J Neurophysiol 120: 2466–2483, 2018.
First published August 22, 2018; doi:10.1152/jn.00205.2018.

REVIEW | *Control of Coordinated Movements*

Long-latency reflexes for inter-effector coordination reflect a continuous state feedback controller

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Submitted 26 March 2018; accepted in final form 20 August 2018

Crevecoeur F, Kurtzer I. Long-latency reflexes for inter-effector coordination reflect a continuous state feedback controller. *J Neurophysiol* 120: 2466–2483, 2018. First published August 22, 2018; doi:10.1152/jn.00205.2018.—Successful performance in many everyday tasks requires compensating unexpected mechanical disturbance to our limbs and body. The long-latency reflex plays an important role in this process because it is the fastest response to integrate sensory information across several effectors, like when linking the elbow and shoulder or the arm and body. Despite the dozens of studies on inter-effector long-latency reflexes, there has not been a comprehensive treatment of how these reveal the basic control organization that sets constraints on any candidate model of neural feedback control such as optimal feedback control. We considered three contrasting ways that controllers can be organized: multiple independent controllers vs. a multiple-input multiple-output (MIMO) controller, a continuous feedback controller vs. an intermittent feedback controller, and a direct MIMO controller vs. a state feedback controller. Following a primer on control theory and review of the relevant evidence, we conclude that continuous state feedback control best describes the organization of inter-effector coordination by the long-latency reflex.

feedback; heteronymous reflex; optimal feedback control

INTRODUCTION

Motor behavior often involves coordinating different parts of the body while interacting with a mechanically uncertain environment. Consider eating a meal with friends or family: you extend your elbow and shoulder to accept a filled bowl from the host, divide the selected portions on your plate with a fork in one hand and knife in the other, and eventually leave the table using your legs, trunk, and arms. Each scenario cannot be fully predicted and requires online adjustments among several body parts to ensure task success: the passed bowl could weigh more than expected, the steak may have adjacent sections of fat and cooked meat, and the chair could slip back when you rise to stand. The present review describes how long-latency reflexes (LLRs) play an important role in coordinating different parts of the body to counter mechanical perturbations.

Long-latency reflexes help compensate mechanical perturbations to the body and ensure task success. They are compensatory bursts of muscular activity evoked by an unexpected displacement of a skeletal body part and situated between the short-latency reflex and voluntary reaction. In the upper limb, the short-latency reflex spans ~20–50 ms, the long-latency reflex spans ~50–100 ms, and the voluntary reactions occur ≥100 ms (Calancie and Bawa 1985; Capaday et al. 1991; Lewis et al. 2005; Lee and Tatton 1982; Nakazawa et al. 1997; Pruszynski et al. 2008). In the lower limb, the short-latency reflex spans ~40–65 ms, the long-latency reflex spans ~65–120 ms, and the voluntary reactions occur ≥120 ms (Corna et al. 1996; Diener et al. 1983; Grey et al. 2001; Toft et al. 1989); the leg muscles tend to have more delayed responses due to longer nerve tracks.

Three key observations demonstrate that long-latency reflexes are relevant to coordinating different effectors. Foremost, LLRs are commonly employed by the nervous system to counter mechanical perturbations. LLRs are expressed throughout proximal and distal muscles of the upper and lower limbs, as well as the trunk, following a displacement of the associated body part. Second, LLRs have been repeatedly shown to integrate information across multiple effectors relevant for achieving a common goal. For example, during a pinch

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task, a LLR in the index finger can be evoked by displacing the opposing thumb (Cole et al. 1984; Cole and Abbs 1987), and during standing, a LLR in the leg can be evoked by a sudden pull on the arm (Cordo and Nashner 1982). Finally, long-latency reflexes rely on supraspinal generators including brain stem circuits (Foysal et al. 2016; Herter et al. 2015; Miller and Brooks 1981; Shemmell et al. 2009; Soteropoulos et al. 2012; Stapley and Drew 2009) and a somato-motor cortical network with primary motor cortex as a major node (Capaday et al. 1991; Cheney and Fetz 1984; Day et al. 1991; Evarts and Fromm 1981; Matthews et al. 1990; Miller and Brooks 1981; Omrani et al. 2016; Pruszynski et al. 2011). Delayed activity of slow spinal circuits (Grey et al. 2001; Lourenço et al. 2006; Marchand-Pauvert et al. 2005; Matthews 1984; Schieppati and Nardone 1997) along with sustained activity of fast spinal circuits (Kurtzer et al. 2010) likely contribute, as well. The supraspinal generators are directly involved in coordinating different body parts and themselves are conditioned by basal ganglia and cerebellum, key centers for sensorimotor function (for review, see Porter and Lemon 1993 and Scott 2004). Accordingly, we should expect that LLRs will exhibit considerable sophistication in coordinating different effectors.

Below we describe results from ~25 studies on inter-effector coordination by the LLR, most involving the upper limb. Each study examined how LLRs integrate information across different portions of the body, such as digits of the hand, elbow and shoulder, and ankle-knee-hip, which may be considered as one effector in other experimental contexts. These studies reflect a relatively small subset from a line of research that started in the mid-1950s (Hammond 1956). To fully appreciate the sensory basis, central generators, and capabilities of the long-latency reflex, we suggest the following reviews: Kurtzer 2015b; Lee et al. 1983; Marsden et al. 1983; Pruszynski and Scott 2012; Scott 2004; Scott et al. 2015; Shemmell et al. 2010.

The following material will highlight important organizational features of the long-latency reflex that are not uniquely wed to a general theory of coordination. Whereas previous reviews [including our own (Cluff et al. 2015)] have advocated that optimal feedback control was a good model to account for the broad range of variables that can modify LLRs, this review focuses on organizational features that set constraints on any candidate model of neural feedback control. Thus, although it may not be necessary to invoke an optimal control model, alternative views must have sufficient complexity to account for key empirical observations.

We considered three contrasting ways that a controller can be organized: multiple independent controllers vs. a MIMO controller, a continuous feedback controller vs. an intermittent feedback controller, and a direct MIMO controller vs. a state feedback controller. These concepts have driven sensorimotor research on both limb and body control with various arguments for continuous processing (Liu and Todorov 2007; Mugge et al. 2010; Saunders and Knill 2003; Sternad and Schaal 1999; van der Kooij and de Vlugt 2007), intermittent processing (Bottaro et al. 2008; Collins and De Luca 1993; Fishbach et al. 2007; Loram and Lakie 2002; Meyer et al. 1988; Milner 1992), direct control (Debicki and Gribble 2004; Gribble and Ostry 1999; Gottlieb et al. 1996; Quaney et al. 2003), and state feedback (Ariff et al. 2002; Gritsenko et al. 2009; Kuo 2005; Merfeld et al. 1999). This engagement further motivated us to clarify the organization of the long-latency reflex. After a primer on control theory, we summarize both long-standing and recent evidence, concluding that the circuits underlying inter-effector coordination by the long-latency reflex are best accounted for by continuous state feedback control. It should be noted that this conclusion does not preclude other control organizations for other behaviors and levels of analyses.

CONCEPTS IN CONTROL THEORETIC MODELS

Basic Definitions and Architecture

A control system can be defined in general as the combination of a plant (S) and a controller (*C*). The plant is characterized by one or several state variables, or simply a state vector, which evolves over time. The evolution of the state variables is called the trajectory, and a controller is an entity that can modify the plant's trajectory. These definitions are very general because the specificity of control models across fields and applications varies widely. Also, although we focus on linear control systems, our general conclusions remain valid for nonlinear systems. In particular, previous studies (some reviewed below) reported a linear scaling of average LLRs with perturbation magnitude across perturbations spanning an order of magnitude, as well as fixed reversal times following perturbations of different magnitude. These observations are consistent with the superposition principle of linear systems and indicate that although the biomechanical system and the neural controller are clearly nonlinear, the analyzed behavior does not depart much from the predictions of a linear model.

Understanding behavior as a control system means finding the plant and controller that accurately describe the perceptual and motor process for the observed behavior. The plant is the biomechanical system composed of bones, muscles, and other tissues (Fig. 1*A*). The state of this plant, accordingly, is joint position, velocity, torques, and muscle dynamics. The controller is the nervous system, which generates motion by driving muscle contraction.

There are two objectives for applying perturbations to a control system. First, the properties of the biomechanical plant, such as the inertial parameters of body segments (Winter 2009), and the viscoelastic properties of muscles (Burdet et al. 2001; Crevecoeur and Scott 2014; Kearney et al. 1997; Mussa-Ivaldi et al. 1985; Perreault et al. 2004; van der Helm et al. 2002) must be identified, as well as their dynamics (Scott et al. 1996; Zajac 1989). Second, one can understand the properties of the controller itself (Burdet et al. 2001; Crevecoeur et al. 2014; Kearney et al. 1997; Mussa-Ivaldi et al. 1985; Perreault et al. 2004; van der Helm et al. 2002). These two approaches are not independent (and are jointly considered in many studies) because accurate models of the plant are necessary for drawing meaningful conclusions about the neural controller. In fact, discrepancies in the estimates of muscles elastic stiffness and viscosity, up to an order of magnitude (Crevecoeur and Scott 2014; Mussa Ivaldi et al. 1985), have led to different conclusions about neural control, an issue that should be explored further. With that caveat, the present review will focus on the properties of the neural controller.

We now define the main aspects of a control system that will be useful to interpret the computational organization of long-latency reflexes to mechanical perturbations. The most fundamental distinction is whether the nervous system creates the

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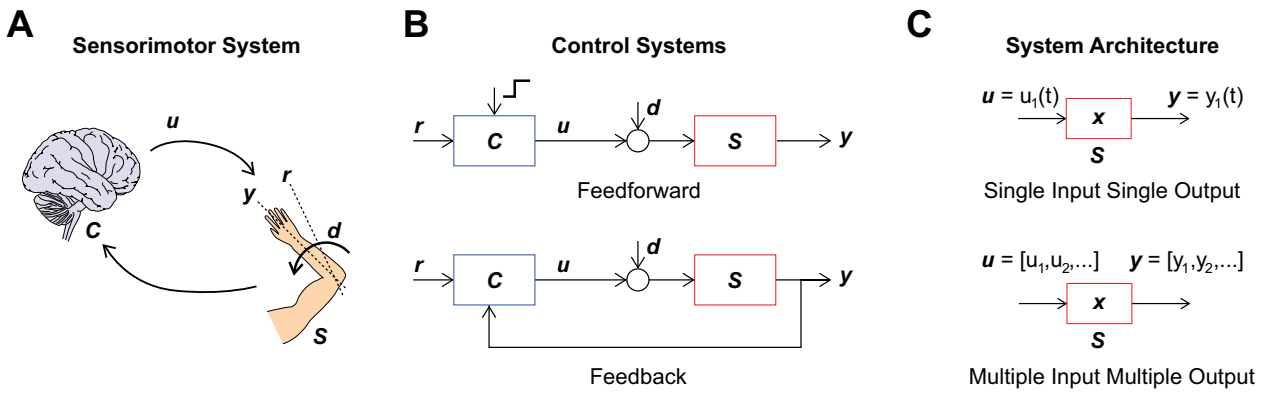


Fig. 1. System architecture. *A*: illustration of the neuromusculoskeletal system with the brain as controller (*C*), sending motor commands (*u*) to the biomechanical plant (*S*) composed of muscles, bones, etc. The system output (*y*) is a measurement of the state of such a position, velocity, higher order derivatives, or mixture of these signals. The reference variable (*r*) represents the desired state to track or around which the controller maintains equilibrium. *d*, Disturbance subsequent to control action. *B*: schematic illustration of control systems with feedforward or feedback. In a feedforward setting, the control is launched or triggered by the occurrence of a perturbation. In a feedback setting, the system output is fed back to the controller. *C*: characterization of single-input/single-output (SISO) or multiple-input/multiple-output (MIMO) systems. A SISO system is characterized by scalar input and output variables. MIMO characterizes systems with vector input or output. See text for variables and equations.

behavior of interest by operating as a feedback (closed loop) controller or a feedforward (open loop) controller (Fig. 1*B*). A defining feature of an open-loop controller is that the control actions, once triggered, do not depend on subsequent disturbances (*d* in Fig. 1, *A* and *B*) because the system output is not used to adjust control. In contrast, the closed-loop controller continuously regulates the output depending on changes in the state. A hybrid controller can be designed as a sequential open-loop controller, which updates its action in selected times based on either available data about the system trajectory or an internal clock. Hybrid controllers are effectively closed loop with intermittent feedback in the sense that sensory information still influences behavior, but only at particular points in time. This is illustrated in Fig. 2, where the switches in the intermittent controller highlight the possibility that feedback may be engaged and disengaged. Although long-latency reflexes (along with other responses) definitely reflect the output of feedback controllers (because mechanical perturbations evoke responses), an issue to be resolved is between continuous and intermittent feedback control.

We use the concept of hybrid or intermittent controllers in a general way to refer to controllers that have intrinsic discontinuity in sensory to motor transformations. Predictable features of hybrid control include hold times between sequences of motor responses, and threshold-like mechanisms that engage the launching of the response (or the closing of the switches). More precisely, a discontinuity relative to time can be conceived as a controller with a continuous sampling of information and a threshold for action, like those extensively used to study decision-making between discrete competing options (Cisek et al. 2009; Gold and Shadlen 2007). Alternatively, the discontinuity could arise from only sampling information at discrete intervals, a concept that dovetails with the well-known phenomenon of sensory gating by descending signals as occurs with presynaptic inhibition in the spinal cord (Rudomin 1999) and central cancellation in the brain (Blakemore et al. 1998). In either case, the controller would be insensitive to perturbations for a range of times and magnitudes below a particular threshold. Such a discontinuity would not preclude the controller's ability to scale with the magnitude for perturbations that exceed the threshold, and thus attention must be paid to small disturbances to disentangle continuous from intermittent feedback. There are clear bottlenecks in the neural control system when individual units are considered: a temporal constraint for sensory or motor neurons is the refractory period of a few milliseconds following a spike. As well, single cells only fire when the membrane voltage crosses a threshold. Ceiling or saturation effects may also affect the overall scaling of feedback responses. Thus the individual components of the sensorimotor system are not continuous, but at the population level

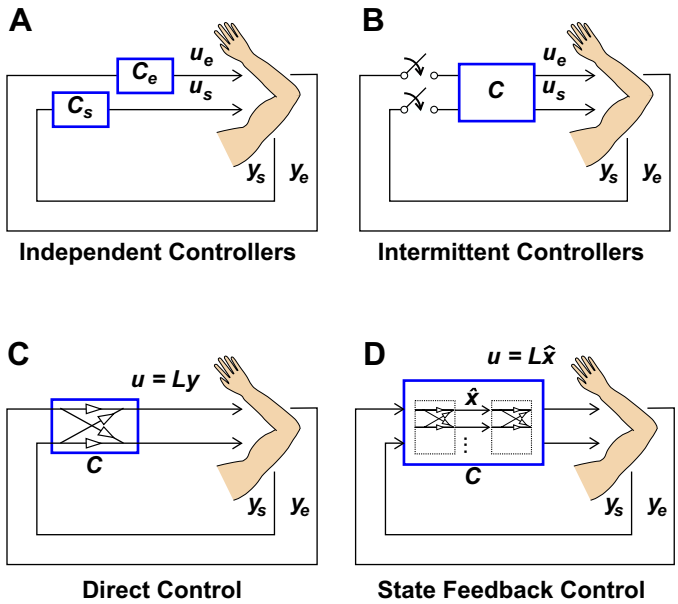


Fig. 2. Candidate controllers. *A*: independent controllers acting at each individual joint such as, for example, multiple controllers for shoulder (y_s) and elbow (y_e) separately. *B*: intermittent control with a feedback loop that opens or closes dependent on thresholds or hold time in the feedback process. *C*: direct control, which we defined as a multiple-input/multiple-output (MIMO) controller with a direct mapping of sensory variables representing the joint outputs onto multi-joint control commands. *D*: state feedback control. Because of imperfect measurements (partial or mixed sensory information, noise, and delays), a state feedback controller may achieve more efficient control by filtering out noise and reconstructing internal or external variables such as the applied perturbation pattern or changes in the environmental dynamics. See text for variables and equations.

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and at the scale of input/output signals that have an impact on joint motion, it is unclear whether or how much these bottlenecks impact behavior. Considering this, a continuous system model of LLRs, in our view (and in light of the evidence reviewed below), remains a conceptually valid candidate.

We should mention the particular case of time-optimal control for completeness because it falls under the category of discontinuous controllers, to which hybrid controllers also belong. In the particular case of a linear system model with bounded control input, a time-optimal controller, that is, a controller that steers the system to the target as fast as possible, is known as a "bang-bang" controller. This term refers to the property of such a controller to use maximal control signals all the time. Given the fine-grained scaling of LLRs with perturbation magnitude (as reviewed below), it is clear that a bang-bang controller is not a suitable model for LLRs (Lewis 1996).

The second fundamental property to consider is the number of system input and output variables. With a single input and single output (i.e., scalar quantities), the system is called SISO (Fig. 1*C*). Imagine a robotic actuator composed of a single-joint arm with a goniometer and torque actuator with current input: the control of the joint angle based on the current can be captured in a SISO system. When there is more than one input or output variable (i.e., dimension > 1), the system is called MIMO (Fig. 1*C*). A good example is the two-jointed arm, which requires monitoring the motion of each joint and controlling two motors. Encoding of distinct variables at the same effector (e.g., joint angle, velocity, and torque in a single joint) or multiple measurements of error also confer a MIMO structure to the system. Likewise, a controller can reconstruct distinct measurements for SISO systems such as the well-known PID controller, which uses control signals proportional to the joint position error, its derivative, and its integral. However, in the current context we mean MIMO as controls based on the integration of information from sensors in different effectors.

Controller Design: Multiple Independent Controllers, Direct Control, and State Feedback

Given that our biomechanical system is MIMO, a basic question is whether the nervous system is composed of multiple controllers acting independently on each effector (i.e., one controller per effector; Fig. 2*A*) or a centralized controller that receives information from multiple effectors and coordinates commands to them (a MIMO controller). The signature of multiple independent controllers is that sensory information at one effector cannot directly influence control at another effector, but only indirectly through mechanical interactions across the distinct effectors. In the context of sensorimotor control, it is the interaction torque at the joints that causes motion, which in turn induces control responses. Thus independent controllers express a cascade of control responses at each joint (or degree of freedom) caused by the mechanical interactions in the periphery. In contrast, a MIMO controller would respond to perturbations through coordinated motor commands to several effectors based on information from multiple sensors (see He et al. 1991 for first application to postural control).

Multiple independent controllers can be eliminated outright when the feedback response of one effector depends on the state of another effector. Two examples were raised in the INTRODUCTION, and many more are elaborated in LITERATURE REVIEW ON THE LONG-LATENCY REFLEX. Accordingly, coordination across effectors in the LLR refutes multiple independent controllers (however complex is each controller) as a viable hypothesis.

To describe MIMO controllers, it is convenient to express the equations of motion in an algebraic form. The continuous time differential equation is based on Newton's law, linking forces with acceleration and, consequently, to velocity and position ($\sum \vec{F} = m\vec{a}$); likewise, filtering models link electrical activity in neurons to force production in muscles as a simple model of muscle dynamics. An algebraic representation of such equations in the context of linear systems takes the following form:

$$x_{t+1} = Ax_t + Bu_t + \xi_t, \tag{1}$$

where x_t and u_t are the state and control vectors at time t, A and B are matrices that capture the system dynamics, and ξ_t represents a random disturbance capturing noise in the process. The matrix A captures the unforced dynamics, that is, the spontaneous system trajectory without any external intervention. For instance, a dissipative system typically includes forces proportional to velocity with opposite sign, which would be expressed in this matrix by a viscous constant. The matrix B describes how changes in the control variable impact the system trajectory. In our example, it would contain the parameters that shape the torque generation as a filtered response to the control variable.

A standard controller in this context is the state feedback controller (Fig. 2). Assuming that the state vector is available, the controller can be represented at each time step by a matrix (L_t) and a control vector in the following form:

$$u_t = L_t x_t. \tag{2}$$

Such MIMO controllers naturally handle the mechanical interaction between effectors, because disturbances to any component of the plant can generate control responses at any other effector through the structure of the gain matrix, L_t. In contrast, controlling MIMO systems through independent controllers at each effector is quite difficult because of the peripheral interaction between loops; they generally require operating at low frequencies and careful tuning of each feedback gain (Astrom et al. 2001). State feedback controllers in the form of *Eq. 2* were introduced to overcome this limitation. Indeed, plugging *Eq. 2* into *Eq. 1* yields a closed-loop dynamic corresponding to

$$x_{t+1} = (A + BL_t)x_t + \xi_t,$$

and the control design reduces to calculating the feedback gains such that $A + BL_t$ has desired properties. Also, the gain matrix in *Eq. 2* can vary over time, which allows one to incorporate time-varying constraints associated with the intended behavior.

Often, the state vector is not known exactly due to several complexities. Biological sensory information can involve a combination of several state variables, such as muscle spindles encoding both fascicle length and velocity, and Golgi tendon organs reflecting both static and dynamic force (Nichols 2018; Proske and Gandevia 2012). Sensory measurements may be corrupted by noise (Faisal et al. 2008), and there are unavoidable temporal delays with the transmission of neural signals

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along axons and intramuscular transduction of chemical processes into mechanical force (Herzog 2000). In the context of linear systems, a delayed and noisy mixture of state variables (called y_t) can be written as follows:

$$y_t = Hx_{t-\delta t} + \omega_t, \quad (3)$$

where H captures the linear combination of state variables encoded in the sensory receptor, δt represents the temporal delay expressed in number of time steps, and ω_t is a random noise disturbance.

For the purpose of this paper, we can define a direct feedback controller as follows:

$$u_{D,t} = L_t y_t. \quad (4)$$

When applied to multiple joints, this controller has a MIMO structure and consists of a direct mapping of sensory inflow into motor commands (Fig. 2*C*).

A more efficient class of controllers, also called state feedback control, compensates for the information loss about the state that is inherent to delays, mixing, and noise. This is possible by reconstructing the state vector with an observer as follows:

$$\hat{x}_{t+1} = A\hat{x}_t + Bu_t + K_t\left(y_t - H\hat{x}_t\right). \quad (5)$$

In *Eq. 5*, the "hat" illustrates the estimation made about the state and K_t indicates the gain factor for estimates, which evolves over time; *Eq. 5* does not address the issue of sensory delay (δt in *Eq. 3*), but this problem can be solved in the same formalism with an augmented system (Crevecoeur et al. 2013). Furthermore, *Eq. 5* describes a general observer that is not necessarily optimal. A particular case is when ξ_t and ω_t follow a Gaussian distribution. In this case it is possible to derive an observer that minimizes the uncertainty captured as estimation variance. Such an observer is known as a Kalman filter (Anderson and Moore 1979). A state feedback controller with partial observation is similar to *Eq. 2* with the difference that it applies the gain matrix to the estimated state (Fig. 2*D*):

$$u_{S,t} = L_t\hat{x}_t. \quad (6)$$

It is important to highlight that *Eq. 1* captures the true system trajectory, whereas *Eq. 5* is a simulated trajectory computed by the controller, and that the controller knows the matrices A, B, and H, i.e., the limb and environmental dynamics are known a priori and allow the current state to be internally computed (Wolpert and Gharamani 2000). That is, the ability to make state estimates is based on the presence of an internal model, and poor state estimates (through a faulty internal model or no delay compensation) can lead to inaccurate and irregular behavior (Crevecoeur et al. 2010).

Summary and Hierarchy of Controllers

We have outlined three contrasting ways that controllers can be organized and summarize their main properties in Table 1. These properties are not exclusive or tied to only one control design, and thus Table 1 only focuses on those aspects most relevant to our discussion:

1. Multiple independent controllers (Fig. 2*A*) that individually handle control at each individual joint vs. MIMO controllers that receive information from several effectors and transmit commands to several effectors. These controllers exhibit continuity but would fail to exhibit coordinated responses because each controller response depends on its effector's motion.
2. Continuous feedback controllers that respond continuously to sensory inputs vs. intermittent feedback controllers (Fig. 2*B*) that exert commands at discrete intervals and amounts. Intermittent or hybrid controllers as defined above can exhibit scaling with sensory information only when disturbances exceed the threshold, predicting discontinuity in the response.
3. Direct MIMO controllers (*Eq. 4*, Fig. 2*C*) whose gain matrix (L_t) can be matched to the plant dynamics and whose control signals are solely determined by the instantaneous sensory information (y_t) vs. state feedback controllers (*Eq. 6*, Fig. 2*D*), which also handle the MIMO structure of the body through a gain matrix and generate motor responses based on internal estimations about the state of the limb. Both direct and state feedback controllers exhibit continuous scaling and coordinated responses. Adaptability and adjustments to limb or environmental disturbances is achievable through ad hoc parameterization. In contrast, state feedback controller has intrinsic parameterization in the internal model; thus it can readily generate commands based on estimated variables or adapt to changes in the environment.

A few points should be kept in mind when considering these three contrasts. First, the designs are partially but not entirely exclusive. For example, multiple independent controllers can be either continuous or intermittent, and MIMO controllers can also be continuous or intermittent. Second, the complexity of organization increases from multiple independent controllers to direct feedback control to state feedback control. Last, in principle, both direct and state feedback controllers can be modified to various complexities in limb mechanics, i.e., context or environment. This property is equivalent to assuming that the control gain matrix (L) is designed dependent on the system dynamics (A and B). This assumption is inherent in state feedback control beaus these matrices are used in the observer, whereas it can be made explicitly in the case of direct controllers by parameterizing them.

Table 1. *Summary of contrasting features of the different control designs*

Control Design	Response Scaling	Coordination across effectors	Estimation/Adaptation
Multiple Independent	Yes	No	Difficult: tuning at low frequencies
Intermittent/Hybrid	Beyond threshold	Beyond threshold	(Not specific)
Direct	Yes	Yes	Difficult: through ad hoc parameterization
State Feedback	Yes	Yes	Easy: intrinsically parameterized

Contrasting features of the different control designs based on functions of the long-latency reflex identified from empirical studies.

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LITERATURE REVIEW ON THE LONG-LATENCY REFLEX

Inter-Effector Coordination Reflects a MIMO Neural Controller

As presented in the computational considerations above, the biomechanical system is MIMO. It is also clear that feedback control involves sending motor commands to multiple muscles. The question arises whether the neural basis of LLR has MIMO structure or whether separated controllers actuate individual joints in isolation. A first strong argument against the idea of multiple controllers was already given in the INTRODUCTION, where a LLR in the index finger can be evoked by displacing the opposing thumb (Cole et al. 1984; Cole and Abbs 1987), and during standing, a LLR in the leg can be evoked by a sudden pull on the arm (Cordo and Nashner 1982). These results indicate that information from one body part drives responses in remote body parts. These are just two of many examples (to be treated in detail later) that provide unambiguous evidence for a MIMO structure in the neural controller. The following is a brief accounting of more of these studies: wrist LLRs dependent on elbow information (Koshland et al. 1991; Latash 2000; Weiler et al. 2016), wrist LLRs dependent on other wrist muscles (Cody and Plant 1989), elbow LLRs dependent on wrist information (Kurtzer et al. 2016), elbow LLRs dependent on shoulder information (Kurtzer et al. 2016), elbow LLRs dependent on contralateral elbow information (Dimitriou et al. 2012), shoulder LLRs dependent on wrist information (Maeda et al. 2017), shoulder LLRs dependent on elbow information (Kurtzer et al. 2008, 2009), ankle LLRs dependent on knee and hip information (Safavynia and Ting 2013a), and ankle LLRs dependent on shoulder and elbow information (Lowrey et al. 2017).

The above summary compactly refers to a particular muscle's LLR depending on particular joint's motion, which, to be clear, means that a muscle that crosses the given joint exhibits a LLR following displacement of a different joint. Accordingly, displacing that joint will not stretch or shorten the muscle of interest, and no afferents within that muscle (muscle spindle and/or Golgi tendon organs) could have evoked its LLR; hence, each example points to a MIMO control structure. Afferents from muscles spanning the displaced joint are the most likely sources for these non-local/heteronymous reflexes, but there is no information on which muscle is responsible or in what combination, nor do we want to exclude cutaneous signals, because skin stretch impacts the perception of limb position (Collins et al. 2005; Edin and Johansson 1995). Hence, we describe the situation as *X*'s LLR depending on *Y*'s motion. A final clarification before moving forward is that biarticulars (muscles that cross several joints) do not inherently provide a MIMO structure because they only relay information about their own stretch and not which joint motion induced that stretch, nor do they relay any information for combinations of joint motion that result in zero length change; for example, the biceps muscles is stretched by either elbow extension or shoulder extension, and so there is a combination of flexion at one joint (stretching the muscle) and extension at the other joint (shortening the muscle) that will lead to no changes in the muscle's length. Biarticular afferents to monoarticular motor centers and vice versa are likely present and would provide MIMO structure but have yet to be experimentally identified in detail.[1]

Further indication that the long-latency reflex involves a MIMO neural controller is the synchronization of response modulation evoked by changes in task goal. Long-latency responses are known to be modulated in amplitude depending on the location or shape of the goal target. The coordination across multiple effectors has revealed that this modulation occurs at about the same time across effectors, or at least close to the minimum response latency imposed by sensorimotor delays. Weiler et al. (2015) examined reflex coordination across wrist, elbow, and shoulder muscles where a spatial target was placed medial to the forearm or lateral to the forearm and applied perturbations could be an elbow flexor or elbow extensor. Accordingly, the same perturbation (and same limb displacement) would push the hand toward or away from the target depending on its position. The elbow flexor torque evoked goal-dependent modulation at ~60 ms in the elbow flexor muscle (stretched by the load), the wrist flexor muscle (shortened by the load via intersegmental dynamics), and the shoulder flexor muscle (neither shortened nor lengthened due to the large inertia of the robot) (Fig. 3, *left*). Because the joint kinematics at this time were the same across conditions, the concurrent modulation of arm LLRs is caused by a coordinated descending command and not by mechanical interactions in the biomechanical plant; similar linked changes occurred in the arm's extensors to an elbow extensor torque. The authors also report positive correlations in the trial-by-trial response magnitude of muscles at adjacent joints, between wrist and elbow muscles and between elbow and shoulder muscles. This further suggests that the LLRs for different muscles are scaled together as part of a coordinated action. Note that the earlier studies by this group (Pruszynski et al. 2008 and Weiler et al. 2015) used different target locations and applied torques for the different muscle groups and were not ideal to examine comodulation.

Using the same paradigm, Crevecoeur et al. (2016a) investigated whether the grip force applied to an instrumented object held in precision grip reflected knowledge about the shoulder response modulated in amplitude by the location of the target (Fig. 3, *middle*). Comodulation of their LLRs would demonstrate such knowledge for inter-effector coordination. The authors found that the electromyography (EMG) of muscles involved in grip force generation was modulated at about the same time as the change in shoulder EMG (~60 ms), and this latency for shoulder muscle was similar to the one measured when participants were not holding any object. The concomitant modulation of shoulder and hand muscles also originated in the neural control, because the perturbation-related motion at the onset of the response modulation was the same across conditions. A positive trial-by-trial correlation between LLR of hand and shoulder muscles, such as that seen in Weiler et al. (2016), was also reported in this study.

[1] To our knowledge, only one study selectively stretched a single muscle and examined reflexes in a different muscle (Cody and Plant 1989). These authors applied a step indentation to the tendon of a wrist muscle and observed short-latency and long-latency reflexes in that muscle. When the short-latency reflex from tendon displacement was matched to the short-latency reflex observed during wrist displacement, the long-latency reflex was smaller, which points to the normal involvement of afferents from synergist wrist muscles. In addition, a long-latency reflex was observed in an unstretched wrist muscle that crossed the same joint.

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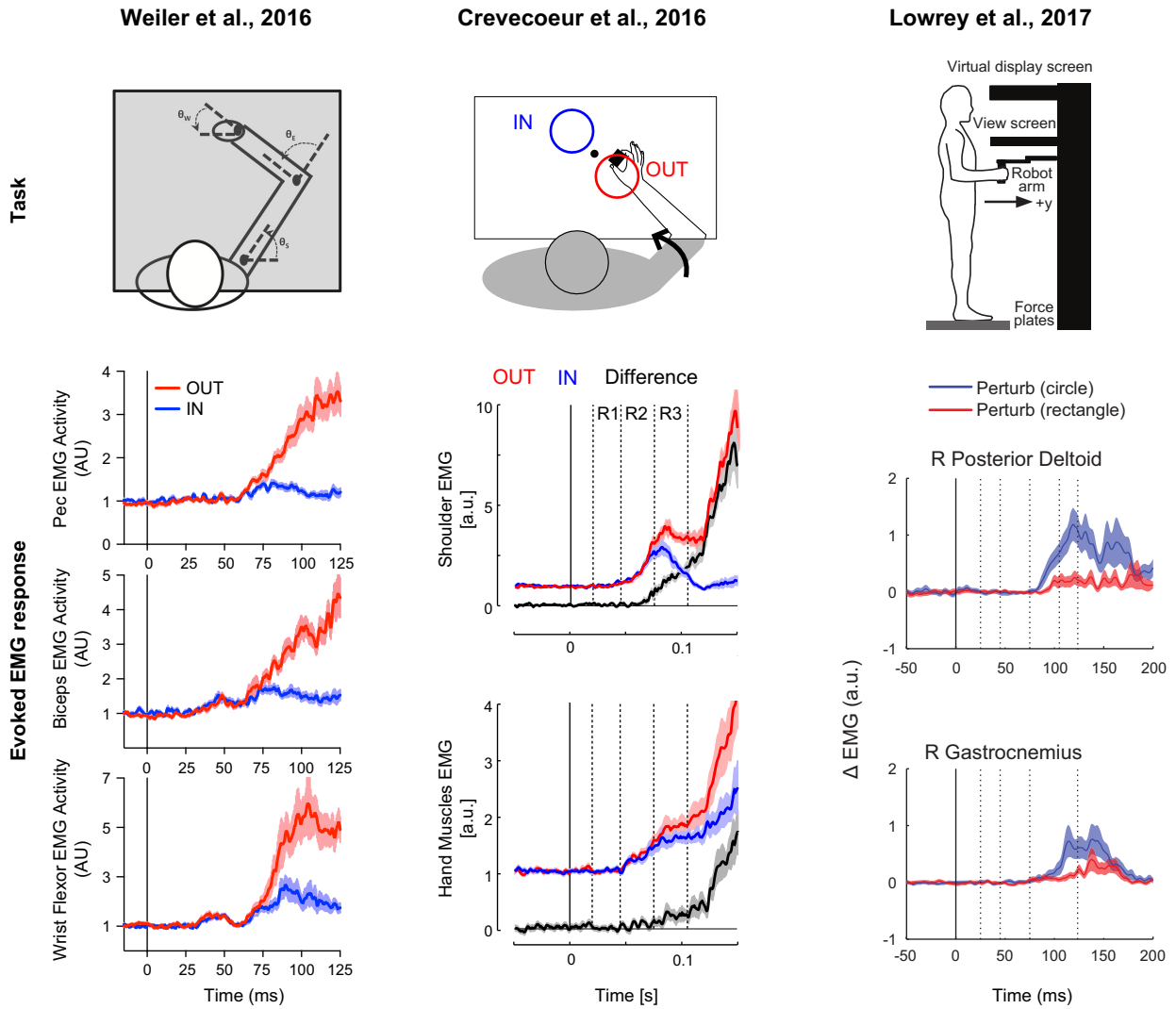


Fig. 3. Coordination of goal-directed feedback. *Left*: IN-OUT task where the same mechanical perturbation could displace the hand toward (IN) or away from (OUT) the goal target. Goal-dependent modulation of activity by the wrist flexor (flexor carpi ulnaris; θ_w), elbow flexor (biceps brachii; θ_e), and shoulder flexor (pectoralis major; θ_s). Perturbations were applied to the elbow. Observe the synchronized electromyography (EMG) response modulation across the muscles. [Adapted from Weiler et al. (2015).] *Middle*: coordination of shoulder extensor (posterior deltoid) and grip muscle (flexor pollicus brevis and adductor pollicus) commands in the IN-OUT paradigm as participants held an instrumented object. Shoulder and hand muscles displayed synchronized modulation of activity dependent on the location of the goal target. [Adapted from Crevecoeur et al. (2016a).] *Right*: coordination of upper limb and lower limb muscles in a reaching task during standing. Goal-directed responses were evoked using a small dot or elongated rectangular target. EMG responses (ΔEMG) are from the upper limb (posterior deltoid) and lower limb (gastrocnemius). Observe synchronized response modulation, with a small delay for lower limb muscles reflecting longer travel times. [Adapted from Lowrey et al. (2017).] AU, arbitrary units; Pec, pectoralis major.

Near-synchronous response modulation was reported by Lowrey et al. (2017), who applied unexpected forward or backward loads to a lateral reach while subjects were standing. Response modulation of upper limb (elbow and shoulder) and lower limb (ankle and knee) muscles was encouraged by altering the shape of the goal target from trial to trial, such that reaching to a dot required a more vigorous response to the perturbation applied to the hand than when reaching to a bar offering a range of successful configurations so one could reduce motor efforts (Lowrey et al. 2017). The authors found target-related changes in the LLR of upper limb and lower limb muscles (Fig. 3, *right*). Again, there was no change in perturbation-related motion that accounted for the response modulation observed at the onset of LLR. It can be observed that LLR modulation started a little later in the lower limb (~80 ms), which is consistent with the slightly longer conduction time needed to reach these muscles.

Interestingly, the routing of motor responses across joints even appears to include rapid pathways to the visual system. By asking participants to visually track their fingertip following perturbations, Crevecoeur et al. (2016b) found a rapid onset of smooth pursuit in the direction of limb motion before 100 ms, possibly as early as 75 ms, which is faster than the oculomotor response to the same visual stimulus without any limb motion. Collectively, these results show a response modulation across muscles that is not accounted for by differences in limb motion, and thus reflect control distributed across effectors. When compared across conditions or effectors, it appears that the delay at which task-related modulation occurred is close to the minimum delay corresponding to the neural transmission times. Thus a series of independent controllers or a cascade of controllers cannot capture these results, contrary to a MIMO neural

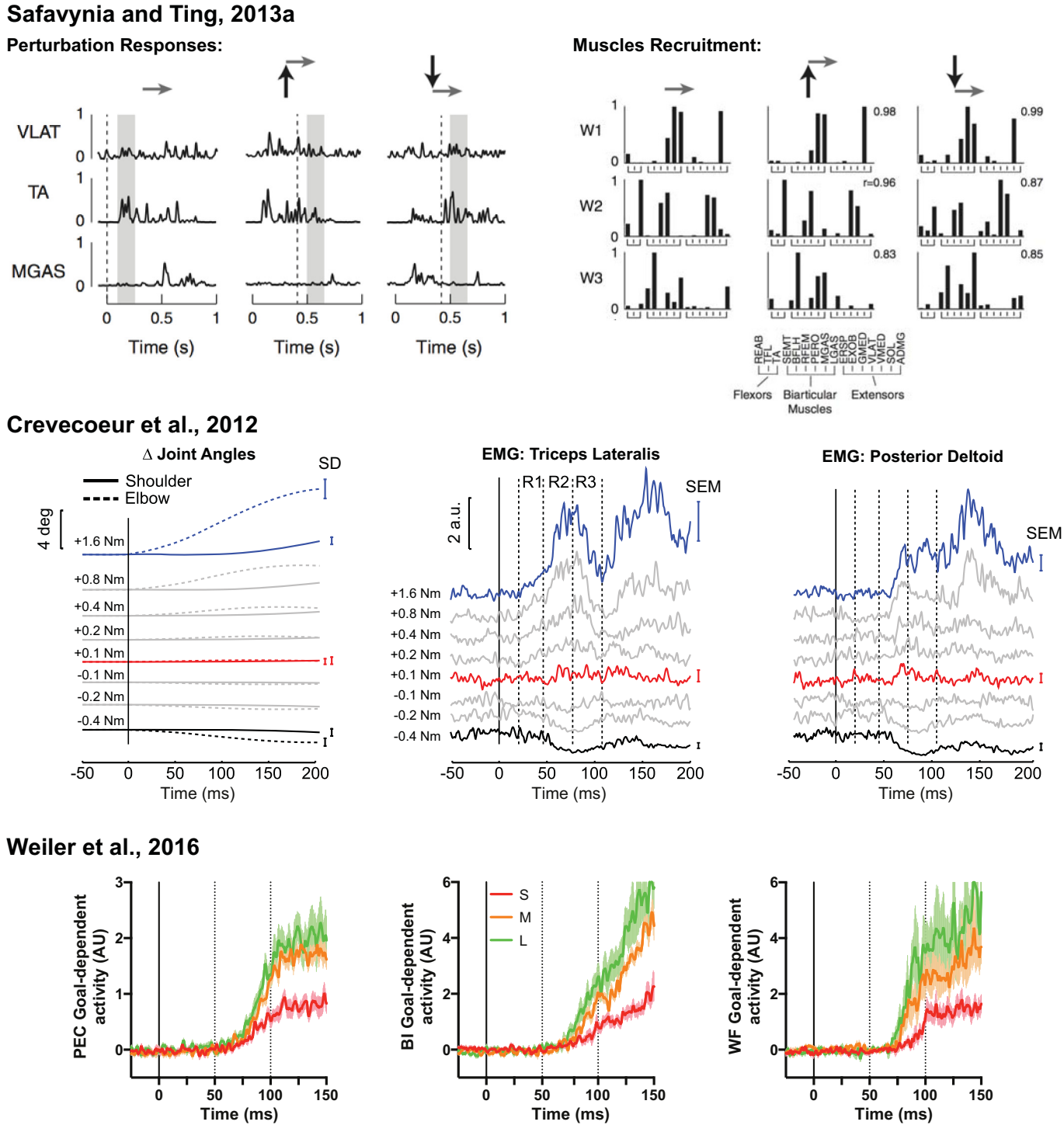
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controller. Of course, there can be internal feedback and cascaded processing supporting more sophisticated functions of later response epochs, but the onset of coordinated responses to meet task demands is supported by a MIMO controller.

Inter-Effector Coordination Best Reflects Continuous, Not Intermittent, Control

A basic issue is whether a controller is organized as a continuous or intermittent process (Fig. 2*B*). There are two domains in which we expect continuity in a continuous control process. First, we expect to see continuity in time so that perturbations applied at any time can generate a motor response. Second, we expect continuity relative to the magnitude of the perturbation so there is no perturbation threshold (above noise) for generating a motor response.

Evidence for continuous responsiveness in the LLR across time was provided by Safavynia and Ting (2013a). They examined the control of whole body posture to different directions of platform motion in a single ramp or delivered on top



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of an ongoing forward or backward displacement (Fig. 4, *top left*). In each case, nonnegative matrix factorization extracted the intermuscular pattern of activity that best accounted of the overall response variance (Fig. 4, *top right*; 3 first components were retained for illustration). Importantly, the collective patterns within the LLRs of leg and trunk muscles were highly consistent across the three situations, i.e., the same multimuscle coordination was evoked from a quiet state and during the ongoing evolution of muscle activity to a forward or backward displacement. A significant limitation of the work is the wide spacing between the two successive perturbations (400-ms delay), which is within the 2- to 3-s update rate reported for intermittent control of body posture (Lakie and Loram 2006) and well above the 70-ms floor reported for monkeys' wrist movements (Fishbach et al. 2007). Partially addressing this is a study by Soechting and Lacquaniti (1988), who examined elbow and shoulder muscle reflexes by using a random sequence of torque pulses with denser occurrence; the m-sequence with bins of 40 ms yielded a modal perturbation spacing of 40 ms and mean perturbation spacing of ~75 ms. Cross-correlation of the evoked activity by the arm muscle responses with the pulse perturbations revealed that the average LLRs incorporated motion of both joints; however, this approach mixed the responses from all perturbation durations, and 25% were $\geq$120 ms. Denser sampling in time would yield a more stringent test. A preliminary study (Kurtzer 2015a) leveraged the observation that a single perturbation displacing the elbow (and only the elbow) evokes a LLR in the unstretched shoulder extensor (Kurtzer et al. 2008). A second elbow displacement was applied 35, 60, or 110 ms after the first elbow displacement and evoked a second burst of shoulder muscle activity (relative to the single sustained step) at a fixed delay of ~50 ms. Likewise, torque offset at 35, 60, or 110 ms led to an attenuation of shoulder muscle activity (relative to a sustained step) at a fixed delay of $\approx$50 ms. If this preliminary reports bears out, then it would either indicate intermittency $\leq$35 ms (far below previous reports) or support the more parsimonious explanation of continuous control.

Continuity of response magnitude relative to the perturbation magnitude was found in long-latency reflexes to mechanical perturbations of the upper limb. Crevecoeur et al. (2012) used very small (often undetected) perturbations ($\pm$0.1 Nm) that displaced the elbow by $<0.2^\circ$ in 50 ms and still found excitatory and inhibitory LLRs in the unstretched shoulder muscle (Fig. 4, *middle*). These LLRs scaled linearly with the small perturbation magnitudes and approached the natural variability of postural maintenance or point-to-point reaching, indicating the fine-grain modulation of inter-joint reflexes. Although response thresholds most likely exist at the level of individual sensory or motor components of the motor system, it appears that these thresholds operate below the magnitudes of changes that may impact behavior and suggest that there is no "dead zone" within which perturbations fail to evoke a LLR.

Supplementing the evidence described above are studies focused on how the LLR changes with different instructed tasks and goals. Hammond (1956) first reported that greater arm LLRs occurred if subjects were instructed to "resist" the displacement rather than "yield" to the displacement. Such changes were described as a "triggered reaction" by Crago et al. (1976) because the LLR was more variable with a "resist" instruction than a "do not intervene" instruction, which presumably assays automatic contributions. Further evidence for a triggered reaction conception is that similar task-related LLRs can be evoked with assistive and resistive perturbations when subjects are instructed to initiate a reach in a specific direction (Ravichandran et al. 2013; see also Koshland and Hasan 2000).

In contrast, other studies show continuous changes in the magnitude of task-dependent activity. Figure 4, *bottom*, shows how the goal-dependent changes in the wrist, elbow, and shoulder LLRs scaled with small, medium, and large perturbations applied to their joint (data from Weiler et al. 2016). Hence, this is a general characteristic of the arm's LLRs. Task-dependent changes in the arm's LLR are also continuously linked to different target locations (Pruszynski et al. 2008), temporal demands on acquiring the target (Crevecoeur et al. 2013), size of the perturbations (Pruszynski et al. 2008; Weiler et al. 2016), likelihood of the perturbation (Rothwell et al. 1980), and the evolving belief of target placement before a perturbation (Selen et al. 2012). Additionally, returning to our first example of multi-joint LLRs, shoulder LLRs express differential task-dependent LLR activity according to the direction of elbow displacement when subjects return their hand to the starting target, i.e., resist perturbations in any direction (Kurtzer et al. 2014).

Taken together, the weight of evidence indicates that the long-latency reflex is engaged continuously in time and mag-

Fig. 4. Continuous control. *Top*: participants stood on a platform that moved along different directions or followed a sequence of perturbations. Response patterns are selected from vastus lateralis (VLAT), tibialis anterior (TA), and medial gastrocnemius (MGAS) muscles following perturbations to the right (gray arrow) in a discrete setting or in a biphasic setting where it was preceded by a forward or backward perturbation (black arrow). Vertical dashed lines indicate onset from a single step perturbation or onset of the second step perturbation. Shaded region following each perturbation indicates the time window for analyzing long-latency reflexes (LLRs) of the leg muscles. Extracted response patterns from all muscle samples across discrete and biphasic conditions (3 first response components) are shown at *right*. Observe that these components are highly reproducible across conditions, which indicates a consistent structure in the response pattern. The following muscles were identified: rectus abdominis (REAB), tensor fascia lata (TFL), TA, semitendinosus (SEMT), long head of the biceps femoris (BFLH), rectus femoris (RFEM), peroneus longus (PERO), MGAS, lateral gastrocnemius (LGAS), erector spinae (ERSP), external oblique (EXOB), gluteus medius (GMED), VLAT, vastus medialis (VMED), soleus (SOL), and adductor magnus (ADMG). [Modified with permission from Safavynia and Ting (2013b).] *Middle*: scaling of shoulder and elbow responses to multi-joint perturbation torque applied to both joints simultaneously, which initially displaces just the elbow joint. Perturbations of distinct magnitudes were applied. The elbow response displayed a short-latency (onset ~25 ms) stretch response followed by long-latency and voluntary activity. The shoulder muscle was initially unstretched and expressed no short-latency activity. However, this muscle exhibited reliable long-latency responses that scaled with the perturbation magnitude (Crevecoeur et al. 2012). *Bottom*: scaling of LLR with perturbation magnitude. The response elicited by a perturbation moving the limb away from the perturbations is contrasted with the response evoked when the perturbation pushing the limb toward the target, thereby extracting the response component related to the target location. Show is the scaling of the target-related response with the perturbation amplitude (S, small; M, medium; L, large). The muscles of interest were the pectoralis major (Pec; shoulder flexor), biceps brachii long head (BI; biarticular elbow flexor), and the flexor carpi ulnaris (WF; wrist flexor). [Adapted from Weiler et al. (2016) with permission.] AU, arbitrary units; EMG, electromyography.

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nitude, which favors continuous control, not intermittent control, as the basis for coordinating different effectors.

Inter-Effector Coordination Reflects the Mechanical Properties of the Body

The studies described above demonstrated that the neural mechanism supporting long-latency reflexes has a MIMO structure. Below we review some studies showing that, in addition, these responses integrate disparate information in a way that is appropriate for the mechanical properties of the body. As previously mentioned, selective displacements of the elbow will evoke LLRs in unstretched/unshortened shoulder muscles (Kurtzer et al. 2008, 2009). These shoulder responses are appropriate to counter the underlying shoulder (and elbow) torque that caused motion at just the elbow; that is, intersegmental dynamics necessitate that motion at one joint is due to torque being applied at multiple joints. Elbow muscles also express LLRs to selective displacement of the shoulder that is appropriate to counter the underlying elbow (and shoulder) torque (Kurtzer et al. 2016). A different example in the upper limb are the LLRs in an elbow extensor to sudden wrist pronation (Gielen et al. 1988). Although the elbow extensors are not directly impacted (stretched or shortened) by wrist pronation, their action counters the elbow flexion from biceps brachii (an elbow flexor and wrist supinator) as it is engaged to compensate the pronating perturbation. Hence, the elbow's LLR is tuned to the chain of interactions that different muscles exert on the skeleton.

Three different research groups have reported wrist LLRs to elbow displacement via an applied elbow torque (Koshland et al. 1991; Latash 2000; Weiler et al. 2015, 2018). Notably, in these situations the wrist muscle activity does not counter the underlying torque, but rather helps bring the hand to the target. Consider that an elbow extensor torque will extend the elbow and flex a supinated wrist via interaction torque. The hand can return toward the starting position by flexing the elbow, flexing the wrist, or flexing both together (Fig. 3, *left*).

Safavynia et al. (2013b) reported complementary findings in a full-body balance control task during which leg muscles integrated disparate information appropriate for the limb's mechanical properties. Their subjects stood on a platform moving in a sequence, which decorrelated the motion pattern of the ankle and the body's center of mass (Fig. 5, *top*). The best reconstruction of evolving ankle muscle activity was achieved by center-of-mass kinematics driving a continuous closed-loop controller with long-latency delay. Local joint kinematics or any combination of two-joint motion gave poorer fits to the data and delays incompatible with the physiology.

Inter-effector coordination by the LLR is not fixed but exhibits considerable flexibility to the body's configuration, the environmental setting, and task demands. Kurtzer et a. (2008) reported that shoulder LLRs to selective displacement of the elbow depended on the elbow's starting angle; greater responses occurred when the arm was maintained in elbow extended posture than when in elbow flexed posture (Fig. 5, *middle*). Similarly, Maeda et al. (2017) showed that wrist position impacted the magnitude of shoulder LLR to elbow displacement; greater LLRs occurred with the wrist extended than when flexed(Fig. 5, *bottom*). In both cases, the change in LLR magnitude appropriately accounts for how the arm's mass distribution varies with joint configuration and, hence, the change in torque (exerted or applied) required to move the limb. Another example of position dependency is the aforementioned LLRs of wrist muscles to elbow torque perturbations. Their LLRs reverse depending on the wrist orientation. With the wrist in a pronated position, an elbow flexion will evoke a LLR in the wrist flexor, but with the wrist in a pronated position, an elbow flexion will evoke a LLR in the wrist extensor (Koshland et al. 1991; Weiler et al. 2018). These changes ensure that the hand is directed to the starting position.

Another set of studies to consider are those examining the mechanical interactions between the limbs and the body. Perhaps the earliest reports of inter-effector coordination by the LLR focused on this situation. Marsden et al. (1981) had subjects (themselves) resist pulls to the thumb of one arm while stabilizing their stance. When their body was completely supported, they exhibited LLRs in hip muscles appropriate to stabilize the trunk. Responses in more remote muscles (including the foot and opposing arm) occurred with suitable positioning, such as leaning forward or bracing a table with the opposite hand. Subsequent researchers built on these initial reports and obtained comparable results. Cordo and Nashner (1982) found that forward pulls on the hand of standing subjects evoked LLRs in leg muscles to tilt the body backward. The reverse situation was also observed given that forward translation of the platform (tiling the body backward) evoked stabilizing LLR of the arm's elbow flexor, which tilted the body forward. Also, as described before, Lowrey et al. (2017) examined postural responses of leg and trunk muscles during perturbations of an ongoing reaching movement. A backward displacing force applied to the reaching arm evoked LLRs of both arm and leg muscles; the leg responses were appropriate to stabilize the body's center of mass as confirmed by recordings of the force plate on which they stood.

Long-latency reflexes can express knowledge of the mechanical properties of the body and environment during tasks that do not require inter-effector compensation, as in the previously described studies, but are benefitted from their involvement. Consider a pinching task where the aperture between the finger and thumb depends on the position of each (Cole et al. 1984; Cole and Abbs 1987). Because perturbations to one digit do not mechanically impact the opposing digit, compensation can be achieved by responses in just the perturbed digit. However, engagement of both digits distributes the work effort, and in fact, flexion perturbations applied to the thumb during a finger-thumb pinching task will elicit a LLR in the opposing finger flexion and even different combinations of inter-phalangeal and metacarpal contribution depending on the perturbation timing appropriate to bring the tips of the two digits together (Cole and Abbs 1987).

Similar task-relevant coordination has been reported by Dimitriou et al. (2012) during a tray balancing task. Each hand controlled one side of the simulated tray, and subjects were instructed to keep the tray level. Perturbations that displaced one side down (pulling the arm forward or pushing one arm back) resulted in a long-latency excitation or inhibition in the contralateral arm to upright the tray. The magnitude of LLR reflexes involving both arms can even be influenced by the

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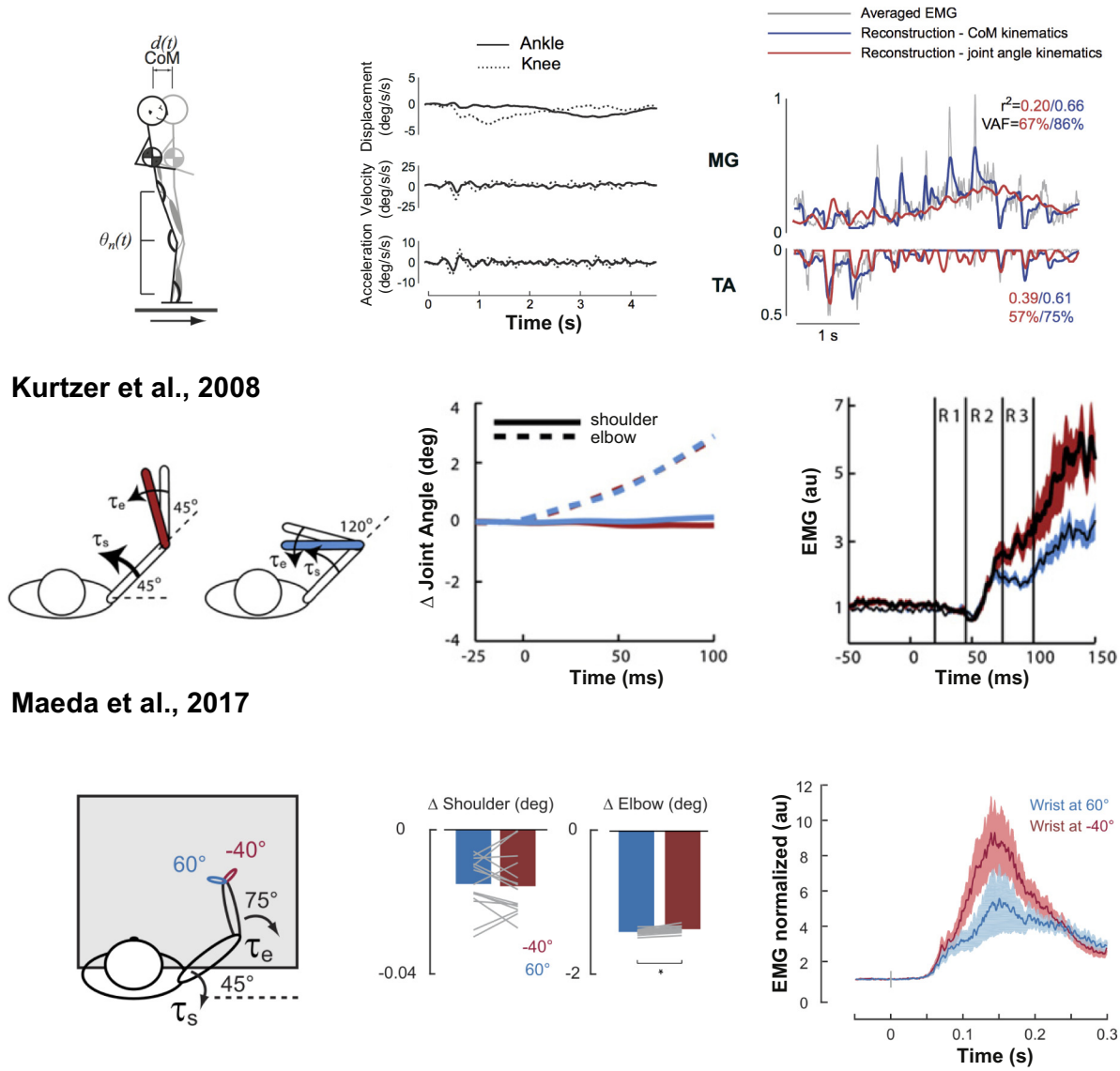


Fig. 5. Internal models. *Top*: illustration of the platform displacement inducing full body motion (*left*). Displacement, velocity, and acceleration of the ankle are shown in a series of perturbations applied to the base of support (*center*). Electromyography (EMG) responses of tibialis anterior (TA) and medial gastrocnemius (MG) were well approximated with a model of control of the center of mass (COM), whereas a feedback control model based on the two joints did not account for the response pattern (*right*). [Adapted from Safavynia and Ting (2013b).] *Middle*: illustration of multi-joint perturbation applied to the shoulder and elbow joints (*left*). Similar amounts of elbow motion for distinct levels of underlying shoulder torque are shown (*center*). Average EMG responses across participants are shown (*right*). The modulation of response gain in the long-latency reflex reflects knowledge of the link between motion and torque across distinct joint configurations. [Adapted from Kurtzer et al. (2008).] *Bottom*: illustration of multi-joint perturbation applied to the shoulder and elbow joints with different initial wrist configurations (*left*). Large changes in elbow angle at 50 ms following the perturbation with little to no motion of the shoulder, with no difference across the two wrist configurations, are shown (*center*). Scaling of the shoulder EMG dependent on the wrist angle was consistent with an internal model of inter-segmental dynamics (*right*). [Adapted from Maeda et al. (2017).]

visuomotor mapping. In a study by Mutha and Sainburg (2009), subjects performed bilateral reaching movements to move a cursor whose lateral position was the average of the two arms' lateral placement. Leftward perturbations applied to the right arm during movements resulted in rightward LLRs from both arms appropriate to move the shared cursor back to center. A related postural study found that perturbing both arms outward resulted in low LLRs when they controlled a single cursor (because little cursor motion was induced due to spatial averaging) than when each arm controlled its own cursor (Omrani et al. 2013).

Many of the previous examples of inter-effector LLRs also exhibit context dependency. Subjects do not exhibit LLRs in their leg to a pull on the arm when bracing the body at the shoulder and so eliminating the mechanical transmission between the arm and body (Cordo and Nashner 1982; see also Marsden et al. 1981). Complete cessation of finger LLRs occurs to thumb perturbations when the finger is pressing on a solid surface (Cole et al. 1984); inter-arm LLRs also disappear when subjects control two different cursors rather than a common object (Dimitriou et al. 2012). However, in other cases, the LLRs appear to be unaffected by mechanical brac-

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ing. Shoulder LLRs to elbow motion (Crevecoeur et al. 2012), elbow LLRs to shoulder motion (Kurtzer et al. 2016), and wrist LLRs to elbow motion (Koshland et al. 1991) are all retained when the respective joint is physically restrained. Another last example comes from LLRs evoked during standing. Corna et al. (1996) examined reflexes of ankle muscles with a tilting platform. When one leg was placed on the platform and the other on a stable surface, both legs exhibited LLRs to platform tilt, albeit smaller in the unperturbed leg. It is not entirely clear what purpose is served by activity in the unperturbed limb because it would not stabilize the body against the imposed perturbation. We will return to these putative exceptions in the DISCUSSION.

Inter-Effector Coordination Reflects State Feedback Control

So far we have argued that inter-effector long-latency reflexes are best accounted for by a continuous MIMO controller that is tuned to limb mechanics. Computationally, this implies that the controller is parameterized in such a way that changes in limb configuration evoke distinct responses for similar amounts of motion. Such parameterization is, in principle, achievable in a direct control design and requires that the control gains be tuned on the basis of an internal model of limb dynamics. We now turn to the adaptability of these responses relative to environmental dynamics, which in the experiments described below could not be directly inferred on the basis of sensed motion or limb configuration. These results thus suggest that internal or external variables not directly measured are internally calculated/estimated to generate a motor response. Ultimately, these features can be reproduced in a direct, parameterized controller setup to account for any feature of environmental dynamics. A simpler design that accounts for these results is a state feedback controller, which includes knowledge dynamics and uses internal estimated state to generate control.

One key property of LLRs is their adaptability to novel environmental dynamics, paralleling studies on motor adaptation to altered dynamics (Lackner and Dizio 1994; Sainburg et al. 1999; Shadmehr and Mussa-Ivaldi 1994). Subjects quickly adapt their anticipatory actions to the introduced movement-dependent forces through updating of a structured representation of limb dynamics, i.e., an internal model (for extensive review see Shadmehr 2014). Feedback corrections are also modified during motor adaptation and reflect changes to an internal model (Wagner and Smith 2008). Most recently, adaptive changes within the long-latency reflex have been identified during motor learning. The perturbation-evoked LLRs mirrored the novel force field and were correlated with the time course and extent of anticipatory adaptation (Ahmadi-Pajouh et al. 2012; Cluff and Scott 2013). Although both these studies involve multiple joint movement and almost certainly the same learning mechanisms, Cluff and Scott (2013) provided clearer evidence of inter-effector changes. Adaptation of reaching movements to a velocity-dependent elbow load resulted in upscaled elbow LLRs to a pure elbow displacement (applied during movement) but less upscaling of shoulder LLRs, consistent with the fact that the change in dynamics primarily affected elbow motion.

Another approach to testing adaptation of inter-effector LLRs involves position-dependent force fields. Krutky et al. (2010) employed a negative spring environment, forces directed away from a particular axis in space, and report scaling of the LLRs to specific directions of instability (not a global change), which suggests selective reweighting of multi-joint LLRs. Across these studies, the joint configuration was controlled (e.g., perturbations at the same time during the reach, or before movement during static holding at the start target), and yet responses differed across contexts. A final example of adaptability supporting LLR was recently given by Weiler et al. (2018). They reported that reversing the visuomotor mapping between limb motion and cursor modified how wrist LLRs to an elbow perturbation flip with supination and pronation; notably, this modification evolved over several days of practice in contrast to the examples above, which took a few minutes to recover near-baseline values after returning to the normal mapping. Thus the control gains are not solely tight to sensory feedback, as in a direct control framework, but also integrate knowledge about the environment, and this modification has different timescales for different rearrangements.

The most complex controller that we defined consisted of a state feedback controller, which, given sensory delays, mixing, and noise, implies the presence of an observer (*Eq. 5*). We must recall that this controller has a MIMO structure, is inherently parameterized to handle mechanical interactions and can represent environmental disturbances as a result of internally generated signals about the presence and properties of an external load. One experiment tested this hypothesis directly in the context of single effector control. Crevecoeur and Scott (2013) applied torques with distinct temporal profiles presented either as catch trials or in a blocked fashion. When presented as catch trials, these profiles had similar rise time and amplitude to standard step perturbations but quickly changed to the opposite plateau value within 50 ms so that the initial rate and final level were negatively correlated, unlike torque steps. The data showed that participants responded to catch perturbation as if they expected a step load, and also that they learned and adapted to the catch perturbations when presented in blocked fashion. Because information about the first 50 ms of the perturbation profile is not available at the response onset, the modulation and adaptation of LLR must reflect the use of internal priors, which is the signature of internal models and state feedback control.

In the context of multi-effector coordination, these results were extended to multisensory integration and eye-hand coordination. The specific prediction of a state feedback controller was that the combination of limb and visual afferent feedback following a perturbation would be linearly combined as expected under static conditions, but it is their extrapolation to the present that are combined, leading to a larger contribution of proprioception after a transient load. Crevecoeur et al. (2016b) had subjects visually track their arm during mechanical perturbations paralleling estimation of voluntary reaches. The paradigm followed that of Ariff et al. (2002), who used visual tracking accuracy during reaching movements as a proxy of an internal estimate of limb motion, or a "real-time predictor," and highlighted transient inhibition of saccadic movements following perturbations consistent with a recomputation of future hand motion. Following the same rationale, visual responses to visual and mechanical perturbations to the cursor and to the limb were used to probe how the nervous system estimated the perturbation-related motion. Applying a

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torque step (at random intervals) to the elbow not only evoked elbow muscle reflexes but also evoked a fast smooth pursuit eye movement in the direction of the moving arm. The time delay of the eye muscle activity was faster than visual responses to the same visual stimulus without any limb motion. Another key observation was that the latency of saccadic responses to the mechanical perturbations was almost the same with or without vision, whereas the estimation variance decreased. These results were consistent with a model including an observer that compensated for the delay of both visual and somatosensory feedback, thereby accounting for similar response latency while reducing the estimation variance specifically from the visual pathway.

The literature review above provides evidence that inter-effector coordination by the LLR is not a "default" mapping of sensory signals into motor commands. Rather, it exhibits considerable flexibility to the body's configuration, the environmental setting, and task demands. These abilities are, in principle, achievable by a direct controller if the control gains can be varied or swapped with a direct controller according to the situation. Such design requires ad hoc tuning of the control matrices to each context or condition adjusted in a specific way. A simpler and unified framework to express similar complexity is to assume an internal model, which explicitly mimics the plant dynamics. Stronger evidence for state feedback control is the reconstruction of complex state variables and state estimation (Fig. 2*D*), which is supported by the adaptability of LLR to visuomotor perturbation or changes in limb or environmental dynamics and by the hypothesis of state estimation underlying rapid feedback responses as well as delay-dependent multisensory integration.

DISCUSSION

The present review attempted to synthesize studies extending over four decades on how the long-latency reflex contributes to multi-effector coordination. Specifically, we examined how these studies illuminated the basic organization according to four classes of controllers: continuous vs. intermittent feedback controllers, multiple independent controllers, a direct MIMO controller, and a state feedback controller. The cumulative evidence points to a continuous state feedback controller. Continuity of responsiveness by the LLR was evident across both time and magnitude. Evidence against multiple independent controllers and for a MIMO controller was provided by simultaneous control signals across multiple effectors in response to a perturbation. Evidence for state feedback control vs. direct control is that LLRs are based on sensory estimates rather than sensory states alone. Further evidence for state feedback control includes the breadth of flexibility in feedback responses to account for the body and environment's mechanical properties. Below we discuss some important issues surrounding our literature review and conclusions.

Multi-Joint Integration is Common for the Long-Latency Reflex and Rare for the Short-Latency Reflex

In all the cited papers on inter-effector LLRs, none found a similar capability for the associated short-latency reflexes. Manning and Bawa (2011) reported that several muscles of the hand and elbow exhibited short-latency reflexes to wrist displacement,[2] and Stevenson et al. (2015) reported cross-leg limb short-latency reflexes to knee displacement. To our knowledge, these are the only reports to show multi-joint responses at short latency to imposed displacements of a limb segment, although other (less ecological) stimulation techniques have some effectiveness, such as electrical stimuli (Cavallari and Katz 1989; Elliott et al. 2011; Iglesias et al. 2008), tendon taps (Lewis and McNair 2010), and muscle vibration (McClelland et al. 2001). We find this scarcity surprising given the rich connectivity of spinal circuits (Pierrot-Deselligny and Burke 2012), plasticity with sufficient training (Thompson and Wolpaw 2014), and the fact that the necessary links are only a few synapses and spinal levels away. The circumstances or contexts under which the short-latency reflex can integrate information from different effectors under different combination remains an important question for prospective studies. From the wide variety of paradigms presented above, we can confidently state that the LLR is the earliest response that exhibits this capability as a general rule. As to the physiological substrates for this specific capability, only the primary motor cortex has been specifically tested and confirmed (Pruszynski et al. 2011), although brain stem and slow spinal circuits are well positioned to contribute (for review, see Kurtzer 2015b). More physiological studies are needed to clarify this issue.

Limitations of Our Current Knowledge and Approach

There are several limitations to the reviewed literature, approach, and conclusions that should be addressed. All but one of the cited studies (Gielen et al. 1988) used surface EMG whose signals are low-pass filtered by intervening skin and adipose, which can obscure the time response of the underlying action potentials. We do not think this significantly impacts the result because similar results were obtained in the study that used single-unit recordings and EMG (Gielen et al. 1988), and another study using fine-grained analysis (such as running receiver operating characteristic) determined that multi-joint integration occurs near the beginning of the LLR window (Kurtzer et al. 2013). That said, single-unit recording would enable one to isolate particular motor units and their recruitment. The few studies on this topic suggest a shift between motor units engaged during the short-latency reflex and during the long-latency reflex. New techniques in decomposing surface recording activity into constituent motor units from high-density recordings (Johnson et al. 2017) would likely help clarify this and help us understand how the control signal is constructed. Single-unit recordings also have the advantage of avoiding cross talk, although we consider this a minor issue. Most studies examined LLRs from muscle response far from those directly impacted (stretched/shortened) by the joint displacements. The multi-joint responses were also expressed in the LLR but not in the earlier short-latency reflex, which argues against cross talk.

Another issue regards the level of detail of the models we considered. These did not involve specific details about sensory transduction, neuron dynamics, interneuron networks, or muscle mechanics. These features are undoubtedly essential for actual behavior and could provide further insight on its modeling along with some constraints. For example, how

[2] A preliminary report by Pruszynski and colleagues appears to confirm and extend the existence of a wrist-to-elbow fast spinal circuit (Weiler et al. 2018).

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might neural oscillations impact the processing of information for sensorimotor control (e.g., Yang, in press), how does cerebellar architecture determine its putative role as an internal model (e.g., Galliano and De Zeeuw 2014), and how does multi-muscle reflex control mediated by cutaneous pathways (e.g., Pratt et al. 1991) relate to proprioceptive processing?

The final issue is the functional significance of the LLR to everyday sensorimotor behavior. We expect that LLRs are engaged in most activities given their recruitment by quite small perturbations and linear increase with perturbation size through a broad range. Certainly, the LLR can exert a measurable affect on behavior during comparison of different movement trajectories with different LLRs (e.g., Crevecoeur et al. 2013). Although their responses tend to be smaller than the subsequent voluntary epoch, that could reflect the combined response of sustained activity by long-latency circuits along with voluntary-specific circuits. Testing this hypothesis (and the previous limitations we raised) will require richer paradigms and analyses for probing the underlying physiology under natural conditions.

Relevance of Optimal Feedback Control

The present review focused on organizational features of the LLR that set constraints on any candidate model of neural feedback control. Optimal feedback control can incorporate these capabilities, but emphatically does so as constraints for designing the optimal control law. One could also design an optimal control law for multiple independent controllers, MIMO direct controllers, or any other of these using intermittent feedback. These are constraints on the basic organization of the system. The optimal control law determines the sequence of gains that achieves the lowest expected cost. Typical cost functions include a term that penalizes motor error (final and during movement when applicable) and a penalty on control variable, which capture metabolic or energetic expenses. It is thus a trade-off between movement efficiency and control-related cost, and we believe that the adjustment of this trade-off constitutes the definition of task success.

Optimal control models have been criticized for the required computational complexity in finding the optimal control law, a requirement that may appear biologically implausible (Friston 2011; Loeb 2012), or accounting for limits in adaptation (de Rugy et al. 2012). Hence, alternative views have sought simpler models with smaller computational load and sometimes more detailed physiological circuits to implicitly solve the computations. These have received some empirical and modeling support (Buhrmann and Di Paolo 2014; Hudson et al. 2010; Liesker et al. 2009; Ota et al. 2016; Raphael et al. 2010; Zhang et al. 2010). Optimal feedback control is a powerful model to capture the most efficient behavior, yet it does not tell much about how the nervous system may converge to the corresponding control solutions, and this remains an open question for optimal feedback control models as well as alternative models. The data sets a constraint on the complexity of the underlying closed-loop model, but this complexity can be distributed across the system representation and the controller design. In our view, the bias of optimal feedback control is to consider state feedback control of a sufficiently complex system model (*Eqs. 1*, *3*, *5*, and *6*; "complex" is used in the sense of having sufficiently many state variables and degrees of freedom), but with these settings, the continuous state feedback control solution emerges in a well-defined framework, leading to the large amount of predictions and experiments inspired by this theory. Alternative theories often take the bias of considering a simpler closed-loop model, such as reflex arcs (Friston 2011), and relegate the necessary complexity to the tuning of each simpler control unit (although simulations of even simple systems are rarely provided). The main drawback is that these views do not capture the complexity of LLR that we highlighted above. In addition, practically speaking, we do not know how to solve these problems efficiently.

Our review focused on LLR coordination across effectors while leaving aside other aspects of their flexibility. Indeed, previous work in the context of single or multiple effectors shows that LLRs change with virtually any change in task demand (Pruszynski and Scott 2012). This aspect in the framework of optimal feedback control can be handled by changing the cost function characterizing task constraints, which has a direct impact on the associated control law. It is clear that in addition to inter-effector coordination, flexibility and task- or goal-related changes in feedback control constitute an essential aspect of LLRs. Although the derivation of the control law may not appear as a plausible mechanisms for sensorimotor control, OFC may in fact be the simplest control theoretic model accounting for both neural control architecture and the expression of flexible, task-related control laws.

Optimal feedback control can also help address two observations. First, the feedback response of different effectors shares responsibility to achieve a given task, such as the LLR in the index finger-to-thumb displacement during a pinch task (Cole et al. 1984). Such sharing is a natural consequence of an optimal feedback law designed to minimize motor effort and maximize accuracy, because each effector exerts less than one alone and signal-dependent noise is diminished as a result (Todorov and Jordan 2002). The result also dovetails with a large number of studies showing a distribution of work across effectors consistent with an optimization processes (Córdova Bulens et al. 2018; Fagg et al. 2002; Kurtzer et al. 2005; Nozaki et al. 2005; O'Sullivan et al. 2009; Todorov and Jordan 2002). Second, in a few instances the inter-effector LLR did not reconfigure to a change in context and instead persisted in actions that were ineffective and/or wasteful. This occurred in the LLRs of wrist (Koshland et al. 1991), elbow (Kurtzer et al. 2016), and shoulder muscles (Crevecoeur et al. 2012) when their respective joints were physically locked. Persistent muscle activity under blocked conditions is also present during voluntary arm action such as phasic shoulder muscle activity during elbow movement even when the shoulder is blocked; a slow decrease was observed after several hundred trials (Debicki and Gribble 2005). We suspect that this persistence reflects the effect of prior history on the internal model. Our intuition is there are fewer occasions where the elbow joint is physically fixed in place compared with external bracing of the body against arm motion, e.g., laying face down on a bed and reaching for a shoe. The few studies recording natural movement statistics have reported that movement frequency is related to movement preference and capability (Howard et al. 2009; Ingram et al. 2008). Studies of reach adaptation have also reported a strong bias to the intrinsic dynamic coupling (Singh and Scott 2003) and the history of prior action (Krakauer et al. 2006) consistent with the internal models

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based on optimal use of current and previous information. Presumably, strong priors also account for why platform tilt of one leg evokes (smaller) LLRs in the unperturbed leg (Corna et al. 1996); the most common situation involves tilt of both, and this forms the prior used in state estimation. In this vein, Weiler et al. (2018) found altered wrist LLRs to reversed vision, but only after several days of practice.

Adopting or not adopting optimal control as a system model of behavior leaves open the question of how neural structures represent or "compute" the control laws. Considerable work needs to be done to clarify processing capabilities, limits, and relations of the long-latency reflex in coordinating different effectors. This effort can be confidently built on a well-defined framework established by the literature reviewed above. This literature and the control theoretic concepts that we proposed were focused on the system level: that is, we analyzed input-output properties of the neural controller based on timing and amplitude of EMG responses across limbs. A clear challenge for future work is to deepen our understanding of the neural basis of rapid feedback control by analyzing how the activity of neurons supports the emergent flexible controller that characterizes behavior.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

F.C. and I.L.K. conceived and designed research; F.C. and I.L.K. interpreted results of experiments; F.C. prepared figures; F.C. and I.L.K. drafted manuscript; F.C. and I.L.K. edited and revised manuscript; F.C. and I.L.K. approved final version of manuscript.

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