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What to Do, or How to Do It?

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In this issue of *Neuron*, Ajemian et al. present a computational model of the activity of neurons in primary motor cortex (M1) during isometric movements in different postures. By modeling the output of M1 neurons in terms of their influence on muscles, they find each M1 neuron maps its output into a particular pattern of muscle actions.

Controlling complex movements is a profoundly challenging problem for the nervous system, and working out how neurons in the motor system solve this problem is an equally challenging problem for neuroscience. The difficulty is that even such apparently simple acts as reaching to a nearby object involve the coordinated action of the muscles controlling the position of several joints. This poses a question: does the activity of neurons represent low-level dynamic aspects of movement such as movement forces and muscle activations, or does it reflect high-level kinematic parameters such as the direction and velocity of hand movements? Signals in spinal motoneurons, plainly, correspond to single-muscle actions; neurons in premotor areas seem to specify movement goals rather than details (Pesaran et al., 2006). But at the level of primary motor cortex (M1), the question of "muscles or movements" remains open and is the subject of active study.

In the 1960s, Evarts recorded the activity of M1 neurons while monkeys performed single-joint movements and found a close relationship between firing rate and muscle force (Evarts, 1968). But subsequent studies of both single- and multijoint reaching movements suggested that M1 neurons encoded such higher-level movement features as the velocity and particularly the direction of movement of the hand, and not the particular muscle activations involved (Georgopoulos et al., 1982, 1986; Crutcher and Alexander, 1990; Moran and Schwartz, 1999). During reaching, the activity of M1 neurons is maximal for movements in a particular preferred direction and falls with the cosine of the angle between this direction and the movement direction, suggesting an explicit representation of movement trajectory (Georgopoulos et al., 1982). A number of subsequent studies have, however, shown that the activity of M1 neurons during a particular reaching movement depends both on arm posture and on external load, suggesting that these neurons also carry lower-level information about muscle activation (Kalaska et al., 1989; Scott and Kalaska, 1997).

It is difficult to analyze M1 coding during an actual reach to a target. Not only do M1 neurons receive input from joint and muscle proprioceptors that changes in the course of the movement, but the forces exerted by each muscle also change continuously throughout the trajectory. The situation can be made more tractable by training animals to exert reach-like forces against a static object under isometric conditions, so that the muscle actions are not confounded with changes in joint position. This strategy was used by Sergio and Kalaska (2003) and Sergio et al. (2005) to study M1 activity during otherwise similar reaching and isometric tasks.

The muscle activity needed to produce a particular arm action depends on the position of the arm because of the different angles of the joints and the different stiffness of the limb in different postures (Figure 1). Sergio and Kalaska (2003) trained monkeys to produce an isometric force in one of eight directions with the hand in nine different positions. The responses of M1 neurons were influenced by posture—the directional tuning of single cells was rotated and their response amplitudes were changed, in an apparently lawful but complicated pattern. In this issue of

Neuron, Ajemian et al. (2008) present a model for this data that is based on analysis of the pattern of muscle activations associated with isometric force generation in different directions at different postures. This model represents a significant advance, because it is strikingly successful in accounting for the way that the responses of individual M1 neurons vary with posture and force direction.

In isometric experiments, force at the hand is generated in two dimensions. It is conventional to think of force generation at the hand in Cartesian coordinates, in which neurons are known to be direction selective (Georgopoulos et al., 1992). The data of Sergio and Kalaska (2003) show that this direction selectivity is not invariant, because it changes with posture. The basis for Ajemian et al.'s model is the geometry of the whole arm. They argue that that M1 cells do have an invariant direction selectivity, not in Cartesian coordinates at the hand but *in the space of joint torques* of the whole arm.

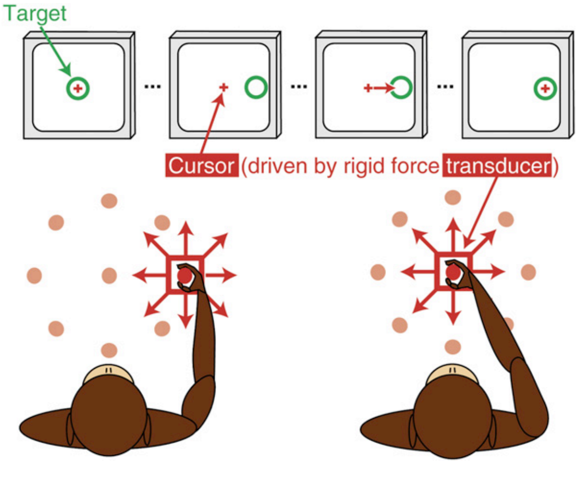

Figure 1. A Schematic of the Task Analyzed by Ajemian et al. (2008) (See Also Sergio and Kalaska, 2003)
A monkey faces a video screen and grasps a fixed manipulandum connected to a force transducer. A trial is initiated when the monkey uses force on the transducer to bring a cursor near the center of a target (green circle). The target jumps in one of eight directions, and the monkey then changes the force delivered to the manipulandum to move the cursor to the new target location and hold it there for 2 s. The task is done on different trials with the arm in nine different postures (pink); two are shown at the bottom, one offset to the right of the midline, one on the midline. The *net* force exerted by the monkey for each movement is the same in all postures, and if M1 neurons encoded only force commands at the hand, their responses would not depend on posture. The muscle actions around each joint, however, depend on posture. Ajemian et al.'s model accurately predicts the change in individual M1 neuron responses in different postures. Adapted with permission from the *Journal of Neurophysiology* (Sergio and Kalaska, 2003).

To generate forces at the hand in this task requires controlling the action of the muscles around two joints (shoulder, elbow); because the shoulder joint can rotate, this calls for four-dimensional control of the torque. Ajemian et al. (2008) transform this four-dimensional space of joint torques into the two dimensions of generated force at the hand. This transformation cannot be specified uniquely, because many different patterns of muscle activation can give rise to the same force at the hand. Ajemian et al. (2008) adopt the reasonable simplifying assumption that the joint torques are generated with minimal coactivation of antagonist muscles, which solves the problem of degeneracy. In the isometric situation, there is then a direct correspondence between joint torques and muscle activation. It is therefore straightforward to convert the preferred direction of each neuron at the central position from Cartesian coordinates at the hand to the underlying joint torques and therefore muscle activations. Because the selectivity in the space of joint torques is fixed, the model predicts the observed changes in direction selectivity across postures. The model's predictions both for the changes in preferred direction and for changes in response magnitude account for a satisfyingly large fraction of the variation in neuronal response observed across postures. In other words, a single tuning curve for each neuron, expressed in the right space, accounts for the full pattern of neuronal responses.

The success of this model is possible in large part because of the relative simplicity of the isometric situation with static forces. This simplicity raises the question of whether Ajemian et al.'s approach will work for actual movements, with all their attendant complexity. A valuable next step would be to study isometric force generation in the presence of time varying loads. Extending the model to this case—and further to the case of real movement—will not be trivial but will probably be necessary to secure its acceptance as a comprehensive account of the role of M1 neurons in programming reaching movements.

The results of Ajemian et al.'s analysis provide strong evidence that it is useful to think of the output of M1 neurons in terms of their influence on muscles. Their model, in effect, defines a "projection field" for each M1 neuron that maps its output into a particular pattern of muscle actions. This is a natural way to think about M1 neurons, especially in the arm region, many of which have strong and direct projections to spinal motoneurons (Lemon, 2008). The simplest interpretation is one that might have been offered by Evarts: M1 neurons control muscle actions. But to say that M1 neurons control muscles is not to say that they do not control movements. The projections of M1 neurons are not confined to small groups of muscles controlling single joints—rather, their output orchestrates a complex pattern of motoneuron activity that leads to coordinated actions affecting multiple joints. This pattern clearly has the *purpose* of programming complex movements.

To capture our understanding, is it better to emphasize the purpose of a neuron or its basis in neural computation? It may help here to consider a different example, the simple cell of the primary visual cortex (Hubel and Wiesel, 1962). Simple cells respond selectively to oriented contours in the visual image and are often casually but reasonably described as "edge detectors." This is a statement of purpose. A more precise statement of how simple cells *work* is that they compute a weighted sum of the visual image over space and time and then modify the result with at least two specific nonlinearities (Lennie and Movshon, 2005). This is a statement of how the purpose is achieved and does not conflict in any way with the statement of purpose that the cell is an edge detector. So perhaps we should set aside the somewhat artificial dichotomy between muscles and movements, between the purpose and its functional basis, and recognize that the activation pattern of motor cortex neurons does two things—it specifies for the peripheral motor system *both* what to do *and* how to do it.

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Finding Gamma

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Neuronal gamma-band synchronization is central for cognition. Respective studies in human subjects focused on a visually induced transient enhancement of broadband EEG power. In this issue of *Neuron*, Yuval-Greenberg et al. demonstrate that this EEG response is an artifact of microsaccades, raising the question of whether gamma-band synchronization can be assessed with EEG.

When networks of neurons are activated, they engage in synchronous rhythmic activity in the gamma-frequency range (30–100 Hz) (Gray et al., 1989). This gamma-band synchronization affects neuronal interactions (Womelsdorf et al., 2007) and thereby subserves several central cognitive functions, including perceptual binding (Gray et al., 1989), attentional selection (Fries et al., 2001), and working memory maintenance (Pesaran et al., 2002). These functions of gamma-band synchronization have been revealed in numerous experiments in animals, using microelectrodes that record single neurons, small groups of neurons, or the local field potential (LFP, a sort of EEG recorded inside the neuropil). The LFP is due to intra- and extracellular current flows that can also be measured noninvasively as magnetoencephalogram (MEG) or electroencephalogram (EEG).

The EEG has been used extensively in human cognitive neuroscience, because it is relatively cheap and easy, but nevertheless delivers noninvasive measurements of human brain activity with millisecond temporal precision. This precision has been exploited predominantly to study brain responses with a strict temporal relation to either a sensory stimulus, a motor response, or any other externally accessible event. The respective event is used to trigger the averaging of EEG epochs to obtain the event-related potential (ERP). The underlying rationale is that any brain response related to the event is phase locked to it and survives averaging, while anything else is noise and is removed through the averaging. However, the absence of phase locking is precisely a characteristic feature of the neuronal gamma-band synchronization that had been observed in animals. The microelectrode recordings in animals revealed consistently that, for example, visual stimuli induced synchronized rhythms that occurred in each trial with a different phase relation to stimulus onset. The variable phase relation makes those components disappear in ERPs, and they can only be revealed if the spectral (frequency-wise) power of neuronal activity is estimated separately per trial and only then averaged.

Such a power analysis in turn retains not only the interesting gamma-band rhythm, but also power from, for example, small muscle artifacts. These muscle artifacts contain power actually predominantly in the gamma band, and it is precisely this reason why most researchers prefer to low-pass filter EEG signals around 30 Hz, eliminating many potential artifacts but also any potential gamma-band activity. Thus, both the