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Past, Present, and Emerging Principles in the Neural Encoding of Movement

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Understanding how the brain controls movement has been of primary interest to the motor control community for over 100 years. Yet even today an intense debate persists as to what and how movement parameters are encoded and whether the concept of parameterization is valid. Contemporary views concur that neuronal representations are dynamic, based on task parameters that are behaviorally relevant, and modifiable via learned associations. The chapters in this section provide both historical perspectives and new insights into the fundamental question of what and how movement parameters are encoded in the brain.

How the cerebral cortex controls and represents movements has been debated since the 19th century based on the motor effects of electrical stimulation of the cerebral cortex (Fritsch & Hitzig, 1870) and motor deficits in patients with epilepsy (Jackson, 1873). These initial investigations lead to the fundamental question of whether the cerebral cortex formulates and controls movements by specifying the activities of muscles or by specifying more global aspects of motor behavior. However, it was not until the 1950's with the development by Jasper (Jasper, 1958) of single unit recording in the behaving monkey and Evarts' (Evarts, 1966) pioneering use of this new technique in the primary motor cortex (M1) that the identification of movement parameters encoded in the discharge of neurons began in earnest.

Beginning with Evarts, a common approach has been to isolate and vary specific parameters of movement in a highly controlled behavioral paradigm to determine how the firing of a neuron is modulated in relation to task parameters. Depending on the region of the nervous system studied and the experimental paradigm used, researchers have emphasized different parameters and their encoding in different regions in the CNS. For example, early studies of M1 generally used movements about a single joint to scrutinize the relation between cell firing and parameters of limb movement (Evarts, 1968; Cheney & Fetz, 1980; Hepp-Reymond, Wyss, & Anner, 1978). Much of the effort emphasized the role of M1 in controlling movement kinetics such as force and/or muscle activity, as opposed to the movement kinematics such as position and direction. Similar efforts at understanding the nature of the motor parameters encoded were undertaken for the cerebellum (Thach, 1970b,a), basal ganglia (DeLong, 1973) and spinal cord (Courtney & Fetz, 1973).

An experimental and conceptual shift occurred in the 1980's as more complex and natural movements were studied (Georgopoulos, Kalaska, Caminiti, & Massey, 1982; Schwartz, Kettner, & Georgopoulos, 1988). Neuroscientists turned from examining the neural

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correlates of movements about a single-joint to examine multi-joint and whole arm movements. Both from behavioral and neurobiological perspectives, it became evident that single-joint movements are insufficient to understand the complexities of limb movement in space or to capture the rich variability in neural activity that occurs in planning and executing arm movements (Soechting & Flanders, 1992; Flash & Hogan, 1985; Kalaska & Crammond, 1992; Georgopoulos, 1991; Ashe, 1997). Neurons in the motor cortical areas were shown to be modulated in relation to many kinematic aspects of reaching movements including direction of movement (Georgopoulos et al., 1982), amplitude (Fu, Suarez, & Ebner, 1993; Messier & Kalaska, 2000), speed (Moran & Schwartz, 1999), velocity and acceleration (Ashe & Georgopoulos, 1994; Reina, Moran, & Schwartz, 2001), static position (Kettner, Schwartz, & Georgopoulos, 1988), and accuracy (Gomez, Fu, Flament, & Ebner, 2000).

With growing evidence that motor cortical neurons are modulated in relation to more global or executive features of movement (Georgopoulos, 1991), the debate intensified as to whether the critical control parameters used by the central nervous system were based on kinematic or kinetic variables and which of these parameters neurons encode (Mussa-Ivaldi, 1988; Todorov, 2000; Reina et al., 2001; Soechting & Flanders, 1992; Scott & Kalaska, 1997). The study of multi-joint and more complex arm movements added to this controversy by raising the question of whether the coordinate system used is intrinsic and related to the joints and muscles or extrinsic and related to the position of the hand in space (Soechting et al., 1992; Todorov, 2000; Flash & Hogan, 1985; Kalaska & Crammond, 1992).

During this same period, the question of ‘how’ movements are represented and controlled by the discharge of neurons also developed rapidly. The traditional view that a single parameter was encoded within the firing of a neuron was replaced with broader concepts including that individual neurons are modulated by multiple parameters and the parameters are encoded across populations of neurons. For example, contributions from direction, amplitude, position, speed and acceleration occur in the discharge of single M1, premotor and cerebellar neurons (Ashe & Georgopoulos, 1994; Fu et al., 1993; Fu, Flament, Coltz, & Ebner, 1997; Johnson, Coltz, & Ebner, 1999; Messier & Kalaska, 2000; Moran & Schwartz, 1999; Roitman, Pasalar, Johnson, & Ebner, 2005). Also, populations of neurons work in concert to plan, control and execute movements. This concept has been validated by the success of population codes to predict arm movement trajectories (Schwartz, 1994; Georgopoulos, Caminiti, Kalaska, & Massey, 1983; Schwartz & Moran, 1999) and control external devices (Taylor, Tillery, & Schwartz, 2002; Schwartz, Taylor, & Tillery, 2001; Wessberg et al., 2000; Lebedev et al., 2005). Population codes also account for processes at the boundary between cognition and motor behavior such as the rotation of the population vector that occurs during a visuomotor transformation (Georgopoulos, Lurito, Petrides, Schwartz, & Massey, 1989).

New analytical approaches have been developed to further probe the question of how movement parameters are encoded in neuronal discharge. A variety of statistical and analytical tools including multi-regression analyses (Fu et al., 1993; Ashe et al., 1994), discriminant analysis (Taira & Georgopoulos, 1993), linear and non-linear filtering (Oram, Hatsopoulos, Richmond, & Donoghue, 2001; Chi, Wu, Haga, Hatsopoulos, & Margoliash,

2006), and information theory (Hatsopoulos, Ojakangas, Paninski, & Donoghue, 1998; Paz & Vaadia, 2004) have provided new insights into how neurons encode and represent movements. Additional coding dimensions have also been uncovered in the firing of single and groups of neurons. Moving beyond the classical focus on firing frequency, analysis of the millisecond timing of spike intervals in M1 has been associated with specific motor behavior (Shmiel et al., 2005). Finally, analyses of neuronal synchronization observed within M1 indicate that neurons are more than independent encoders of movement. Correlation and mutual information among the firing of simultaneously recorded neurons suggest that neurons also engage in mutual interactions when coding specific aspects of motor behavior such as direction (Hatsopoulos et al., 1998) as well as global processes (Donoghue, Sanes, Hatsopoulos, & Gaal, 1998) and timing of behavioral events (Vaadia et al., 1995).

The five chapters in this section illustrate contemporary conceptual and experimental approaches to addressing the question of ‘what movement parameters are encoded in the brain?’ Focused on the cerebral cortex, the first chapters revisit the debate over kinematic/extrinsic versus kinetic/intrinsic encoding. Both Kalaska and Miller (Chapters 1 and 2) emphasize the role of M1 neurons in encoding kinetic/intrinsic parameters of movement. The degree to which a population of neurons is coupled to movement kinematics or kinetics is not only a function of the motor region being studied but also of the task. The latter principle is illustrated by the Merchant and colleagues, work (Chapter 3) on the neuronal representation of target interception in the posterior parietal and primary motor cortex. Chapter 4 by Paz and Vaadia raises another critical factor, that of motor learning and its implications for the encoding problem. Finally, Chapter 5 by Reimer and Hatsopoulos asks for a reconsideration of the fundamental premise on which the search for encoding motor parameters is based.

As discussed above, one of the oldest issues in motor control is whether the primary motor cortex explicitly controls arm kinetics in an intrinsic coordinate system or kinematics in an extrinsic coordinate system. Originally framed as a question of whether movements or muscles are controlled by the primary motor cortex, the controversy has not subsided in the face of numerous experimental studies over the last 40 years. Chapter 1 by Kalaska provides an in depth review and examination of this critical question from three levels. First, acknowledging that kinematic and extrinsic signals are present in the discharge of many M1 neurons, evidence from Kalaska’s laboratory and others indicate that M1 neurons are also modulated by intrinsic parameters of movement. The essential observation has been that during a reach task changes in arm posture alter the directional tuning of individual M1 neurons and the overall distribution of preferred directions in M1 even though the hand moves along the same path (Cabel, Cisek, & Scott, 2001; Gribble & Scott, 2002; Scott & Kalaska, 1997). Therefore, the discharge of M1 neurons reflects control signals operating at the joint or muscle level. Second, there have been numerous demonstrations that M1 neurons are modulated in relation to kinetics. Early studies of movements about a single joint found that the firing of M1 neurons varies as a function of force (Cheney & Fetz, 1980; Evarts, 1968; Evarts & Thach, 1969). For multi-joint reaching movements, the discharge of M1 neurons are modulated by loads applied at the hand (Kalaska, Cohen, Hyde, & Prud’homme, 1989) and at specific joints (Cabel et al., 2001; Gribble & Scott, 2002). During various

isometric tasks, M1 neurons are also highly modulated and tuned to the direction of isometric force (Georgopoulos, Ashe, Smyrnis, & Taira, 1992; Sergio & Kalaska, 2003; Taira & Georgopoulos, 1993; Sergio, Hamel-Paquet, & Kalaska, 2005). Finally, there is the question of whether M1 neurons, particularly those in the caudal bank, directly control muscle activity. Here, Kalaska argues that the evidence is more circumstantial and only correlative. For example, there are similarities in the temporal patterns of muscles and M1 neurons (Kalaska et al., 1989; Sergio & Kalaska, 2003) and there is sufficient information in small numbers of M1 neurons to extract signals that are similar to muscle activity (Morrow & Miller, 2003; Carmena et al., 2003). Demonstrating that M1 neurons causally signal muscle activity remains a challenge.

Chapter 2 by Miller and colleagues also focuses on the debate whether kinematics or kinetics are controlled by M1 neurons. Starting where Kalaska's review leaves off, this next chapter asks whether M1 neurons directly control muscle activity. Instead of emphasizing the relation between an M1 neuron and a muscle, these authors work from the premise that M1 neurons are likely to control groups of muscles in functional synergies. The concept of synergies has a long history as a potential CNS strategy for reducing the complexity of controlling elaborate biomechanical systems (Arbib, Iberall, & Lyons, 1985; Santello, Flanders, & Soechting, 1998; D'Avella, Saltiel, & Bizzi, 2003; Soechting & Lacquaniti, 1989; Cordo & Nashner, 1982). Spike triggered averaging has shown that a single M1 neuron makes functional connections to many muscles (Fetz & Cheney, 1980). Therefore, this chapter hypothesizes that the discharge of M1 neurons encodes the activity of muscle synergies rather than single muscles or global movement parameters.

Two approaches by Miller and Colleagues are used to examine the muscle synergy hypothesis. First, cross-correlations are computed between the firing of a single cell and EMG activities of a group of muscles during a grasp task. The result is a characterization of the muscle-space preferred direction for an M1 neuron that is defined as the vector of physiologically plausible maximum correlations of a neuron's activity with each muscle. The authors interpret the stability and distribution of this muscle-space representation as evidence that M1 neurons control a group of muscles. The second approach uses a linear impulse response filter to correlate the firing of many M1 neurons to the activity of a single muscle. The results show strong correlations between the cell firing and the muscle activity and that the weightings can be used to predict subsequent EMG responses. The authors conclude that although single neurons do not necessarily reflect the activity of any single muscle, a group of neurons with similar functional properties are involved in the control of a group of muscles.

Chapter 3 by Merchant and colleagues underscore an additional principle concerning the encoding of motor parameters; different tasks may require different control parameters and that the weight given to a parameter may depend on the task requirements and control strategy. Merchant and colleagues consider the problem of interacting with a moving object using an interception task. A successful interception requires that the hand and the object be at the same place at the same time, requiring both spatial and temporal matching. In addition to encoding information about the movement of the hand, the task necessitates processing information on the movement of the target including position, direction, and velocity. In

most interception tasks the key parameter is the time-to-contact (TTC), a parameter which incorporates both distance and velocity. Merchant and colleagues were the first to show the neural correlates of TTC in the posterior parietal cortex (area 7) and the motor cortex (Merchant, Battaglia-Mayer, & Georgopoulos, 2004).

Merchant and colleagues studied two different versions of intercepting a circularly moving target. For the first the moving target was continuously shown (real motion) and for the second the target was extinguished except at discrete points (apparent motion). For each version, trials with (GO) and without the actual interception (NOGO) were utilized. Both area 7a and M1 neurons signaled the interception and the angular position of the target but the percentage of cells was dependent on whether the task was GO or NOGO. The results suggest that TTC is the key parameter encoded in M1 during apparent motion. The key parameter in area 7a is the angular position of the target with TTC as the second most important parameter. The authors conclude that neurons in area 7 and M1 process different parameters of the stimulus depending on the type of the stimulus motion. These findings reinforce the concept that the neurons encode the behaviorally relevant parameter.

Chapter 4 by Paz and Vaadia adds another dimension to the neural control of movements, the ability to learn new sensorimotor skills. Learning requires developing new mappings among brain activity, sensory inputs and motor output. Learning therefore challenges the concept of static or dominant kinematic/extrinsic representations versus kinetic/intrinsic representations. Studying the processes of learning can provide new insights into how the brain represents parameters of movement. How the motor system generalizes from a few trials to more general conditions is particularly relevant to the question of how movement parameters are encoded. Learning should also shed light on whether the encoding of any parameter is a predetermined feature of a motor structure or simply a learned association. As the authors point out, the brain is likely to produce adaptations in the relevant behavioral variables (i.e., if the learning involves controlling velocity, the brain will alter the encoding of velocity), minimizing the variance in the relevant task parameter (Harris & Wolpert, 1998; Todorov, 2004).

Paz and Vaadia examine learning in the motor system from the perspective of motor primitives. A motor primitive is a set of basic functions that when weighted and combined produce the desired behavior. Direction of movement and tuning to velocity or subsets are examples of likely primitives. Learning can change both the weights and shapes of the primitives. Learning can also show how motor primitives are linked to patterns of generalizations. Chapter 4 demonstrates these concepts by showing that the directional tuning curve of subpopulations of M1 and supplementary motor area (SMA) neurons can be modified during adaptation to a visuomotor transformation. Only those subsets of neurons with preferred directions closest to the training direction exhibited changes indicating a generalization (though limited to one direction) of a previously learned behavior to a similar task. The changes in SMA neurons occurred earlier during learning than those in the M1 neurons, consistent with a hierarchy of learning. Having implications for a number of questions in motor learning such as generalization, acquisition of internal models, and source and extent of plasticity, the results illustrate that the encoding of movement parameters is dependent on training.

Over the past 40 years the motor control literature has provided evidence that M1 neurons are modulated in relation to almost every movement or task parameter tested. The final chapter by Reimer and Hatsopoulos questions whether the concept of the encoding of a movement parameter is meaningful. Reimer and Hatsopoulos' central idea is that the traditional way of thinking about neurons as controlling or encoding single or multiple parameters of movement might not be accurate. Many movement parameters considered in the literature are spatially or temporally correlated. For example, in a center-out task the position and velocity signals are correlated, having lower velocities at the start and end of the movement and higher velocities in the middle. Using tasks such as random pursuit tracking to decouple instantaneous position and velocity signals still leaves parameters correlated at some other lag. Others have pointed out the strong correlation among extrinsic and intrinsic parameters during arm movements (Reina et al., 2001). Earlier studies had also shown that the neurons might be encoding different parameters during different stages of a task based on the task requirements. For example, the discharge of dorsal premotor and M1 neurons encode different parameters of movement during the progression of the reach, in which movement direction is signaled first followed by movement amplitude (Fu et al., 1993; Gomez et al., 2000; Johnson, Mason, & Ebner, 2001). This was referred to as a "temporal parcellation scheme" as opposed to the "multiplexing strategy" found for cerebellar Purkinje cells (Johnson et al., 2001; Johnson & Ebner, 2000). The authors suggest that single neurons in the motor cortex dynamically encode movement trajectories over time and not simply instantaneous single or multiple parameters of movement. Neurons are conceptualized as having "preferred trajectories" as opposed to preferred directions or tuning to other specific parameters. In essence, neurons encode simple or complex probabilistic trajectories through space referred to as movement "fragments." To illustrate this concept the movement trajectory before and after a spike is computed and these trajectories can vary greatly with respect to the instantaneous movement direction. The authors suggest that the pursuit of parametric encoding alone will limit our understanding of how the motor system functions due to the diverse and sometimes contradictory results obtained on the encoding of motor parameters. Rather than focusing on developing experimental frameworks that strive to reduce parametric dependencies, the authors suggest using an alternative interpretative framework based on such concepts as task goals, intent, or movement coordination.

In conclusion, there has been great progress in understanding how movements are represented in the discharge of central neurons. Both concepts and experimental approaches continue to evolve. There has been a shift from focusing on the encoding of single parameters to multiple parameters and now researchers are asking whether motor primitives, synergies or movement fragments are the critical variables. Recent demonstrations that stimulation of M1 can generate complex movements to an endpoint suggest a possible functional organization based on such elements (Graziano, Aflalo, & Cooke, 2005). There has also been a shift from studying movements about a single joint to more physiological multi-joint movements. Recent studies suggest the need to investigate natural behaviors, as the parameters encoded in M1 during natural movements may differ from those observed in more constrained laboratory paradigms (Aflalo & Graziano, 2006). Also required are investigations into the unique contributions of different structures to the control of

movement, including how neuronal representations differ in time and structure. Because motor structures are plastic and have the capacity to “learn” new sensory-motor mappings and control strategies, long term chronic recordings are needed to understand the sources and extent of this plasticity. Therefore, what is emerging is a dynamic view of motor representations optimized to meet task demands (Aflalo & Graziano, 2006; Johnson et al., 2001; Todorov & Jordan, 2002; Scott, 2004). The challenge will be to understand the principles underlying such representations of movements.

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