Available online at www.sciencedirect.com
ScienceDirect
Journal of Physiology - Paris 101 (2007) 9–21
Journal of Physiology Paris
www.elsevier.com/locate/jphysparis

The functional role of different neural activation profiles during precision grip: An artificial neural network approach

Bernard Grandjean [a,b,c], Marie-Claude Hepp-Reymond [d], Marc A. Maier [a,b,c,*]

[a] *Inserm, U742, Paris F-75005, France*
[b] *Université Pierre et Marie Curie-Paris6, Paris F-75005, France*
[c] *Université Diderot-Paris7, Paris F-75013, France*
[d] *Institute of Neuroinformatics, University – ETH Zurich, Zurich CH-8057, Switzerland*

Abstract

A dynamic and recurrent artificial neural network was used to investigate the functional properties of firing patterns observed in the primary motor (M1) and the primary somatosensory (S1) cortex of the behaving monkey during control of precision grip force. In the behaving monkey it was found that neurons in M1 and in S1 increase their firing activity with increasing grip force, as do the intrinsic and extrinsic hand muscles implicated in the task. However, some neurons also decreased their activity as a function of increasing force. The functional implication of these latter neurons is not clear and has not been elucidated so far. In order to explore their functional implication, we therefore simulated patterns of neural activity in artificial neural networks that represent cortical, spinal and afferent neural populations and tested whether particular activity profiles would emerge as a function of the input and of the connectivity of these networks. The functional implication of units with emergent or imposed decreasing activity was then explored.

Decreasing patterns of activity in M1 units did not emerge from the networks. However, the same networks generated decreasing activity if imposed as target patterns. As indicated by the emerging weight space, M1 projection units with decreasing patterns are functionally less involved in driving alpha motoneurons than units with increasing profiles. Furthermore, these units did not provide significant fusimotor drive, whereas those with increasing profiles did. Fusimotor drive was a function of the (imposed) form of muscle spindle afferent activity: with gamma (fusimotor) drive, muscle spindle afferents provided signals other than muscle length (as observed experimentally). The network solutions thus predict a functional dichotomy between increasing and decreasing M1 neurons: the former primarily drive alpha and gamma motoneurons, the latter only weakly alpha motoneurons.

Keywords: Precision grip; Neural network; Firing pattern; Grip force; Motor cortex; Somatosensory cortex

1. Introduction

Force production in the precision grip, i.e. between the thumb and the index finger, depends on the co-activation of antagonist muscles. Thus, electromyographic (EMG) activity of task-related finger, wrist or elbow muscles increases as a function of increasing precision grip force (Smith and Bourbonnais, 1981; Hepp-Reymond et al., 1989; Maier and Hepp-Reymond, 1995). This seems to be specific to the precision grip since digit or wrist movements of simple flexion or extension require activation of agonist muscles and deactivation of antagonist muscles (Fetz and Cheney, 1980).

Studies in the behaving monkey have shown that neurons located in several motor as well as in sensory regions are strongly modulated during the control of force in the precision grip. Non-identified cells in the hand representation of the primary motor cortex (M1) fall into two classes: those that increase their firing activity with increasing force

* Corresponding author. Address: UMR-742 Inserm/Université Paris-6 et Paris-7, Université Pierre et Marie Curie, BP 23, 9, Quai Saint Bernard, Bât. C, 6ème étage 75005 Paris, France. Tel.: +33 (0) 1 44 27 34 21; fax: +33 (0) 1 44 27 34 38.
E-mail address: Marc.Maier@snv.jussieu.fr (M.A. Maier).

0928-4257/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jphysparis.2007.10.005

and those that decrease their activity with increasing force (Hepp-Reymond and Diener, 1983; Wannier et al., 1991; Hepp-Reymond et al., 1999). The discharge patterns of these neurons have been categorized into tonic, phasic–tonic and phasic components, each of which can either increase or decrease as a function of force (Table 1). The existence of a relatively large percentage of neurons with decreasing firing patterns in M1 is a puzzling finding in view of the fact that none of the muscles shows a similar behavior. It was even shown that identified corticomotoneuronal (CM) cells with post-spike facilitation of target muscles can decrease their activity with an increase of target muscle activity (Maier et al., 1993). Moreover, neurons with decreasing activity as a function of increasing grip force have also been shown to be present in other cortical motor areas, such as the premotor area (Hepp-Reymond et al., 1994, 1999), in subcortical structures such as in pallidal (Anner-Baratti et al., 1986), cerebellar neurons (Smith and Bourbonnais, 1981) and motor thalamic nuclei (Anner-Baratti et al., 1986), or as in sensory areas such as the primary somatosensory (S1) cortex (Wannier et al., 1991). Neurons with decreasing activity seem to be exclusively activated in precision grip and seem to be necessary for the co-activation of antagonist muscles.

However, how exactly these neurons with a decreasing activity are implicated in providing muscular co-contraction is not known. Dynamic and recurrent artificial neural networks with continuous (analog) units provide a tool for probing the interaction between connectivity and activity in a given network. We used such artificial neural networks to investigate the functional properties of these firing patterns. We therefore simulated patterns of neural activity in networks that represent cortical and spinal neural populations and tested whether particular activity profiles would emerge as a function of the input and of the connectivity of the networks. In particular, we asked (i) under which conditions (in terms of network connectivity and network activity) are cells with decreasing activity an emergent property of the network, and (ii) what is the functional role of cortical cells with increasing and in particular with decreasing activity profiles during control of precision grip force?

2. Materials and methods

2.1. Simulated tasks

The artificial networks were designed to simulate a precision grip task and the corresponding time-varying activity of multiple populations of neurons involved in the control of force. The monkeys were trained in a visually guided step-tracking paradigm to generate force on a transducer held between thumb and index finger (Wannier et al., 1991). The monkey increased and then held the grip force at a first lower level (1st step) and

Table 1
Type and percentage of activity profiles observed during force control in precision grip in the monkey for unidentified neurons in M1 and S1 and for the EMG (data from Wannier et al., 1991 and Hepp-Reymond et al., 1989)

Pattern	Profile	M1 (%)	S1 (%)	EMG
Tonic (t+)		20	18	Extrinsic digit muscles
Phasic (p+)		19	33	
Phasic–tonic (p+t+)		8	28	Intrinsic digit muscles
Tonic decreasing (t−)		27	10	
Phasic decreasing (p−)		6	4	
Phasic–tonic decreasing (p–t−)		9	3	
Phasic increasing– tonic decreasing (p+t−)		11	4	

then increased again the force and held it at a second higher level (2nd step). Force was released at the end of the trial, which lasted about 4 s. Thus, monkeys performing this task transform a visual signal that indicates the target force into actual precision grip force. Accordingly, our networks receive as input a target force and are required to provide as output the typical activity profiles of motor units recorded from flexor and extensor muscles (Fig. 1). This transformation is achieved within a network of four modules, each with specific connections within and among them. These modules correspond to a motor cortical (M1), a somatosensorial (S1) and segmental network as well as muscle afferents.

In addition, networks were also trained to combine the precision grip task with a subsequent alternating flexion–extension task. This forces the networks to use a single weight space for achieving both tasks, i.e. to co-activate antagonist muscles for grip force control and to activate reciprocally first the flexor and then the extensor muscles to provide a step-change in flexion and a step-change in extension. This further constrains the networks so as to generate different responses, since biological networks perform a large range of different behaviors.

2.2. Network architecture

Two network architectures have been used: (i) a basic model that includes the motor cortical and segmental network and the muscle afferents with a total of 45 units, interconnected by a 680 weights, and (ii) an extended model that adds the somatosensorial module to the basic network. This extended network consists of 59 units, interconnected by a total of 944 weights. The interconnectivity of the modules is shown in Fig. 1a and b, respectively, and provides a coarse correspondence between units in the network and neurons in specific brain regions. The operation of the force step-tracking networks is as follows.

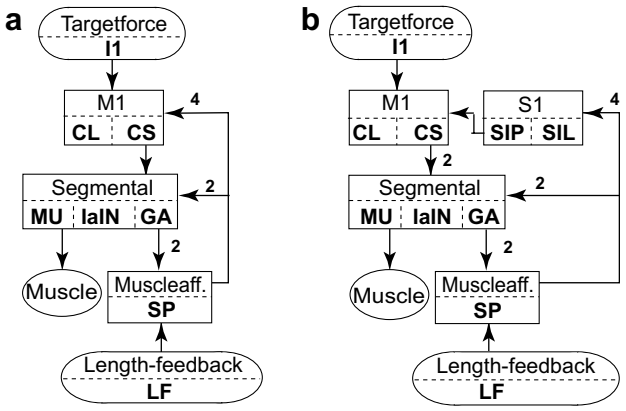

Fig. 1. General architecture of the step-tracking precision grip network. (a) Basic version. The basic version comprises three different modules: motor cortex units, spinal units and muscle afferents. The M1 module consist of an equal number of excitatory projection units (CS) and local inhibitory units (CL) which are mutually interconnected. The target force input is relayed to the M1 module, whose corticospinal projection units (CS) forward their activity to all units of the segmental population, i.e. to alpha (MU) and gamma motor (GA) units projecting to the muscle, and to units corresponding to Ia-inhibitory interneurons (IaIN). Muscle afferents, driven by a muscle length feedback (LF) and gamma (GA) units, project back to the segmental and the M1 module. The muscle activity is not modeled. A one step time delay applies to interactions between units of the same module and longer time delays between modules are indicated in number of time steps. (b) Extended version. The extended version adds a S1 module to the basic network. The S1 module has an equal number of excitatory projections units (S1P) mutually interconnected to local inhibitory units (S1L).

The *input* to the network is provided to the cortical module and is for the precision grip task represented by a step-change from a lower level (first 55 time steps) to a higher level of force (second 55 time steps). The input is represented by two units (If1, Ie2) corresponding to the (visual) target force over time (Fig. 3). For the precision grip task, these two input units change their activity in parallel (Fig. 3, 'CC'), whereas for the reciprocal flexion–extension task, these two input units are activated one after the other: first a flexion cycle (Fig. 3, 'F') indicated by a step-change in the flexion input unit (If1), while the extension input unit (Ie1) is deactivated. The opposite is the case for the subsequent extension step-change (Fig. 3, 'E').

A further two input units mimic the corresponding length changes of the flexor and extensor muscles (LFf1, LFe1) and provide the input to the respective flexor and extensor muscle spindle afferents (SPf, SPe), since there is no explicit model of the muscles, the proprioceptors or of the mechanics of the thumb and index finger in our neural networks. For the isometric precision grip task, the two inputs show a step-decrease,

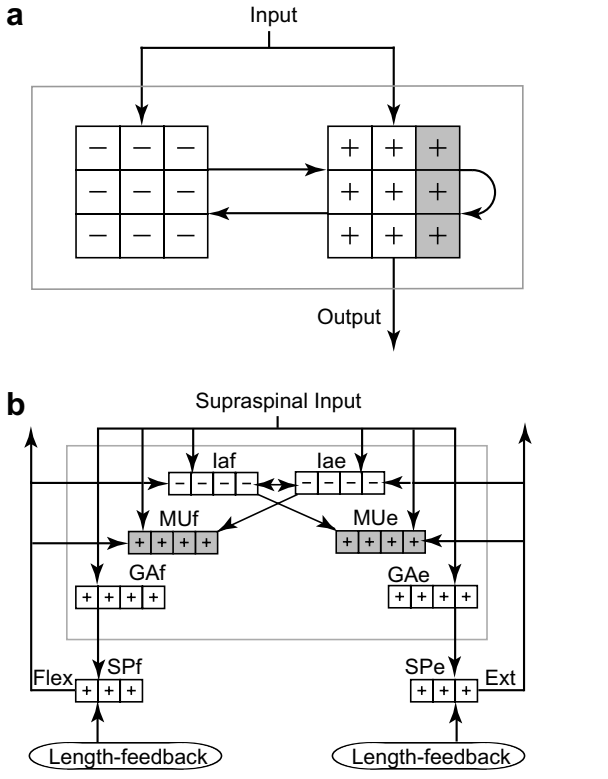

Fig. 2. Architecture of the cortical and spinal modules. (a) The M1 and S1 intra-cortical modules consist of equal numbers of excitatory and inhibitory units that are mutually interconnected. The excitatory units themselves are mutually interconnected (but without self-connections). Some excitatory units (shaded) have target activations corresponding to known firing patterns of M1 and S1 cells. The input to the cortical modules is distributed to both types of units, and the output arises from the excitatory projection units. (b) The spinal cord (segmental) module consists of units corresponding to alpha motoneurons (MU), gamma motoneurons (GA) and Ia-inhibitory interneurons (Ia), each divided into a flexor (f) and extensor (e) group. The connections between these groups are modeled according to the classical stretch reflex connections. In addition, gamma motor units drive the muscle afferents (SP). Muscle spindle afferents feed back to alpha motor and Ia-inhibitory units, as well as to supraspinal units. All alpha motor units (shaded) have target activation patterns. The supraspinal input to the segmental module is distributed to all units; the segmental output consists of alpha and gamma motor units.

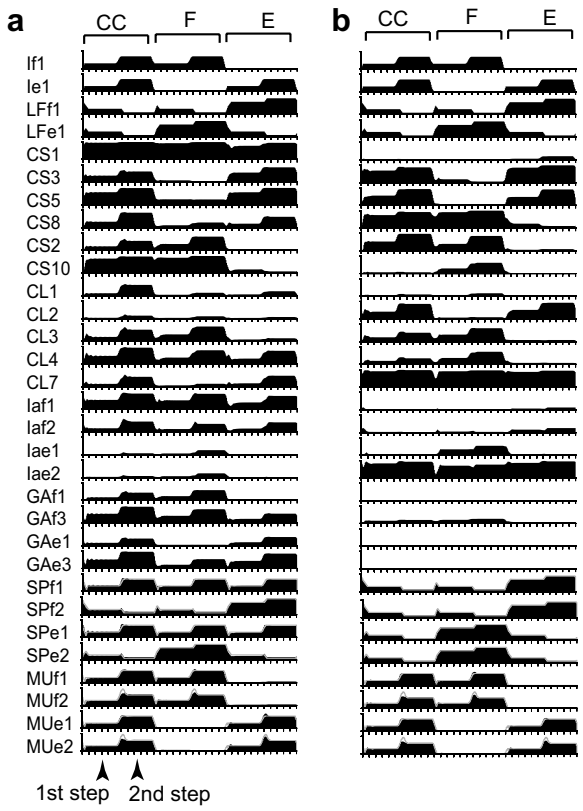

Fig. 3. Activation patterns in the basic network with constrained spinal connectivity. Precision grip task (needing co-contraction, CC) followed by flexion (F) and extension (E). For illustration purposes, the network was reduced to 31 units by eliminating units with negligible activity or weights and by combining redundant units. Input units: If1, Ie1 LFf1, LFe1. Output units with target activity patterns: alpha motor units MUf1-2, MUe1-2 and muscle spindle afferent units (SPf1,2, SPe1,2). All other units are hidden units. After learning, the purely tonic input (If1, Ie1 LFf1, LFe1) is transformed into the tonic and phasic–tonic activity profiles of the flexor (MUf) and extensor (MUe) motor units, which are first co-contracted then activated reciprocally. (a) Two types of target profiles for muscle spindle afferent units: SPf1 and SPe1 increase with grip force and with flexion–extension. SPf2 and SPe2 signal muscle length, i.e. decreasing activity during agonist contraction and increasing activity during agonist lengthening. (b) Single type of target profiles for muscle spindle afferent units: SPf1,2 and SPe1,2 signal muscle length.

which indicates the shortening of the flexor as well as of the extensor muscles with increasing force. For the reciprocal and non-isometric flexion–extension task, these two inputs diverge: for flexion, the flexor length (LFf1) signals a step-decrease, whereas the extensor signals at the same time a step-increase. The former corresponds to flexor shortening, the latter to extensor lengthening during flexion. The opposite input is given for extension. Muscle rest length is indicated by an activity of 0.5, lengthening is >0.5, shortening is <0.5.

The *motor cortical module* (Fig. 2a) corresponding to M1 consists of 10 projection units and 10 local units. This is a highly simplified model of the generic cortical circuitry and captures only the interconnectivity between local inhibitory units (CL) and excitatory projection units (CS). The input to the cortical module (i.e. 'visual' target force and muscle afferent feedback via omitted bulbar and thalamic relays) is distributed to both types of units (Porter et al., 1990). The interconnectivity between CS and CL units is modeled as follows (Fig. 2a): each local unit is reciprocally connected with all projection units and projection units are mutually interconnected (Baranyi et al., 1993), whereas local units are not interconnected. The output of the motor cortical module consists of the excitatory projection units that correspond to corticospinal neurons. In some simulations, a combination of 'free' CS units and CS units with target activations have been used.

The *segmental module* (Fig. 2b) consists of three types of units corresponding to flexor and extensor alpha motor units (MUf/e), gamma motoneurons (GAf/e) and Ia-inhibitory interneurons (Iaf/e). The 4 MU units, the 6 Ia and 6 GA units receive inputs from the cortical projection units. The spinal interconnections of these units (Fig. 2b) are based on anatomical and physiological data (Jankowska, 1992) and reflect the concept of Hultborn et al. (1979) for the spinal control of antagonist muscles. The output of the module consists of alpha and gamma motor units.

The *afferent module* represents muscle spindle afferents, i.e. units (SPf/e) driven by gamma motoneurons (GAf/e) and the equivalent of the muscle length feedback (LFf, LFe). The six afferent units feed back to the segmental level (i.e. to the homonymous alpha motor units and their corresponding Ia-inhibitory units) and supraspinal levels (i.e. to the motor cortical module in the basic network or to the somatosensorial module in the extended network).

The *somatosensorial module* corresponding to S1 consists of two types of units: 7 excitatory projection units (S1P) and 7 local inhibitory local units (S1L). The internal connectivity is similar to the motor cortical module (Fig. 2a). The module receives input from the muscle afferents, and it provides output to the motor cortical module.

2.3. Target activation patterns

The time-varying alpha motor unit activity of the flexor and extensor muscles corresponds to the main target outputs. In some simulations, we further constrained the network by incorporating representative profiles of physiological activity (target activity over 110 time steps) in particular subpopulations of units. Table 1 gives a summary of experimentally determined response classes and their frequency in the precision grip step-tracking task (Wannier et al., 1991). Briefly, primary motor cortex (M1) cells showed tonic increasing (t+) and phasic increasing (p+) activity, but also tonic decreasing activity (t−). Other firing patterns were found less often. Cells in the somatosensory cortex (S1) fell into the same classes but showed less decreasing activity. We have chosen to implement target patterns for M1 (CS) and S1 (S1P) units if they occurred in at least 5% of the task-modulated neurons. Table 1 shows the corresponding time-varying target patterns.

Motor units (EMG) showed tonic and phasic–tonic increasing discharge patterns in extrinsic and intrinsic digit muscles, respectively, and no decreasing activity (Hepp-Reymond et al., 1989) and this for agonist (flexor) and antagonist (extensor) muscles. Furthermore, the target patterns for the flexor motor units during flexion had the same profiles as during co-contraction, but the extensor motor units were inactive during this flexion period (and vice versa for extension).

In this precision grip task, the patterns of activity of spinal interneurons or gamma motor units are not known, neither that of muscle afferents. However, a microneurographic study in humans showed that muscle afferents respond to isometric contractions by increasing as well as decreasing patterns (Edin and Vallbo, 1990). The muscle spindles with decreasing patterns, to a first approximation, signaled muscle length, i.e. their decreased activity followed the shortening of the muscle. In contrast, the muscle spindles with increasing patterns signaled the opposite, i.e. they increased their activity during shortening of the muscle. Thus, target patterns for muscle spindles were implemented as increasing phasic–tonic target patterns as well as decreasing patterns, the latter following the shortening of the muscle during increasing and isometric precision grip force.

2.4. Network training

To obtain the dynamic recurrent networks of continuous units we used the temporal flow algorithm (Williams and Zipser, 1989), a backpropagation through time algorithm that incorporates time-varying activation patterns (110 time steps for the co-contraction step-tracking network and 330

time steps for the combined co-contraction and flexion–extension step tracking). The learning rate (ε) was limited to a range of 10^{-1}–10^{-4}. Starting from a configuration with initially random weights, the networks were trained for 1000 cycles. The error for each target unit corresponds to the integral of the time-varying difference between the actual and the target activation. The training procedure is not intended to resemble biological learning but provides appropriate networks that generate the required behavior. Learning curves showed a quick decrease of the error within the first 200 cycles and afterwards asymptotic behavior.

3. Results

3.1. Basic network (excluding cortical target patterns)

We tested first whether decreasing activation patterns would emerge in a network corresponding to Fig. 1a, i.e. including motor cortex units, spinal units and muscle afferents. We started with a minimally constrained version, where neither cortical target units nor any weight limitations were imposed. Starting from random connection weights, the network converged rapidly to a solution where the cortical units transformed their tonic step input into tonic and phasic–tonic motor unit output patterns. This was the case after learning the precision grip task (average error of the motor units after 1000 training cycles: 3.6%), as well as after learning precision grip and reciprocal flexion–extension task (average MU error: 4.6%). However, the flexor and extensor motor unit activations were driven essentially by the cortical projection units, whereas the other spinal units (Ia-inhibitory units, gamma motor units) and the afferents showed weak or no activations. Emergent activations of the (free) cortical projection and local units showed tonic and phasic–tonic increasing, but no decreasing patterns. Furthermore, the muscle spindle afferents all showed an increasing pattern, none a decreasing (i.e. following muscle length). In other words, the only emergent pattern, i.e. that not provided by the input, was a phasic–tonic increasing activation.

In order to provide activations of the spinal units, the spinal weight space was restrained: the minimal weight was non-zero for the following connections: gamma units projected obligatorily to spindle afferents (GA => SP), the spindle afferents projected in turn to homonymous Ia and motor units (SP => Ia, SP => MU), and the Ia units in turn inhibited the heteronymous motor units and Ia units (Ia => MU and Ia => Ia). Thus, the spinal network was constrained to the classical connectivity for the control of antagonist muscles, i.e. activation of the agonist muscle via afferents and reciprocal inhibition via Ia interneurons. Under these conditions of a spinally constrained weight space, the network still accomplished the dual tasks, with an MU error of 5.9%. Still, there were no emergent cortical units with a decreasing pattern.

We then tested how a particular muscle spindle target activity would affect the network solution. We therefore imposed two different sets of muscle spindle targets: first (Fig. 3a), a mix of muscle spindles that signal muscle length (decreasing for the co-contraction task) and those that did not (increasing pattern for muscle shortening). Second (Fig. 3b), all four muscle spindle afferents signaled muscle length. The network trained to the first case (error 4.2%), as well as that trained to the second case (error 3.5%) were able to fit their respective motor unit and spindle target activities. How did the network provide these solutions and what was the function of the cortical projection units? The weight space gives a first answer since the input–output transformation is completely determined by the weight matrix and its associated activity patterns.

Fig. 4a shows the (reduced) weight space of the network that learned the combined co-contraction and reciprocal task (its corresponding activity patterns are shown in Fig. 3a). The activity patterns for the co-contraction and subsequent flexion–extension step-changes are shown on the left as well as in the top row of Fig. 4a. The divergence of connections of any unit to other units is given by its row of output weights, and the convergence to any unit is given by the column of its input weights.

Most cortical projection units as well as local units showed tonic increasing (e.g. CS5,8) and phasic–tonic increasing activity (e.g. CS3). A single cortical projection unit showed a high, but non-modulated activity (CS1). Cortical projection units with increasing activity patterns (e.g. CS3,5,8,2,10) strongly projected to motor units, that with a non-modulated activity projected only weakly to motor units (CS1). Furthermore, cortical projection units with increasing activity during co-contraction and during flexion (e.g. CS2,10) primarily projected to flexor motor units (MUf1,2). In contrast, cortical projection units with increasing activity during co-contraction and during extension (e.g. CS3,5,8) primarily projected to extensor motor units (MUe1,2). Cortical projection units also connected to gamma motor units (GAf, GAe) and again, cortical projection units activated primarily during flexion (e.g. CS10) projected to 'flexor' gamma motor units (e.g. GAf1) and vice versa (CS3 => GAe1), although not all gamma motor units were driven in only one of the flexion–extension phase (e.g. GAf3, GAe3). Muscle spindles (SP) were driven by the convergent input of gamma motor units (GA) and the muscle length feedback (LFf1, LFe1). The exclusively increasing gamma drive provided the muscle spindle activity for those with (imposed) increasing profiles that did not follow muscle length (e.g. SPf1, SPe1), but much less so for muscle spindles that followed muscle length (e.g. SPf2, SPe2). Note that these two types of muscle spindles received the same weights from the muscle length feedback, thus the difference of increasing vs decreasing muscle spindle activity was solely due to gamma drive.

Figs. 3b and 4b, respectively, illustrate the activity profiles and the weight space for the case where all muscle spindles signal muscle length. Under these conditions, cortical projection units (CS) still connected to alpha motor units (MU) as seen previously, however, their connections to gamma motor units (GA) was generally much weaker and gamma motor unit activity was absent. Note that although the cortical network received decreasing activity

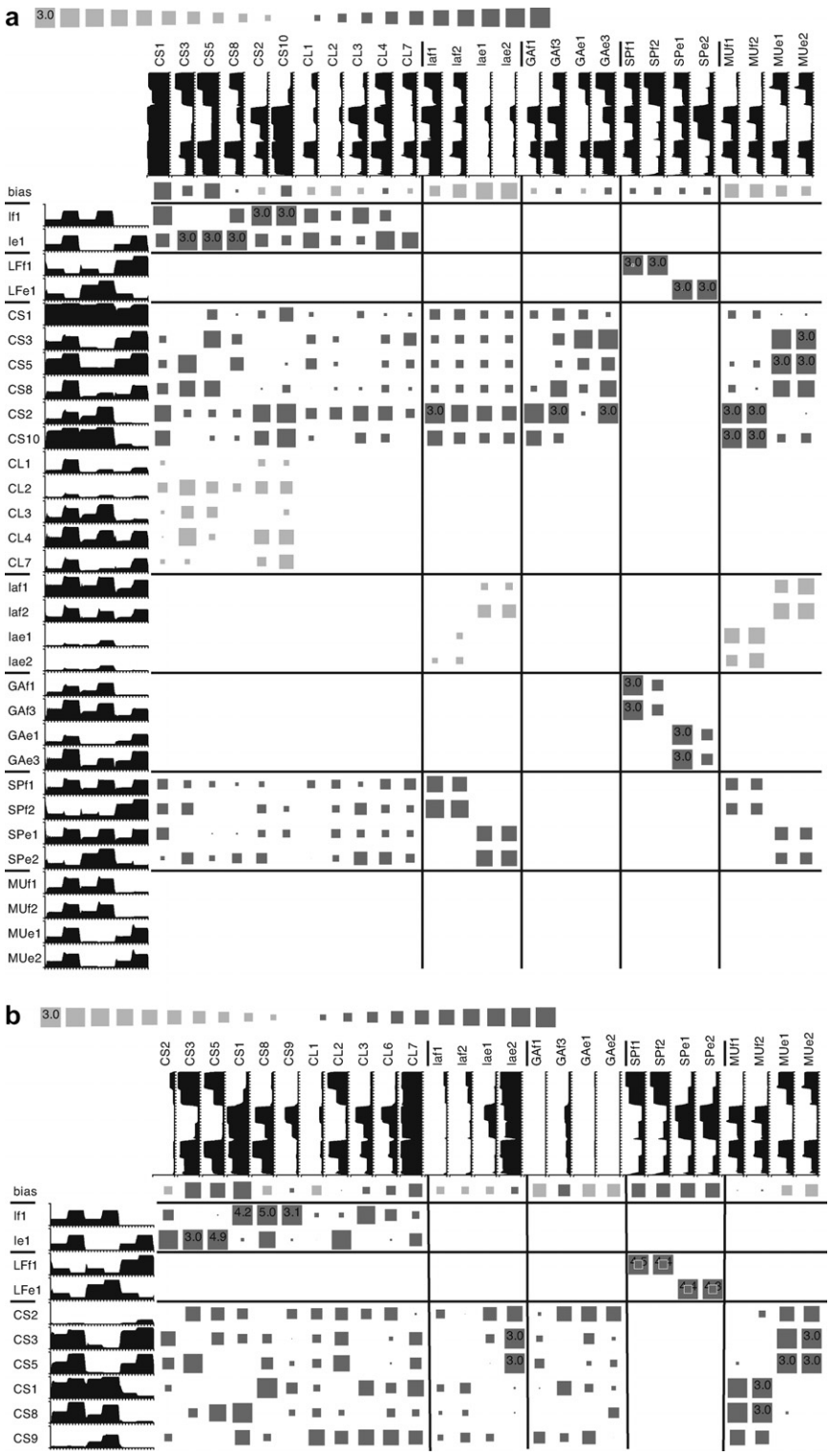

Fig. 4. Weight matrix of the basic network with constrained spinal connectivity for the combined co-contraction and reciprocal flexor–extensor task. For illustration purposes, the network was reduced to 31 units as in Fig. 3. Names and activity of units are shown at the left and along the top. The bias unit has constant maximal activity. The connection strength from row unit to column unit is symbolized by the area of the square in the range calibrated at the top $\{-3,3\}$. Excitatory and inhibitory connections are represented by black and grey squares, respectively. (a) Network weight matrix corresponding to the activations shown in Fig. 3a (mixed muscle spindle responses). The emergent weight space shows strong weights from increasing cortical projection units (CS3,5,8,2,10) to increasing spinal alpha motor units (MUf, MUe), in phase with extension (CS3,5,8 to extensor motor units MUe1,2) or with flexion (CS2,10 to flexor motor units MUf1,2), but weak weights to spinal units with decreasing activity (GAf2, GAf3, GAe3). (b) Partial (corticospinal) weight matrix corresponding to the activations shown in Fig. 3b. Imposed purely increasing muscle spindle activity. Since there is no decreasing spindle activity, the gamma motor units are inactive (and the weights between the cortical projection units and the gamma motor units can be considered zero).

via the spindles (SP), no emergent decreasing cortical profiles emerged during co-contraction (Fig. 3b).

3.2. Basic network (including cortical target patterns)

No decreasing cortical activity patterns emerged in the previous simulations (Section 3.1), nor emerged all known types of increasing profiles: in particular, purely phasic (increasing or decreasing) activity patterns were not found. This indicates that the network was not sufficiently constrained. In addition to the constraints imposed in these networks, we therefore imposed the observed cortical target patterns in the cortical projection units. Since there are no experimental data available that show the different cortical activity patterns for a reciprocal finger flexion–extension task, we started with the use of a simple network trained only for the precision grip task. Fig. 5 and 6a show the resulting weight space and corresponding activations. Under the same constraints used previously, the network converged to a solution with an average error of 5.0% and clearly produced decreasing activity profiles if given as targets (Fig. 6a): a tonic decreasing (CSt4), a phasic decreasing (CSt5), a phasic–tonic decreasing (CSt6) and a mixed phasic-increasing, tonic-decreasing unit (CSt7). In addition, also the phasic increasing cortical projection unit (CSt2), which did not emerge previously, was now present.

How was the decreasing cortical activity produced? The cortical units received two kinds of input: a direct 'visual' and increasing input (If1, Ie1) and the muscle afferent input (SP). The tonic visual input connected strongly to cortical

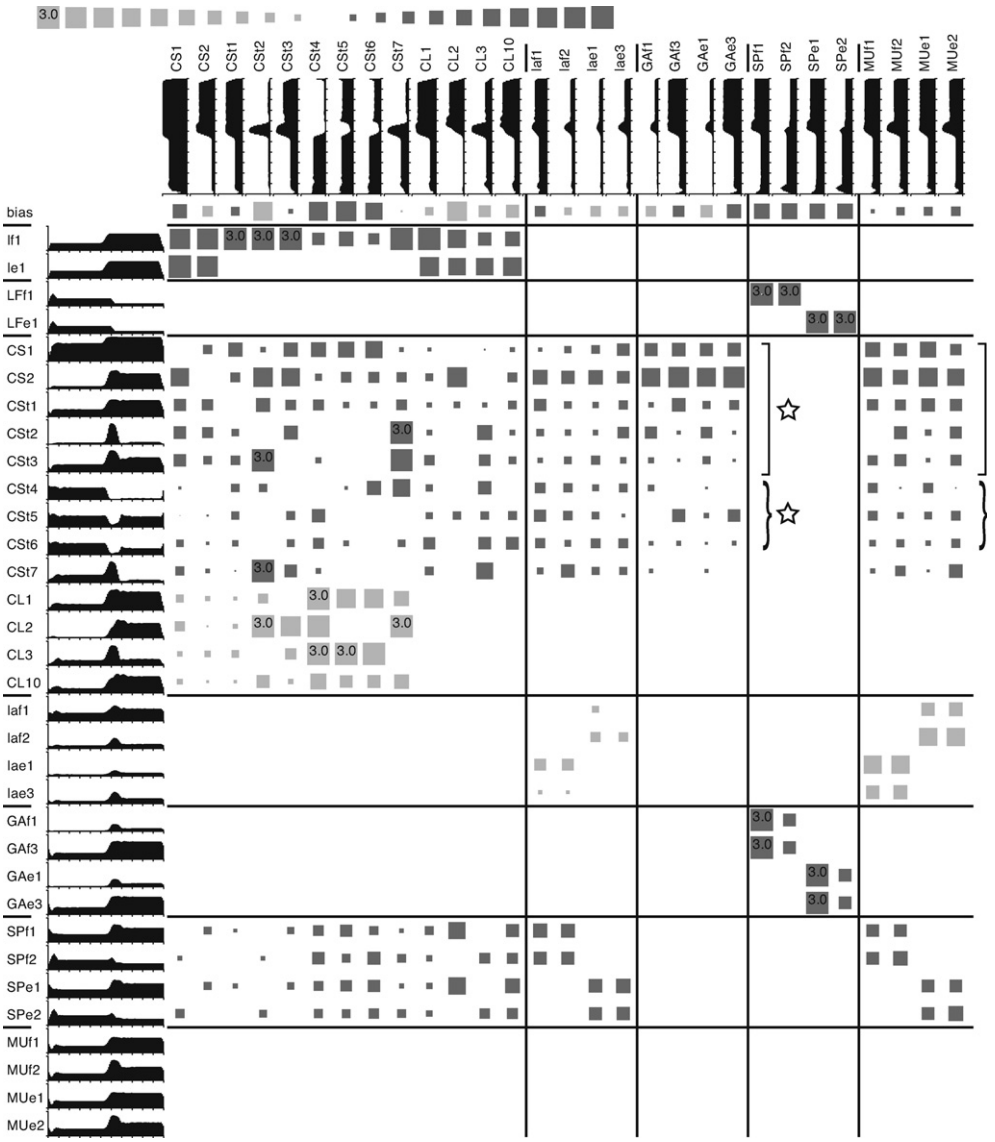

Fig. 5. Weight matrix of the basic (and reduced) network with cortical target patterns and constrained spinal connectivity for the co-contraction task only. Note stronger weights between increasing cortical projection units (CS1,2 and CSt1,2,3) and alpha motor units (MUf/e; to the left of the square bracket) compared to decreasing projection units (CSt5,6,7, left of curly bracket). Their corresponding weights to gamma motor units are shown to the left of the stared square and curly bracket, respectively.

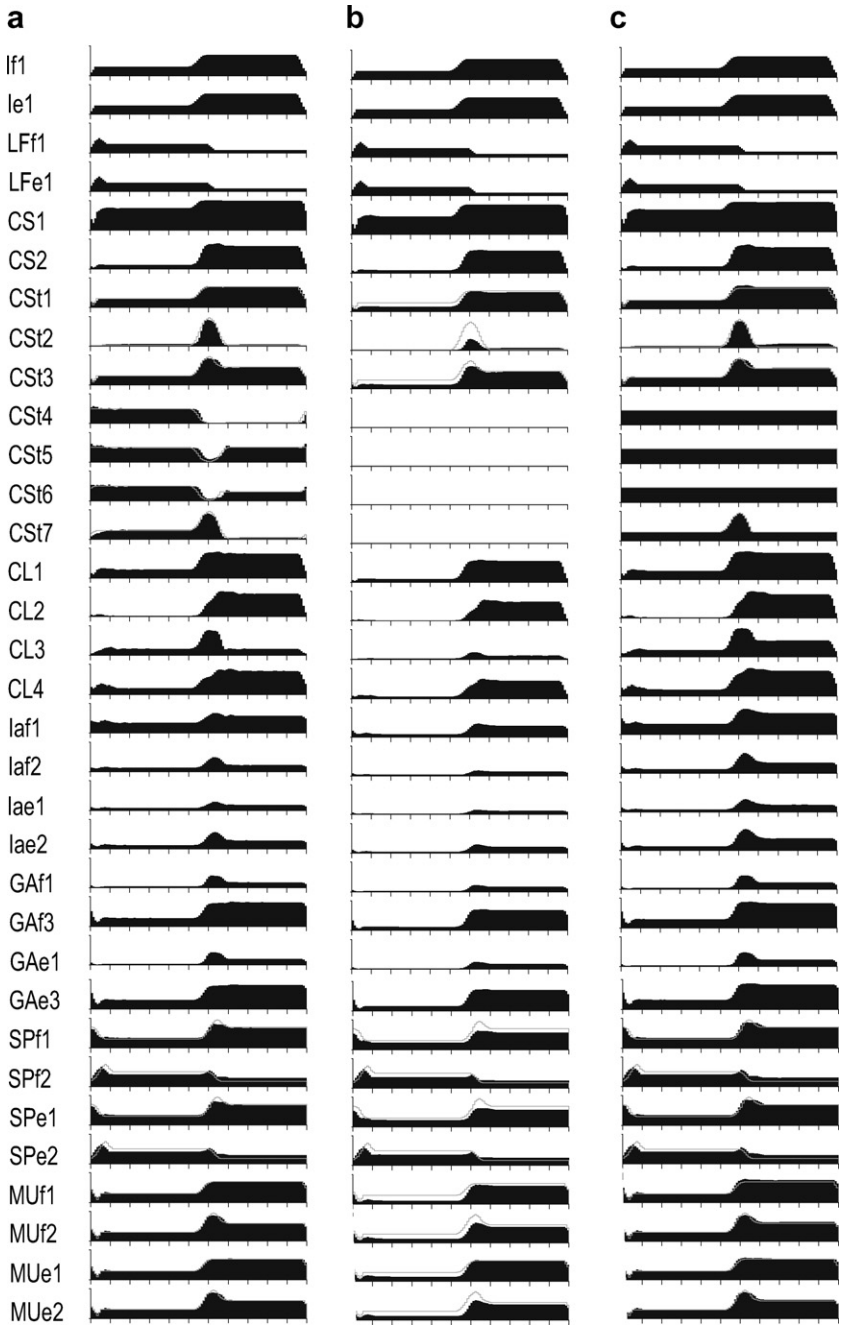

Fig. 6. Activity patterns for the network with M1 target patterns for the co-contraction task (shown in Fig. 5). (a) Activity patterns corresponding to the (intact) network shown in Fig. 5. (b) Activity patterns after elimination of M1 target units with decreasing patterns (CSt4-7). Lack of these units produces a decrease mainly of the cortical activity. (c) Activity patterns after elimination of the decreasing modulation of M1 target units. Lack of this modulation produces a slight over-activity in cortical units.

units with tonic profiles and less so to those with phasic components. The cortical input from the muscle spindles was weak for projection units with increasing profiles, stronger for those with decreasing profiles. However, decreasing cortical projection units received a mix of increasing and decreasing muscle spindle feedback. In addition, the decrementing activity also emerged from the interaction between inhibitory and excitatory cortical units: the local inhibitory units had all increasing activity patterns. They inhibited strongly the decreasing projection units and much less so the increasing projection units.

What was the function of the cortical projection units with different activity profiles in the network? Those with increasing profiles (CS1, CS2, CSt1,2,3) projected strongly to alpha motor units (Fig. 5, weights indicated to the left of the square bracket) and somewhat more weakly to gamma motor units (to the left of the stared square bracket). In contrast, those with decreasing profiles

(CSt4,5,6) projected much more weakly to the alpha motor units (Fig. 5, to the left of the curly bracket) and very weakly to gamma motor units (to the left of the stared curly bracket).

Purely phasic (increasing or decreasing) activity patterns were not found in the basic network without cortical target patterns. However, if a target given, the networks were able to produce purely phasic activity: increasing phasic activity (e.g. CSt2, Fig. 6) was achieved by convergence of inhibitory bias combined with mainly excitatory drive from projection units (Fig. 5). The opposite held for decreasing phasic activity: convergence of excitatory bias and mainly inhibitory drive from local cortical units, which are the only source for acquiring a phasic decreasing activity (Fig. 5). Furthermore, a clear pattern of connectivity between units with similar patterns of activity emerged: cortical projection units with an increasing phasic component (CSt2) projected preferentially to alpha and gamma motor units with phasic–tonic or phasic profiles or other units with phasic components. The unit with a decreasing phasic activity (CSt5) tended to project more strongly to purely tonic units (e.g. MUf1, MUf2, GAf3, GAe3) in order to counter-balance any concurrent phasic increasing input.

In order to further investigate the role of cortical units with decreasing activity patterns, we employed two techniques: (i) we deleted decreasing units, i.e. 'lesioned' the network after learning, and observed the resulting network activity, and (ii) we eliminated the task modulation of decreasing units, i.e. their activity for the second force level was the same as for the first force level. We thus eliminated their decreasing modulation, but kept their 1st level background activity.

Lesioning the cortical projection units (CSt4-7) with decreasing patterns results in the following changes (Fig. 6b): at the cortical level, both local and increasing projection units showed reduced levels of activity. This resulted in a modified spinal activity: weaker Ia activity but virtually unchanged gamma activity. In turn, the muscle afferent activity was only slightly decreased. Finally, the alpha motor unit activity was not markedly diminished.

Eliminating the decreasing part of the modulation of cortical projection units had a different effect. Fig. 6c shows that the non-modulated activity of the cortical projection units (CSt4-7) with decreasing patterns resulted in only subtle changes during the second force step: a somewhat increased activity in local cortical and spinal Ia units, but no clear effect on gamma, spindle and motor unit activity.

3.3. Extended network (including S1)

Since the decreasing firing patterns have not only been observed in the motor cortex (M1) but also in the somatosensory cortex (S1), we extended our basic network architecture in order to simulate units corresponding to the somatosensory area (Fig. 1b). In this configuration, the muscle afferent feedback was no longer delivered directly to the M1 units, but to the S1 units, whose projection units in turn connected to the M1 units.

We chose again to constrain the spinal weight space, as we did in the basic network that included M1 target units (Section 3.2). Adding S1 units without any target patterns did not fundamentally change the network solution. In this case, the network 'short-circuited' S1 and converged to solutions without activity in the S1 units. This is not surprising, since the basic network architecture was already sufficient for solving the task. However, applying target activations (t+, p+, t+p+, t−) to some of the S1 projection units induced activity in free S1 units, whether local or projection units.

Fig. 7 shows the resulting (and reduced) weight space for the combination of the precision grip and flexion–extension task. The network fitted successfully the S1 target patterns as well as the other target patterns (average error = 6.7%). Cortical target patterns from the co-contraction cycle were repeated for the flexion–extension cycle. S1 projection units indeed developed weights to M1 units, more strongly to local M1 units than to M1 projection units. In contrast, the tonic decreasing S1 target unit (SIPt4) projected preferentially to M1 projection units. The decreasing activity of this unit was generated through a strong input from local inhibitory and increasing units (SIL2,6) acting on a positive bias. It received no concomitant excitation from other excitatory S1 units (Fig. 7).

M1 projection units showed similar tendencies as described for above: increasing M1 projection units connected strongly to alpha and gamma motor units and this in phase with their predominant flexion or extension activity, but not both. Decreasing M1 projection developed weaker weights to alpha and gamma motor units.

4. Discussion

4.1. Task and data base

Our dynamic neural networks simulate experimentally obtained temporal activity patterns in a network architecture that, in a simplified way, differentiates units in the motor cortex, from units in the somatosensory cortex, from spinal units and from afferent units. These networks incorporate thus physiological and anatomical constraints and elucidate the operation of certain types of units during a simulated force-tracking task in the precision grip. In addition, these networks combine the precision grip task with a reciprocal flexion–extension task. These, as well as previous models (Maier et al., 2003, 2005), focus on the physiological issue of how motor neurons are driven by convergent input from several sources: excitatory corticospinal input, inhibitory spinal input and excitatory afferent feedback. Each of these sources provides synaptic input of a particular temporal form: here we focus on the temporal profile of cortical input during control of precision grip. One important difference to a previously published model (Maier

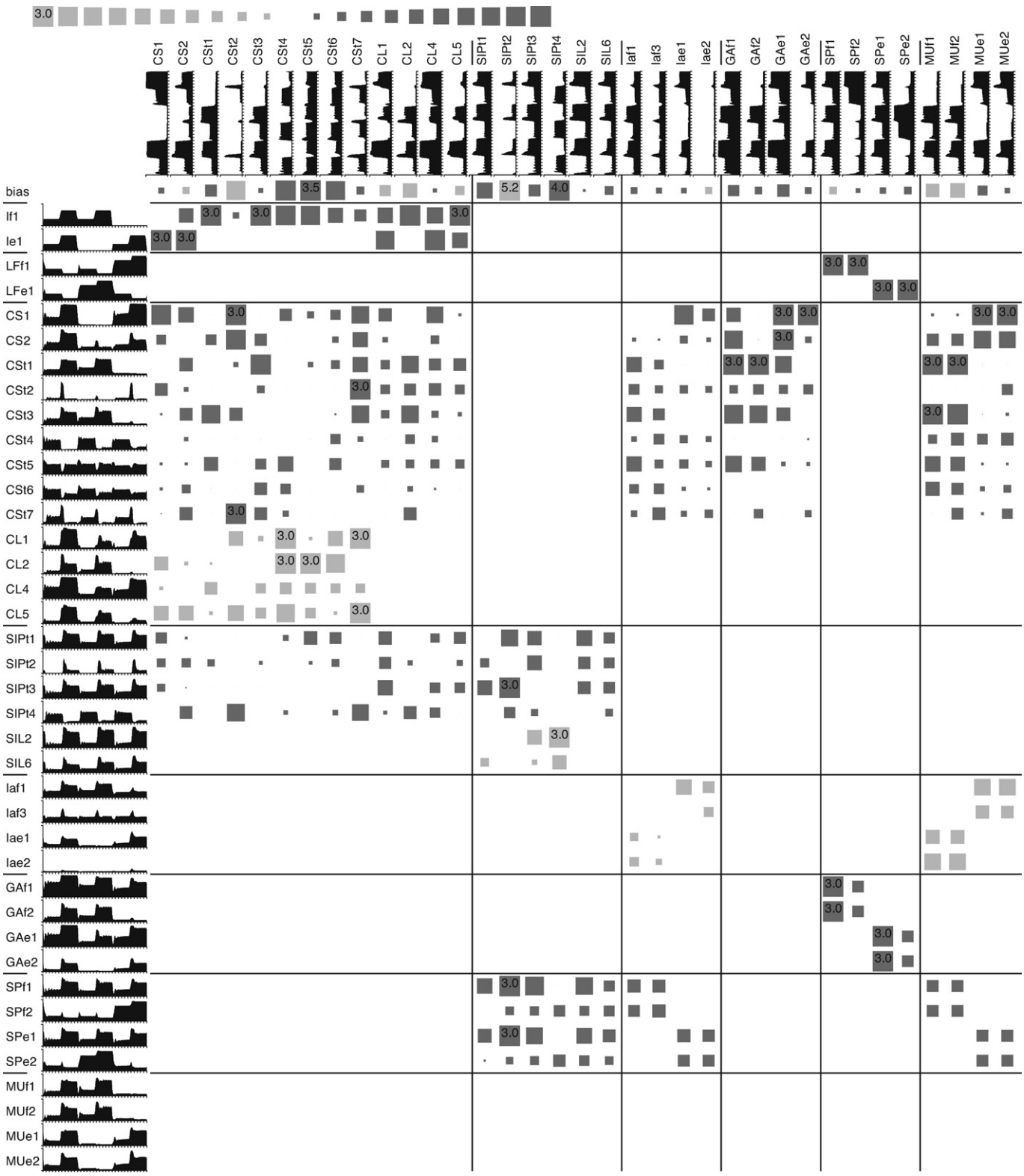

Fig. 7. Weight matrix of the extended network with M1 and S1 target patterns for the co-contraction and flexion–extension task.

et al., 2005) lies in the form and significance of the afferent feedback: here we modeled specifically muscle spindle feedback and provided as input the variation of muscle length, whereas a force feedback was provided in this earlier model.

Our modeling approach differs from approaches that also predict time-varying activity patterns based, not on the connectivity, but on the resulting movement (e.g. Todorov, 2003; Guigon et al., 2007; Trainin et al., 2007). Usually, these analytical models simulate the resulting

movement kinematics and dynamics based on optimality criterions, but they do not or only schematically simulate the central nervous aspects in terms of connectivity and 'identified' populations of neurons. In contrast, our approach is complementary and favors the central aspects, but does not simulate the resulting movement.

Single cell recordings from the behaving monkey showed that neurons in M1 cluster into different firing patterns during an isometric precision grip force task: in order to increase the grip force from a low to a higher level, neurons fall into two classes (Table 1): (i) neurons that increase their activity with force and (ii) neurons that decrease their activity with the increase in force (Wannier et al., 1991). In contrast, the EMG (and hence the motor units) of agonist and antagonist muscles showed exclusively increasing activity with an increase in force (Hepp-Reymond et al., 1989; Maier and Hepp-Reymond, 1995). M1 neurons with increasing firing patterns are assumed to drive, either directly or indirectly, spinal motor neurons. Indeed, it has been shown that many corticomotoneuronal (CM) cells provide a monosynaptic excitatory drive to their target muscles, which increases as a function of precision grip force (Maier et al., 1993). However, the function of M1 neurons with a decreasing activity profile remains to be elucidated.

4.2. Non-emergence of decreasing activity patterns in M1

In our minimally constrained networks, i.e. those where only the patterns of motor unit activity were imposed, units with decreasing activity did not emerge in the artificial neural network, whether trained for precision grip only, or for precision grip and flexion–extension. However, the same networks were able to generate decreasing activity in cortical projection units if imposed as target. Therefore, the connectivity of the network is sufficient to produce decreasing cortical activity, but the conditions or constraints are such that they do not emerge by themselves. In particular, the simplification with respect to the peripheral system, i.e. the lack of an explicit model of the muscles, the proprioceptors and the mechanics of the thumb and index finger, may contribute to the non-emergence of decreasing units.

4.3. Role of imposed decreasing vs increasing units in M1

After having imposed the cortical target patterns, we can ask what the functional role of cortical units with decreasing (and with increasing) activity profiles is during control of precision grip force. In all networks with cortical target patterns, the emergent weight space showed that cortical projection units with increasing activity patterns projected strongly, those with decreasing activity profiles projected weakly to alpha motor units. This is consistent with the observation that during a wrist (not finger) flexion–extension task, corticomotoneuronal (CM) cells all had increasing activity profiles (Fetz and Cheney, 1980). Furthermore, M1 projection units developed strong weights to motor units in phase with the flexion–extension task similar to CM cells that showed preferentially connections to agonist muscles, i.e. to flexors when active during flexion and vice versa (Fetz and Cheney, 1980) or to synergist, but not antagonist muscles during a precision grip task (Buys et al., 1986). Moreover, our network predicts that cortical projection units with decreasing profiles are not devoid of weights to alpha motor units. This prediction is in line with a small sample of CM cells that showed a decrease of activity with an increase of precision grip force. However, these CM cells did not show weaker post-spike facilitation than other CM cells (Maier et al., 1993).

There was a clear difference with regard to their respective projection to spinal gamma motor units: increasing cortical projection units projected more strongly to gamma motor units than decreasing projection units. Clearly, the gamma drive depended on the activity of the muscle spindle units. In the networks with (imposed) muscle spindle afferent target profiles that followed the changes in muscle length, gamma motor unit activity was absent, and hence there was no functional connectivity between cortical projection units and gamma motor units. However, when some muscle spindles signaled muscle length and showed a decreasing profile, and other spindles had an increase of activity with muscle shortening, gamma drive was present and was provided by cortical projection units. In this case, increasing cortical projection units provided more gamma drive than decreasing units.

It was this fusimotor drive that enabled muscle spindle units to acquire a signal different from the changes in muscle length. There is indirect experimental evidence for the presence of gamma (fusimotor) drive: muscle afferent activity in the primate increased well before movement onset in a wrist flexion extension task (Flament et al., 1992) and muscle spindle activity increased during isometric contractions of human finger extensor muscles (Edin and Vallbo, 1990). Indirect evidence also indicates that attention modulates fusimotor drive in humans (Hospod et al., 2007). However, the time course of gamma drive in the precision grip task is not known: the absence of decreasing afferent activity during muscle shortening was interpreted as evidence for an increasing drive (Flament et al., 1992). Similarly, the presence of an increasing spindle response during isometric muscle shortening was observed in 3/4 of the recorded muscle spindles and interpreted as excitatory fusimotor drive (Edin and Vallbo, 1990). However, the temporal profile of gamma drive has so far not been experimentally determined in tasks such as precision grip force control. Our model predicts that fusimotor drive is primarily provided by corticospinal neurons that increase their activity with the simultaneous increase in force, akin to the concept of α–γ co-activation.

In our model, as has been observed experimentally for corticospinal neurons (Jankowska, 1992; Baranyi et al., 1993), cortical projection units not only developed connections to motor units, but also to spinal Ia-inhibitory units as well as to each other and to local cortical inhibitory

units. Therefore, the function of decreasing cortical projection units cannot be limited to their action on motor units. We tested their global involvement in the neural network by performing artificial 'lesions' or by eliminating their task-related (decreasing) modulation. The elimination of the cortical projection units with decreasing activity had small effects on the spinal level: this is coherent with their relatively weak connectivity to alpha motor units and even weaker connectivity to gamma motor units. More marked effects were seen on the cortical level: the projection units with increasing profiles and the local cortical units showed lower levels of activity. Eliminating simply the decreasing task modulation of cortical projection units had only marginal effects on the network.

4.4. Tonic vs phasic activity patterns

The development of phasic components was a general emergent property of our networks. The networks did not receive any phasic input, neither the 'visual' input at the cortical level, nor the muscle length feedback at the afferent level had a phasic component. However, through the mutually connected cortical network of inhibitory and excitatory units, the tonic input was transformed into a phasic–tonic activity that provided excitatory drive to the one half of the alpha motor units with phasic–tonic target profiles. However, purely phasic increasing or decreasing activity was not an emergent property of our networks. The cortical network was able to provide purely phasic activity if such target patterns were given, via the interplay of excitation and inhibition in the cortical network. Our networks predict that neurons with a phasic component are preferentially connected among each other, and the same would hold for neurons with purely tonic activity. Furthermore, units with purely tonic activity received input from units with increasing and from units with decreasing phasic components: these two counteract each other to provide a purely tonic convergent output.

4.5. Addition of S1

The networks that included S1 units did not fundamentally alter the network operation compared to those where the muscle afferent signal was directly fed back to the M1 units. As in the M1 module, also the S1 module was able to produce increasing as well as decreasing activity if corresponding target patterns were provided. Again, the decreasing activity was essentially produced through the interaction of local inhibitory and excitatory projection units.

5. Conclusions

Our artificial neural networks predict the operational role of M1 neurons during the control of precision grip force. First, the model replicated several well-known facts: (i) The majority of corticomotoneuronal (CM) cells increase their activity as a function of grip force and also as a function of flexion–extension (wrist) torque. CM cells thus provide a major driving force of motor units. (ii) CM cells project preferentially to motor units active during the same phase of a flexion–extension task. (iii) Muscle spindle activity during isometric contraction and during flexion–extension does not correspond to a signal directly proportional to muscle length.

Based on the replication of these key elements of corticospinal function, these models also provide some predictions with respect to the involvement of M1 neurons that show a decreasing activity as a function of increasing precision grip force: (i) As indicated by the emerging weight space, corticospinal neurons units with decreasing patterns will functionally be less involved in driving alpha motoneurons than units with increasing profiles. (ii) M1 neurons with decreasing activity will not provide significant fusimotor drive, whereas those with increasing profiles do. (iii) 'Lesions' of decreasing M1 neurons will only weakly affect motoneuronal activity, but will modify (and generally decrease) the remaining cortical activity.

Therefore, a putative role of M1 neurons with decreasing activity may be the fine-tuning of cortical activity profiles within a network of excitatory and inhibitory neurons. This fine-tuning may be a requisite of muscular co-contraction for the control of precision grip force.

Acknowledgements

This work was in part supported by Inserm. The recurrent neural network simulator was initially developed by L.E. Shupe in the Laboratory of E.E. Fetz, Department of Physiology and Biophysics and Washington National Primate Research Center, University of Washington, Seattle, WA 98195.

References

Anner-Baratti, R., Allum, J.H., Hepp-Reymond, M.C., 1986. Neural correlates of isometric force in the "motor" thalamus. Exp. Brain Res. 63 (3), 567–580.

Baranyi, A., Szente, M.B., Woody, C.D., 1993. Electrophysiological characterization of different types of neurons recorded in vivo in the motor cortex of the cat: I. Patterns of firing activity and synaptic responses. J. Neurophysiol. 69, 1850–1864.

Buys, E.J., Lemon, R.N., Mantel, G.W., Muir, R.B., 1986. Selective facilitation of different hand muscles by single corticospinal neurones in the conscious monkey. J. Physiol. 381, 529–549.

Edin, B.B., Vallbo, A.B., 1990. Muscle afferent responses to isometric contractions and relaxations in humans. J. Neurophysiol. 63 (6), 1307–1313.

Fetz, E.E., Cheney, P.D., 1980. Postspike facilitation of forelimb muscle activity by primate corticomotoneuronal cells. J. Neurophysiol. 44 (4), 751–772.

Flament, D., Fortier, P.A., Fetz, E.E., 1992. Response patterns and postspike effects of peripheral afferents in dorsal root ganglia of behaving monkeys. J. Neurophysiol. 67, 875–889.

Guigon, E., Baraduc, P., Desmurget, M., 2007. Coding of movement- and force-related information in primate primary motor cortex: a computational approach. Eur. J. Neurosci. doi:10.1111/j.1460-9568.2007.05634.x.

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

Hepp-Reymond, M.C., Wannier, T.M., Maier, M.A., Rufener, E.A., 1989. Sensorimotor cortical control of isometric force in the monkey. Prog. Brain Res. 80, 451–463.

Hepp-Reymond, M.C., Husler, E.J., Maier, M.A., Qi, H.X., 1994. Force-related neuronal activity in two regions of the primate ventral premotor cortex. Can. J. Physiol. Pharmacol. 72 (5), 571–579.

Hepp-Reymond, M.C., Kirkpatrick-Tanner, M., Gabernet, L., Qi, H.X., Weber, B., 1999. Context-dependent force coding in motor and premotor cortical areas. Exp. Brain Res. 128, 123–133.

Hospod, V., Aimonetti, J.M., Roll, J.P., Ribot-Ciscar, E., 2007. Changes in human muscle spindle sensitivity during a proprioceptive attention task. J. Neurosci. 27 (19), 5172–5178.

Hultborn, H., Lindstrom, S., Wigstrom, H., 1979. On the function of recurrent inhibition in the spinal cord. Exp. Brain Res. 37, 399–403.

Jankowska, E., 1992. Interneuronal relay in spinal pathways from proprioceptors. Prog. Neurobiol. 38, 335–378.

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

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

Maier, M.A., Shupe, L.E., Fetz, E.E., 2003. Recurrent neural networks of integrate-and-fire cells simulating short-term memory and wrist movement tasks derived from continuous dynamic networks. J. Physiol. (Paris) 97 (4–6), 601–612.

Maier, M.A., Shupe, L.E., Fetz, E.E., 2005. A dynamic neural network model for the premotoneuronal circuitry controlling wrist movements in primates. J. Comput. Neurosci. 19 (2), 125–146.

Porter, L.L., Sakamoto, T., Asanuma, H., 1990. Morphological and physiological identification of neurons in the cat motor cortex which receive direct input from the somatic sensory cortex. Exp. Brain Res. 80, 209–212.

Smith, A.M., Bourbonnais, D., 1981. Neuronal activity in cerebellar cortex related to control of prehensile force. J. Neurophysiol. 45 (2), 286–303.

Todorov, E., 2003. On the role of primary motor cortex in arm movement control. In: Latash, M.L., Levin, M.F. (Eds.), Progress in Motor Control III (Chapter 6). Human Kinetics, Champaign, IL, pp. 125–166.

Trainin, E., Meir, R., Karniel, A., 2007. Explaining patterns of neural activity in the primary motor cortex using spinal cord and limb biomechanics models. J. Neurophysiol. 97 (5), 3736–3750.

Wannier, T.M., Maier, M.A., Hepp-Reymond, M.C., 1991. Contrasting properties of monkey somatosensory and motor cortex neurons activated during the control of force in precision grip. J. Neurophysiol. 65 (3), 572–589.

Williams, R.J., Zipser, D., 1989. A learning algorithm for continually running fully recurrent neural networks. Neural Comput. 1, 270–280.