the coding of different movement parameters in neuronal activity, and so on. This was in fact a real breakthrough in neurophysiology. Together with the recording of slow potentials preceding and accompanying movement (Kornhuber & Deecke 1965), this method promoted the appearance of modern ideas concerning organization of movement.

Now, however, the analysis of single-neuron activity yields less and less new basic data. This has stimulated researchers to develop new methods that are more global and effective for explaining the organization of movement. Pribram (1973), for example, has proposed a holographic theory of memory storage which is again cited in the target article. Another modern and promising approach to analysing the organization of movement is neural network modeling. Such models could explain the interrelations among different units in the control of movement as described in the target article.

Other methods are also becoming more popular now, for example, brain imaging, which allows us to represent the general picture of different structures, their timing and interrelations in the preparation, initiation, and performance of movement. The analysis of chemical mechanisms of motor control is also very interesting. For example, the chemical nature of postural asymmetry produced by unilateral lesions of cerebellum, motor cortex and so on is being studied. It has been shown, in particular, that vasopressin is one of the substances responsible for such postural asymmetry (Vartanyan & Klemen'ev 1991).

In general, one can say that a synthetic approach - including the methods of stimulation and lesioning, the recording of single-neuron and multineuronal activity, neural network modeling, brain imaging, the analysis of chemical mechanisms of motor control as well as other methods - is probably the appropriate way to study brain mechanisms of movement organization.
Second, cells representing movement at different hypothetical hierarchical levels could still all show a correlation to a particular task variable. For example, many possible control parameters, such as output forces at the hand or handspace "virtual positions," joint torques, and multimuscle or single-muscle activation patterns will all covary with an external load (Kalaska et al. 1989). The tasks typically used cannot distinguish among these or other possible parameters, and so could mask a hierarchical sequence of transformations within a "channel."

Third, the correlation of neural activity with a given parameter may have quite different origins and functions in different areas. A muscle-like representation might be generated in one area, appear in a second area as a corollary discharge of the activity in the first, and be produced in a third region by reafferent peripheral input. One should be very cautious in linking these neurons together into a single distributed channel with one function. For example, many cells in both the premotor cortex and parietal cortex area 5 show directionally tuned activity changes during the instructed-delay period prior to reaching movements (Crammond & Kalaska 1989; Weinrich & Wise 1982). One could argue that these cells form part of a single functional "channel" for the preparation of movement. Alternatively, the parietal activity could be a corollary discharge about the intended movement that is required, according to several models of kinesthetic sensation, to interpret the complex reafferent input from proprioceptors (Kalaska 1991a). The parallel representations of motor intention in premotor and parietal cortex would thus have different roles.

Fourth, binary classification of cells (correlated vs. noncorrelated) ignores important quantitative differences in their responses. For instance, according to a rigorous analysis-of-variance (ANOVA) test, the activity of many cells in both the motor cortex and area 5 is significantly correlated with external loads (Kalaska et al. 1990). The load-dependent variation of activity in area 5 is several times smaller than that in the motor cortex, however, and its directional tuning bears no consistent relation to the motor task. As a result, single-cell variations cancel out at the population level in area 5 and cannot contribute a meaningful signal for the compensation of external loads, unlike the motor cortex. The ANOVA results on their own give the false impression of a similarity between motor and parietal cortex function.

Conversely, labeling cells according to their best statistical correlation could create a false impression of functional divisions, such as segmented planning "channels," by ignoring the true complexity of cell properties. In fact, most cortical cells show partial correlations with many different attributes of both movement preparation and execution (Hochner & Wise 1991; Kalaska et al. 1989; Thach 1978; Weinrich & Wise 1982). This is consistent with the complex combinations of response properties predicted by network models (see Fetz and Robinson, this issue) but it is not consistent with separate parallel "channels."

Traditional models assume that single cells perform a specific role and that a given function can therefore be attributed to an identifiable population, which could be either a discrete anatomical structure or a distributed but segregated "channel." For the sake of debate, we would like to suggest an alternative hypothesis for the nature of representations within the motor system that is also inspired by network models. The partial correlations of cellular activity with several movement parameters indicate that the activity of each neuron is determined by many different convergent inputs reflecting different aspects of motor planning and execution. Each cell can thus be viewed as a multichannel processor that transmits complex combinations of signals and contributes simultaneously to the representation of several different analytical levels of motor planning (Kalaska 1991b; Kalaska & Crammond 1992). The relative importance or weighting of the contribution to each representation varies from cell to cell. The representation of a particular analytical level of
movement planning or of a particular movement attribute is therefore the sum of the corresponding single-cell response components distributed across a population of cells. Furthermore, different representations are distributed across overlapping populations of neurons and do not correspond to separate cell populations. In this model, sequential sensorimotor transformations are produced by the patterns of convergence and divergence of connectivity within the motor system, which result in a gradual change in the relative weighting of different levels of movement representation by single cells across the distributed network. There is no absolute localization of function in the traditional sense, but the representation of different analytical levels of motor planning may still be preferentially concentrated in different cell populations or structures.

**On networks and neurophysiology.** A superb discussion is provided by Fetz of some fundamental problems in interpreting the results of single-unit neurophysiological studies of the cerebral cortical mechanisms of motor control. He argues that they usually do not provide adequate information to demonstrate causality and that attempts to interpret neural activity in terms of arbitrary engineering parameters such as force, torque, or velocity are the naive equivalent of pounding square pegs into round holes (see also Robinson and Alexander et al.). Fetz intended his target article to be provocative. He has succeeded. Although we agree with much of what he says (Kalaska & Crandall 1992), we have been provoked to defend chronic single-unit studies to counterbalance what seems to be an unjustly pessimistic evaluation of their utility.

First, Fetz criticizes attempts to identify sequential activation of different neural populations because the latency distributions in different structures show extensive overlap, so that most cells are coactive at any given instant during a movement. Saying that they are active “more or less in parallel” (sect. 2.1, para. 3) does not necessarily mean simultaneous activation, however, and it does not preclude a moment-to-moment serial flow of information among components of the network. Overlapping but sequential recruitment of different neuronal populations within and across neuronal structures is seen repeatedly (Kalaska & Crandall 1992). Because the motor command evolves in real time prior to and during the movement, a sequence of planning transformations can still occur within a distributed network with small time delays between the representations of each planning level and so the neurons contributing to those different planning levels would be coactive during most of the movement.

Second, it is true that many cells show complex or paradoxical relations to movement parameters such as velocity, torque, or muscle motor-unit responses. The usefulness of this observation, however, is only as good as its implicit assumption that these are the actual parameters used by the central nervous system, which is questionable.

A major premise of Fetz’s target article is that the ultimate goal of neurophysiological motor-control studies is to have a complete description of the causal mechanisms for the planning and initiation of movement. To attain this “Holy Grail,” one must have a description of the activity of all the cells in the circuit, but also a complete description of all intercellular connectivity. One could take the even more radical position that we must have intracellular records of all subthreshold membrane events. Attempts at complete cell-by-cell causal understanding of the circuit, besides being technically impossible, may be a quixotic endeavor (see Robinson), however. Fetz himself notes that a broad (if not infinite) range of arbitrary network configurations can be taught to converge on the desired output and that each instantiation of each network configuration results in a unique causal solution. If each biological system likewise represents a unique solution, of what generalizable value is such a profound description? We would argue that this depth of description is unnecessary, and that network models suggest it is pointless. Moreover, this criterion renders futile all neurophysiological studies of sensory systems, because the final output is a sensation that is experienced introspectively and is not independently measurable, making causal inferences impossible.

Fetz suggests that his network model can provide useful insights into biological motor control and that it transforms a step change in target position into motor unit activity (sect. 4.2, para. 2). It must also be acknowledged, however, that the network is just a curve-fitting matrix that transforms arbitrary input waveforms into a variety of output waveforms that are merely low-pass-filtered and differently weighted combinations of the inputs. We see no evidence, for instance, that it solves any of the sensorimotor transformations required to convert target spatial location into a multidimensional intrinsic reference frame of muscular activity. Given that the hidden units show many different waveforms, some of them will resemble actual cellular response patterns by chance alone. Thus, indiscriminate comparison of the “responses” of elements in a network with the discharge patterns of single cells can be as seductively misleading as correlating that discharge to parameters of Newtonian mechanics. Moreover, the network is interpreted only in terms of the relatively small population of corticospinal and rubrospinal cells that synapse directly on spinal motoneurons. This ignores all the other cells, including the many corticospinal neurons that do not synapse on spinal motoneurons and influence movement indirectly through the intermediary of spinal interneuronal networks. Does Fetz mean to imply that those cells play no significant role in motor control? On the contrary, others have proposed that spinal networks are the critical system that determines muscle activity patterns (Georgopoulos & Grillner 1989).

It is disconcerting that both Fetz and Robinson, who have made such important contributions to this field, would now appear so critical of the utility of the single-unit method. It is interesting to reflect on the history that has led us to this situation. Traditional motor-control models simplistically predicted that single cells would unambiguously encode a discrete parameter of movement. This assumption justified the single-unit recording method. Paradoxically, the results of those studies did not fit readily into those schemes and so helped invalidate traditional serial models as biologically implausible. Network models have suggested other information-processing mechanisms, in which the resultant single-cell response patterns can be complex combinations of movement-related signals that do not fit readily into any formal physics or mathematics coordinate system. Despite the tone of Fetz’s target article, however, this does not invalidate the single-unit recording method. On the contrary, we would like to reemphasize the fact that it was single-unit recording studies that indicated that networks are potentially more valid models for brain processes. Properly designed single-unit recording studies have revealed, and will continue to reveal, important differences in the response properties of neurons in different structures under different task conditions from which one can infer, if not literally then at least symbolically, the nature of the information being processed by neurons in different areas. These data can also be used to develop better computational models. As we have stated elsewhere (Kalaska & Crandall 1992), one of the critical tests of any motor-control model that claims biological validity will be how well it can replicate the response properties of cells observed in single-unit recordings, not the other way around. We have no intention of hanging up our electrodes in the foreseeable future.

**The role of directed attention in egocentric spatial perception:** An artful dodge? The target article of Stein addresses the fascinating question of how the central nervous system combines inputs from different sensory systems to generate what we perceive introspectively as a unified supramodal Euclidean representation of our immediate surroundings. Evidence for an explicit map of "real" space is scanty and probably the straw man of this target article. The central issue is whether there is a
single supramodal coordinate system for spatial perception and motor control, but how information encoded in any coordinate system is made available to systems using a different reference frame, be it in perception (sensory - sensory) or action (sensory - motor) systems.

The evidence is indeed compelling that the posterior parietal cortex (PPC) is the site at which information from a sufficient number of sensory and cognitive systems converges in order to allow transformations between different reference frames. For example, some cells in PPC areas 5 and 7b with clearly defined somatic sensory receptive fields may also respond to visual stimuli in a volume of space immediately adjacent to the somatic field, possibly in expectation of stimulation from approaching objects (Duhamel et al. 1991; Leinonen et al. 1979; MacKay & Crammond 1987). The function of such neurons may be to map visual input about objects in peripersonal space onto a body map in personal space, leading to the creation of a multimodal representation of objects in egocentric space (Duhamel et al. 1991). A critical test of Stein's hypothesis is the degree to which directed attention is responsible for this alignment of somatic and visual reference frames. (For instance, repeated visual stimulus presentation can quickly lead to attenuated responses.)

This function may not be limited to PPC, because cells with similar properties have also been found in the postcentral premotor cortex (Gentilucci et al. 1988).

The hypothesis that the deliberate and conscious process of directed attention mediates the alignment of and transformation between different maps is more speculative in the domain of action systems. Moreover, it might be a virtually bullet-proof hypothesis, impossible to disprove. It is difficult to see, for example, how one could completely eliminate some degree of directed attention in a conditioned voluntary motor task or devise experiments to demonstrate the existence of accurate spatial perception in a situation in which we are confident that no attention is involved. For example, the influence of directed attention on parietal activity was demonstrated in a complex behavioral context in which a motivated monkey attended to loci in space at which it was conditioned to expect behaviorally relevant stimuli (Goldberg & Bruce 1985; Mountcastle et al. 1981). During the intertrial interval, when the monkey was idly scanning the task environment and not expecting any stimuli, those effects were absent. Yet it is difficult for us to believe that the animal's spatial perception was in any way degraded during that period. Does this mean that one must begin to invoke different degrees, shades, or flavors of directed attention to account for spatial perception and for sensorimotor transformations in different behavioral contexts? An alternative proposal, which is to some extent merely playing with semantics, is to suggest that the transformations result when signals describing the intention to move are relayed to the PPC, where the relevant information in different reference frames is then integrated. This is one possible explanation for the finding that neuronal activity recorded in the PPC during an instructed delay period prior to arm (Crammond & Kalaska 1989) and eye (Gnadt & Andersen 1988) movements encodes the direction of the intended movement. The problem posed by Stein's hypothesis, however, concerns how one can disprove the possibility that this delay-period activity arises because some form of attention is directed to the target location or even to the body part that will be moved. Furthermore, the direction of attention and of movement are not always colinear, and movement does not always require a high degree of directed attention. Finally, the mere act of directing attention to a locus in space to receive a pertinent instruction leaves open an infinite range of motor responses, each of which will require unique sensorimotor transformations. Hence, we do not see how implicating directed attention clarifies or resolves any of the problems of spatial representations and sensorimotor transformations.

In conclusion, Stein is probably right that a cartographic multimodal map of egocentric space does not exist. Neverthe-
The identification of corticomotoneuronal connections

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[EEP] Within the admirably well-balanced target article by Fetz, an old, unresolved issue is lurking: the definition of corticomotoneuronal (CM) cells. In the first paragraph of section 3 these cells are said to "directly affect motoneurons" and in section 3.2 they "can be said to causally affect force." However, as Fetz also states in the first sentence of section 3, these cells are defined by a "correlational linkage," that is, their firing is only statistically related to motoneuron firing. My criticism is that the causal link is not secure: When Fetz (and others) define CM cells, they mostly use postspike facilitations (PSFs), which do not allow an accurate identification of a direct link; hence CM cells may well be misidentified. The issue is important because if Fetz wishes to use connectivities as constraints on his neural models, the connectivities must be accurate.

The problem is that a peak in a correlogram or PSF may result from excitation of the motoneurons not by the cortical neuron recorded but by some other neuron(s) synchronized to it, such as other CM cells, that is, other neurons involved in the common task. To demonstrate this is not so for a correlogram, criteria for the durations or latencies of the peaks must be met, as described elsewhere (e.g., Davies et al. 1985; cf. Kirkwood & Sears 1991). Although these criteria are not absolute and must be separately argued for each situation, the durations must be short, in the msec or sub-msec range, and latencies are critical within a msec. However, the durations of the PSFs are usually 10 msec or more and the latencies are hard to define by virtue of rather slow initial rates of rise. These durations are inevitable because, in the transformation from somatic motoneuron discharges to the PSF, temporal dispersion occurs in the motoneuron axons and muscle fibres. Latency and duration information is lost and there are therefore no criteria which can reliably be used on the PSFs to distinguish a genuine direct connection from one due to synchronization in the cortex.

In his defence, Fetz might cite evidence from CM cells that were identified with a PSF and then shown to give a narrow cross-correlogram peak when their spikes were correlated with those of single motor units in the muscles giving the PSF. Such peaks can be good evidence for the existence of a direct connection, but it does not necessarily follow that the PSF represents the same connection. In particular, the narrow peaks seen in illustrated cross-correlograms often sit on top of lower-amplitude but broader peaks (e.g., Fig. 11F of Lemon & Mantel 1989; Fig. 1B of Mantel & Lemon 1987; or Fig. 2 of Smith & Fetz 1989). Because these other components are of lower amplitude and have a quite different time-course, the narrow peaks can be very clearly discriminated from them and the broader ones can be ignored. However, the area of the broad peak may well be as large as or larger than the area of the narrow one; so when either effect is measured via the filter represented by the peripheral temporal dispersion, either could give a peak with a time-course similar to that of the PSF, with similar peak amplitudes. Thus, even for those units giving good evidence of a direct connection, one would reasonably suspect that 50% of their PSFs originated in other mechanisms. The rather smaller (and often noisier) PSFs that form the subsidiary projections defining the motoneuronal "fields" of CM cells would seem to be even less secure. Nevertheless, these PSFs still tell us something: At the very least they indicate that the unit concerned and the "muscle field" are closely co-activated during a given movement. I believe, however, that what they have in common may not be a direct connection from the unit to the motoneurons of each muscle but a linkage one or more synapses further back in the network. The issue is equally important in studying changes in the PSF between different states or movements when, because cortical cells may be activated in different combinations, changes in their synchronization would be expected to occur.

Fetz and his colleagues have always been aware of the possibility of synchronization effects and, in an important paper, Smith and Fetz (1986) tried to assess them. The conclusion then was that the effects could be considerable. Each spike of a CM cell could be accompanied by, on average, one other spike from the colony of other CM cells converging on the motoneurons of a given muscle. This supports the view expressed above that typically 50% of the strongest PSFs could arise via cortical synchronization. The "sharply rising, later component of the PSF," write Smith and Fetz, "may still be interpreted as evidence for a direct connection." However, in published illustrations, many PSFs do not have such clear sharp components. Smith and Fetz demonstrated that a major problem exists, but Fetz appears to proceed as if it does not.

Could one do better in establishing the connectivities? The general use of single-unit cross-correlations would probably be too difficult. A possible alternative might be to look more assiduously for positive signs of synchronization, that is, for "common input" effects in the PSFs. At present assessments of periodic features in the PSFs (together with consideration of the unit autocorrelograms) are very undervalued. For these features, applying criteria set out more than 20 years ago (e.g., Moore et al. 1970) might at least allow the recordings most likely to be contaminated by cortical synchronization to be weeded out.

In conclusion, I would not at all wish to dissuade Fetz (and others using a similar technique) from pursuing their present course of combining connectivity studies with large-scale modelling. I would only put in a plea for a more critical approach when attempting to establish the connectivities.
To understand the output functions of the motor system Fetz quite rightly stresses the importance of studying identified output neurons, such as CM and RM cells, because of the causal influence the STA reveals them to have over their target muscles. Here it is very important to distinguish between the central "representation" of a movement and how the activity that is so represented actually controls and communicates with the interneurons and motoneurons involved in the execution of the movement. But in addressing the organisation of these outputs we must carry this point to its logical conclusion: What, if any, is the significance of the "muscle field" that is the signature of a given output neuron? In their original study Cheney and Fetz (1980) stated that they could not find any obvious relationship between the muscle fields of CM cells and their pattern of discharge during a ramp and hold wrist flexion/extension task. Many of the muscles active during these movements, however, are also active for extension or flexion of the digits, and the paradigm used in these studies cannot address the significance of the pre-motoneuronal unit in question for these other movements.

In a precision grip task, requiring independent control of thumb and index finger, and in which the same group of muscles studied by Fetz and his colleagues is active, we have found evidence that the muscle field may be a very good indicator of the way a particular CM unit is recruited (Bennett 1992; Bennett & Lemon 1991). These CM cells tend to be most active when the balance of activity in a number of synergist finger muscles is that corresponding to the relative "weighting" or strength of PSF produced in these same muscles by the CM cell, that is, there is a congruence in the pattern of synaptic connectivity and of recruitment during movement. This relationship, however, only became apparent through examination of the highly varied patterns of muscle activity used by the monkey to shape its hand prior to the onset of the precision grip task. The considerably stronger facilitation that CM cells exert on intrinsic hand muscles than on long forearm muscles (Lemon et al. 1991) also implies that even single cells can exert a significant influence over the level of activity in a given hand muscle.

A problem for many parametric studies is to decide precisely how a neuron might encode a given parameter of movement. In most studies the mean rate of a neuron's discharge has been taken to be a reliable indicator of its activity in relation to that parameter. Much less attention has been paid to the pattern, as opposed to the rate, of cellular discharge. In the case of monkey CM cells, where it is possible, using STA, to assess directly the action of the cell upon its target muscle, there is clear evidence that the pattern of discharge is important. As predicted by earlier work on temporal facilitation at the CM synapse (see Porter 1970), when CM cells fire with very short interspike intervals (<10 msec), these spikes produce strong postspike facilitation (PSF) of EMG activity in their target muscles. Paradoxically, spikes with long interspike intervals (>30 msec) can produce equally strong effects when these are measured as the size of the PSF relative to the ongoing, background EMG level. Cell discharge in midrange intervals (15–30 msec) produced weaker effects than either very short or long intervals (Lemon & Mantel 1989). This shows that both firing pattern and rate have important consequences for muscle activity: It is therefore misleading to equate the output of a given cell simply in terms of mean firing rate alone, yet this has been the approach adopted in most parametric studies.

The meaning for movement of activity in single cortical output neurons

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[EEF] Fetz has written a really useful and thought-provoking target article. In it he has highlighted a common scientific problem: To what extent are the results obtained simply a consequence of the experimental design? This error is all too easy to make in the field of motor control where the essential operation of the motor system remains a truly hidden unit!

The search for a representation of different movement parameters at the level of single-cell activity has not been as rewarding as some early studies indicated. We may have missed important clues that are present in the organisation of the motor output map, not only in the primary motor cortex but in other frontal motor areas. Hughlings-Jackson hypothesized that the hand muscles in particular would have a large cortical representation because "they serve in more numerous movements." The multiple representation of outputs to individual motoneurons and muscles and the extensive overlap in these representations must mean that the different output units be they single cells or cell clusters, are likely to make quite different contributions to the measured parameter (Humphrey 1986; Lemon 1990), and this is probably why it is possible to find task-related cells over wide areas of cortex and in different cortical regions (Lemon 1990). In many studies there has been an insistence on the monitoring and measurement of the "encoded" parameter, to the exclusion of more natural movements. The stereotyped nature of most tasks comes up against the versatility of the motor system in finding many different solutions for the same motor task.

The spike-triggered averaging (STA) technique, introduced by Fetz and Cheney for the identification of pre-motoneuronal cells has allowed us to determine the output targets of different units within the motor system. Since most cortico- and rubromotoneuronal (CM and RM) cells facilitate more than one muscle, it is clear that multiple muscle control is the key feature of output organisation for both the motor cortex and the red nucleus. Each cell facilitates a particular combination of muscles, the "muscle field" of Fetz and Cheney (1980).
To what extent are brain commands for movements mediated by spinal interneurones?

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[EEF] The initial studies of unit recording in behaving animals seemed to be based on the assumption that the motor cortex is interested solely in motoneurones even though it was known at that time that corticospinal volleys influence many spinal mechanisms, including interneurones of almost all spinal reflex pathways to motoneurones, to ascending pathways, and to many of the pathways producing presynaptic inhibition by their action of primary afferent terminals. It was an important advance in this field when Fetz and Cheney (1980) introduced the method of recording from cortico-motoneuronal (CM) cells identified by their EMG postspike facilitation. Even so, caution is required and I believe that some interpretations are based on doubtful assumptions. An inherent assumption seems to be that only the monosynaptic pathways from the motor cortex and the red nucleus matter. The cat does very well without these connections and I am convinced that the major command also in primates is via spinal interneurones, implying that the monosynaptic pathways, though important, contribute only a fraction of the command, perhaps producing some fractionation of muscle activation and final adjustment of the movement. If so, a causal relationship between cell and muscle activity would not always be expected.
Two examples of command mediating interneuronal systems in cats should be mentioned. The C3-C4 propriospinal system is particularly interesting because behavioural studies have shown that it can mediate the command for target-reaching (Alstermark et al. 1981b; Alstermark & Kümmel 1990). The C3-C4 PNs have powerful connections with forelimb motoneurones and receive monosynaptic convergence from all major descending pathways except the vestibulospinal tract; they are also influenced (mainly inhibitorily) from the forelimb which they govern (Alstermark et al. 1984; Illert et al. 1977; 1978). It is worth noting that the C3-C4 propriospinal system exists in humans (Malgren & Pierrot-Desilligny 1988a; 1988b) and that it is activated during movements (Baldissera & Pierrot-Desilligny 1989) resembling those used by Fetz as tests. It is therefore likely that the command for wrist movements is mediated in parallel by CM and RM cells and by the C3-C4 PNs, with the latter contributing the major part. Such parallel processing obviously makes it extremely difficult to determine the contribution of individual systems and a close resemblance of activity in a given premotoneuron and muscle activity may even be fortuitous; consider that the pattern of motoneuronal activation is also influenced by segmental reflexes from proprioceptors activated by the movement.

Another example of a spinal premotoneuronal system is provided by interneurones activated by group II secondary spindle afferents which may servoassist movements commanded from the brain. Some of these interneurones are excited by cortico- and/or rubrospinal volleys (Edgley et al. 1988; Lundberg & Voorhoeve 1961) and it has been suggested that the corticospinal command is mediated by this pathway initially is phasic, activating the interneurones and/or the motoneurones. Once the movement has started it might be governed from the brain partly or largely via secondary afferents driven by tonic activation of static γ-motoneurones (Lundberg et al. 1987b). The hypothesis is clearly of interest in relation to the finding that the rubro-motoneuronal (RM) cells are predominantly phasic. It is possible that some of the tonic rubrospinal neurones, which do not project to motoneurones, instead control static γ-motoneurones and exert tonic action on motoneurones via secondary afferents and group II excitatory interneurones. A sharp division between phasic and tonic neurones would not be expected since the proportion between direct descending α-activation and group II activation may differ; phasic-tonic cells clearly may be incorporated within the framework of the group II hypothesis.

The subdivision by Lawrence and Kuypers (1980) into lateral and medial descending systems may prove fallacious. Cheney et al. (1988) accept this division and assume that the commands for wrist movements are mediated entirely by the lateral system, that is, the cortico- and rubrospinal tracts (CST and BST). It is noteworthy that after complete transection of the CST and BST in cats, reticulospinal pathways can under some conditions mediate the entire command not only for target-reaching (which includes activation of proximal and distal muscles) but also for food-taking, which requires manipulatory toe movements (Alstermark et al. 1987). It can by no means be excluded that reticulospinal pathways contribute to the command even when the CST and BST are available; note that a very large part of the corticofugal output ends in the brain stem.

Playing the role of devil’s advocate, Fetz remarks about the finding by Muir and Lemon (1983) that some CM neurones are preferentially active during a precision grip between thumb and forefinger but inactive during a power grip. This finding is unexpected only if you believe that each target muscle has its own exclusive cortical neurones through which the brain must operate whatever movement involving this muscle it wishes to command. If you accept that “The brain knows nothing of muscles, it only knows movements” (Hughlings Jackson 1932) then it is not surprising to find different CM cells active during different movement conditions. I also fail to be surprised by the above observation that CM cells strongly modulated in a finely

controlled ramp and hold tracking task were inactive during rapidly alternating ballistic movements that engaged the same target muscles. In cats there is a special pathway from the motor cortex exciting fast twitch but not slow motoneurones (Alstermark & Sasaki 1986; Alstermark et al. 1981a). It would be advantageous to activate fast motoneurones selectively during rapidly alternating movement because lingering tension in slow motor units of antagonists would then not prevent agonist shortening. A ramp and hold task, on the other hand, is better served by CM cells contributing to the usual recruitment order.

A recent study of fractionation in another premotoneuronal system — the C3-C4 PNs — has revealed that some PNs project only to motoneurones, others to both motoneurones and reciprocal la inhibitory neurones (Alstermark et al. 1990). The latter neurones may be used for commanding reciprocal movement and the former for other movements. It would not be surprising if the same subdivisions exist among CM neurones projecting to a given motor nucleus. Furthermore, a study of the termination of individual C3-C4 PNs has revealed branching to different motoneurones with multiple termination in different combinations; some PNs terminate on both motoneurones to proximal and distal muscles (Alstermark et al. 1990; Tsutsumi 1990). Such findings indicate that different muscle synergies are laid down in the divergent projection of the PNs. This principle has already been established in a study of CM cell activity related to wrist and finger movements in monkeys (Lemon, personalcommunication). Premotoneurones to a given motor nucleus may accordingly be differentially used depending on the motor synergy represented in their projection pattern.

I am impressed by Fetz’s thoughtful comments on population vectors.

To some extent I find the pessimism in the target article unjustified. The relationships between cell activity and the type of movement described as paradoxical are highly interesting as are the observations regarding convergent activity from different sources and the different response pattern in CM and RM cells. With the new method introduced by Fetz the whole field has been transformed and the investigation of unidentified cells now seems almost meaningless.

Fetz closes his essay expressing hope that the combination of two methods will resolve the issue of network mechanisms generating motor behaviour. I hope he is willing to admit that a thorough knowledge of spinal circuitry and its control from the brain, lesion experiments, and the new various activity-dependent histochemical techniques is also required.
Cortical area-specific activity not yet found?

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[EEF] Apart from the issue of neuronal coding of movement parameters, Fetz's target article presents a number of views on the organization of multiple motor areas. Although he does not deny the specialization of different areas, the author warns against a simplistic view that different areas subserve different functions. The following points of fundamental importance are clearly made: (1) Studying relative timing of cellular activity does not provide any basis for determining the causal hierarchy among different areas. (2) Neurons related to the activation of muscles as well as to motor set are widely distributed over many areas, suggesting broadly distributed representation of these motor processes. (3) No such thing as preferential coding of particular movement parameters has been found in a single motor area. I agree entirely that a given motor area would be involved in diverse functions, so that cell types of enormous diversity will be observed in each area. It is about time to abandon an excessively simplistic view that motor areas are patchworks of regions involved in totally different functions.

As much as I admire Fetz's article, I must challenge the inference that no area-specific differences in properties of neuronal activity have been reported. Reading this article, one would conclude that only neurons of the same type have been found everywhere in motor areas and in more or less the same quantity. This may be true in relation to muscle activation or "motor set" (for future movements in different directions), as described in detail in the text. One should not underestimate recent studies, however, which report area-specific preferential relations of neuronal activity to particular aspects of motor behavior (Humphrey & Freund 1991; Rizzolatti & Gentilucci 1988; Tanji & Kurata 1989).

Let us take an example of a recent report from our own laboratory (Mushiake et al. 1991). Neuronal activity was examined while monkeys were performing sequential movements either under visual guidance or on the basis of memorized information. Most neurons in the primary motor cortex were typically related to movements in a similar way, regardless of whether they were guided by visual signals or memory. Exceptions were extremely rare. On the other hand, a majority of neurons in secondary motor areas exhibited preferential relations to either visually guided or memorized movements. Premotor cortical neurons were more active when visually guided, whereas neurons in the supplementary motor area were more active with memorized sequential movements. These differences are not at all trivial and point to the presence of specialization in cortical areas.

There is also a report describing profound differences of neuronal activity in primary and secondary motor areas in relation to the use of one hand or both hands together (Tanji et al. 1988). [See also MacNeilage et al.: "Primate Handedness Reconsidered." BBS 10(2) 1987.] I do not believe that secondary motor areas are the only essential ones in these specialized aspects of motor behavior. In this sense, I agree with Fetz that "a region's specialized function need not be its only function, and certainly should not be the only standard for interpreting what each of the cells in this region is coding." On the other hand, just because one fails to find area-specific differences in neuronal activity in relation to relatively easy motor tasks, it does not follow that one cannot find aspects of regional specialization by observing cellular activity.

The statement in the target article: "Thus, the notion that cortical functions are segregated into different cortical areas can be preserved only by imposing different interpretations on similar experimental evidence" is accordingly not acceptable. I wish to point out the effectiveness of surveying neuronal activity in experimental conditions addressed to well-defined behavioral specificities. The question we pose is: "When the organism needs to perform a particular motor task in a particular behavioral condition, what type of neuronal activity in which area is used?" After such studies (as mentioned in relation to secondary motor areas) have been undertaken, we can proceed to the problem of how the variety of activity found in different areas can give rise to the requisite motor performance. As discussed extensively in Fetz's article, this will require computational modeling.
Saving the baby: Toward a meaningful reincarnation of single-unit data

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Several commentators (Alexander, Fuchs et al., Kalaska & Crammond, Lundberg, and Tanji) described my target article as unduly pessimistic about the utility of single-unit recording in behaving animals. Alexander suggests I have concluded that "the response properties of central neurons are meaningless or uninterpretable." Having performed many chronic recording experiments, and having every intention of continuing such studies, I should first clarify that I think chronic unit recording is not only useful but quite essential for understanding neural mechanisms controlling movement. Without these experiments we would not be in the present situation of having a wealth of information for evaluating their significance. My skepticism concerns more the utility of simplistic interpretations of neural response patterns in terms of correlated movement parameters and the assumption that neural networks operate through explicit coding of abstract conceptualized variables. In sensory systems the coding of stimulus features seems more secure, although Bridgeman raises corresponding con-
cerns even there; the idea that movement parameters are similarly coded in the motor areas is intuitively seductive but not convincingly supported by the accumulating experimental evidence. This does not mean, however, that chronic unit recording should be discarded along with the dubious interpretations. Although neural mechanisms controlling movement may not operate through explicit coding of movement parameters, the responses of neurons still offer crucial clues to neural computation.

The basic limitation of single-unit data is that they provide a very selective sample of a complex system, leaving a wide gap between highly restricted unit activity and overall system behavior. I would question the utility of bridging this gap by inference or leaps of faith. To better explain how neural networks control movement, we can fill this gap more effectively with neural network simulations. So, rather than being pessimistic about the utility of single-unit recording, I would be optimistic in hoping that single-unit data can finally be put into a causal framework: By incorporating the observed responses of units into neural network simulations we can generate more complete working models that can help explain the functional meaning of neural patterns.

The target article by Alexander et al. (this issue) seems to argue much the same point on the systems level that Robinson's target article (this issue) and mine have argued on the cellular level, namely, that the operations of biological neurons do not conform to popular conceptual schemes that are imposed upon the recorded data. In his commentary Alexander suggests I would argue that "neural correlates of movement parameters...are only meaningful if they covary with the activity of the muscles with which that neuron is ultimately connected." Although I chose premotoneuronal (PreM) cells and their target muscles as useful examples of elements in the motor system with a correlational linkage that can be proven independently of their firing patterns, I do not believe that the relation of central neurons to movement parameters must all be analyzed in terms of these elements. In principle, higher-order cells could code parameters very well, and the literature is full of suggestive evidence for such coding, including, ironically enough, my target article. The tonic firing rate of certain PreM cells codes static muscle force much better than the motor units that produce that force, as shown in Figure 3 of my target article. Whereas individual motor units have a highly nonlinear relation to net force because of their recruitment threshold and saturation, many rubromotoneuronal (RM) and corticomotoneuronal (CM) cells have a linear relation to static force over a considerably wider range.

Alexander's commentary raises the important point that the evidence for the coding of a movement parameter can be strengthened when the relation between unit activity and a candidate parameter is tested under "a variety of system level input/output conditions." This strategy is crucial for determining whether a particular behavioral variable is reliably correlated with the activity of a neuron. For example, the contention that a central neuron codes direction of limb movement is strengthened when it correlates best with that direction independently of the force required to make the movement, or the part of extrapersonal space in which the movement is made. Unfortunately, there do not appear to be many motor cortical cells that pass such a battery of tests. As more behavioral situations are used to confirm the coding of a particular parameter, fewer neurons appear to correlate consistently with that parameter.

The use of multiple behavioral tasks is related to another excellent point raised by several commentators, namely, that additional techniques are important for providing a full picture of the role of cells in controlling movement. Lundberg and Ioffe mention the classical strategies of stimulation and lesions, which can be performed both electrically and pharmacologically. Iansik points out that the converging approaches should also include evidence from clinical observations. I agree that converging evidence from different techniques strengthens the functional arguments (Fetz 1981), but in the role of devil's advocate I would have to point out the pitfalls involved for interpreting unit data: Stimulation and lesions at best reveal the net effects of the majority of the affected cells and cannot reflect the function of every neuron in the affected region. Relying on the consequences of lesions and stimulation for interpreting the meaning of unit data has led to systematically underestimating the diversity of neural types in a region and the multiplicity of possible functions in which a particular region can participate.

Additional evidence from a number of procedures, including lesions, stimulation, and a repertoire of behaviors, would also be helpful in constructing realistic neural networks that could replicate the range of observations. The inability of biological neurons to consistently code a specific parameter under variable circumstances is bad news for simplistic concepts of neural coding, but these additional behavioral conditions are grist for the neural network mill. Simulating a battery of behavioral situations and responses to lesion and stimulation provides important additional constraints for neural networks. A neural network model becomes more plausible to the degree that it can simulate a range of experimental conditions.

In light of their curious antipathy to neural network modeling Fuchs et al. are relatively generous regarding my model and instead take issue with my comments about coding. They state that my target article describes paradoxical unit responses as presenting some "irreconcilable problems" for single-unit recording. In fact, I welcome those paradoxical responses as significant clues that mechanisms other than explicit coding are operating, and I agree entirely that these responses are "easily interpretable when there is a more complete understanding of the system"; this was precisely my point in discussing the insights provided by neural network simulations. We have two ways to deal with such paradoxical units: Robinson's target article and the commentary of Fuchs et al. suggest that neural networks operate successfully despite the existence of so-called rogue cells because these cells are simply outnumbered by those with more appropriate activity. On the basis of simulations I would suggest the possibility that such rogue cells, which have counterintuitive properties individually, may have some rationale in the context of other such cells; that is, their inappropriate components may cancel, resulting in an appropriate contribution.

I would also take issue with the implication of Fuchs et al. that I consider nonlinear relations to be a problem.
Their statement that "the only disadvantage of nonlinear relations is that they tax the mathematical capabilities of the modelers" might apply to those theoreticians who try to capture the behavior of the networks in analytical form. In fact, most modelers are simulating networks with nonlinear units and have no problem with nonlinear behavior.

In comparing the oculomotor and somatomotor systems, this commentary indulges in the common conceit of some oculomotor physiologists that their system is somehow superior for being simpler. Thus it is claimed that "at least in the oculomotor system, a robust relation seems to exist between synapses from the motoneuron." Of course, one can find examples of such relations, if one is looking for them and is willing to ignore cells with more complex combinations of signals. However, not all oculomotor physiologists (e.g., Robinson) are convinced that the coding is as simple and clean and unequivocal as Fuchs et al. like to argue.

Gandevia points out that much of the complexity of neural activity in relation to movement may arise from the complexity of muscle activities involved in performing a motor task. This point is well taken and underlies the rationale for dealing first with much simpler alternating flexion/extension movements. As Gandevia further notes, even such simple movements may involve complicated coactivation patterns in proximal stabilizing muscles and distal finger muscles that can differ from reciprocal agonist/antagonist activity. This again is the rationale for focusing on those PreM cells that have a demonstrable correlational effect on the agonist muscles. Despite such restrictions, even PreM cells exhibit a variety of response patterns relative to their facilitated target muscles; one would think that inferring the relation of central cells to other muscles in more complex tasks would quickly become prohibitively complex.

Iansek raises the concern that if chronic unit recording data are presumed to be deficient, neural network models based on such data would also be flawed. In fact, the deficiency is not so much in the recorded data per se, which must be accepted as an experimental fact, but in the missing information about the rest of the system. Neural network simulations can help fill in the picture in a relatively objective manner, by tying the scattered observations together into a complete working model. So, neural network simulations actually provide a complementary method of analyzing and understanding the significance of the recorded single-unit data, even when the data alone provide a hopelessly selective sample of the system.

Kalaska & Cromand preclude the usefulness of obtaining a "complete description of the causal mechanisms for the planning and initiation of movement." This "Holy Grail" is dismissed as unattainable, which it is, if one considers the term "complete" to mean a comprehensive description of the state and connectivity of every relevant neuron. Obviously, such an exhaustive compilation of all the details in the biological nervous system is not only impossible to obtain but impossible to synthesize, and a description to this depth is unnecessary. Some simplifications must certainly be made, but we can still pursue solutions that are "complete" in the sense intended in my target article, namely, having a sufficient number of elements to implement a working dynamic solution. The network simulations are obviously simplified in many ways, but they can still provide a more complete representation of the neural mechanisms that can generate a behavior than a patchwork of scattered observations of individual neurons. Obtaining a causal model is ultimately a worthier scientific goal than intuitive reading of selected neural patterns.

Kalaska & Cromand appear to dismiss the neural network simulation in the target article as merely a "curve-fitting matrix" that transforms the inputs by low-pass filtering and weighted combinations of the inputs. Such networks, including this one, actually do more than simple linear operations on the inputs. As reviewed elsewhere (Fetz, in press), dynamic, recurrent neural networks can simulate the nonlinear operations of the oculomotor system (cf. Robinson's target article, this issue), reflex responses with local sign (Lockery et al. 1990), autonomous oscillations that resemble central pattern generators (Rowat & Selverston 1991), and short-term memory tasks (Zipser 1991). My particular model was intended as an example of the method, rather than a physiologically realistic model of the sensorimotor system. Therefore, the fact that Kalaska & Cromand "see no evidence that it solves any of the sensory transformations required to convert target spatial location into a multidimensional intrinsic reference frame of muscular activity" is obviously because the network was never designed or trained with this task in mind. However, there is no fundamental limitation precluding the development of such a model.

Kalaska & Cromand make a good point that looking for parallels between activity patterns of hidden units and responses of biological neurons can involve the same sort of selection bias as correlating neural discharge to parameters of movement, and may be just as misleading. This concern can be addressed by determining whether the analogous neurons and hidden units each typify a representative set of elements involved in the task. In some cases the response properties are so distinctive that there is little question of the uncanny similarity of hidden-unit patterns (for example, the discharge patterns of cortical neurons and network units involved in short-term memory tasks; Zipser 1991). There is a very important difference between interpreting the meaning of response properties of single neurons in behaving animals and interpreting the response patterns of hidden units in the network. In the animal data, one is only guessing about their function. In the network models, one can demonstrate explicitly what that function is by tracing their connections. Therefore, to the degree that hidden-unit activity resembles activity of neurons in animals performing the same task, one can make inferences about the possible function of the biological patterns.

Kirkwood has a very particular bone to pick regarding the relation between postsynaptic facilitation (PSF) and anatomical connections. We have taken PSF to indicate a correlational linkage between the PreM neuron and its facilitated target muscles, and have used it to define both operationally. But as Kirkwood points out, it is conceivable that some of these facilitations may be mediated not by a monosynaptic connection of the triggering cell, but by other cells whose spikes are sufficiently synchronized with the trigger cell. As he indicates, we have analyzed this issue directly by cross-correlating CM and
neighboring cortical cells and found their cross-correlation peaks to be too broad to mediate the primary postspike effects (Fetz et al. 1991; Smith & Fetz 1989). Kirkwood suggests that more careful analysis of the PSF would be helpful in discriminating effects likely to be mediated by direct connections versus those mediated indirectly by synchrony, as previously described by Davies et al. (1985). This sort of analysis has been applied in a recent paper on the postspike effects of afferent fibers (Flament et al. 1992). A useful criterion is the latency of poststimulus effects, which can help define the minimal latency of postsynaptic effects of the trigger unit. Whether all the PSF in previous reports were mediated by direct monosynaptic connections or only some lesser proportion is not critical to the main point of my discussion, which concerns the response patterns of PreM cells. This issue would be relevant to my argument that PreM cells include a variety of response types if all examples of some particular response type were erroneously identified as PreM cells. This is highly unlikely, because each response type had many units with clear PSF that met the most stringent criteria.

The commentary by Lundberg makes several important points. Spinal cord neurons form a very important component of the motor system and we are indebted to Lundberg and his colleagues for their prodigious work in elucidating the segmental circuitry involved in reflex and voluntary movements. Although my target article describes primarily cortical and rubral PreM neurons, we do not assume that "only the monosynaptic pathways from the motor cortex and the red nucleus matter." Our experimental emphasis on the CM and RM cells is based primarily on their greater accessibility in behaving primates and on the fact that they do form a significant component of the supraspinal neurons that affect motoneurons directly. However, we do not believe that they are the only important controllers of motoneurons (Cheney et al. 1981). Regarding the points in the target article, they do provide a significant example of the sort of coding that can appear in cells directly linked to motoneurons. A major remaining experimental challenge is to elucidate the response properties of PreM cells in the spinal cord and we are currently trying to document cervical interneurons that affect motoneurons. The extensive work of Lundberg and colleagues (e.g., Alstermark et al. 1984; Baldissera et al. 1981; Illert et al. 1977; Jankowska & Lundberg 1981) will provide an essential context for identifying cells in such studies. Although the circuitry in the cat will provide important guidance in the monkey studies, significant differences between the cat and the primate, such as the existence of the monosynaptic corticomotoneuronal pathway, should also be remembered. The propriospinal neurons (PN) form an important disynaptic linkage from cortex to motoneurons in the cat (Illert et al. 1977), yet spike-triggered averages of EMG from cortex have so far failed to show that this linkage is sufficiently potent to mediate PSF. Determining whether similar PNs exist at the same extent in the monkey is a primary goal of our current investigations. We agree with Lundberg's suggestion that the CM cells may resemble the C3-C4 PNs in having two subgroups: those cells that project only to synergistic motoneurons and others that project both to motoneurons and Ia inhibitory interneurons (Fetz et al. 1990; Kasser & Cheney 1985).

Another difference between primate and cat may be the degree to which the lateral and medial descending systems play separable roles. Lundberg says it is noteworthy that complete transection of the corticospinal tract and the rubrospinal tract in cats does not abolish commands for target-reaching and manipulatory movements. This result differs from those reported by Lawrence and Kuyper (1968) for the monkey, again suggesting significant interspecies differences. As Lundberg points out, reticulospinal pathways may also play a significant role in controlling primate motoneurons, another challenge for the spike-triggered averaging technique.

The relation of CM cells to movement is further discussed by Lemon, whose work has elucidated the function and connections of CM cells related to distal hand and finger muscles in natural precision grip movements. His work provides new insights into the relations between PSF patterns and responses of the monkey hand. Lemon raises the important point that it is helpful to document the response of PreM cells in relation to relatively normal limb movements in addition to a simple flexion-extension task. He says that when activity of CM cells is related to free hand movements "there is a congruency in the pattern of synaptic connectivity [shown by the PSF] and of recruitment during movement." An important caveat here follows from the fact that PSF can be detected only in those muscles coactivated with the cell; thus, during free movements involving variable activation of different muscles, this condition itself will tend to produce a congruence between the cell's facilitated muscles and the coactivated muscles.

Tanj raises an objection that calls for clarification. According to Tanji, my target article suggests "that no area-specific differences in properties of neuronal activity have been reported" and implies that "only neurons of the same type have been found everywhere in motor areas in more or less the same degree." In fact, my paper does state, perhaps not emphatically enough, that different cortical regions clearly show differences in the relative proportions of cells involved in different functions. Indeed, the work of Tanji and colleagues is particularly exemplary in providing persuasive evidence for regional specializations (e.g., Mushiake et al. 1991). Their work has documented the proportions of cells in different areas under behavioral tasks designed to elucidate these functional differences, and has provided ample data supporting specializations. My point is rather that cells of the same response type can be found distributed over many regions and that these like-minded cells probably form functional groups. The degree to which any particular cell type is found experimentally can also be proportional to the degree to which it is sought; therefore, recording bias should also be carefully controlled in experiments involving a search for different types of neurons. I agree entirely with Tanji's point that the experimental data "point to the presence of specialization in cortical areas" and with Grobstein's similar point that we are "not in general dealing with a fully distributed system but rather with one having discrete 'information processing blocks.'"

What may have led to this misunderstanding is my statement that given a sufficient variety of cell types one can find examples to support any hypothesis from a completely random data set. This statement was designed to make a point but does not reflect a belief that the neural
data are in fact random. There is good evidence for preferential relations between neural discharges and components of movement, and efforts to resolve what those discharge patterns actually mean are certainly worthwhile. My main point is to caution against inferring their meaning by conceptual projections, as opposed to determining their meaning in a causal framework; the latter can now be approached by neural network simulations that replicate these patterns and provide a mechanistic basis for interpreting their computational significance.

References


