

Modular Organization of Spinal Motor Systems

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The vertebrate nervous system produces a wide range of movement flexibly and efficiently, even though the simplest of these movements is potentially highly complex. The strategies by which the nervous system overcomes these complexities have therefore been of interest to motor physiologists for decades. In this review, the authors present a number of recent experiments that propose one strategy by which the nervous system might simplify the production of movement. These experiments suggest that spinal motor systems are organized in terms of a small number of distinct motor responses, or "modules." These distinct modules can be combined together simply to produce a wide range of different movements. Such a modular organization of spinal motor systems can potentially allow the nervous system to produce a wide range of natural behaviors in a simple and flexible manner. *NEUROSCIENTIST* 8(5):437–442, 2002. DOI: 10.1177/107385802236969

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In the natural world, some complex systems are discrete combinatorial systems—they utilize a finite number of discrete elements to create larger structures. The genetic code, language, and perceptual phenomena are examples of systems in which discrete elements and a set of rules can generate a large number of meaningful entities that are quite distinct from those of their elements. A question of considerable importance is whether this fundamental characteristic of language and genetics is also a feature of other biological systems. In particular, whether the activity of the vertebrate motor system, with its impressive capacity to find original motor solutions to an infinite set of ever-changing circumstances, results from the combinations of discrete elements.

The ease with which we move hides the complexity inherent in the execution of even the simplest tasks. Even movements we make effortlessly, such as reaching for an object, involve the activation of many thousands of motor units in numerous muscles. But is this hidden complexity simply the result of combinations of a small number of discrete building blocks? This idea, which is central to our understanding of the neural control of movement, has been offered over the years by a number of investigators. Reflexes (Sherrington 1910), elements of central pattern generators (Grillner 1981), simple movement strokes, spinal force fields (Bizzi and others 1991), and synergistic muscle contractions (Saltiel and others 2001) have variously been suggested as possible building blocks. The problem for the experimentalists that have made these suggestions, however, has been to establish qualitatively and quantitatively the existence of these conjectured building blocks, and most important,

to state the rules subserving the combinations of the discrete elements into behaviorally significant movements.

In the last few years, our group and collaborators have asked a specific question: Are there simple units (motor primitives) that can be flexibly combined to accomplish a variety of motor tasks? We have addressed this fundamental and longstanding question in experiments that utilize spinalized frogs (Bizzi and others 1991; Giszter and others 1993) and rats (Tresch and Bizzi 1999), whereas other investigators have generated corroborative evidence in cats (Lemay and Grill 2000). With an array of approaches such as microstimulation of the spinal cord, NMDA iontophoresis, and cutaneous stimulation of the hindlimb, we have provided evidence for a modular organization of the frog's and rat's spinal cord. In the present context, we use the term *module* to mean a functional unit in the spinal cord that generates a specific motor output by selecting a specific pattern of muscle activation.

The original evidence suggesting a modular organization of frog spinal motor systems came from experiments using microstimulation. In these experiments, the motor responses evoked by spinal microstimulation were characterized in terms of force fields. A force field is a mapping that associates each position of the frog's hindlimb with a corresponding force generated by the neuromuscular system. Force fields were measured by placing the frog's ankle in different locations in the leg's workspace and recording at each location the isometric force evoked in response to microstimulation of the same site in the spinal cord. The majority of force fields generated by stimulation of different areas of the lumbar gray were found to converge toward an equilibrium point (Fig. 1). In addition, such convergent force fields (CFFs) could be grouped into only a small number of classes (Giszter and others 1993). In a series of control experi-

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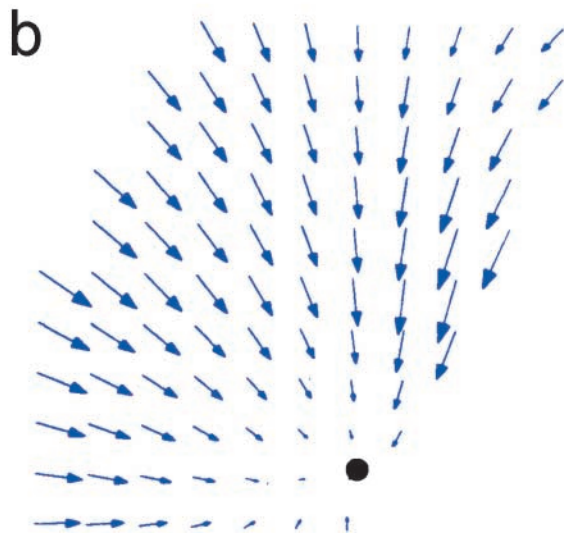
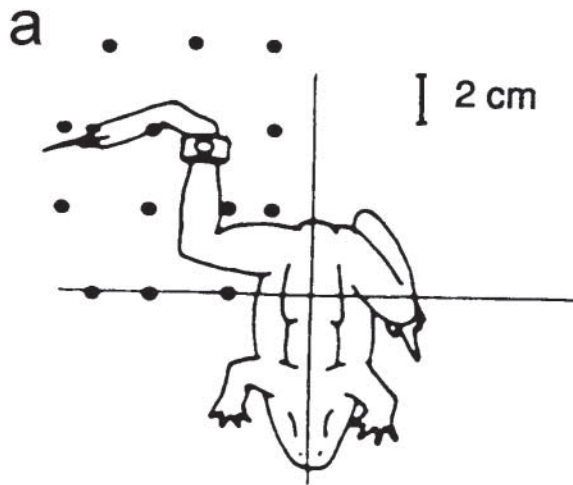


Fig. 1. Force fields evoked from microstimulation of the interneuronal regions of the frog spinal cord. *a*, The ankle of spinalized frogs was attached to a force transducer and fixed at different locations in the workspace of the leg, indicated by the filled circles in the figure. The same site in the spinal cord was electrically stimulated with the ankle in each location, and the resulting isometric force was measured. *b*, shows an example of a force field resulting from the stimulation of one such site in the spinal cord. Reproduced from Bizzi and others (1991).

ments, we have shown that this pattern of forces is not the result of current spread or random activation of the motor neurons. Neither can it result from activating the fibers of passage of the descending fibers and those of the sensory systems. On the basis of these results, Giszter and others (1993) and Saltiel and others (1998) concluded that distinct interneuronal networks of the spinal cord must be the source of specific types of CFFs.

In subsequent work obtained by evoking motor responses with focal iontophoresis of NMDA to the interneuronal regions of the spinal cord, we have confirmed the findings derived from electrical microstimulation. As with the forces evoked by electrical stimula-

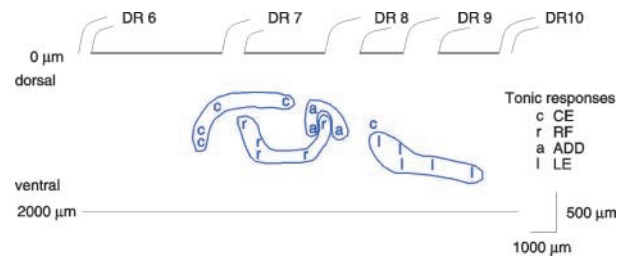


Fig. 2. Topography of spinal cord sites where NMDA elicited a tonic force response. Depth is vertical with the dorsal and ventral surfaces at depths of 0 and 2000 μm , respectively. Rostrocaudally dorsal roots DR6-DR10 delimit the positions of segments 7-10. Note the different scales for the dorsoventral and rostrocaudal axes. All sites were located 150-350 μm from the midline. The four different kinds of tonic responses are indicated by the different letter symbols. Outlines have been drawn to suggest how these tonic responses define a coarse topography. c = caudal extension, r = rostral flexion, a = adduction, l = lateral extension. Reproduced from Saltiel and others (1998).

tion, the forces evoked by NMDA stimulation fell into a small number of distinct classes. The distinct classes defined by NMDA stimulation of interneuronal sites were very similar to those defined by electrical stimulation of the same sites. Moreover, there was a topographic organization of the different classes of forces, such that each class was preferentially evoked from a distinct region of the spinal cord (Fig. 2). Taken together, the discreteness of force orientations emitted by the spinal cord and their organized mapping in the spinal cord, first noted with electrical stimulation and subsequently confirmed with NMDA stimulation, supports the concept of a modular organization of the spinal cord motor circuitry.

In addition to a single tonic force response, focal NMDA stimulation of the spinal cord more commonly elicited a rhythmic sequence of forces, where the force alternated between two or three directions. Remarkably, the directions of these rhythmic forces fell in the same classes as the tonic forces. Moreover, the topographic organization in the spinal cord of the rhythmic forces paralleled that of the tonic forces. Most of the NMDA-elicited rhythms could be grouped in a few classes characterized by the directions between which the force alternated. Each class of rhythms was elicited from two or three separate regions in the cord, and these were located close to those areas producing tonic forces of the same directions as those characterizing the rhythm (Saltiel and others 1998). Taken together, the similarity between the rhythmic and tonic forces and their related topography suggest that one mechanism for the nervous system to produce a complex (here rhythmic) behavior is through the sequential activation of spinal modules.

Another observation derived from electrical microstimulation of the frog's and the rat's spinal cord is that the fields induced by the focal activation of the cord follow the principle of vector summation. Bizzi and others (1991), Mussa-Ivaldi and others (1994), and more recently, Lemay and others (2001) showed that the simultane-

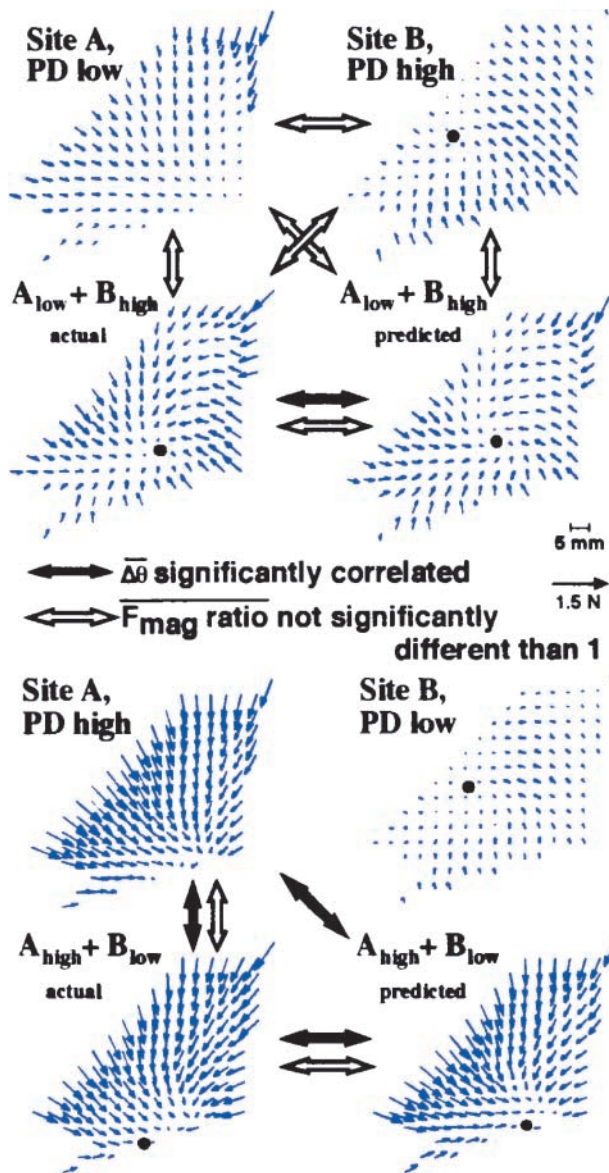


Fig. 3. Vector summation of force vectors when costimulating sites at different activation levels. The top panel shows the individual fields obtained when site A was stimulated at the lower pulse duration (PD) and site B at the higher one, and the actual (site A and B activated simultaneously) and predicted (from linear summation of the forces at each position) fields obtained from costimulation of the two sites. The bottom panel shows the results when the levels of activation were switched. Similarity between fields is indicated by a black arrow indicating no difference in average angular deviation across the measured vectors, and a white arrow indicating that the force magnitude ratio across positions is not different than 1. The fields produced by the two combinations of activation levels (*top* and *bottom* panel) were different from each other, showing the possibility of creating a variety of fields by modulating the contribution of each original site to the summated response. Reproduced from Lemay and others (2001).

ous stimulation of two sites, each generating a different force field, results in the vector sum of the two fields in most instances (Fig. 3). When the pattern of forces recorded at the ankle following costimulation were com-

pared with those computed by summation of the two individual fields, Mussa-Ivaldi and others (1994) found that the “costimulation fields” and the “summation fields” were equivalent in more than 87% of cases. Similar results have been obtained by Tresch and Bizzi (1999) by stimulating the spinal cord of the rat. Recently, Kargo and Giszter (2000) showed that such a principle of force field summation also underlies the control of limb trajectories in the spinalized frog during natural behaviors.

Vector summation of force fields implies that the complex nonlinearities that characterize the interactions both among neurons and between neurons and muscles are in some way eliminated. More important, this result has led to a novel hypothesis for explaining movement and posture based on combinations of few modules. These modules may be viewed as representing an elementary alphabet from which, through superimposition, a vast number of actions could be fashioned by impulses conveyed by supraspinal pathways and/or by the reflex pathways. Through computational analysis, Mussa-Ivaldi and Giszter (1992) and Mussa-Ivaldi (1997) verified that this view of generation of movement and posture has the competence for controlling a wide repertoire of movements.

The force vectors that characterize the fields described by Bizzi and others (1991), Mussa-Ivaldi and others (1994), and Giszter and others (1993) are the expression of specific groups of synergistically active muscles evoked either by the microinjection of NMDA or by the electrical stimulation of the interneuronal areas of the spinal cord. Recently, our laboratory has developed a novel method to identify muscle synergies with the help of a computational analysis.

The question of the existence of muscle synergies has been addressed in the past by studying the correlations between pairs of muscles involved in different forms of a motor task. This approach has failed, in many cases, to provide clear evidence for muscle synergies. For example, only a few pairs of hand muscles involved in isometric precision grip in humans appeared to be correlated at different levels of force magnitude (Hepp-Reymond and others 1996). An earlier study of human elbow muscles during isometric force production over a range of directions also found that the patterns of coactivation of muscle pairs are in most cases more complicated than expected for a synergy (Buchanan and others 1986).

One problem with the use of correlations to assess the existence of synergies is that if the same muscle is recruited simultaneously in more than one synergy, muscle correlations may be weak even within a synergy. The simple example in Figure 4 illustrates this point. If three muscles are recruited as part of a single synergy (as in Fig. 4a), their activities lie on a one-dimensional subspace (Fig. 4b), that is, these activities are all generated scaling a single vector. The activation of each pair of muscles is therefore highly correlated (Fig. 4c). When the same muscles are recruited by two synergies (Fig. 4d), each with a specific balance, their activities lie in a

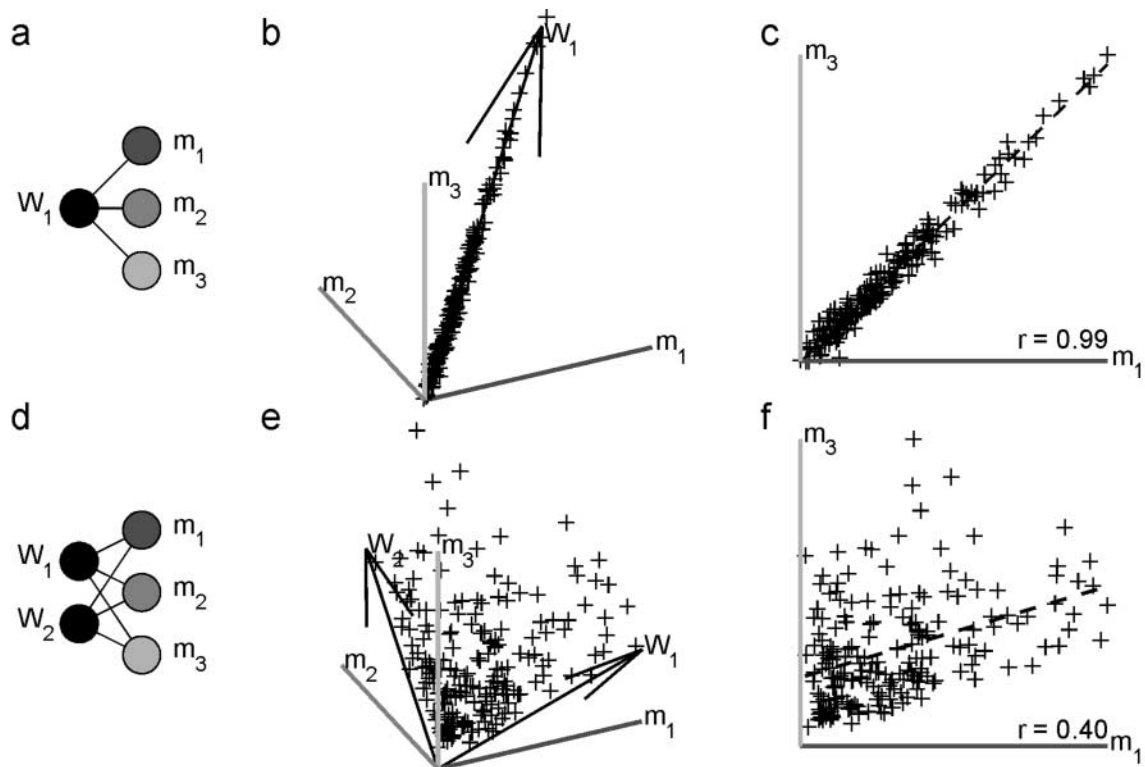


Fig. 4. Responses generated by combinations of muscle synergies may show low correlation between the activities of muscle pairs. A muscle synergy is defined here as the recruitment of a group of muscles with a specific balance of activation. If only one synergy is activated at a time (a), a set of responses obtained by changing the level of activation of a synergy is obtained by scaling a single vector in the muscle activity space (b). In this case, all pairs of muscles have highly correlated activations (c). If instead two synergies are coactivated (d), the set of responses are generated by combining two vectors and the activities of the muscles lie on a plane (e). The correlation between two of the three muscles is now much lower (f).

two-dimensional subspace (Fig. 4e) and their correlations are much weaker (Fig. 4f). Nonetheless, the fact that these activations are generated by scaling and combining two synergies is reflected by the low dimensionality of the activation subspace with respect to the total number of muscles. This simple example suggests that to recover a synergistic structure in the observed muscle patterns, it is necessary to examine their multidimensional structure.

We developed a new method to extract muscle synergies from a large set of muscle patterns. This method identifies a set of N vectors $\{\mathbf{w}_i\}_{i=1..N}$ in muscle activity space, that is, muscle synergies, which can be scaled and combined to best reconstruct all the observed patterns $\{\mathbf{m}_j^{obs}\}$, that is,

$$\mathbf{m}_j^{obs} \approx \mathbf{m}_j^{pre} = \sum_{i=1}^N c_{ij} \mathbf{w}_i.$$

Because muscle activation is a nonnegative quantity, we imposed a nonnegativity constraint on both synergies and combination coefficients. These synergies are obtained by minimization of the total squared reconstruction error $E^2 = \sum_j \|\mathbf{m}_j^{obs} - \mathbf{m}_j^{pre}\|^2$ using an iterative optimization procedure. After initializing synergies and coefficients with random positive values, the following two steps are iterated until the error stops decreasing. First, given the synergies, for each observed pattern \mathbf{m}_j^{obs} , a nonnegative least-squares minimization is used to find

a set of nonnegative coefficients c_{ij} for which the predicted pattern is closest to the observed one. Second, given the coefficients, a new set of synergies is constructed, muscle by muscle, using again nonnegative least-squares minimization. This iterative procedure is terminated when the reconstruction error stops decreasing.

Using these computational methods, a recent study has examined whether the muscle activation patterns evoked by noxious cutaneous stimulation consist in the combination of a small number of muscle synergies.

Tresch and others (1999) examined the muscle activation patterns produced in the withdrawal reflexes evoked by noxious cutaneous stimulation of the hindlimb of spinalized frogs. By scratching different regions of the hindlimb skin surface, they evoked a range of muscle activation patterns. These patterns varied systematically with the location of the stimulation, such that the muscle activations tended to move the limb away from the site of stimulation. Figure 5a shows an example of responses evoked from stimulation of one site of the hindlimb, on the front of the leg near the knee. Figure 5b shows the averaged EMG activity for each muscle in the responses shown in Figure 5a. This stimulation evoked responses that, although generally similar, showed a degree of variability from one response to the next. Tresch and others (1999) then examined whether this variability in

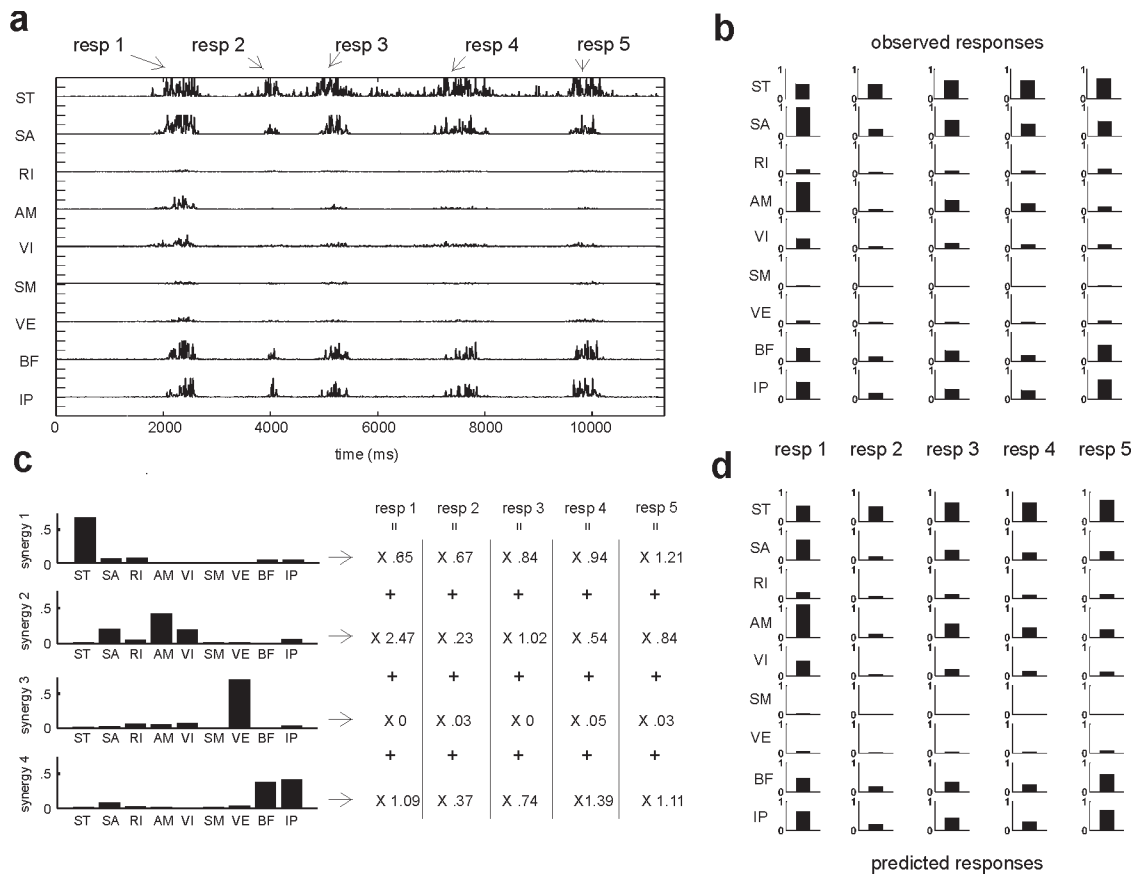


Fig. 5. Example of muscle covariation patterns within evoked responses. (a) shows the raw EMGs for five responses evoked from stimulation of the same skin region near the rostral surface of the knee. (b) shows the averaged, normalized activation for the muscles recorded in each of the responses shown in (a). Note that each muscle was normalized to the maximal value observed for that muscle across all responses evoked from any stimulation site in this animal. As a result, the muscle balances seen in (a) are slightly different than those shown in (b). (c) shows how these responses could be explained as a linear combination of a set of muscle synergies. The synergies obtained from applying the algorithm described in the text to the entire set of responses obtained from this animal are shown to the *left*. The weightings of each of these synergies used to reconstruct the responses in (b) are shown to the *right*. (d) shows the responses resulting from the combination of muscle synergies shown in (c). Reproduced from Tresch and others (1999).

responses evoked at a particular site, as well as the systematic variation between responses from different sites, could be explained as the combination of a small number of muscle synergies.

Figure 5c shows the four synergies extracted using the methods described above and how they reconstructed the responses observed in Figure 5a. For example, in reconstructing the first response, the algorithm used 0.65 times the first synergy plus 2.47 times the second synergy, 0 times the third synergy, and 1.09 times the fourth synergy. This weighted sum of these synergies gave the predicted responses shown in the Figure 5d, using equation 1 of the previous section. As can be seen from the figure, the algorithm reconstructed the observed responses with a high degree of fidelity, predicting greater than 90% of the variance over the entire set of responses in all frogs examined. Thus, the results of this study suggested that the muscle activation patterns evoked from noxious cutaneous stimulation of the frog hindlimb could be explained as the combination of a small number of muscle synergies.

Also of interest is the fact that Tresch (1997) compared the distinct muscle synergies derived from cutaneous stimulation with the patterns of muscle activation evoked by microstimulation of the frog spinal cord (the CFFs identified by our previous research). Tresch found that the two sets of EMG responses were very similar to one another. In addition, the synergies evoked by NMDA (Saltiel and others 2001) appear to be qualitatively similar to those described by Tresch.

There remains the concern as to whether the synergies that we have extracted might simply represent the outcome of a statistical fitting technique rather than synergies genuinely encoded by the spinal cord. Again the comparison of our synergies to those extracted from many natural behaviors should help address this question. In particular, finding substantial sharing of synergies extracted from different EMG data sets, for example, NMDA, a broad range of cutaneous behaviors, and locomotion, would support the idea that these synergies represent building blocks for the construction of movement by the spinal cord. The preliminary finding of sim-

ilarity between the synergies extracted from two data sets, NMDA and cutaneous as mentioned above, is a first step in that direction.

In summary, the experiments described in this review provide evidence for a modular organization of spinal motor systems. Using a range of behavioral, physiological, and computational techniques, these experiments identified a small set of “modules” organized by spinal motor systems. From this limited set, a wider range of movements could be produced utilizing simple combinatorial mechanisms, and recent experiments have provided evidence that such combinations are in fact utilized during natural behaviors in the frog. Taken together, this work suggests that, similar to other complex systems in nature, the vertebrate motor system utilizes the flexible combination of discrete elements to produce a wide range of motor behaviors.

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