Erratum

Erratum to "Force and the motor cortex"
[Behavioural Brain Research 86 (1997) 1–15][1]

James Ashe

Brain Sciences Center (11B), VAMC, One Veterans Drive, Minneapolis, MN 55417, USA

The Publisher regrets that this article was printed without incorporating several Author's Corrections. The corrected article is reprinted in the following pages.

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[1] PII of original article: S 0166-4328(96)00145-3

Review Article

Force and the motor cortex

James Ashe *

Brain Sciences Center (11B), VAMC, One Veterans Drive, Minneapolis, MN 55417, USA

Abstract

The relation between the activity of cells in the motor cortex and static force has been studied extensively. Most studies have concentrated on the relation to the magnitude of force; this relation is more or less monotonic. The slope of the relation, however, shows considerable variation among different studies and seems to be inversely associated with the range of forces over which the cell activity has been studied. Cells in the motor cortex also show variation in activity with the direction of static force. When both the direction and the magnitude of static force are allowed to vary, a majority of cells show significant changes in activity with direction of force alone, an intermediate number relate to both direction and magnitude, while a small number relate purely to the magnitude. This suggests that the direction of static force can be controlled independently of its magnitude and that this directional signal is especially prominent in the motor cortex. In general, it has been more difficult to study the relations to dynamic force. There is a correlation between motor cortex cell activity and the rate of change of force. The direction of dynamic force is also an important determinant of cell activity. When both static and dynamic force output are required (for example, with arm movement in the presence of gravity) it is the dynamic signal that is most clearly reflected in motor cortex activity. The relations between motor cortex activity and static or dynamic force are not invariant, but may be modified by the behavioral context of the motor output. © 1996 Elsevier Science B.V.

Keywords: Monkey; Force; Static; Dynamic; Motor cortex; Isometric

1. Introduction

The investigations into the relation between the parameters of movement and the activity of cells in the motor cortex were strongly influenced from the beginning by the work of Sherrington and his colleagues [32,49]. This work has been used to support the conception that there is a fixed relation between specific areas (or cells) in the motor cortex and the muscles involved in movement. Although Leyton and Sherrington [49] did refer to the "punctate localization" of muscles within the motor cortex, their experiments clearly documented a much more complex association between the cortex and muscles. Neither did they consider that the

relation between the cortex and elements of the motor output was fixed, in fact, they state explicitly that "the motor cortex is a labile organ" (Ref. [49], p. 144). As regards function, they suggested that "the upbuilding of larger combinations (*of movements*) varied in character ... is one of the main offices performed by the motor cortex" (Ref. [49], p. 178). One of the conclusions in their paper is that the motor cortex performs an integrative function wherein whole movements are constructed, and does not subserve the control of single muscles. This is in keeping with the earlier suggestion of Hughlins Jackson that "muscles are represented in the nervous centres in thousands of different combinations – that is, as very many different movements" [42,43]. Nevertheless, later work continued to use what was assumed (erroneously) to be the imprimatur of Sher-

* Fax: (1) (612) 725 2291; E-mail: ashe@maroon.tc.umn.edu

rington, in putting forward what were regarded as similar results [9]. Consequently, the idea that cells in the motor cortex are literally 'upper motor neurons' has been the dominant one which has been tremendously influential in neurology and neurophysiology.

If one accepts the hypothesis that muscles are represented within the motor cortex then force is the most obvious motor parameter to study as force is generated by muscle activity. To imagine that the activity of cells could relate to another parameter, such as amplitude, velocity, or direction, assumes a more sophisticated relation between motor cortex and muscle than was generally allowed. Therefore, from the earliest motor behavioral experiments in the monkey, force was the parameter that has received most attention. Force is a vector, and as such, has both magnitude and direction. However, it is the magnitude of force, which could be related to the activity of a single muscle, rather than the direction that has been the main focus of research. There have been several recent developments in the study of force coding by the motor cortex that question previous views of the motor cortex as a controller of muscles and take us closer to Sherrington's concept of the function of the motor cortex as one of integration.

In addition to reviewing the work on force, we will attempt to outline how our current understanding of the way in which this variable is controlled is in keeping with changing attitudes to the role of the motor cortex in motor output. The review deals predominantly with experiments using the technique of single cell recording in awake behaving animals which gives fine grain information about the activity of cells in the intact organism.

2. Relations to magnitude of force under static conditions

Following the introduction of the technique of extracellular single cell recording in awake behaving animals in the late 1950s [39,60], Evarts [13] was the first to usefully apply it to the study of motor function. Many of the experiments were done under static isometric (or semi-isometric) conditions; it was expected that these behavioral conditions would lead to the least ambiguous results concerning the motor cortical coding of the magnitude of static force. Recent work suggests that the relation between cell activity and activity in target muscles is quite more complex than originally conceived; therefore, even the simplest behavioral studies need to be interpreted in this light.

2.1. Force as a controlled variable

In the early experiments, Evarts [13,14] recorded from pyramidal tract neurons (PTNs) while a monkey made flexion and extension movements at the wrist against opposing and assisting loads, or maintained postural fixation while resisting similar loads. The overall conclusion from these experiments was that activity in the PTNs was related to the forces exerted rather than to the position or displacement of the wrist. Schmidt and colleagues [64] were unable to document a strong relation to the magnitude of force, and suggested that the cells were primarily involved in the selection of muscle groups used in the task. Thach [72] expanded on the findings of Evarts using a more sophisticated paradigm in which position, force, and the direction of the upcoming movement were dissociated, and found that the activity of cells in the motor cortex related to all three parameters (force, direction, position) in approximately equal proportions. Motor cortical cell activity may be modulated by both joint torque and joint position under static conditions [10,15,20,74]. The force developed by a muscle for a given amount of muscle activation is dependent on its length. Consequently, it has been suggested that the change in activity of some motor cortex cells is most consistent with the length–tension relation of the muscles involved in the task [15,20,74]. The general conclusion that can be drawn from these dissociation studies is that a proportion of cells in the motor cortex relate to static force output in some meaningful way.

2.2. Characteristics of the relation

The relation between motor cortex cell activity and force is often monotonic as first suggested by Evarts [14], and subsequently corroborated by Thach [72]. However, this relation may not hold for all cells [11]. In addition, the relation may only apply over a restricted range of forces. The technique of spike triggered averaging [56] has been used to identify cells that have a presumed monosynaptic connection to muscle [10,17], and the activity of these cells has been characterized under isometric and auxotonic conditions [10]. In these experiments [10], the relation between cell activity and static force was found to be monotonic over part of the force range used. The relation did not hold for forces at the extremes of the range and the overall function (cell activity vs. force) was often S-shaped. The implication was that there is an optimal range of force within which cells show their maximum force sensitivity, and this range could vary for different cells. There may be a number of distinct populations of cells each with a different relation to force. For some of these cells, the relation is linear throughout the range of forces tested, while for other cells, the linear relation holds only for forces in the middle of the range, and tends to plateau at the extremes [10,15]. A number of investigators have suggested that the greatest modulation in cell activity with static torque occurs during small changes in

torque about zero [15,20,74]. This would imply that a particular function of motor cortex cells is the regulation of small incremental changes in force. In these studies, however, the change in torque about zero was confounded with change in the direction of the torque. The increase in sensitivity to torque about zero may represent the combined effect of the direction and the magnitude of torque on the cell; many cells in these studies were related to both direction and magnitude of torque. This last issue was not studied rigorously, perhaps due to the relatively restricted nature of the behavior.

2.3. Precision grip

The precision grip behavioral task has been an important probe in uncovering the relations between motor cortical cell activity and static force output for a number of reasons. (1) It involves the co-ordinated action of many muscles across a number of joints in the hand and forearm, thus presenting a relatively rich and meaningful behavior which can then be correlated with cell activity. (2) The control of the motor output of the hand and fingers has long been regarded as an important function of the motor cortex. (3) There are direct monosynaptic connections from motor cortical cells to motoneurons supplying the muscles of the hand. Hepp-Reymond and colleagues used this task to study the control of forces exerted by the fingers [35,36,51,70,73]. They found that the relation between motor cortex activity and force output was monotonic [35,36,51,73]. Although an early study [70] failed to show any consistent relation between the magnitude of static force and cell activity. This monotonic relation seems to hold true irrespective of the body part or joint at which the forces are exerted. The overall force levels used in the precision grip task were relatively small, varying between 0.1 and 2.5 N. The slope of the relation between cell activity and force output at the fingers was generally higher than that at other joints (see below), with one exception [15]. This may reflect the specialization of the hand, and the fingers, in particular, for the control of small precise incremental changes in force. Because higher levels of force were not tested, it is not clear over what range the relation between cell activity and static force remained linear.

2.4. Complexity of the relation between motor cortical cells and muscles

The monotonic relations between cell activity and force produced by single muscles, or by groups of agonist and antagonist muscles across several joints, must be interpreted in the light of the distributed anatomic connections and the complicated functional relations between cells in the motor cortex and limb muscles. The monotonic relations described above are remarkable in their apparent simplicity given the complexity of cell–muscle interactions.

There is great divergence in the corticospinal projection from the motor cortex to the motoneurons in the spinal cord. Individual corticospinal axons make contact with motoneurons projecting to multiple muscles in the cat [68], and in the monkey [67]. In addition, corticospinal neurons have collaterals at many different levels of the spinal cord [69]. In contrast to the divergent projections from the motor cortex, the input to the motoneurons is convergent, with a single motoneuron receiving input from neurons over a wide expanse of the cortical surface [47]. This arrangement would be sufficiently complicated if the connections between motor cortex cells and muscle were direct. However, this is only the case for cells in the motor cortex that project to distal muscles; and perhaps to a small proportion of proximal muscles [59]. The motoneurons of all other muscles receive cortical input indirectly via a system of interneurons in the spinal cord further complicating the task of specifying motor output on the basis of the action of single muscles. It is remarkable that we see any relatively simple relations under these circumstances.

To better define the relation between motor cortical cells and muscle, it has been useful to study corticomotoneuronal (CM) cells: these cells are thought, on the basis of post spike facilitation (PSF), to have monosynaptic connections to the motoneurons in the spinal cord [17,48]. In a study examining the distribution of projections of single corticomotoneuronal cells, 33% of the cells were connected to muscles operating across two or more joints [55]. This suggests that these cells may serve to co-ordinate the activity of muscles in a multi-jointed limb toward some behavioral goal (e.g., net force or direction of the limb). Further evidence that the primary function of CM cells may not be the specification of the activity of single muscles comes from behavioral studies in which there was a lack of a clear and consistent relation between CM cell activity and activity in target muscles: "we found no clear relation between the response pattern of a CM (corticomotoneuronal) cell and its target muscles, with respect to either the number of facilitated muscles or their location" (p. 778, [10]). Therefore, a demonstrable physiological connection between a cell and a muscle (or muscles) does not assure a consistent functional relation between cell and muscle activity (see below). The paradoxical relations between cell activity and force in an isometric precision grip task also relate to this issue [51]. In this study, 33 CM cells were identified, eleven had positive correlations to the force exerted, while six had negative correlations despite activation of the target muscles. In fact, the average correlation coefficient between cell activity and the total force exerted

(from Table 1 in [51]) was higher for the cells with negative relations ($r = -0.38$) than for those with positive relations ($r = 0.31$). The finding of a negative correlation is particularly surprising as none of the muscles to which the cells were related behaved in a similar way. The authors suggest that these negatively correlated cells may enable co-contraction of muscles in the task by a reduction in excitatory drive to Ia inhibitory interneurons: while, plausible this is purely speculative. Recent behavioral studies may help to explain the more puzzling aspects of the results referred to above. The isometric precision grip involves the co-ordinated activity of up to 15 different muscles of the hand and forearm and there may be a significant amount of trial-to-trial variability in muscle activation during the task [53]. This suggests that the same behavior may be performed using different combinations of activation strengths in the various muscles. The electromyogram from these muscles showed few examples of either spatial or temporal synergy between pairs of muscles recorded simultaneously [52]. Therefore, it would seem that the activation of groups of muscles is not fixed during the performance of a particular task and, given the extent of the variability in muscle activation during different repetitions of the same behavior, it is unlikely that this variable is controlled directly by the activity of motor cortical neurons. This finding is in keeping with the variable nature of the CM cell interactions already discussed.

Table 1
The force range over which the relation to static force was monotonic, the slope of this relation and the body part at which the force was exerted for a number of different studies

Study	Body part	Force range (N)	Slope (impulses/s/N)
1. Hepp-Reymond et al. [36]	Finger	0.90	66.5
2. Wannier et al. [73]	Finger	0.80	69.0
3. Evarts [14]	Wrist	3.92	4.7
4. Thach [72]	Wrist	3.89	2.4
5. Cheney and Fetz [10]	Wrist	5.98	2.8
6. Evarts et al. [15]	Elbow	0.07	180.1
7. Hoffman and Luschei [37]	Jaw	72.00	0.6
8. Taira et al. [71]	Shoulder/elbow	4.89	10.9

3. Relations to magnitude of force under dynamic conditions

The relations of cell activity to force under dynamic conditions (i.e., when the force is changing) have not been studied extensively. In addition, there have been numerous aspects of experimental design which have complicated the interpretation of data dealing with the control of dynamic force: actual forces were not measured, the behavioral tasks also involved movement, and the behavioral repertoire of the tasks was limited.

Evarts, in his original work, suggested that cell activity related to the rate of change of force in addition to the magnitude of force [13]. However, he drew no distinction between the primacy of one of these variables over the other in accounting for cell activity. Some cells related to both the rate of change and the magnitude of force suggesting a flexible relation between cell activity and the control of static and dynamic force output. Evidence for the non-exclusive relation between cell activity and either static or dynamic force output was also found in other studies in which the majority of cells changed activity during both conditions [36,70].

The use of behavioral tasks in which static and dynamic force was produced under isometric conditions simplified the interpretation of task related cell activity [35,36,70]. While the majority of cells changed activity during *both* static and dynamic force production, some cells related exclusively to either the static or dynamic components of the task [36,70,73]. There was a statistically significant correlation between cell activity and the rate of change of force in the majority of cells which were related exclusively to dynamic force. Among the cells which related to both static and dynamic force, the proportion with statistically significant correlations to the dynamic aspects of force was smaller, but the strength of these correlations was within the same range as that of the purely dynamic group. This suggests that the *nature* of the relation to the magnitude of dynamic force is similar in the two groups. Other work by Hepp-Reymond and her colleagues [36] showed a smaller proportion of cells relating to the rate of change in force; in addition, this relation was often conditional on other aspects of the motor behavior (see below).

Other studies have also documented a fair proportion of cells in the motor cortex which relate to dynamic force output. However, in many instances, the findings were not elaborated upon, or presented in detail. For example in one study, it was found that about 25% of cells in the motor cortex discharged only during change in force [73]. Apart from this statement, no further analysis was presented on these cells. Cheney and Fetz [10] showed a relation between activity and the rate of change of isometric force in 3 of 10 CM cells; again, no details were given, perhaps because the relation to static

force was the primary focus of the study. In the same vein, Conrad and colleagues [11] found a number of cells which showed an increase in the frequency of discharge associated with movements opposing forces of increasing magnitude. The results, however, are difficult to interpret, as the actual forces exerted by the arm were not measured and movement related activity could not be distinguished from that related to force.

Humphrey and colleagues devised a novel approach to the analysis of the relation between cell activity and the coding of various movement parameters, which cast some light on the relation to force under dynamic conditions [41]. Two assumptions were inherent in this analysis: (1) the time course of cell activity could be used to predict the time course of different parameters during movement; and (2) the time course of several simultaneously recorded neurons provided a more accurate prediction of the time course of movement parameters than that of any single neuron. The smoothed discharge frequency of each neuron was multiplied by a constant (derived separately for each neuron using multiple linear regression) and the resulting values from all neurons were summed at each time point, giving a predicted time course for each parameter (force, rate of change of force, displacement, velocity). The behavioral task comprised both static and dynamic components as it involved alternating flexion and extension at the wrist, with a hold period in both flexion and extension. Under dynamic conditions, cell activity was related to the instantaneous force or to the rate of change in force. The time course of activity from five neurons recorded simultaneously best predicted the time course of instantaneous force output suggesting that this variable may be coded by motor cortex cells under dynamic conditions.

Recent work on the neural relations to force under dynamic conditions examined the specification of this parameter [61]. The writings suggested that force was specified independently of movement amplitude and it appeared that different populations of cells were involved in the coding of these two variables. In an extension of these studies, it was also found that both the direction of movement, and the magnitude of dynamic force, may be reflected in the activity of motor cortex cells in a preparatory period before a signal to move as well as during the movement itself [62].

4. Nature of the relation to force

The studies reviewed briefly above, raise a number of issues about the nature of the relation between neural activity and the magnitude of force.
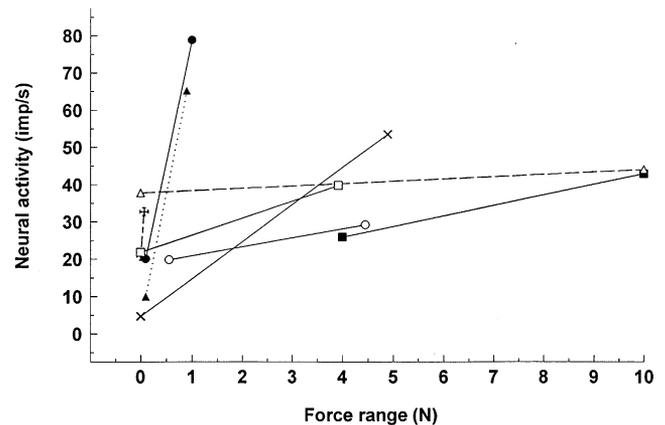

Fig. 1. Average cell activity (impulses/s) plotted against the maximum and minimum values in Newtons (N) of the static force over which the relation to cell activity was monotonic (to a maximum level of 10 N) for the eight different studies outlined in Table 1. The symbols used relative to the numbered studies in Table 1 are as follows: filled circle (1), filled triangle (2), empty square (3), empty circle (4), filled square (5), cross (6), empty triangle (7), X (8).

4.1. Are small and large forces controlled differently by the motor cortex?

The range of forces used in different experiments has been largely determined by the body part performing the task (e.g., finger, wrist, jaw, or elbow). The monotonic relation between cell activity and static force holds for different body parts and over a wide range of forces. The slope of the monotonic relation can vary greatly, depending on the magnitude of the forces used. In general, the slope is much greater for small [15,36,51,73] than for large forces [10,37,72]. This is illustrated in Fig. 1, in which the increase in cell activity (impulses/s) is plotted against the range of forces used in for a number of different studies. The data were derived from tables and figures in the original publications (see Table 1); only cells showing an increase in activity with force in a specific 'preferred' direction were included. There appears to be a relation between the slope of the increase in cell activity and the range of forces used. In fact, the relation between the two variables is linear (Fig. 2). There are a number of possible explanations for this finding. As the force range covaried in many cases with the body part used to perform the task, it is possible that the variation in the slope reflects the differential relations of neurons relating to different body parts to force output rather than to the range of force per se. However, when very small forces are exerted at large joints, such as at the elbow [15], then the slope can be exceedingly high reflecting not a fixed relation of cortical cells to force produced at particular joints, but instead an inverse relation of slope to the range of forces produced. Another possible interpretation of these data is that the slope may reflect the number of increments in force that need to be specified

over a particular force range, rather than a relation to the range itself. If for example, in one case N-levels of force must be specified (i.e., discriminated) over a given range of force, and in another case 10 N-levels over the same range, then a much higher rate of cell activity per unit force will be needed in the latter case, *if force levels are to be discriminated equally well in both cases*. At present, there are insufficient data available to decide this last issue.

4.2. Do cells in the motor cortex preferentially relate to extensor muscles?

The idea that primary motor areas are preferentially involved in controlling the extensor muscles of the upper limbs came from observations in human subjects following stroke affecting the upper limbs, in whom the extensor muscles showed greatest weakness. Of the 23 PTN documented by Evarts [13] as having a monotonic relation to force, 16 were more active with extensor loads. Cheney and Fetz [10] also found more cells relating to extensor than to flexor forces. The most compelling evidence that there may be a fundamental difference in the way in which cells in the motor cortex relate to these different groups of muscles comes from the slopes of the regression lines of cell activity against force which were greater for flexor and than for extensor muscle groups [10]. The average increase in discharge for each Newton increase in force was 4.8 and 2.5 impulses/s for the extensor and flexor muscles, respectively. In another study [72], motor cortex cells also showed more modulation per unit force for wrist extension (8.3 impulses/s/N) than for wrist flexion (3.3 impulses/s/N). Therefore, within a limited motor behav-

ioral repertoire, more cells in the motor cortex relate to and are more strongly modulated by forces exerted by extensor than by flexor muscles. However, the relevance of this finding is not clear in the context of the normally functioning multi-jointed limb.

4.3. Do all cells in the motor cortex have similar relations to force output?

Cells within the motor cortex may project to neurons in many different areas, such as other cortical areas, subcortical structures, brainstem and spinal cord. It makes intuitive sense that the best relations to motor output should be found for those cells which have direct connections to spinal motor structures, especially to motoneurons which are the final common pathway to the muscles. PTN course through the medullary pyramids and putatively project to the spinal cord, although their target structures are not clear. On the other hand, CM cells are thought to have monosynaptic connections to the motoneurons in the spinal cord [17,48]. Hepp-Reymond and co-workers have used a common behavioral task (precision grip) in a number of experiments during which recordings were made from different cell types in the motor cortex. These the cells were either: (1) unidentified as regards target structures [35,36,70,73]; (2) CM cells [51]; or (3) PTNs [70]. The findings in these experiments can be used to directly compare the relations to force of the various cell types. There were no major differences in the relations between the different cells types and force output: unidentified and PTN had the same general relation to force output and similar overall response characteristics [70], and the proportion of unidentified and CM cells which showed a positive correlation with static force was similar [36]. Surprisingly, the correlation coefficients between cell activity and force, were less for the CM than for the unidentified cells: the range of correlation coefficients for 33 unidentified neurons with positive relations to force was $r = 0.5$–0.94 [36], while the range for 11 CM cells was $r = 0.19$–0.5 [51]. In addition, the force sensitivity, as reflected in the mean force–rate slopes, was also lower for the CM (32.4 impulses/s/N) than for the unidentified cells (54 impulses/s/N). This is not to suggest that CM cells generally show less sensitivity to force than do unidentified cells, it is merely to illustrate that the relation between cell activity and force is often complex, even for cells that have the clearest functional connection to motoneurons. The differences in force sensitivity in these cells groups may reflect small differences in the force range that used in the tasks, or indeed, the somewhat different behavioral paradigms.

The unidentified cells referred to above were chosen for study because of a relation to force output. None of the cells were tested to establish whether they were
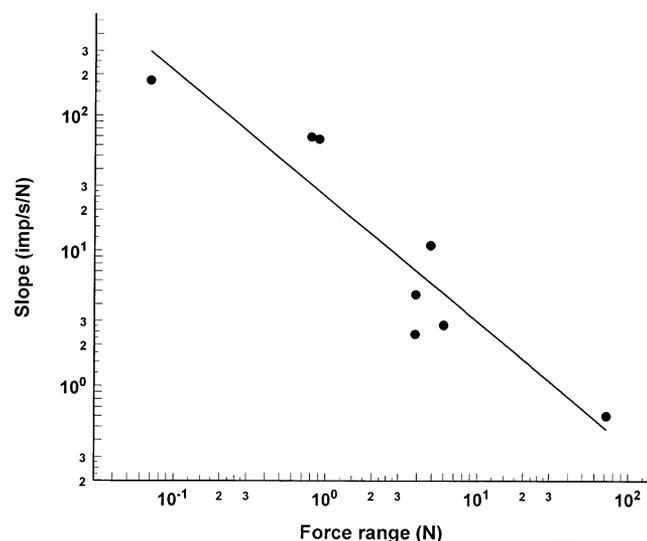

Fig. 2. The slope of the increase in cell activity (impulses/s/N) graphed against the force range in a log–log plot (data from Table 1) with superimposed regression line. The relation is linear with an r^2 of 0.88 ($P < 0.001$).

PTN or CM, and conceivably these cells could have fallen into either category. In a number of studies, however, task-related cells were explicitly identified as PTN or non-PTN [15,41,74]. The proportions of these two cell types that were task related during force output were similar [74]. In addition, the *nature* of the relation between cell type and force was similar [15,41,74]. Given the conditional nature (see below) of the relation between cell activity in the motor cortex and motor parameters, the functional anatomic connectivity per se seems to be an unreliable predictor of the behavioral correlates of cell activity.

4.4. How are changes in force magnitude reflected in cell activity?

Is the process of increasing the magnitude of force subserved by recruitment of additional force related cells or by increased firing frequency in the cells already recruited at lower force levels? Although this issue has not been the primary focus of a study it has been addressed by a number of investigators. Evarts [15] did discuss the recruitment of PTN both in relation to different functional groups of neurons and to the antidromic response latency of individual neurons; however, as the direction and magnitude of the force were confounded, the data are difficult to interpret. In general, increases in force have been accompanied by an increase in the firing rate in cells already recruited rather than by recruitment of additional cells [10,15]. The modulation of firing frequency was the mechanism employed by cells to code for changes in the magnitude of force; this was true for over 80% of the force range employed in one study [10]. These findings are at variance with the results of some other studies [35,73]: in which, although, most neurons showed modulation of firing frequency with increase in force, up to 25% [73] seemed to be recruited at higher forces.

4.5. Are static and dynamic forces controlled by different processes?

Static and dynamic force output may be controlled by fundamentally different processes [27]. During isometric force production in the cat the magnitude of force, or its derivative, increased linearly with the target amplitude, whereas the time to peak force, or its derivative, remained relatively constant and independent of the total force exerted [29,28]. Taking account of the response characteristics of muscle, Ghez [27] has proposed a pulse-step model of force control, in which the duration of the force pulse is constant and its amplitude is related to peak force, while the step involves an increase in output to maintain a steady state. This is similar to the model proposed for the control of saccades [4,63], though in oculomotor models it is the duration of the pulse rather than its amplitude that determines the amplitude of the saccade. Ghez further speculated that separate structures might be involved in controlling the pulse and step. The existence of separate dual control mechanisms (see below) within the motor system is supported by the results of studies on eye movements [63], the vestibular ocular reflex [66], arm movements in human subjects [18,19,38] and in experimental animals [21,25].

Supporting evidence for the existence of two different control systems for the control of motor output comes from the work of Humphrey and Reed [40] who examined changes in cell activity in the motor cortex associated with the production of torques about a joint: a monkey held his wrist in a static position in a manipulandum and opposed reciprocal dynamic torques, in the form of a sinusoid, delivered at different frequencies. At lower frequencies, there was reciprocal activation in the extensor and flexor muscles operating about the joint, while at higher frequencies, the stiffness of the joint was increased through the co-activation of both sets of muscles. The authors found two distinct populations of cells within the wrist area of the motor cortex, one primarily related to the control of reciprocal muscle activation and the other to the control of joint stiffness.

5. Behavioral context of neural activity

The earliest comprehensive study of the behavioral context of neural activity examined the relation between isometric contraction in pairs of agonist/antagonist muscles in the arm and the activity of cells in the motor cortex [16]. Beginning with the premise that motor cortex activity and muscle activity were related in some general way, the authors sought to characterize this relation. Eight of ten cells examined changed activity during the contraction of more than one of the muscles. Only one of the cells exhibited reciprocal relations to agonist and antagonist muscles. Many cells were active during both agonist and antagonist muscle activation across a single joint, or during muscle activity at more than one joint. The results also demonstrated that it was possible, through the use of operant conditioning, to change the apparent relation between a cell and a muscle. For example, a motor cortical cell that increased discharge consistently during the contraction of a particular muscle could be 'conditioned' so that muscle activity no longer was associated with change in cell activity. However, dissociation in the other direction could not be achieved, namely: the conditioning of the occurrence of muscle activity without concomitant activity in the cell with which it had been consistently associated. These findings in relation to 'conditioning' have two implications. First, as the authors conclude: ''precentral cells have more complex

and variable relations to muscles than simple and consistent covariation with a single muscle..." (p. 219, [16]). Secondly, the association between a cell and a muscle may differ depending on which element is regarded as the dependent one in the relation.

The activity profile of individual neurons can change relative to the strategy used in the performance of a particular behavior. In one experiment, a monkey used two different strategies to perform a task [36]. The animal increased force at the finger tips in either a slow controlled ramp-like or in a ballistic fashion. For at least one cell, the linear regression coefficient relating cell activity to dF/dt was negative during ballistic force output, although it was positive during the force ramp. In addition, there were a number of cells which showed significant positive correlations with peak dF/dt or mean force during the controlled ramp; the relations were not significant in the ballistic task. Cheney and Fetz [10] also documented differential activity in three CM cells during a task performed using two different strategies. In one strategy, the animal performed rapid ballistic flexion–extension movements at the wrist, while in the other, the movements were performed in a more controlled ramp-and-hold fashion. The CM cells discharged briskly during the ramp and hold and were almost silent during the ballistic movements although the facilitated muscles were active in both conditions.

The activity of CM cells does not necessarily relate to the activity of the facilitated muscles per se, but is often critically dependent on the level of force exerted [10]. Even when the level of force exerted by a facilitated muscle remains constant, CM cell activity may depend on other features of the task. Muir and Lemon [57] recorded from CM cells, while a monkey performed two different tasks: a precision grip and a power grip. The first dorsal interosseous muscle was equally active in both tasks, however, a CM cell facilitating this muscle was active only during the precision grip. This result illustrates the extent to which cell activity may depend on the behavior irrespective of muscle activity. Other examples of the complex relation between cell activity and muscle output are to be found in studies of locomotion in the cat [2] in which chronic electrodes implanted in the motor cortex of the cat were used to study cells which increased activity linearly in relation to the speed of locomotion. In this experiment, cell activity did not change significantly when the locomotion was on a 10° incline, although there were substantial increases in the amount of EMG activity. The are other examples to be found in studies of locomotion. The activity of PTNs was much higher in a cat required to accurately place the limbs while walking on the rungs of a horizontal ladder, than when walking at a similar rate on a treadmill, although, the muscle activity was similar in both conditions [1,5]. Large changes in PTN activity, relative to normal walking, were also seen when cats had to lift a limb to clear objects placed on a treadmill [12]. In this last example, a major difference between the two conditions was in the temporal sequence rather than in the total amount of muscle activity, and it was presumably this difference that contributed to the large change in PTN activity.

6. Directional aspects of static force

Force is a vector and as such has both direction and magnitude. The majority of studies on force and its relation to cell activity in the motor cortex have failed to take account of the directional nature of force. This is not to say that the direction of force output has not been a consideration in these studies, but that the experimental design was such that force was generally examined in one dimension only: for example, flexion and extension at the elbow [11] or the wrist [10,72], supination/pronation of the forearm [15], or opposition of the thumb and index finger [35]. It is not possible to adequately study the relations to the direction of force under such restricted behavioral conditions. The first study to take full account of the directional aspects of force output was that of Kalaska and colleagues [44,45] who extended the investigation of the neural relations to static force to the direction of multi-joint, two-dimensional (2D) forces. They examined the activity of cells in the motor cortex while monkeys held a manipulandum, steady at the center of a work-surface, against loads operating in eight different directions. They found that cell activity in the motor cortex varied with, and was broadly tuned to, the direction of force.

Recently, these observations have been extended to conditions in which forces of different direction *and* magnitude were exerted in 3D [8,71]. The relations between the steady-state frequency of discharge of 188 cells in the arm area of the motor cortex of the monkey and the direction and magnitude of the three-dimensional (3D) static force exerted by the arm on an isometric manipulandum were analyzed using stepwise multiple linear regression. In 154/188 (81.9%) cells, the regression model was statistically significant ($P < 0.05$). In 121/154 (78.6%) cells, the direction, but not the magnitude of force, had a statistically significant effect on cell activity; in 11/154 (7.1%) cells only the magnitude effect was significant; and in 22/154 (14.3%) cells, both the direction and magnitude effects were significant. The same analysis was used to assess the effect of the direction and magnitude of force on the electromyographic (EMG) activity of 9 muscles of the arm and shoulder girdle. For all of the muscles studied, the regression model was statistically significant. In 4/9 (44.4%) muscles only the direction effect was significant, whereas in the remaining 5/9 (55.6%) muscles, both the direction and magnitude were significant. No
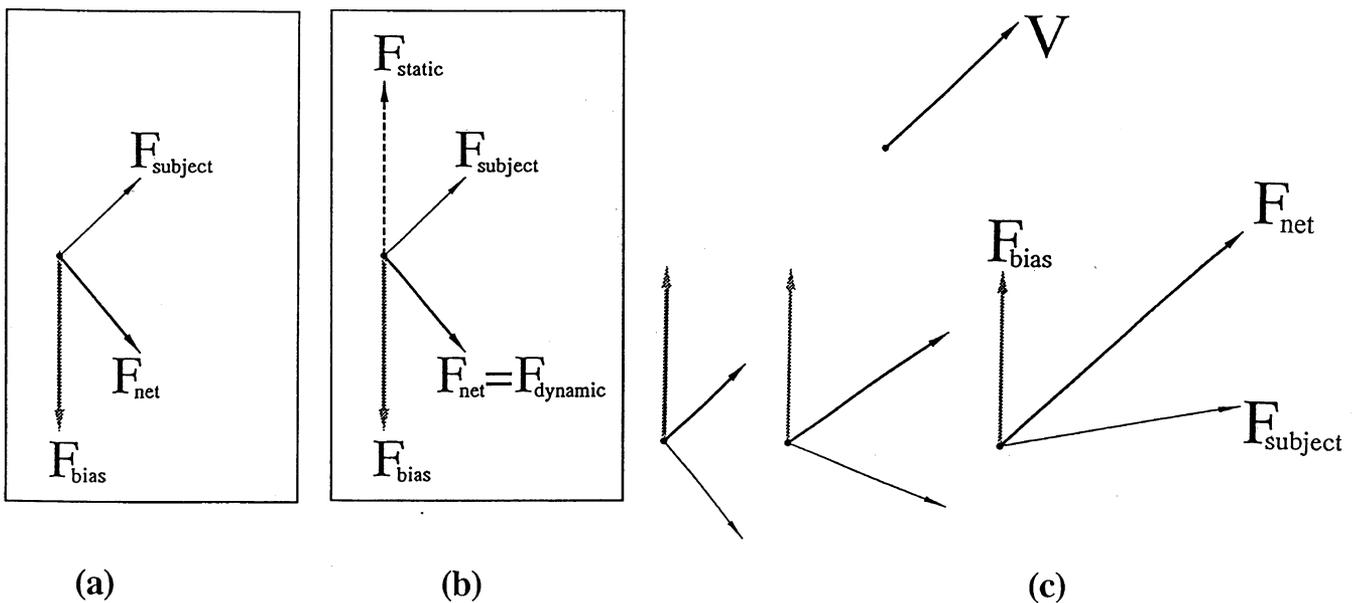
Fig. 3. (a,b) Forces defined in the text: force bias (F_{bias}), force exerted by the subject (F_{subject}), static force (F_{static}), dynamic force (F_{dynamic}), and net force (F_{net}). (c) Time-varying changes in these forces when F_{dynamic} increases in magnitude and is in the visually instructed direction V (arbitrary data). Italic letters (bold in figure) indicate vectors. (Adapted from Georgopoulos et al. [21].)

muscle studied showed a significant effect of force magnitude alone. The differences in the frequency of occurrence of direction and magnitude effects between cells and muscles were statistically significant. These findings underscore the fundamental importance of the direction of force in space for both motor cortical cells and proximal muscles and underline the differential relations of cells and muscles to the direction and magnitude of force. With respect to the latter (muscles), these results indicate that the specification of the magnitude of 3D force is embedded within the directional signal; this combined direction + magnitude effect was 3.9 times more prevalent in the muscles than in the cells studied. In contrast, the pure directional effect was 1.8 times more prevalent in the cells than in the muscles studied. This suggests that the direction of force can be controlled independently of its magnitude and that this directional signal is especially prominent in the motor cortex.

7. Directional aspects of dynamic force

The control of force output under two dimensional dynamic conditions has recently been specifically addressed [21]. A task was designed in which a monkey exerted dynamic force in two dimensions under isometric conditions. Constant bias forces were incorporated into the task which dissociated three force variables: the force exerted by the subject, the net force and the change in force. This dissociation of forces allowed for the simulation under isometric conditions of the situa-

tion that pertains during movement where gravity acts as a constant bias force which when summed vectorially with the subject's force results in the net force that carries the limb in the desired direction. The different force vectors involved under normal gravitational conditions, and simulated in this experiment, are shown graphically in Fig. 3a. In order to exert forces in a desired direction (F_{net}) in the presence of a constant bias force (F_{bias}), such as gravity, then the subject must exert force (F_{subject}) which when summed vectorially with the bias force will produce force in the desired direction. We assume that the actual force exerted by the subject under these circumstances can be further decomposed into static and dynamic components (Fig. 3b). The static component (F_{static}) is equal to and opposite the bias force while the dynamic component is the equivalent of the net force. Fig. 3c shows how the subject's force can be resolved into two component vectors, as force of increasing magnitude is exerted in direction V: the static component is equal and opposite to the force bias, while the dynamic component is identical to the net force. Finally, the change in force, which was defined as the difference between successive force vectors at time t and $t+1$, is the same for the subject force and the net force, as the bias force remains constant.

In the task, a monkey exerted force on an isometric manipulandum to control movement of a force–feedback cursor on a video display. To begin the task, the animal had to align the force-feedback cursor to a central target and maintain the cursor in that position during a 'hold' period. At the end of the hold period, a
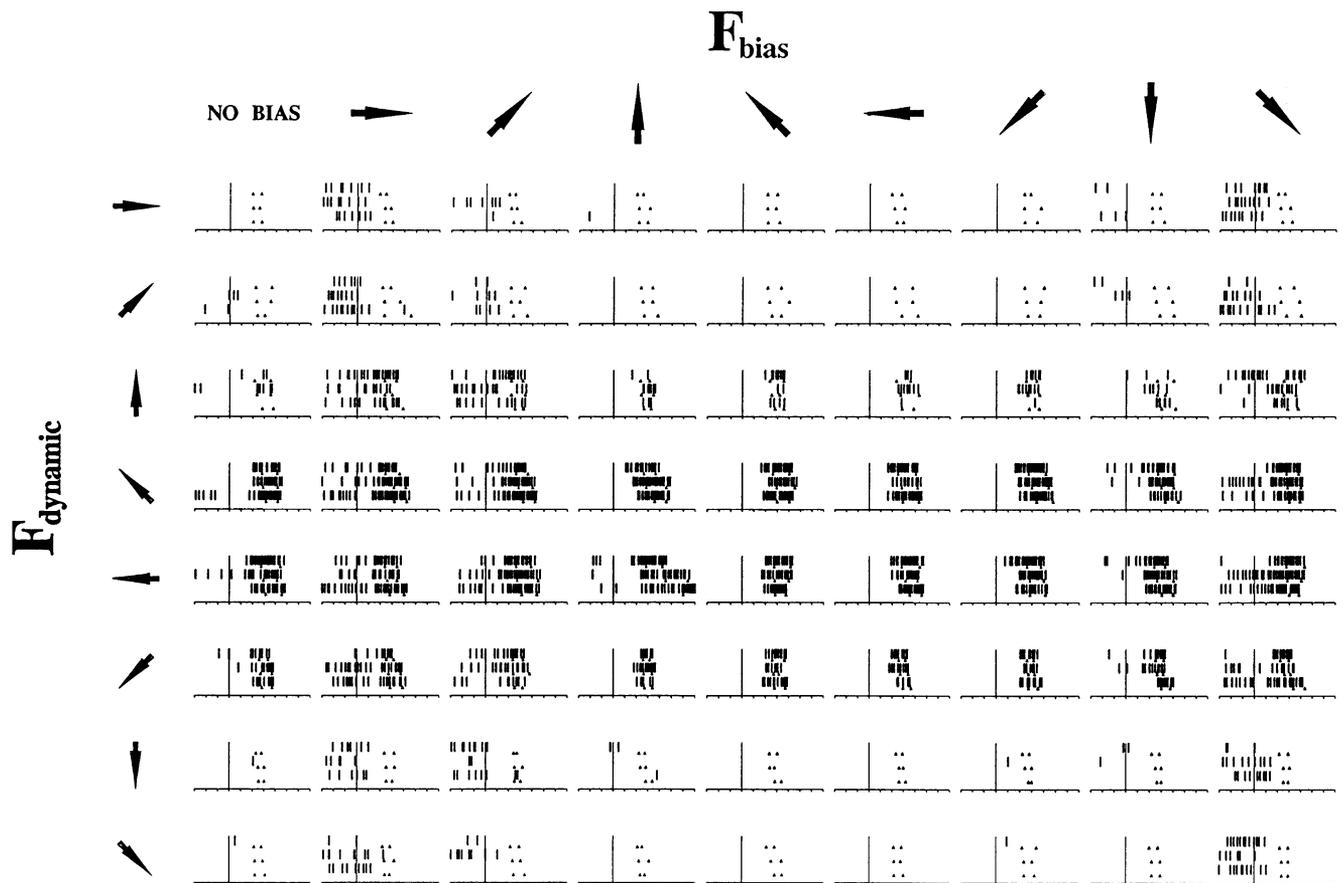
Fig. 4. Force directional tuning and its invariance across force biases are illustrated for the impulse activity (three repetitions) of one cell in the motor cortex. The directions of dynamic force and force bias are shown in the rows and columns, respectively, including the case of no force bias (first column). Rasters are aligned to the onset of the peripheral stimulus (0 time); the time scale time scale is 100 ms per division. Reprinted with permission from Georgopoulos et al. [21]. Copyright 1992 American Association for the Advancement of Science.
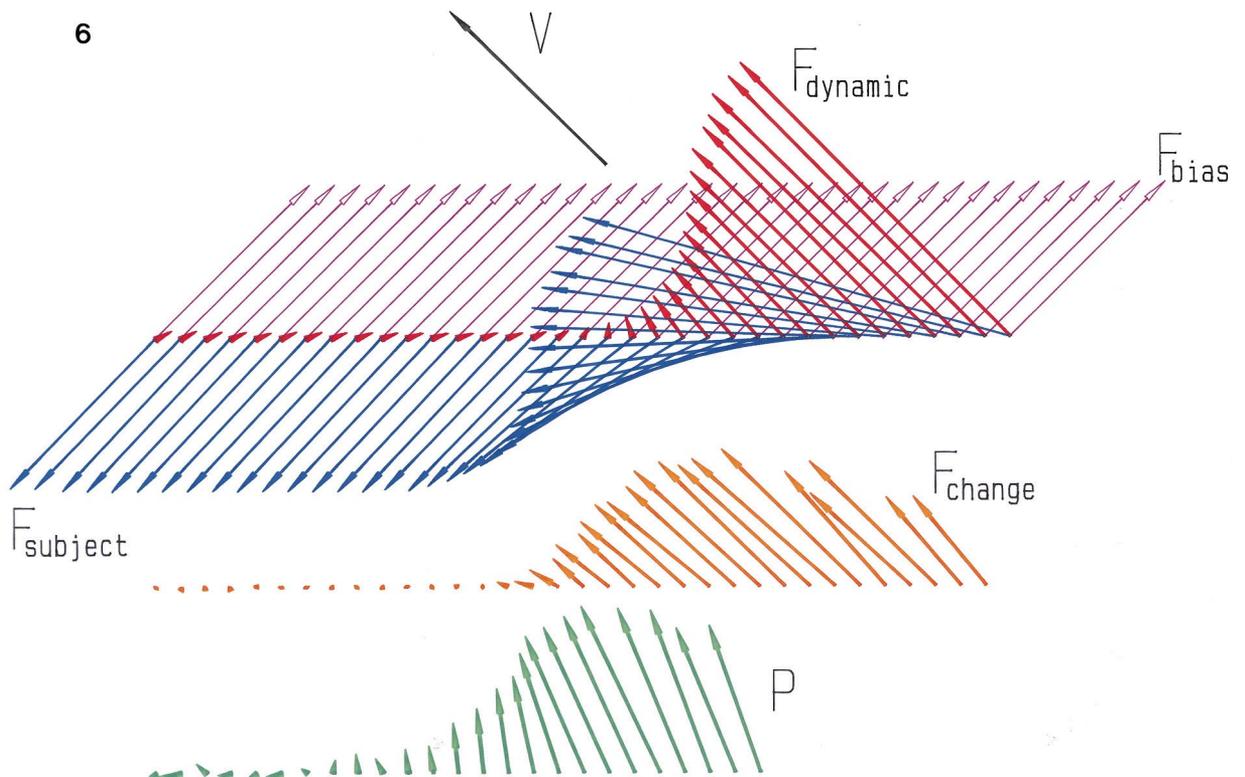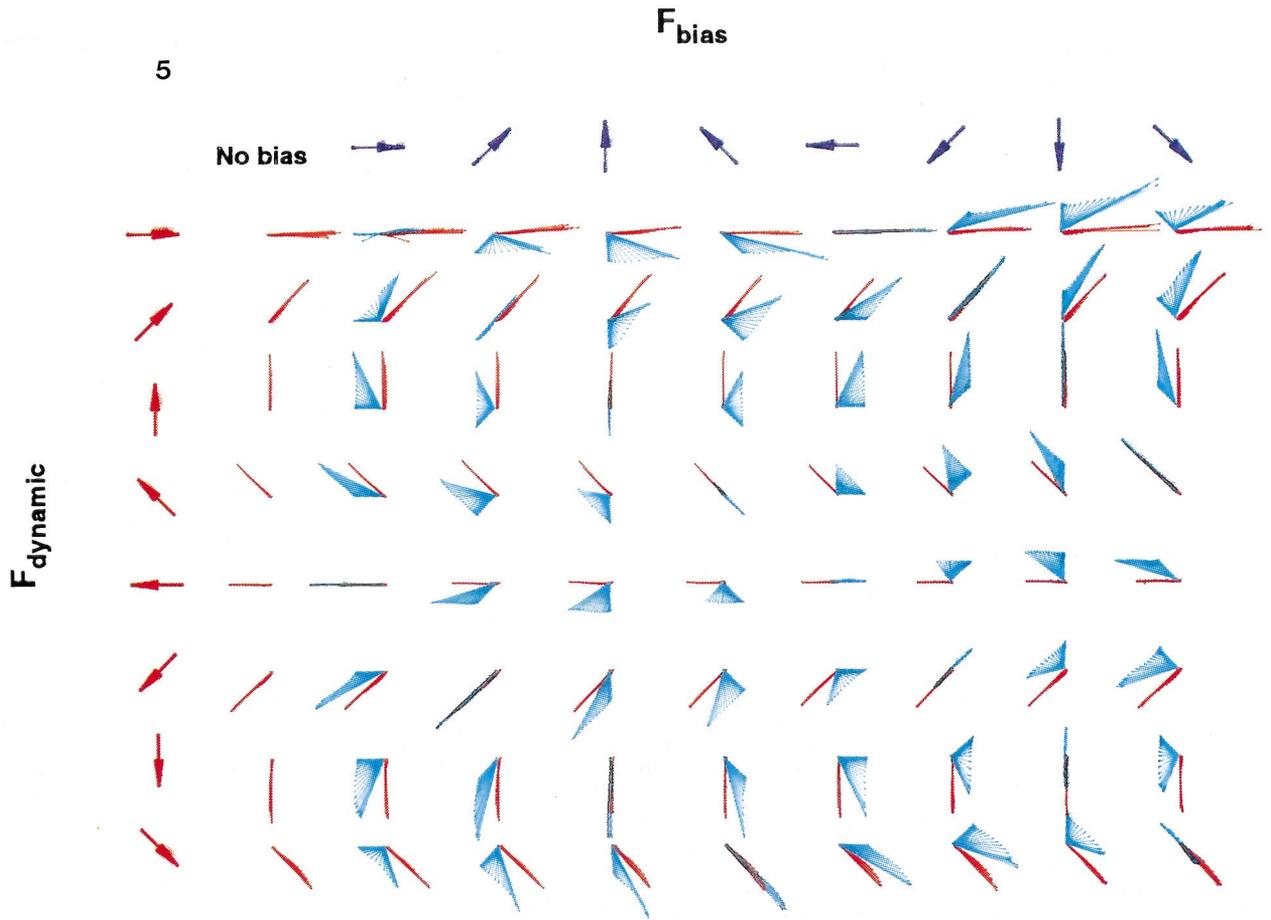
target appeared in one of eight peripheral locations on a circle of 100-g force radius, and the animal was required to produce a force pulse so that the net force-feedback cursor would move in the direction ($\pm$ 22.5°) of the target; the animal was rewarded when this cursor moved past the target, which corresponded to a net force > 100 g force. The force pulses were produced in the presence of a constant force bias (45 g) in eight different directions; in addition, the same force pulses were produced in the absence of force bias.

The main finding in the study was that 56% of the cells recorded in the motor cortex during the performance of the task were directionally tuned during the reaction and force production time; this tuning was preserved across the different force biases used (Fig. 4).

This finding suggested that the cell activity varied with the dynamic force, but not with the force exerted by the monkey ($F_{subject}$), given that the latter, unlike the former, changed dramatically dependent on the force bias (Fig. 5). The direction of the change in force and the visually defined direction also remained invariant and congruent across different force biases and could be among the directional variables to which cell activity is related. The relations of neuronal activity to the various forces were confirmed using the time-varying neuronal population vector [22,26], which was compared to: (1) the time-varying dynamic force; (2) the force exerted by the subject; and to (3) the change in force (Fig. 6). This figure clearly shows that the population vector related to the dynamic force or force change, but not to the

Fig. 5. Time-varying dynamic forces (red) and forces exerted by the subject (blue) in the presence of bias forces (purple) in various directions. Forces are averages of 10-ms samples from all trials during which tuned cells were recorded. In the No bias case (first column) the dynamic force and the subject's force were the same. Conventions are as in Fig. 4. Reprinted with permission from Georgopoulos et al. [21]. Copyright 1992 American Association for the Advancement of Science.

Fig. 6. The neuronal population vector (P) points in the direction of the dynamic force ($F_{dynamic}$), or force change (F_{change}), but not the total force exerted by the subject ($F_{subject}$). All vectors illustrated are time-varying (every 10 ms) for a particular force bias and instructed visual direction. The length of force change is 6 times that of the other force vectors. Reprinted with permission from Georgopoulos et al. [21]. Copyright 1992 American Association for the Advancement of Science.

F$_{bias}$

5

No bias

F$_{dynamic}$

6

V

F$_{dynamic}$

F$_{bias}$

F$_{subject}$

F$_{change}$
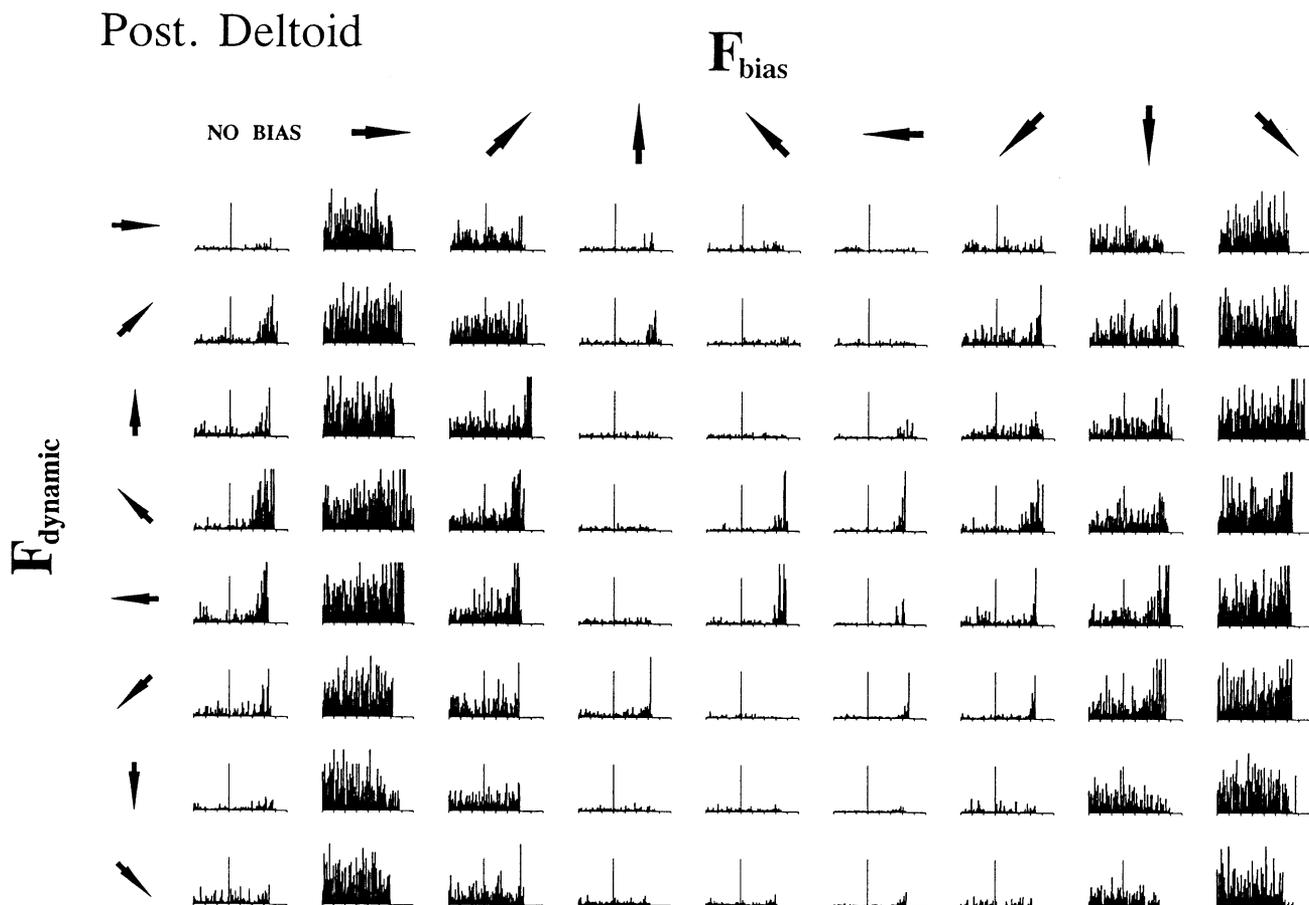
P

Post. Deltoid

$$F_{bias}$$

Fig. 7. Electromyographic activity in one muscle (posterior deltoid) recorded during the performance of the task. The activity in this muscle changes appreciably with the constant force bias. The conventions are as in Figs. 4 and 5.

force exerted by the subject. The neural activity contrasted sharply with that of the electromyographic activity from muscles active in the task which changed appreciably with the force bias (Fig. 7).

The experimental design enabled various forces to be dissociated as mentioned above. Also by design, the force pulse was truly dynamic, uncontaminated by any static components, as would have been the case had the subject been required to stop at a particular target force level. The neural activity was related to the net force and not to the subject force. Lest this appear counterintuitive, however, one must remember that the net force is equivalent to the dynamic component of the force exerted by the subject (see Fig. 3b).

Therefore, under dynamic conditions, the motor cortex seems to be preferentially involved in the control of the dynamic component of the force. An obvious corollary is that the neural activity, similarly, did not reflect the total muscle activity, but its dynamic component [75]. The findings in relation to control of dynamic force do not suggest that the motor cortex is not engaged during static force output. In fact, motor cortical cells clearly reflected the static force applied to counteract the force bias at the beginning of each trial

(see Fig. 4). When a dynamic process is superimposed on a static one, as was the case in this experiment, then the dynamic process assumes primary importance, and this is reflected in the activity of motor cortex cells.

While the study did not involve movement, the results raise a number of interesting issues about the relation between neural activity and movement parameters. Directional tuning has been documented in both static isometric [44,45,71], dynamic isometric [21] and movement [23,24,46,65] conditions. This activity cannot relate to kinematic planning of the upcoming motor output, because by definition, there are no kinematics in the isometric case. Another possibility is that this common directional tuning may relate to muscle activity [22,44,51,58,62]. However, in this isometric experiment, the directional tuning and the muscle activity were not congruent. Force is another parameter common to movement and isometric conditions, but the mechanical conditions for generating the directed motor output are very different in these two cases, that is when a mass to be accelerated is present (movement) or absent (isometric force). The presence, then, of directional tuning in both of these cases suggests that the common underlying factor for motor cortical activity

may relate to an abstract spatial representation of the motor trajectory [6,33,34,54].

The study also raises the issue of the representation of the force exerted by the subject under dynamic conditions in which only the dynamic component of the subject's force is reflected in the activity of motor cortex cells. The static component is behaviorally essential in the presence of a force bias and must be coded at some level. It is possible that the force exerted by the subject is represented at the level of the motoneuronal pools by the convergence of dynamic and static (postural) inputs from separate supraspinal structures [27,25,30] and spinal interneuronal systems [7,31], providing an ongoing integrated signal.

8. Spinal interneuronal systems and force

In a series of experiments using a spinal frog preparation, Bizzi and colleagues [7,31] microstimulated the spinal gray matter while measuring forces produced at the ankle. The animal was immobilized, and the force transducer on the ankle functioned as a clamp, allowing isometric forces to be measured. The frog leg was positioned at various locations on a two-dimensional work-surface and the forces acting on the ankle were measured at each location during stimulation of a point within the spinal gray matter. A map of the resultant force vectors showed that convergent force fields could be produced by stimulation, and these fields centered around an equilibrium point at which the forces acting on the ankle were zero. The interpretation of the force data was simplified when the forces produced by stimulation were regarded as being a composite of resting forces (static or postural) acting on the ankle prior to stimulation and 'active' forces (dynamic) generated by the stimulation. The force field produced by simultaneous stimulation at two sites within the spinal cord could be reproduced by the vector summation of the force fields obtained when each site was stimulated separately. The equilibrium points of the 'active' force fields produced by stimulation at multiple sites within the cord centered around three principal directions within the work surface.

These findings have a number of implications: (1) there is an integrated interneuronal system within the spinal cord that is capable of producing complex multijoint behaviors; (2) these complex behaviors are best understood by consideration of a separate static and dynamic control systems; and (3) force fields produced by stimulation of separate areas within the spinal gray matter are integrated by a process of vector summation. The results also relate directly to the work of Georgopoulos and colleagues [21], showing how the convergence of dynamic and static (postural) inputs from separate supraspinal structures and spinal interneuronal systems could be integrated at a spinal level.

Other spinal interneuronal systems, such as the propriospinal system in the cat [50], have been shown to be important in the patterned activation of the different muscles required for reaching. Propriospinal neurons at the C_3–C_4 level in the cat have monosynaptic connections to motoneurons supplying proximal muscles. These propriospinal neurons, in turn, have monosynaptic connections to several supraspinal systems, including the corticospinal tract. Interruption of the projections from the interneurons results in abnormal reaching movements [3]. These propriospinal interneurons may participate in the integration of reaching movements at a spinal level, and effectively translate signals from cells in the motor cortex that relate to the direction of force output of the whole limb [21] into appropriate patterns of muscle activation.

Acknowledgements

References

[1] Amos, A., Armstrong, D.M. and Marple-Horvat, D.E., Changes in the discharge patterns of cortical motor neurons associated with volitional changes in stepping in the cat, *Neurosci. Lett.*, 109 (1990) 107–112.

[2] Armstrong, D.M. and Drew, T., Discharges of pyramidal tract and other motor cortical neurones during locomotion in the cat, *J. Physiol. (Lond.)*, 346 (1984) 471–495.

[3] Alstermack, B., Lindstrom, S., Lundberg, A. and Sybirska, E., Integration in descending motor pathways controlling the forelimb in the cat. 9. Differential behavioral defects after spinal cord lesions interrupting defined pathways from higher centres to motoneurones, *Exp. Brain Res.*, 42 (1981) 299–318.

[4] Bahill, A.T., Clark, M.R. and Stark, L., The main sequence, a tool for studying human eye movements, *Math. Biosci.*, 24 (1975) 191–204.

[5] Beloozerova, I.N. and Sirota, M.G., Role of motor cortex in control of locomotion. In: V.S. Gurfinkel, M.E. Ioffe, J. Massion and J.P. Roll (Eds.), *Stance and Motion: Facts and Concepts*, Plenum, New York, pp. 163–176.

[6] Bernstein, N., *The Coordination and Regulation of Movements*, Pergamon Press, Oxford, 1967.

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

[8] Boline, J., Ashe, J., Taira, M. and Georgopoulos, A.P., Motor cortex and isometric force: dynamic vs. static processes, *Soc. Neurosci. Abstr.*, 19 (1994) 983.

[9] Chang, H.T., Ruch, T.C. and Ward, A.A., Topographical representation of muscles in motor cortex of monkeys, *J. Neurophysiol.*, 10 (1947) 39–56.

[10] Cheney, P.D. and Fetz, E.E., Functional classes of primate corticomotoneuronal cells and their relation to active force, *J. Neurophysiol.*, 44 (1980) 773–791.

[11] Conrad, B., Wiesendanger, M., Matsunami, K. and Brooks, V.B., Precentral unit activity related to control of arm movements, *Exp. Brain Res.*, 29 (1977) 85–95.

[12] Drew, T., Role of the motor cortex in the control of gait modification in the cat. In: M. Shimamura, S. Grillner and V.R. Edgerton (Eds.), *Neurobiological Basis of Human Locomotion*, Japan Scientific Societies, Tokyo, 1991, pp. 201–212.

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

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

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

[16] Fetz, E.E. and Finocchio, D.V., Correlations between activity of motor cortex cells and arm muscles during operantly conditioned response patterns, *Exp. Brain Res.*, 23 (1975) 217–240.

[17] Fetz, E.E. and Cheney, P.D., Postspike facilitation of forelimb muscle activity by primate corticomotoneuronal cells, *J. Neurophysiol.*, 44 (1980) 751–772.

[18] Flash, T. and Hogan, N., The coordination of arm movements: an experimentally confirmed mathematical model, *J. Neurosci.*, 5 (1985) 1688–1703.

[19] Flanders, M. and Herrmann, U., Two components of muscle activation: scaling with speed of arm movement, *J. Neurophysiol.*, 67 (1992) 931–943.

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

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

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

[23] Georgopoulos, A.P., Kalaska, J.F., Caminiti, R. and Massey, J.T., On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex, *J. Neurosci.*, 2 (1982) 1527–1537.

[24] Georgopoulos, A.P., Kettner, R.E. and Schwartz, A.B., Primate motor cortex and free arm movements to visual targets in three-dimensional space. II. Coding of the direction of movement by a neuronal population, *J. Neurosci.*, 8 (1988) 2928–2937.

[25] Georgopoulos, A.P. and Massey, J.T., Static versus dynamic effects in motor cortex and area 5: comparison during movement time, *Behav. Brain Res.*, 18 (1985) 159–166.

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

[27] Ghez, C., Contribution of central programs to rapid limb movement in the cat. In: H. Asanuma and V. Wilson (Eds), *Integration in the Nervous System*, Igaku-Shoin, Tokyo, 1979, pp. 305–319.

[28] Ghez, C. and Vicario, D., The control of rapid limb movement in the cat. I. Response latency, *Exp. Brain Res.*, 33 (1978) 173–189.

[29] Ghez, C. and Vicario, D., The control of rapid limb movement in the cat. II. Scaling of isometric force adjustments, *Exp. Brain Res.*, 33 (1978) 191–202.

[30] Gibson, A.R., Houk, J.C. and Kohlerman, N.J., Relation between red nucleus discharge and movement parameters in trained macaque monkey, *J. Physiol. (Lond.)*, 358 (1985) 551–570.

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

[32] Graham Brown, T. and Sherrington, C.S., On the instability of a cortical point, *Proc. R. Soc. Lond. Ser. B*, 85 (1912) 250–277.

[33] Grobstein, P., Organization in the sensorimotor interface: a case study with increased resolution. In: J.-P. Ewert and M.A. Arbib (Eds.), *Visuomotor Coordination: Amphibians, Comparisons, Models and Robots*, Plenum Press, New York, 1988, pp. 1–32.

[34] Grobstein, P., Between the retinotectal projection and directed movement: topography of a sensorimotor interface, *Brain Behav. Evol.*, 31 (1988) 34–48.

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

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

[37] Hoffman, D.S. and Luschei, E.S., Responses of monkey precentral cortical cells during a controlled biting task, *J. Neurophysiol.*, 44 (1980) 333–348.

[38] Hollerbach, J.M. and Flash, T., Dynamic interactions between limb segments during planar arm movement, *Biol. Cybern.*, 44 (1982) 67–77.

[39] Hubel, D.H., Single unit activity in striate cortex of unrestrained cats, *J. Physiol. (Lond.)*, 165 (1959) 559–568.

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

[41] Humphrey, D.R., Schmidt, E.M. and Thompson, W.D., Predicting measures of motor performance from multiple cortical spike trains, *Science*, 170 (1970) 758–762.

[42] Jackson, J.H., On the comparative study of diseases of the nervous system, *Br. Med. J.*, 2 (1889) 355–362.

[43] Jackson, J.H., On the anatomical investigation of epilepsy and epileptiform convulsions. In: J. Taylor (Ed.), *Selected Writings of John Hughlins Jackson, Vol. 2*, Hodder and Stoughton, London, 1932, p. 113.

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

[45] Kalaska, J.F. and Hyde, M.L., Area 4 and area 5: differences between the load direction-dependent discharge variability of cells during active postural fixation, *Exp. Brain Res.*, 59 (1985) 197–202.

[46] Kettner, R.E., Schwartz, A.B. and Georgopoulos, A.P., Primate motor cortex and free arm movements to visual targets in three-dimensional space. III. Positional gradients and population coding of movement direction from various movement origins, *J. Neurosci.*, 8 (1988) 2938–2947.

[47] Landgren, S., Phillips, C.G. and Porter, R., Cortical fields of origin of the monosynaptic pyramidal pathways to some alpha motoneurons of the baboon's hand and forearm, *J. Physiol. (Lond.)*, 161 (1962) 91–111.

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

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

[50] Lundberg, A., Integration in a propriospinal motor centre controlling the forelimb in the cat. In: H. Asanuma and V. Wilson (Eds.), *Integration in the Nervous System*, Igaku-Shoin, Tokyo, 1979, pp. 47–69.

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

[52] Maier, M.A. and Hepp-Reymond, M.-C., EMG activation patterns during force production in precision grip. II. Muscular synergies in the spatial and temporal domain, *Exp. Brain Res.*, 103 (1995) 123–136.

[53] Maier, M.A. and Hepp-Reymond, M.-C., EMG activation patterns during force production in precision grip. I. Contribution of 15 finger muscles to isometric force, *Exp. Brain Res.*, 103 (1995) 108–122.

[54] Masino, T. and Knusden, E.I., Distinct neural circuits control horizontal and vertical components of head movement in the barn owl, *Nature*, 345 (1990) 434–437.

[55] McKiernan, B.J., Marcario, J.K., Karrer, J.H. and Cheney, P.D., Corticomotoneuronal (CM) post-spike effects on shoulder, elbow, wrist, digit and intrinsic hand muscles during a reaching task in the monkey, *Soc. Neurosci. Abstr.*, 20 (1994) 983.

[56] Mendell, L.M. and Henneman, E., Terminals of single Ia fibers: distribution within a pool of 300 homonymous motor neurons, *Science*, 160 (1968) 96–98.

[57] Muir, R.B. and Lemon, R.N., Antidromic excitation of motoneurons by intramuscular electrical stimulation, *J. Neurosci. Methods*, 8 (1983) 73–86.

[58] Mussa-Ivaldi, F.A., Do neurons in the motor cortex encode movement direction? An alternative hypothesis, *Neurosci. Lett.*, 91 (1988) 106–111.

[59] Palmer, E. and Ashby, P., Corticospinal projections to upper limb motoneurones in humans, *J. Physiol. (Lond.)*, 448 (1992) 397–412.

[60] Ricci, G., Doane, B. and Jasper, H., Microelectrode studies of conditioning: technique and preliminary results. In: *Premier Congres International des Sciences Neurologiques*, Snoeck-Ducaju, Brussels, 1957, pp. 401–415.

[61] Riehle, A., MacKay, W.A. and Requin, J., Are extent and force independent movement parameters? Preparation- and movement-related neuronal activity in the monkey cortex, *Exp. Brain Res.*, 99 (1994) 56–74.

[62] Riehle, A., Requin, J., Neuronal correlates of the specification of movement direction and force in four cortical areas of the monkey, *Behav. Brain Res.*, 70 (1995) 1–13.

[63] Robinson, D.A., Oculomotor unit behaviour in the monkey, *J. Neurophysiol.*, 33 (1970) 393–404.

[64] Schmidt, E.M., Jost, R.G. and Davis, K.K., Reexamination of the force relationship of cortical cell discharge patterns with conditioned wrist movements, *Brain Res.*, 83 (1975) 213–223.

[65] Schwartz, A.B., Kettner, R.E. and Georgopoulos, A.P., Primate motor cortex and free arm movements to visual targets in three-dimensional space. I. Relations between single cell discharge and direction of movement, *J. Neurosci.*, 8 (1988) 2913–2927.

[66] Sejnowski, T.I. and Lisberger, S.G., Sites of motor learning in the vestibulo-ocular reflex (VOR) predicted by a dynamical network model, *Soc. Neurosci. Abstr.*, 17 (1991) 1382.

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

[68] Shinoda, Y., Yamaguchi, T. and Futami, T., Multiple axon collaterals of single corticospinal axons in the cat, *J. Neurophysiol.*, 55 (1986) 425–448.

[69] Shinoda, Y., Arnold, A.P. and Asanuma, H., Spinal branching of corticospinal axons in the cat, *Exp. Brain Res.*, 26 (1976) 215–234.

[70] Smith, A.M., Hepp-Reymond, M.-C. and Wyss, U.R., Relation of activity in precentral cortical neurons to force and rate of force change during isometric contractions of finger muscles, *Exp. Brain Res.*, 23 (1975) 315–322.

[71] Taira, M., Boline, J., Smyrnis, N., Georgopoulos, A.P. and Ashe, J., On the relations between single cell activity in the motor cortex and the direction and magnitude of three-dimensional static isometric force, *Exp. Brain Res.*, 109 (1996) 367–376.

[72] Thach, W.T., Correlation of neural discharge with pattern and force of muscular activity, joint position and direction of intended next movement in motor cortex and cerebellum, *J. Neurophysiol.*, 41 (1978) 654–676.

[73] Wannier, T.M., Maier, M.A. and Hepp-Reymond, M.-C., Contrasting properties of monkey somatosensory and motor cortex neurons activated during the control of force in precision grip, *J. Neurophysiol.*, 65 (1991) 572–589.

[74] Werner, W., Bauswein, E. and Fromm, C., Static firing rates of premotor and primary motor cortical neurons associated with torque and joint position, *Exp. Brain Res.*, 86 (1991) 293–302.

[75] Wise, S.P., Monkey motor cortex: movements, muscles, motoneurons and metrics, *Trends Neurosci.*, 16 (1993) 46–49.