

Stimulating News about Modular Motor Control

Jörn Diedrichsen^{1,*} and Joseph Classen^{2,*}

¹Institute of Cognitive Neuroscience, University College London, London, United Kingdom

²Department of Neurology, University Hospital, Leipzig, Germany

*Correspondence: j.diedrichsen@ucl.ac.uk (J.D.), joseph.classen@medizin.uni-leipzig.de (J.C.)

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How does the motor system efficiently control dexterous finger movements? A study by Overduin et al. (2012) shows that muscle activity patterns elicited by cortical microstimulation matched those extracted from natural movements and hence could constitute the building blocks for movement production.

Among all rich movement repertoires, primate finger movements occupy a uniquely large space. Accomplishing the generation of such dexterous movements represents a special challenge to the nervous system. Many muscle and joint movements need to be controlled efficiently and accurately. How does the brain perform this complicated task with such apparent ease?

To obtain a deeper insight into this question, we must study the system against the background of the movements that it performs regularly. In visual neuroscience, there is a good precedent for this approach. Our understanding of the visual system has been greatly advanced by considering how the statistics of natural images shapes the tuning properties of individual neurons (i.e., Olshausen and Field, 1996). Equivalently, the neuroscientific investigation of the motor system needs to consider the natural statistics of movement. The paper “Microstimulation Activates a Handful of Muscle Synergies” by Overduin and colleagues in this issue of Neuron (Overduin et al., 2012) now provides an important step in this direction, and shows how the cortico-spinal motor system encodes neural patterns related to generating frequently performed movements.

The authors stimulated the rostral motor and caudal premotor cortices in two awake behaving monkeys, and carefully recorded the muscle EMG and hand movements. For each stimulation site, they found a slightly different pattern of muscular activity in the 15–19 recorded muscles. The evoked patterns displayed certain regularities: they occupied a relatively low-dimensional subspace in the space of all possible muscular activation patterns. Hence, a large portion of the

variance could be explained by a restricted set of linear factors, so-called *muscle synergies*. Crucially, however, the evoked patterns occupied the same subspace as the muscular activation patterns that were observed when the monkeys manipulated objects of different shape. The muscle synergies extracted from stimulation and from natural behavior, therefore, were in a good agreement. This reflects that the patterns of muscular activity derived from the stimulation match those that underlie the highly practiced everyday activities of the monkey.

The observation that movement activity can be well *characterized* by a set of muscular synergies then leads to the hypothesis that movements may be *controlled* by a small set of flexible modules. Empirical evidence for muscle synergies has come mostly from studies that show that muscle activities or joint movements can be described by combinations of a small set of linear features (Santello et al., 1998). From this observation alone, however, we cannot conclude that muscle synergies are explicitly encoded within the nervous system, let alone that they are encoded at any particular level. Rather, constraints of the tasks (Diedrichsen et al., 2010) and the musculoskeletal system (Kutch and Valero-Cuevas, 2012) may explain many of the observed regularities in the behavior. Therefore, studies employing electrical neuronal stimulation (Bizzi et al., 1991) are important in gaining further insight into the neural representation of synergies.

The current study now provides a strong and compelling demonstration of the principle that the output organization of the cortico-spinal system reflects to a large

degree the structure of the activities performed by the animal. With this insight, it provides a substantial extension of studies in human subjects using TMS stimulation and kinematic recording (Gentner and Classen, 2006).

An important methodological feature of the study is the use of relatively long (150ms) stimulation trains. Previous work by Graziano and colleagues (Graziano et al., 2002) have suggested that activation of neural circuits by long stimulation trains drive the limb to a specific endpoint posture that is independent of its starting position. To achieve this kinematic pattern, muscular activity evoked by stimulation ought to depend on the starting posture of the arm, because different movement directions require different forces. The evidence for such posture-dependent synergies, however, has been mixed. While some authors have found such dependencies (Graziano et al., 2004), other authors, using relatively similar techniques, have not (Griffin et al., 2011). The current study by Overduin et al. (2012) now demonstrates that, while stimulation tended to drive the hand toward certain postures, the patterns of muscle activity appeared to be relatively stable over different starting postures of the hand. This apparent discrepancy of the results, however, may be at least partially explained by the passive forces arising from the biomechanical properties of muscles and tendons, which act on fingers of relatively low mass.

From a functional perspective, at least, it is clear that the motor cortical activity should show postural dependency. What matters in the end to the animal is not whether the correct patterns of muscles are activated, but whether the movement and forces produced by the

hand lead to successful task performance. For this, muscular activation patterns need to be dependent on the current posture; however, whether activity in motor cortical circuits should drive the limb invariantly to certain endpoint positions is less clear. Rather, it is possible that the motor cortex encodes relatively stable muscular synergies, which are gated by posture (i.e., the muscles show multiplicative tuning between the desired force and postural input).

Another interesting open question concerns the level at which regularities in muscular activation patterns are represented; it is possible that some aspects are encoded in spinal circuits. Clearly, muscle activity evoked by spinal stimulation indicates that there is already much structure here (e.g., [Hart and Giszter, 2010](#)). It is conceivable that much of the observed muscle activation patterns were mediated by spinal interneurons, especially because the stimulation was performed on the crest of the precentral gyrus. Indeed, viral tracing studies suggest that corticospinal projection neurons in these areas project mostly to spinal interneurons ([Rathelot and Strick, 2009](#)). Direct cortical projections to ventral horn neurons, and hence innervations of individual muscles, arise predominantly from more caudal aspects of primary motor cortex in the anterior bank of the central sulcus. Thus, one may expect that the contribution of spinal circuits may be less pronounced when stimulating in the depth of the sulcus.

The regularities in the stimulation-evoked muscle activation are likely influenced by the organization of motor cortex: both the pattern of divergent projections from motor cortical neurons to subcortical targets and the strength of the lateral connections between different motorcortical circuits will heavily influence the evoked patterns. While somewhat marginal to the central claims of the current paper, the location of these regularities becomes important when considering the plasticity of these circuits. Even short-term practice (20–30 min) can dramatically alter the movements that can be evoked by TMS stimulation of motor cortex ([Classen et al., 1998](#)). We would expect that such plasticity is a function of modulation of cortical activation states and lateral connections. On the other

hand, there are also very long-lasting changes through experience. For example, life-long musical training alters the movement patterns evoked from M1 stimulation in a way that even reflects the specific instrument played ([Gentner et al., 2010](#)).

One challenge for the future is to decipher the mechanisms of plasticity on short and long timescales that underlie these changes. It is relatively easy to see that Hebbian-type learning (what fires together, wires together) would invariably reinforce the most often used combinations of neural activation patterns throughout the systems hierarchy, while weakening others. However, it is likely that multiple learning mechanisms at multiple sites interact in giving rise to both short- and long-term changes.

The evidence provided by the authors—especially about the spatial distribution of evoked activity patterns—has the potential to shed new light on the functional relevance of this cortical organization. As stated by the authors, there is a strong intuition that synergies reflecting natural movement statistics make planning and control of movements “easier.” While we share this intuition, we also believe this argument deserves some further scrutiny. Specifically, the next challenge is to understand more precisely in what respect the structured organization of motor cortical outputs promotes the production of skilled movements. So let us take a step back and ask again: why do synergies make control easier?

The original argument put forward by [Bernstein \(1967\)](#) was that synergies remove superfluous degrees of freedom and, therefore, reduce the dimensions of the available control space; that is, it is easier for the nervous system to find the correct activation pattern of 7 synergies than the correct activation patterns on 19 muscles. It is now clear that this argument is misleading in two aspects. First, the strict definition of synergies as a “dimensionality-reduction device” would imply that some muscle activation patterns and, therefore, some hand postures simply cannot be achieved. When having fewer synergies than muscles, the “simplicity of control” would be gained by accepting a restriction of the possible control space. However, recent data indi-

cates that even unusual and arbitrary muscle activation patterns *can* be learned ([Radhakrishnan et al., 2008](#)). Thus, while synergies seem to impose a useful structure of the control space, they do not necessarily reduce its size in a deterministic sense. Second, despite some spatial regularity, each stimulation site exhibited a different pattern of evoked muscle activity ([Overduin et al., 2012](#)). If we consider the activated network for each stimulation site as one cortical controller, it quickly becomes clear that the motor cortex (given the smoothness of the stimulation map and the size of the hand region) has a higher number of controllers than the number of hand muscles it controls; thus, rather than reducing redundancy, this cortical organization would expand redundancy.

The answer to the question of why synergies make control easier must, therefore, ultimately be probabilistic. It likely relates to the distribution of the output properties of motor cortical controllers in the high-dimensional space, which in turn reflects the probability distribution of neural activation patterns related to hand movements (or muscle activities) within the practiced motor repertoire. Thus, activation patterns optimal for generating a repertoire of frequently practiced movements must differ from those associated with movements with relatively low probability. Currently, we do not fully understand where this difference lies. One possibility is that a well-practiced movement can be quickly generated from very few muscular activation patterns, each of which is encoded in a dedicated corticospinal circuitry. Thus, when executing the movement, the system would only need to activate very few cortical controllers—in the extreme case, only a single cortical module. This would imply that the motor cortex uses a sparse coding approach ([Olshausen and Field, 1996](#)). Alternatively, the motor cortex may use more distributed patterns of activity, which would allow it to produce the encoded movements with less variability than improbable movements. Finally, the encoding of synergies may also lead to a reduction of the overall activity, and, hence, (neural) energetic effort. We believe that understanding which criterion the motor cortex optimizes through the encoding

of synergies will further our understanding as to how the brain controls the hand. In answering this question, the paper has provided an important step in the right direction.

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There and Back Again: The Corticobulbar Loop

Anne-Marie Oswald^{2,3,*} and Nathaniel N. Urban^{1,2,3,*}

¹Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA 15213, USA
²Department of Neuroscience and Center for Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA
³Center for the Neural Basis of Cognition, Pittsburgh, PA 15213, USA
 *Correspondence: amoswald@pitt.edu (A.-M.O.), nurban@cmu.edu (N.N.U.)
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Feedback is a ubiquitous anatomical feature of sensory processing in vertebrates. In this issue of *Neuron*, two papers (Boyd et al., 2012, and Markopoulos et al., 2012) analyze the features of feedback from olfactory cortex to olfactory bulb.

The simplest view of sensory processing is a series of feedforward stages each extracting successively more complex features of incoming stimuli. A somewhat more sophisticated view incorporates parallel or divergent feedforward streams that are customized for processing of different stimulus features—such as the “what” versus “where” pathways of the visual system. However, even this view neglects a prominent anatomical attribute of all sensory pathways—extensive feedback connections that transmit activity from higher-order areas to more primary structures. Moreover, in many cases, feedback connections outnumber the feedforward connections between these same areas. The function served by these retrograde signals for the most part is unknown. How does the brain use feedback signals, which could be thought of as an “echo” of the output returning to its source?

Understanding the functional role of feedback connections requires answering two key questions. What patterns of activity are generated in the downstream areas? And what are the functional and anatomical properties of the feedback projections? Recent work from a number of groups has made strides toward addressing these two questions and provided a greater understanding of the role of feedback in olfaction. Electrophysiological and imaging studies have provided detailed analyses of how odors are represented in olfactory cortex (Miura et al., 2012; Poo and Isaacson, 2009; Stettler and Axel, 2009; Wilson and Sullivan, 2011). In this issue of *Neuron*, two papers (Boyd et al., 2012, and Markopoulos et al., 2012) use optogenetics to reveal specific features of the feedback connections from olfactory cortex to olfactory bulb, providing an important step in under-

standing the functional role of feedback in this sensory pathway (Figure 1). Olfactory processing begins when odorant molecules bind to olfactory receptor proteins on the membrane of sensory neurons in the nose. Each sensory neuron expresses one of about one thousand different olfactory receptor genes found in the rodent genome. The axons of olfactory receptor neurons (ORNs) converge in structures called glomeruli that tile the surface of the olfactory bulb. In each glomerulus, the axons of ORNs expressing the same receptor form excitatory synapses with the dendritic tufts of excitatory mitral and tufted cells. Mitral and tufted cells send a primary apical dendrite to a single glomerulus; therefore, all the afferent input to these cells is provided by a single type of olfactory sensory neuron. Several classes of inhibitory neurons within olfactory bulb