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Muscle, Biomechanics, and Implications for Neural Control*Lena H. Ting^{1,2} and Hillel J. Chiel³*¹*Department of Biomedical Engineering, Emory University and Georgia Institute of Technology, Atlanta, GA, USA*²*Department of Rehabilitation Medicine, Division of Physical Therapy, Emory University, Atlanta, GA, USA*³*Departments of Biology, Neurosciences, and Biomedical Engineering, Case Western Reserve University, Cleveland, OH, USA***12.1 Introduction**

Understanding neural and biomechanical interactions is fundamental to motor control. Nervous systems arose in the earliest motile animals, allowing them to move purposefully through the environment. For example, some tunicates have a complex nervous system in their juvenile stages that allows them to swim as tadpoles, before affixing to a rock and becoming sessile filter feeders with greatly reduced and simplified nervous systems as adults (Zaniolo et al. 2002; Meinertzhagen et al. 2004). Across species and at multiple scales, the biomechanics of muscular structure, body form, and environmental forces influence how animals move (Vogel 1988). Neural mechanisms must act through the complex biomechanics of the body and the environment to generate motor behaviors (Chiel and Beer 1997; Chiel et al. 2009). Of equal importance, neuromechanical interactions define whether and how neural signals can influence motor function, and can reveal seemingly paradoxical relationships between neural signals and body movements. Because there are no one-to-one relationships between neural signals and biomechanical variables, variations in neuromotor signals must be carefully interpreted with respect to the biomechanical properties of the organism and its environment, which can vary with movement context. As a result, biomechanical properties determine whether neural signals simply excite the natural dynamics of the system, in which case variability has little effect on motor output, or whether neural signals must be precisely controlled to achieve the correct motor function. Our ability to “read” the neural motor code is thus intimately entwined with decoding the physical dynamics of the system receiving the neural signals. In this chapter, we focus on the key principles of biomechanics and motor control that underlie motor behaviors.

How do neural and biomechanical systems interact to produce functional sensorimotor behaviors? While muscles and neural circuits need to be studied in isolation to understand many of their properties, recent studies suggest strongly that it is only in a

functional and physiological context that their role in producing movement can be fully understood. There is astonishing variety across animals of the types of muscle, body plans, and environments that determine the neuromechanical properties and interactions that underlie movement. We use examples from invertebrates and vertebrates to demonstrate how understanding the mechanics of motor behaviors helps make sense of this great diversity.

In the first section of this chapter, we describe how the transformation of neural activity into individual muscle forces depends on both intrinsic neuromuscular properties and muscle function. We then examine how the effects of activating a muscle in producing a behavior depend on body structure, interaction with environmental forces, and behavioral context. The third section discusses how multi-functional biomechanical interactions influence neural strategies for movement and our interpretation of neuro-motor patterns. We argue throughout that, in both vertebrates and invertebrates, muscle multi-functionality versus specialization drives the relative complexity of neural versus muscular adaptations in generating motor behavior.

12.2 Behavioral Context Determines How Motorneuron Activity Is Transformed into Muscle Force and Power

In this section, we review the neuromuscular transform from motorneuron activity to muscle force, the first step in the transformation of neural signals to biomechanical outputs. Classically, motorneurons have been considered the “final common pathway”, acting as a relay that transmits information from descending commands to muscle. More recently, motorneurons from many species, including humans, have been shown to perform complex processing and modulation of descending commands that can greatly alter the pattern of muscle activation. Moreover, although motorneuron action potentials are reliably transformed into neurotransmitter release at the neuromuscular junction, the resulting force of the muscle is not uniquely determined by this transformation, but also depends upon the state of the muscle at the time of activation as well as its recent and long-term history of activity (Hooper and Weaver 2000).

Classical analysis of isolated muscle separates forces into independent components dependent on muscle length, velocity, and activation level. Studies of muscle properties have therefore often been done on isolated muscle under conditions in which muscle force, velocity, or length were held constant (Hill 1938, 1953; Gordon et al. 1966; Rack and Westbury 1969). This work has defined multiple well-known muscle properties (Enoka and Pearson 2013) that have been used in a wide variety of phenomenological muscle models (Zajac 1989).

Muscle Force Summation over Time Varies with Activation Frequency Muscles act as low pass filters of motorneuronal activity (for an example of an extreme functional consequence, see Fig. 10.3d). Muscle activity can therefore outlast neural excitation, and muscles may fail to respond to low levels of neuronal activity. This property is often referred to as the “force-frequency” or “muscle twitch” characteristic, describing the rate of muscle force activation and deactivation. In response to repeated stimuli, force summation depends on the difference between motorneuron interspike interval and muscle twitch duration; no summation occurs for interspike intervals longer than twitch duration, and

summation becomes increasingly greater as interspike interval becomes increasingly less than twitch duration. A consequence of this interplay is that activation amplitude can depend on either spike number or spike frequency (Morris and Hooper 1997; Hooper et al. 2007).

Muscle Length Alters Muscle Force Production The number of myosin heads that can engage the actin filament increases as thick and thin filament overlap increases. For any given activation level, muscle force therefore varies as a function of muscle length. This property is referred to as the “force-length” or “length-tension” characteristic of a muscle. Thus, when muscle is held at a fixed length (i.e., undergoes an isometric contraction), if the fixed length is other than the optimal length, the muscle develops less than its maximum possible tension.

Muscle Velocity Alters Muscle Force Production The ability to form cross-bridges between actin and myosin also depends on the speed with which the thick and thin filaments move relative to each other. This property is referred to as the “force-velocity” characteristic of a muscle. Generally, forces decrease as the rate of muscle shortening increases, and increase as the rate of muscle lengthening increases.

Even When Muscles Receive no Neuronal Activation, They Resist Lengthening Stretched unactivated muscles generate force, primarily due to stretching of sarcomere-spanning muscle giant proteins (for references see Hooper and Thuma 2005). This property is referred to as “passive muscle force” and increases with muscle length. Passive force is independent of acto-myosin interactions (Thuma and Hooper 2010), and is therefore typically considered to act in parallel with the active muscle force arising from cross-bridge interactions.

Muscle models often treat force-frequency, force-length, and force-velocity properties as independent functions that can be simply multiplied by one another, and to which the passive properties are added. They also typically assume that whole muscle force generation properties are the same as the properties of individual muscle fibers or sarcomeres. However, as studies have been extended to analyses within behaving animals, and to physiological activation patterns of muscles and motorneurons, more complexity has emerged, which must be understood to properly predict muscle function.

12.2.1 The Neuromuscular Transform Is History-Dependent

The transformation from motor neural action potentials to muscle force can have varying time-histories. A classical view of the neuromuscular junction (Enoka and Pearson 2013) starts with the activation of the motorneuron innervating the muscle, which faithfully responds to its synaptic inputs and then releases transmitter at its pre-synaptic terminal, i.e., the neuromuscular junction. Transmitter binding by post-synaptic receptors generates a strong depolarization that induces the entire innervated motor unit (the motorneuron and muscle fibers it innervates) to generate an action potential, activating calcium release from internal stores in the muscle fibers. This triggers myosin binding to actin and initiates a contraction, usually referred to as a twitch. However, recent studies have demonstrated that each step of this process is more complex, and subject to extensive modulation (Hooper and Weaver 2000). In general, such non-classical

properties are referred to as “history-dependent” because muscle force depends not only on current levels of activation, length, and velocity, but also events in the recent past.

12.2.1.1 Motorneurons Are Subject to Neuromodulation and History-Dependence That Can Significantly Alter Their Output

Motorneurons cannot be considered simple relays or integrators of synaptic input; rather, they can strongly affect the degree to which muscle can be activated. The same synaptic input to a motorneuron can generate vastly different firing rates as a result of neuromodulatory effects on motorneurons. As a consequence, the voluntary activation of a muscle, even at maximal effort, may elicit a wide range of force levels depending upon the neuromodulatory state of the motorneuron. The existence of persistent inward currents (PIC) in motorneurons, carried by sodium and calcium ions, leads to bistability: sustained motorneuron firing can continue after synaptic input is removed (Heckman et al. 2008) (see also Chapter 8). Neuromodulators can act on metabotropic receptors and, through their actions on the PIC, increase motorneuron sensitivity to excitatory inputs by 6-fold in vertebrates (Lee and Heckman 2000). Furthermore, different patterns of descending inhibitory input can alter the ability of motorneurons to recruit motor units (Powers et al. 2012). Thus, the level and pattern of descending synaptic input onto motorneurons have a complex relationship to the final activity of the muscles.

12.2.1.2 Presynaptic Neurotransmitter Release at the Neuromuscular Junction Is History-Dependent

After a rapid volley of action potentials (a tetanus), the presynaptic terminal may release higher amounts of transmitter than it would have in a resting state, and this post-tetanic potentiation appears to be due to increased levels of calcium in the presynaptic terminal (Zucker and Regehr 2002).

12.2.1.3 Post-Synaptic Muscle Excitation Is History-Dependent and Subject to Modulation

In both vertebrate skeletal (Enoka and Pearson 2013) and invertebrate muscle, whether a train of impulses temporally summates depends, as explained above, on the difference between interspike interval and twitch duration. In non-spiking invertebrate muscle and vertebrate smooth muscle, excitatory junction potentials can summate spatially as well as temporally. Invertebrate and smooth muscles are also subject to neuromodulation both from dedicated modulatory neurons or circulated neuromodulators (extrinsic modulation), and modulatory substances released from the muscle’s own motorneurons (intrinsic modulation) (Katz and Frost 1996). Such modulatory compounds (often biogenic amines or peptides) may not induce force changes on their own, but rather change the strength and speed of response to the conventional transmitter released by the motorneuron, thus allowing the muscle to respond to both low and high rates of motorneuron firing (Brezina et al. 2000). A recent study in intact animals demonstrated that motorneuronal activity during one behavior (an attempt to grasp food) did not generate significant force, but prepared the muscle to generate much stronger forces in response to the same motorneuron firing at higher frequencies during a subsequent behavior (swallowing) (Lu et al. 2015).

12.2.1.4 Contractile Dynamics of Cross-Bridge Interactions Are History Dependent

The properties of active muscle force generated through actin–myosin interactions are also history-dependent; some of these properties are discussed in more detail below. Examples include the level of muscle force depending on the history of muscle excitation, length, and lengthening or shortening velocity (Vandenboom et al. 2013). This history-dependence can result in skeletal muscle generating increasingly higher “staircase” force profiles in response to identical stimulation pulse trains. In smooth muscle, prior stretch can remodel the actin–myosin filaments, altering muscle force-length properties; resetting the force-length relation allows muscles that interact with soft organs to continue to generate force even as they are steadily stretched (e.g., as occurs during lung inflation in breathing, Gunst et al. 2003).

These multiple modulatory and history-dependent features of the motor unit mean that defining the context and history of muscle activation is critical for determining the forces that muscles generate (Hooper and Weaver 2000; Perreault et al. 2003; Siebert et al. 2007). Furthermore, this list of history-dependent properties is not exhaustive, and in particular does not include the effects of muscle fatigue on the neuromuscular transform (Enoka et al. 2011).

12.2.1.5 The Molecular Motors of Muscles Give Rise to the Functional and History-Dependent Properties of Muscle Force Generation

The phenomenological properties of whole muscle described above all result, ultimately, from active and passive molecular processes in the muscle. The active properties arise from the dynamics of the force-generating actin–myosin interactions (Huxley 1957). Simulations of populations of actin–myosin interactions (Fig. 12.1), using mechanistic models of cross-bridge dynamics, can reproduce muscle force-frequency, force-length, and force-velocity properties (Zahalak 1986; Zahalak and Ma 1990). Several other history-dependent muscle properties are not included in phenomenological muscle models but have important functional roles in movement.

Catch and Latch Catchlike properties of muscles may be important for force enhancement to maximize muscle performance, and have been found in a variety of species including humans (Binder-MacLeod and Kesar 2005). Some molluscan muscles, such as the anterior byssus retractor muscle of the mussel *Mytilus edulis*, show a powerful *catch* property in which a short neural activation results in sustained tension that is maintained without fatigue and using very little energy. Catch is due to binding of a thick filament protein, twitchin, to the thin filaments, thus locking the thick and thin filaments rigidly together, and is regulated by twitchin phosphorylation state (Funabara et al. 2005; reviewed in Hooper et al. 2008). Vertebrate and (non-catch) invertebrate smooth muscles show a phenomenologically similar *latch* state in which sustained contractions are maintained with relatively low levels of intracellular calcium and ATP consumption. This state arises via phosphorylation of a myosin regulatory light chain, which slows cross-bridge cycling, in particular cross-bridge detachment (Murphy and Rembold 2005). Yu et al. (1997) used a biophysically-based model of this process to create a non-isometric smooth muscle model that effectively captures the latch properties of a wide variety of vertebrate and invertebrate muscles.

Short Range Stiffness The force a muscle produces when stretched after a prolonged rest is higher than that predicted by the force-length relationship (Nichols and Cope 2004;

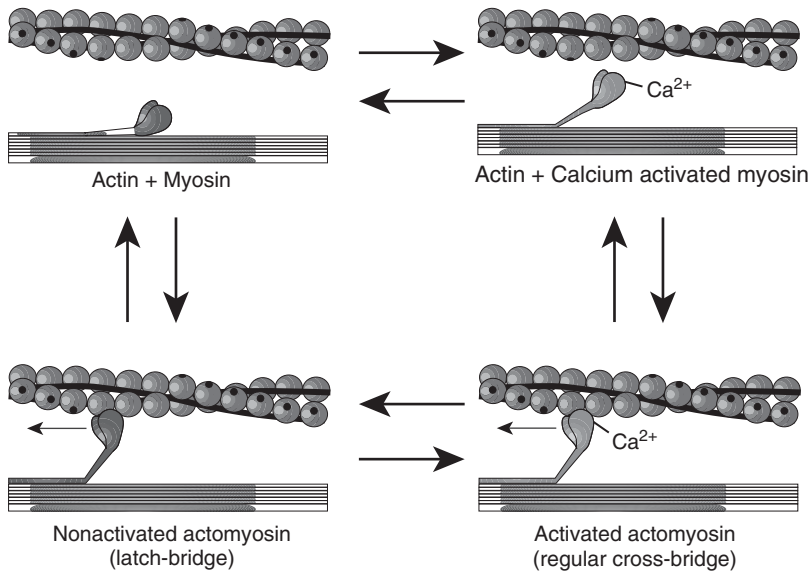


Figure 12.1 Cross-bridge interactions underlying classical and history-dependent characteristics of muscle force generation. Formation of cross-bridges that generate muscle force. Top left: thin (actin) filament above thick (myosin) filament; unbound myosin head is shown. Top right: calcium exposes myosin binding sites (in vertebrate muscles) or directly induces contraction by binding to myosin (molluscan muscle). Bottom right: ATP induces the dissociation of the actin–myosin complex and ATP hydrolysis causes a conformational change that moves the myosin head, which binds to a new position on the actin. As the myosin head returns to its initial position, the actin filament slides relative to the myosin. Bottom left: Under appropriate circumstances, a latch cross-bridge forms, which can maintain the attachment and thus tension with very little requirement for energy. The mechanism of latch is still an area of active investigation (e.g., Yu et al. 1997). Catch, which occurs in invertebrate muscles and results in the ability to maintain tension with less or even no energy use, occurs via a conceptually similar connection of the thin and thick filaments by the giant sarcomere associated protein, twitchin (see Hooper and Thuma 2005, Hooper et al. 2008 for references).

Nishikawa et al. 2007). This force is present in activated and isolated muscle fibers, and is likely due to differences in the relative population of attached and unattached actin–myosin molecules in isometric vs. shortening or lengthening muscles (Getz et al. 1998; Campbell and Moss 2002). This property is referred to as short-range stiffness (Rack and Westbury 1974; Morgan 1977) and plays an important role in producing restoring forces in response to muscle stretch in isolation (Kirsch et al. 1994) and during limb movement (Joyce et al. 1974; Perreault et al. 2004). Short-range stiffness also alters sensory information encoding by proprioceptive afferents in response to muscle stretch, with proprioceptive response increasing when the muscle has zero (isometric) vs. non-zero velocity (Haftel et al. 2004). This history-dependence in proprioceptive response plays an important role in the motor control of standing balance (Loram et al. 2009; Welch and Ting 2009; Safavynia and Ting 2013) [See also Chapter 9].

Force Enhancement and Depression Muscle forces during isometric contraction also depend upon the past history of stretching, with higher forces being produced after active stretch (Abbott and Aubert 1952; Edman et al. 1982) and lower forces after active shortening (Abbott and Aubert 1952; Marechal and Plaghki 1979; Herzog et al. 2000).

Although the mechanisms have been debated (Minozzo and Lira 2013), the current view is that contributions from actin–myosin interactions (Amemiya et al. 1988; Bartoo et al. 1997; Herzog et al. 2008), engagement of passive elements within muscle sarcomeres (Edman and Tsuchiya 1996; Herzog and Leonard 2002), and sarcomere non-uniformity may all play a role (Morgan 1990; Edman 2012).

12.2.2 Muscle Power Depends on Behavioral Context

Most of the work mentioned above examining muscle properties was performed by varying muscle activation, length, and velocity individually. *In vivo*, however, muscle activation, length, and velocity typically change independently and simultaneously. The work loop technique (Josephson 1985; Ahn 2012) was developed to allow muscle force production to be studied under the kinematic conditions that muscles experience *in vivo* during motor behaviors. In this technique an isolated muscle is exposed to the time-varying pattern of activation, length, and velocity that it would experience *in vivo*, demonstrating interactions between the force-frequency, force-length, and force-velocity properties that can radically change the function of a muscle. By plotting muscle force versus length (Fig. 12.2), the magnitude and sign of power generation in the muscle can be visualized. This work reveals that a muscle can act as a motor, strut, spring, or brake depending on when it is activated relative to when it shortens and lengthens. To produce energy, i.e., to act as a motor, a muscle must be active primarily during muscle shortening. To absorb energy, i.e., to act as a brake, a muscle must be active primarily during muscle lengthening. Without themselves producing (mechanical) energy, muscles can transmit energy, i.e., act as a strut, by being isometric, and store energy, i.e., act as a spring, by being elastic.

Muscles acting in all these fashions are found in vertebrates and invertebrates alike (Dickinson et al. 2000). Because of these complex interactions among activation, length, and velocity, plots of force versus velocity during motor behaviors depend heavily on behavioral context (Kawakami and Fukunaga 2006; de Brito Fontana et al. 2014) and do not look like those identified when only one of activation, length, and velocity are allowed to vary (Kawakami et al. 2002; Finni et al. 2003). We use three examples to demonstrate these concepts:

Two muscles that are innervated by the same motorneuron and have similar isolated muscle properties play opposite roles in cockroach locomotion: one acts as a motor and the other as a brake (Ahn and Full 2002; Ahn et al. 2006). The two muscle share similar activation patterns and cross the same joint. However, the collective effects of small differences in behavioral context and intrinsic muscle properties cause one muscle to produce energy, whereas the other absorbs it (Fig. 12.2C). The motor muscle is active as it shortens. The brake muscle is activated shortly later, causing it to be active late in shortening and, importantly, at the onset of lengthening. This difference in activation timing relative to when muscle length changes is compounded by the brake muscle having a longer muscle deactivation time constant, and the larger range of the muscle force-length relationship that the brake muscle visits, and the larger strains (length changes) it experiences, during lengthening. When subjected to identical experimental conditions, however, each muscle can be made to produce and absorb energy. Therefore, the functional difference between the two muscles arises from the different behavioral contexts in which they perform.

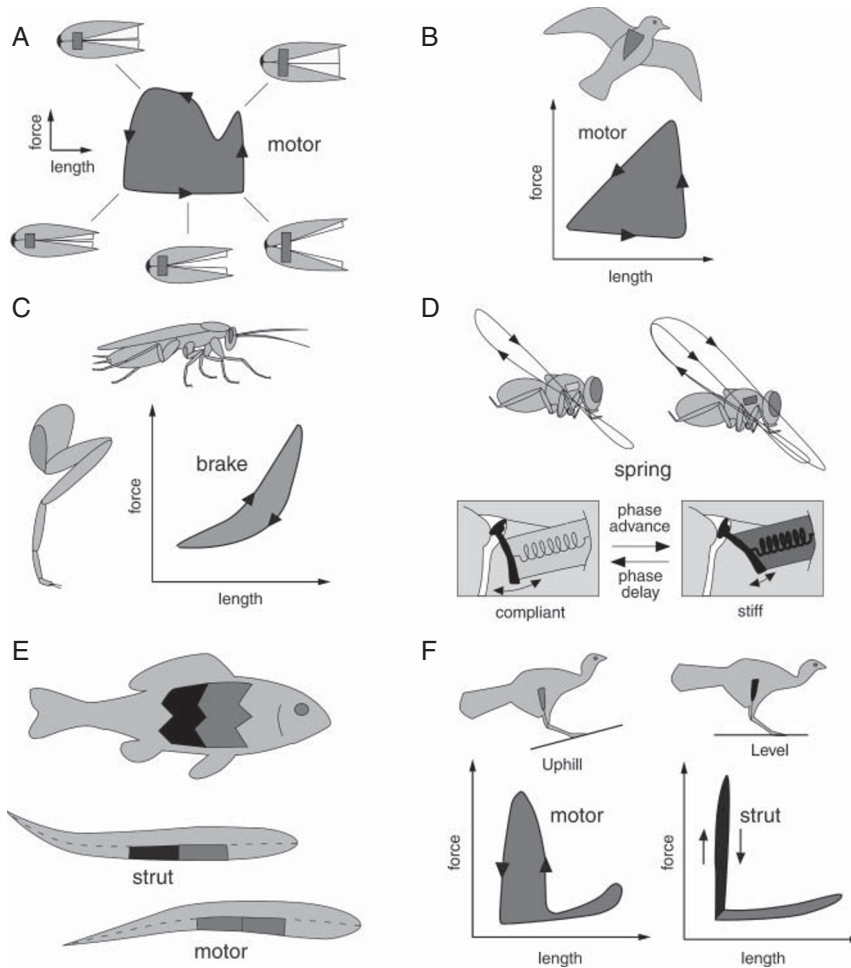


Figure 12.2 Work loop analysis reveals function of muscles as motors, brakes, springs, and struts. The work generated by a muscle is indicated by the area within the loop (shaded areas). Counterclockwise arrows indicate mechanical energy generation (e.g., A, B, F), whereas clockwise loops indicate mechanical energy absorption (e.g., C). When a muscle acts as a spring or strut, no mechanical energy is generated (D, E, F). [The “mechanical” distinction being made because, even in cases in which mechanical energy is being absorbed or the muscle is acting as a strut, the muscle is generally activated during at least part of the movement cycle and hence ATP—chemical energy—is being consumed.] (A) Scallop swimming generates positive work. Starting at the bottom right with the shell fully open, muscle activation causes a rise in force that closes the shell. The muscle deactivates in the upper left, and force drops as the shell continues to close. The shell then opens using no muscle force through active recoil of elastic hinge elements. (B) The pectoralis muscle of birds generates positive power for flight. (C) In running cockroaches, muscles suited for shortening and power production instead absorb energy, and thus act as brakes. (D) In flies, an intrinsic wing muscle acts as a spring to steer and direct power production by flight muscles. (E) In some fish, muscle acts as both a motor and a strut during the locomotor cycle. Cranial muscle fibers first shorten and produce power, which is transmitted by more caudal muscle fibers acting as struts. The more caudal muscle then generates power that is transmitted caudally. (F) *In vivo* muscle force and length measurements in running turkeys indicate a dual role for the gastrocnemius muscle. It generates positive power during uphill running. During level running, it acts like a strut, allowing energy storage and recovery in spring-like tendons. Modified from Dickinson et al. 2000 with permission.

In flight muscles of the moth *Manduca sexta* the function of flight muscles varies with the gradient of temperature along the wing (George et al. 2013). The proximal portion of the muscle is at a higher temperature and generates power, whereas more distal portions of the muscle are cooler and able to store elastic energy in linked cross-bridges due to slower activation and deactivation time constants.

In human jumping, counter-movements take advantage of both classical and history-dependent muscle properties. To reach a maximal jump height, humans use a countermovement technique in which the center of mass is lowered before it is raised. Simulations have shown that the counter-movement increases the force applied during the propulsive phase by allowing muscle force to increase over time as muscles lengthen during the lowering phase (Pandy and Zajac 1991). The active stretching also takes advantage of muscle force enhancement, a history-dependent property in which active muscle force generation increases after stretch (McGowan et al. 2013). The change in posture may further increase force by changing muscle length, and thus position on the force-length curve. Energy storage in tendon and muscle also contribute to increased jump power (Bobbert and van Ingen Schenau 1988; Voigt et al. 1995). Therefore, the countermovement generates a behavioral context in which muscle force and power production are increased.

12.2.3 Muscle Specialization Reflects Behavioral Repertoire

The degree of muscle specialization, plasticity, and history-dependence likely depends upon the mechanical and functional context of movement. As described above, the force that results from a given descending neural command can be modified by modulators and history-dependent properties. As a consequence, muscles may be quite diverse and may lie on a continuum between being highly modifiable to having relatively stereotyped and predictable dynamic responses.

We believe it reasonable to combine these observations into a principle: *the degree of specialization of muscle properties depends on how multi-functional the muscle is throughout the natural history of the animal*. The more singular the function of a muscle, the more likely specialization occurs peripherally, i.e., at the level of muscle contractile properties. In contrast, the more behaviors the muscle contributes to, the more likely it is that modulation occurs centrally, i.e., in motorneuron properties.

Some examples may illustrate this principle. In muscles that interact with soft organs requiring sustained force production at varying lengths, changing muscle fiber properties (e.g., attachment points of the myosin head and the actin filament) may solve the problem. However, in skeletal muscles that play roles in both posture and movement, the ability to produce sustained or dynamic forces may be modulated at the level of the motorneuron (Heckman et al. 2008). Similarly, specialization in muscle force-frequency, force-length, and force-velocity properties are observed in muscles with more stereotyped functions, such as flight power muscles (Biewener 2011) or vocal muscles (Elemans et al. 2004). Human leg muscles show substantial specializations (Lieber and Ward 2011), and insect hindlimb muscles are more specialized than forelimb muscles (Ritzmann et al. 2004). The specific demands of propulsion vs. posture may, respectively, drive the differences in twitch rate found in human gastrocnemius, composed primarily of fast-twitch motor units, and soleus, composed primarily of slow-twitch motor units, calf muscles. Although soleus is important for standing, it cannot be rapidly activated

and deactivated, and is inhibited during rapid postural responses to perturbation (Macpherson 1988; Macpherson and Horak 2013). Arm and forelimb muscles tend to be more heterogeneous in their properties, and to have greater flexibility through modulation at both motorneuronal and higher levels. In summary, considering desired behavioral outputs can shed light on how muscle and muscle control systems are structured, and at what levels specialization and flexibility occur.

12.3 Organismal Structures Transform Muscle Force into Behavior

Muscles do not function in isolation: both the structures in which they operate, and the environment in which an animal behaves, affect muscular function. This section focuses on the transformation from muscle force to the body forces and movements that generate motor behavior. An important general issue is that muscle function cannot be deduced from a simple read-out of motorneuron activity or muscle force alone, but rather requires consideration of *all* forces acting on the body structure. Furthermore, although muscle forces directly affect accelerations, some physical forces, e.g., viscosity, depend on velocity, and the forces of gravity and elasticity depend on position. These observations imply that animal configuration, movement speed, limb or animal scale, and environment properties (e.g., the viscosity of the medium through which an animal moves: for example, air versus water) are all important for understanding any given muscle's role in generating a movement. Depending on whether inertial, viscous, or elastic forces dominate, muscle activity can appear to be directly related to movement acceleration, velocity, or position. We illustrate how the functional effects of the force of a single muscle cannot be interpreted in isolation, but depend upon mechanical interactions throughout the body from both active and passive structures. It is thus critical to focus on the overall *behavioral* context to understand the neuromechanical interactions that transform muscle forces to functional movements.

Classical descriptions of muscle function are based on anatomical arrangements describing muscles as having singular functions. The structures of muscles observed within the body provide a useful first approximation to their function. These anatomical characteristics are important for building the lumped, phenomenological muscle models typically used in musculoskeletal models (Zajac 1989). The architecture of the muscles, tendons, joints, and soft tissue structures leads to a first-order functional description of muscles as cable-like force actuators that move the individual joints that they span (Delp and Loan 2000). While these models are very useful for understanding muscle control of movement, as a result of their simplifying assumptions, they cannot account for the complexities of muscle anatomy and function observed during the majority of real behaviors.

Muscle Shape Muscles are often considered to be fusiform with distinct tendinous attachments to a skeleton. Thus, muscle function is frequently characterized by describing the joints they span and how they generate torques at these joints. However, muscles have a wide range of forms and ways of attaching to both hard and soft tissues. Furthermore, the mass and deformation of the muscle itself must also be considered (Blemker et al. 2005; Pai 2010). This is particularly true for muscles in the tongue and in

soft-bodied animals that have no skeletal attachments, in which muscles both generate support and act as a skeleton.

Motor Unit Distribution Motor units are often assumed to be uniformly distributed within a muscle such that the muscle is homogeneously activated according to the size principle (Henneman 1957; Duchateau and Enoka 2011). However, *in vivo* work demonstrates that regions in single muscles can be differentially activated and have different effects on movement. Regionalized variations in muscle contractile properties and architecture are also observed.

Properties of Surrounding Structures Muscle function is often considered in isolation based on the forces and/or torques the muscle produces on the structures to which it attaches. However, the responses of these structures depend on the mechanical properties of the structure and the forces and accelerations the structure receives from other muscles and from the environment. It is impossible to describe a muscle's function without considering these other factors.

12.3.1 Effects of Muscle Force Depend on the Properties of the Body and the Environment

Biomechanical affordances and constraints arising from interactions with other parts of the body and the environment affect the degree of neural control required to perform a movement. Biomechanical *affordances* refer to types of movements facilitated by the body structure, and how body structures define ways of moving that require little energy or neural control to produce. Biomechanical *constraints* refer to movements that are difficult or impossible to achieve with a given structure or refer to the neural input required to achieve a movement, e.g., precise timing or activity of a particular muscle. Again, the structural and material properties of the body affect how muscle activation alters body motion or shape to produce movement. For example, musculoskeletal systems can apply precise, concentrated forces to the environment that are useful for legged locomotion. Unlike soft-bodied structures, however, they cannot apply distributed forces along the body, nor assume complex shapes to conform to undulating terrain or find their way through tortuous crevices and curving structures. Ultimately, what a neural motor pattern “means” for a behavior depends on biomechanical affordances and constraints.

12.3.1.1 The Relative Importance of Inertial, Viscous, and Spring-Like Forces Affect the Role of Muscle Force

We first discuss the relative importance of different environmental forces for shaping motor output, and then give examples of how biomechanical structures affect the neural control of muscles for motor function. We examine different types of body structure that play a significant role in shaping movement: musculoskeletal systems, tendons and fascia, hydrostatic structures, and muscular hydrostats. Rather than focusing on anatomical descriptions, we discuss how different body structures and their interactions with the environment determine the kinds of motor functions that a muscle can produce.

For all structures, the relative importance of inertial, viscous, gravitational, and elastic forces determine the dynamics of movement resulting from muscle activity. Important

determinants include the size of the animal or limb, movement speed, and the medium within which the movement occurs. As a rule of thumb, larger, terrestrial animals are dominated by acceleration-dependent inertial forces and position-dependent gravitational forces, whereas small terrestrial animals are dominated by velocity-dependent viscous forces and position-dependent elastic forces. Note that the dominating force within a large animal might not be inertial if it is moving a small part of its body (Charles and Hogan 2012); similarly, the dominating force within a small animal may not be viscous or positional if it is engaged in a highly rapid strike movement, dominated by inertial forces. The nature of the forces directly affects the dynamic equations of motion that determine whether a system is stable, oscillatory, or decaying in nature. For example, acceleration- and position-dependent force interactions are described by an oscillating system (i.e., a second order differential equation), whereas interactions between velocity and position-dependent forces are described by an exponentially decaying system (i.e., a first order differential equation).

In general, large animals tend to activate their muscles in shorter durations relative to movement duration, relying on the inertial forces to complete the movements of the large masses of their limbs, whereas smaller animals must continuously activate muscle during movement, since the smaller masses of their limbs result in movements dominated by viscous or elastic forces (Hooper et al. 2009; Hooper 2012). Some animals can employ ballistic movements, in which an impulse of force can initiate a movement, such as a jump. In contrast, viscous forces are highly dissipative. For this reason, small and/or aquatic animals must generate power to overcome viscous forces within their environment. As a consequence, muscles must be continuously activated or the organism will cease to move (Hooper 2012). Movements in a viscous environment can be more ballistic and require less fine motor control, since the environment is inherently stabilizing and dampens oscillations.

Such considerations are also important when moving different body parts or at different speeds. Inertial, viscous, and elastic forces are also determined by the properties of the tissues themselves. Inertial and gravitational forces are much more important in larger appendages such as the arms and leg, although movement through water versus air can also alter the relative importance of viscous versus gravitational forces. For example, simulations and passive dynamic walkers illustrate that little to no muscle activity is necessary to produce walking-like movements (Collins et al. 2005; Kuo 2007). This means that a transient impulse to a muscle can set in motion a complex movement that relies on kinetic and potential energy exchange of pendulum dynamics. It is likely, however, that muscles play more of a role in stabilization and control of walking, since gravitational forces are destabilizing when changing postures, and because perturbations can induce undamped oscillations (Ting et al. 2009). In contrast, human fingers have small mass and higher damping properties than larger limbs (Lin and Rymer 2001; Deshpande et al. 2012; Park et al. 2014). Insect limbs have low mass, a great deal of elasticity (Blickhan 1986; Sensenig and Shultz 2003) and can also have significant energy absorption through hysteretic damping (Dudek and Full 2006). In fact, in the stick insect, if swing muscle activity were to cease at any time during swing, swing leg movement would cease (Hooper et al. 2009). As a consequence, muscle activity is associated only with limb propulsion and is not required for braking limb movement.

The specific dynamics of the body and environment determine whether muscles are required to power the body or limb in a stable environment, or to stabilize the body

or limb in an unstable one. In the swimming lamprey, the inclusion of water viscosity is critical to generating the traveling wave necessary for propulsion (Bowtell and Williams 1994; McMillen et al. 2008). Moreover, neuromechanical modeling shows that changing body stiffness would alter the swimming motions caused by identical muscle activation patterns (Tytell et al. 2010). Similarly, when subjected to unpredictable forces, human arm stiffness and damping is increased in the direction of the applied forces, thus reducing the need for corrective neural control of arm position and desired movement trajectory (Franklin et al. 2004).

12.3.1.2 Muscle Function Depends on Behavioral Context and Environmental Forces

Behavioral context (body configuration and velocity) and environmental forces alter the relative sensitivity to, and hence the effects of, muscle force. As Bernstein (1967) stated: “...one and the same impulse...may produce completely different effects because of the interplay of external forces and because of variations in the initial conditions.” For example, computer simulations of human walking demonstrate a posture-dependent (crouched vs. upright) effect on whether a muscle generates extensor joint torques or center of mass acceleration (Hicks et al. 2008; Steele et al. 2010).

A salient example of this difference can be demonstrated by introducing additional neural impulses to a cockroach limb muscle during two different behaviors: postural control and running (Sponberg et al. 2011b). Introducing artificial muscle action potentials during postural control caused graded linear effects on body rotation and velocity. In contrast, the same action potentials introduced during running had a wide range of complex effects—including no effect—on locomotion. More action potentials were generally required to elicit any measurable effects, which were generally non-linear. The effects of muscle stimulation varied dramatically depending on stimulation phase, increasing vertical velocity in one gait phase but turning the body in another. Furthermore, when investigated with the work loop technique, the muscle absorbed energy when stimulated as it would be during normal running (Full et al. 1998) but, due to interactions with the kinematics of the limb at the time of stimulation and consistent with the behavioral effects, produced positive work with added action potentials (Sponberg et al. 2011a).

12.3.1.3 Biomechanical Affordances and Constraints of Body Structures Affect Muscle Functions

Skeletal Systems Musculoskeletal systems such as human arms and legs are familiar and intensively studied structures. These systems are defined by a muscle attaching to hard skeletal elements, externally in vertebrates (an endoskeleton), internally in insects and other arthropods (a hard cuticle containing muscle, an exoskeleton). The articulations between bones (vertebrate) and body or limb segments (arthropod) define kinematic degrees of freedom for body and limb movements. Bones do not deform enough under load to contribute to movement control, but exoskeletal elements can sometimes deform and store energy necessary for movement.

Muscles generate multiple joint torques defined by the complexity of skeletal structure. In vertebrates and invertebrates alike, some joints move in multiple degrees of freedom (multiple directions), and some muscles span multiple joints. Muscle moment arms relative to the articulated joint centers determine the leverage of the muscle force that

generates joint torque. Limb muscles are commonly referred to as uniarticular (spanning a single joint) or biarticular (spanning two joints). Articulated joints often have multiple kinematic degrees of freedom that define the different ways in which they can move, which must be considered in combination when a muscle is activated. For example, the ball and socket hip joint supports flexion-extension, adduction-abduction, and internal and external rotation. At a minimum, “uniarticular” hip muscles produce torques that affect three kinematic degrees of freedom at the hip, each of which must be coordinated with other muscles to produce a functional movement. The human knee joint also has multiple degrees of freedom, such as flexion–extension and varus–valgus rotation. Linear motion at both joints may also need to be considered. Thus, even simple line-of-action models (Delp et al. 1990) of the biarticular muscles crossing the hip and knee require specifying the joint torque contributions of five moment arms. In finger muscles, muscle tendons diverge and converge with the tendons of other muscles and span multiple joints (Valero-Cuevas et al. 1998, 2007; Valero-Cuevas 2005). Abdominal muscles have even further complexity due to their sheet-like structure and their ability to generate torques across multiple vertebrae via both hard and soft-tissue connections.

Muscle moment arms also change with posture due to geometric considerations that alter the joint torques they produce (Young et al. 1992; Murray et al. 2000). Moment arms are often thought to decrease as joints move away from a neutral position, resulting in constant muscle force producing less torque. However, in cat hindlimb, the moment arms of ankle muscles in the medial-lateral direction increase with displacement from the neutral configuration (Young et al. 1992), generating restorative torque even with constant muscle force. As a result, frontal plane motion of the cat hindlimb can be intrinsically stable to external perturbations, but sagittal plane motion may require more neural control (Bunderson et al. 2008). Moment arms of human shoulder muscles change substantially with arm posture, and do so in a systematic way that may simplify the transformation between joint postures and joint torques (Buneo et al. 1997).

Particularly ingenious musculoskeletal interactions are present in insects. In addition to joint motions, some insect muscles produce sufficient deformation of the exoskeleton to store and release energy that contributes to movement (Gronenberg 1996). In the proximal hind-tibia of the locust, a specialized region composed of resilin acts as a shock absorber as it buckles, preventing the leg from damaging itself when the animal kicks against a substrate (Bayley et al. 2012). Nymphs of the planthopper *Issus* have interdigitating cogs—i.e., a gear—that ensure exact coordination of both legs during jumping, synchronizing their movements within milliseconds and minimizing yaw movements (Burrows and Sutton 2013). Both mechanisms limit the degree of precise neural timing of muscle activation required to control and coordinate movements.

Tendinous and Fascial Connections The tendons that connect muscles to bone have a wide range of mechanical properties that play an important role in muscle function. The interactions between muscle and tendon architecture determine the capacity of the muscle to generate force, to lengthen over large excursions, and to generate power (Wilson and Lichtwark 2011). *Muscle architecture* refers to the arrangement of muscle fibers and tendon. At one extreme, long parallel muscle fibers attach to a tendon at the end of the muscle, allowing for a large range of motion. Short muscle fibers, alternatively, are typically pennate, inserting along the length of a tendon or aponeurosis that runs

through the muscle, which provides high force and power generation but limits the capacity for length change.

Tendon elasticity allows muscle fiber kinematics to differ substantially from musculotendon kinematics based on the relative motion between the skeletal insertions of the muscle. As a consequence, lengthening or shortening of the musculotendon unit cannot be directly related to the direction of muscle fiber lengthening and shortening. Tendons can be actively stretched through muscular contraction and the interaction with environmental forces such that energy is stored. *In vivo* measurements of muscle fascicle length have revealed that gastrocnemius muscles are largely isometric both during highly dynamic tasks such as running (birds: Roberts et al. 1997; humans: Wilson and Lichtwark 2011) and in less dynamic tasks such as standing balance (humans: Loram et al. 2009).

The gastrocnemius remaining at near constant length as the length of its musculotendon unit changes in, say, running, means that the tendon elastically stretches (energy storage) during ankle flexion and lengthens (energy release) during ankle extension, and hence stores and releases mechanical energy across the step cycle. This is an example of a general mechanism of mechanical energy storage in running, in which elastic elements in the stiffened (by extensor muscle contraction) leg store energy through the beginning of stance and return it during the end of stance (Dickinson et al. 2000). It is important to note that this ability to store mechanical energy comes at a metabolic cost. In the case at hand, as the gastrocnemius tendon lengthens it exerts force on the gastrocnemius muscle, whose activation must therefore increase for the muscle to maintain a constant length. Moreover, maximum muscle efficiency is not at isometric contraction, but in contractions about one-quarter of maximum muscle velocity (see Lichtwark and Wilson 2008 for references). Total efficiency of the musculotendon unit, alternatively, depends on contraction velocity, tendon compliance, muscle fiber length, and muscle volume. Theoretical work on human legs shows that no single combination of these parameters is optimal for both running and walking, and that human values are intermediate between the optima for the two gaits (Lichtwark and Wilson 2008). Consequently, the isometric gastrocnemius data, and the braking and spring-like activities shown in Fig. 12.2, are an example of a repeating theme in biomechanics, that it is the entire ensemble (neurons, muscles, tendons, bones) that is selected for, not the maximum efficiency (or any other aspect) of any single member of the ensemble, and that this selection is made across some sort of weighted sum of the entirety of the animal's behavioral repertoire.

The sheets of fascia around muscle and muscle compartments also have connections between them that can transmit substantial force (Huijing 2003; Maas and Sandercock 2010). These connections allow muscles to generate torques about joints they do not span. For example, the rectus femoris, a quadriceps muscle, has a knee extensor moment arm. When the muscle insertion is surgically relocated to produce a knee flexion moment arm, activation of the muscle nonetheless generates knee extensor torque. This presumably occurs because the muscle belly remains connected via fascia with other quadriceps muscles that still have extensor moment arms (Riewald and Delp 1997; Asakawa et al. 2002). Torques about distant muscles can also be generated through fascia. A striking example is the crural fascia, a thick band of fascia that transmits force from thigh muscles to the ankle joint (Stahl and Nichols 2014) and is particularly pronounced in cheetah (van Ingen Schenau 1994). In decerebrate preparations, in which motorneuron output can be completely controlled, disrupting the crural fascia

causes ankle and foot lateral motions to become more variable. This demonstrates that additional neural control of the ankle would be necessary without the forces transmitted by the crural fasci.

Hydrostatic Structures Several structures in vertebrates, and many entire bodies in invertebrates, contain no hard tissues, but instead only muscle surrounding a central fluid-filled cavity. Such systems are called *hydrostatic skeletons* (Kier 2012). Familiar examples are worms and caterpillars (Trimmer and Lin 2014) and human and turtle penises. Because biological tissues and fluids are mostly water and water is nearly incompressible, contraction of one part of these structures leads to expansion of other parts. Appropriate arrangements of muscles around the central fluid cavity can allow the structure to contract along its length (longitudinal muscles), contract strongly at particular locations along its length (circumferential muscles), or twist (helical muscles). These systems have an essentially infinite number of degrees of freedom (as opposed to musculoskeletal systems, in which the degrees of freedom are constrained to specific joints) and consequently can readily conform to complex, irregular terrains and assume very complex shapes.

Models of hydrostatic skeletal structures have provided important insights into the relationship between neural control and biomechanics. An early attempt to model the leech body applied forces to the model elements and determined the equilibrium shape that minimized potential energy (Wadepuhl and Beyn 1989). Kristan and Skalak subsequently developed a model incorporating more details of the passive and active properties of leech musculature, again determining equilibrium shape by minimizing potential energy (Skierczynski et al. 1996). They demonstrated that only patterns of neural activity that were observed *in vivo* produced model activity resembling that observed in normal animals. Using neural patterns from semi-intact preparations or isolated nerve cords, in both of which sensory feedback is altered or absent, resulted in the model producing abnormal body shapes (Kristan et al. 2000). Cohen and colleagues have developed a neuromechanical model of *C. elegans* (Boyle et al. 2012) that accounts for transitions from swimming to crawling on the basis of the viscosity of the environment and the effect of changes in viscosity on sensory feedback. These studies illustrate the vital importance of understanding the structural and environmental context in which muscles function.

Muscular Hydrostatic Structures Muscular hydrostats (tongues, trunks, tentacles) are structures completely occupied by muscle with no central fluid-filled cavity, and which thus have hydrostatic skeletons (Kier and Smith 1985). Longitudinal, circumferential, and helical muscles in these structures allow them to generate shortening, lengthening, stiffening, bending, and twisting motions. These complex shapes alter the effect of a muscle's contraction on the structure based on the geometry of the muscles. For example, shortening the helical fibers while maintaining a constant volume cylinder can either lengthen or shorten the structure, depending on whether the helical muscles are at an angle greater or less than 54° , respectively, predictions confirmed by measurements in squid tentacles.

Length change speed in muscular hydrostats depends on muscle geometrical arrangement and changes in muscle properties. For example, squid tentacles, which strike and capture prey, can elongate in 20 to 40 ms, reaching peak velocities of 2 m/s and peak accelerations of 250 m/sec^2 (Kier and Leeuwen 1997). Comparison of the muscle fibers in the tentacle (which can elongate rapidly) versus the arms (which cannot) suggest that

the tentacle's ability to lengthen rapidly is due to the short lengths and oblique arrangements of tentacle muscle fibers (Kier and Schachat 2008). A computational model of the squid strike (Van Leeuwen and Kier 1997) suggests that the remarkably high velocity of shortening of these fibers is due to the cross-striations of the muscle fibers and their unusually short thick filaments.

Kinematics and kinetics must both be considered when analyzing tongue function. The tongue of the lizard, *Tupinambus nigropunctatis*, consists of two adjacent longitudinal muscles that shorten the tongue wrapped in circumferential muscles that elongate it. A model of tongue function (Chiel et al. 1992) showed that the relative effectiveness of the circumferential and longitudinal muscles was determined both by kinematics (the constant volume constraint) and kinetics (the relative forces in the muscles). The forces generated by each muscle depend on the shape of the muscular hydrostat and determine the forces that protrude and retract the tongue. As a consequence, the effects activating the muscles depend on tongue length. For example, to generate lapping behavior, strong activation of the circumferential muscle combined with low activation of the longitudinal muscle generates a large protrusion, with a small increase of activation of the longitudinal muscle rapidly retracting the tongue. The model also suggested that the low-pass filtering properties and mechanics of the muscles would require significant transformations of neural inputs to create fast lapping movements. In contrast, when animals use pharyngeal tamping to swallow prey, the model predicts that the tongue should be relatively short to make it stiff and able to cope with large mechanical loads. In general, the model demonstrated that, to be properly understood, neural control and mechanics must be analyzed together.

12.3.2 Muscles Are Multi-Functional

Different Regions in Single Muscles Can Have Different Functions during Motor Behaviors Because the structural and contractile properties of single muscles can be highly heterogeneous, a muscle's motorneuron pool cannot be treated as a single entity. Muscles are comprised of many fiber types and, in addition to their distinct neural innervations, motor units can have different physical arrangements. These different arrangements, acting through both hard and soft-tissue connections, can result in parts of the muscle serving different functions, including generating forces at multiple locations. *In vivo* observations of muscle activity have revealed that different muscle subregions and compartments can be differentially activated during motor behaviors.

For example, the cat biceps femoris is a sheet-like muscle with an origin at a tendinous insertion on the pelvis that spreads out to a thin membrane-like attachment that lies over the musculature of the hip, knee, and ankle (Fig. 12.3). The anterior portion of the muscle consequently produces only hip extension torque, whereas the posterior portion produces both hip extension and knee flexion torque. The internal architecture of muscle fascicles and tendons also varies across the muscle. During behavior, a continuum of activity occurs across the muscle. The anterior region is active in slow walking, with more posterior regions being recruited as speed increases (Chanaud et al. 1991). However, the anterior and posterior regions can have opposite activity patterns, one being excited when the other is inhibited (Chanaud and Macpherson 1991). Thus this single muscular structure can generate a continuum of hip and knee torque combinations. As mentioned above, fascial connections also transmit forces to other

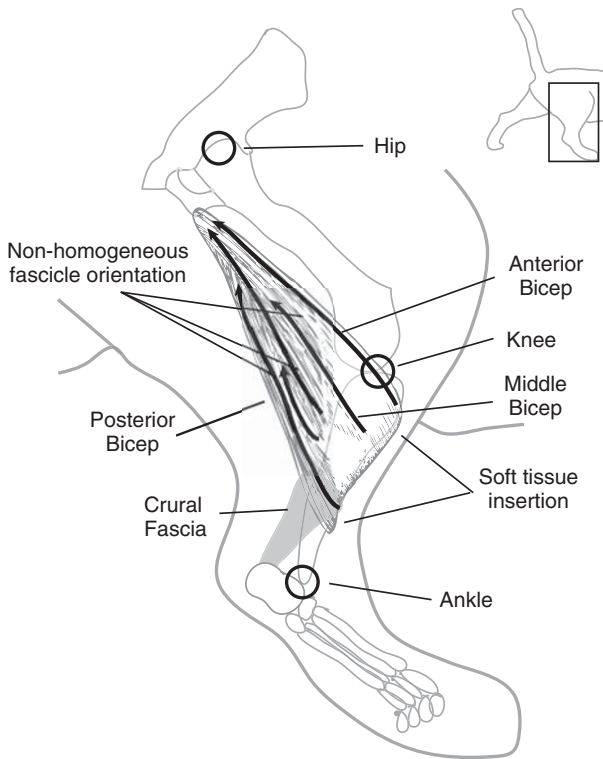


Figure 12.3 Complex muscle and connective structure in cat biceps femoris muscle. The biceps femoris muscle has a “classic” distinct origin on the pelvis. The muscle then fans out in a sheet-like organization and inserts into the soft tissue overlying other muscles. The lines of action of the various muscle fibers are complex because of the differing muscle architecture, but, in general, the joint torques generated when the muscle is activated can be estimated from the moment arms about the joints they span. As a consequence, the anterior biceps has a large moment arm at the hip allowing hip torque generation, but its line of action is coincident with the knee joint center, and so it generates little knee torque. In contrast, the posterior biceps generates hip torque as well as large knee flexion torque because of its large moment arm about the knee. Although the biceps femoris does not span the ankle joint, the crural fascia transmits force from it to the calcaneus bone, and thus it also generates ankle torque.

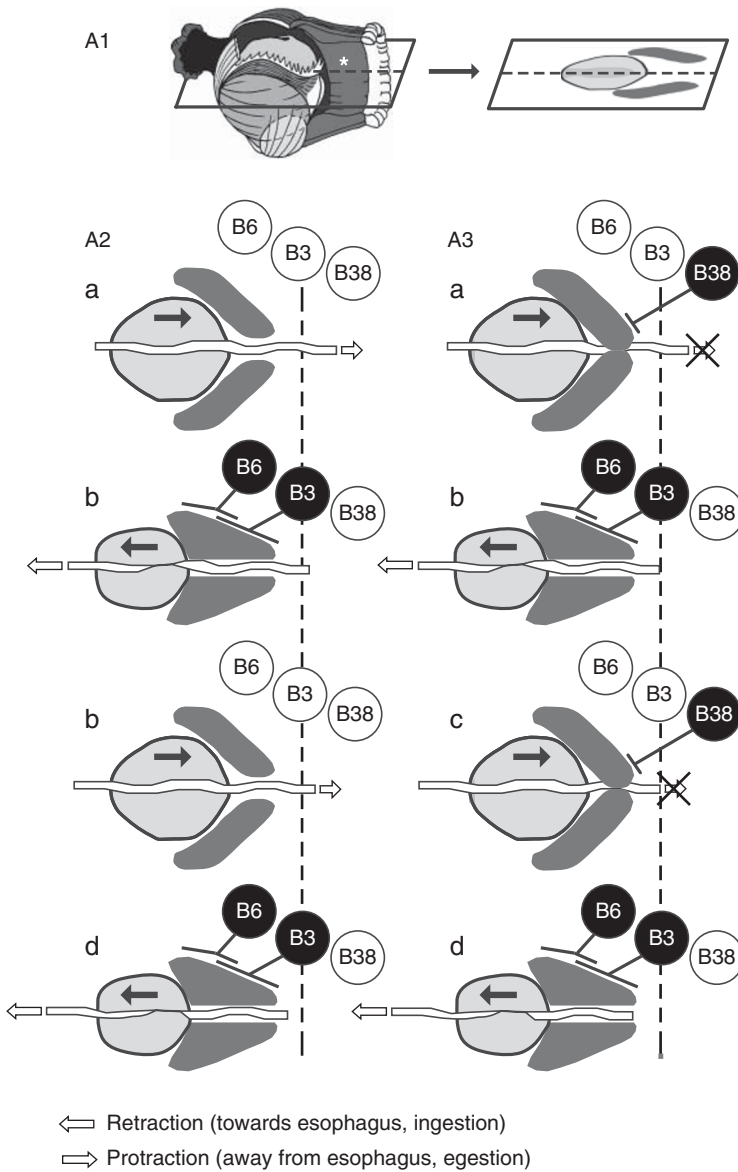
muscles and joints, contributing to both medial-lateral and sagittal ankle torque (Stahl and Nichols 2014).

In more distal muscles such as the gastrocnemius, even more extreme intra-muscle variations in muscle contractile properties, architecture, and tendon arrangements are found (reviewed in Higham and Biewener 2011). Thus, differential activation of muscles can depend on the different torques they generate about joints (Higham and Biewener 2008), but also on different contractile properties and architectural arrangements that interact differently with movement mechanics to facilitate both power generation and absorption (Wakeling 2009; Daley and Biewener 2011). Muscle properties can also contribute to rapid stabilization of the body in the face of perturbation without immediate changes in neural activity (Jindrich and Full 2002; Daley and Biewener 2006; Bunderson et al. 2010).

Differential muscle compartment activation is also important in invertebrate muscle. Independent activation of motoneurons projecting to the same muscle can be related to distinct motor functions. For example, the marine mollusk, *Aplysia californica*, feeds on strips of seaweed by grasping the strip, pulling some into the buccal cavity, releasing the grasper from the seaweed but still holding the seaweed in place in the cavity, repositioning the grasper further along the strip, and then again pulling more into the cavity. To hold the seaweed in place when the grasper is repositioned (protracted) to pull in more, the identified motoneuron, B38, fires to contract only the anterior part of the retractor (I3) muscle (Fig. 12.4). Once the grasper has again closed on the seaweed, other motoneurons fire to contract the entire I3 muscle and thus pull the grasper towards the buccal cavity (retraction) (McManus et al. 2014). Unlike all other I3 motoneurons, B38 is active during protraction rather than retraction. Effectively, the different regions of the muscle are used as if one were pulling a bucket out of a well by a rope and used one hand to pull the rope and the other to hold the rope in place when the first hand was repositioned forward on the rope.

Muscle Function Depends on Adjacent and Distant Muscles In addition to the joint torques that muscles produce about the joints that they span, they can also contribute to accelerations, torque, and power throughout the body. The Newtonian dynamics of a skeleton idealized as a system of interconnected rigid links reveals that a muscle can accelerate all joints in the skeleton because forces are transmitted through the rigid connections between segments (Zajac and Gordon 1989). Thus, acceleration of one skeletal segment accelerates the segments attached to it in a manner dependent on segment inertias and the connections between the segments. The net behavioral effect of a muscle therefore depends on the simultaneous actions of muscle acting at the same and other joints. For example, simulation of the cat hindlimb demonstrated that posterior biceps femoris force either accelerates the toe or, if toe movement is resisted by an external force, generates a force to counter that force (van Antwerp et al. 2007). The direction of toe

Figure 12.4 The dual roles of the I3 muscle increase the efficiency of swallowing. A1) A schematic of the feeding apparatus—the buccal mass—of *Aplysia californica* (left panel); the plane of section (right panel) indicates the level at which the schematics in A2 and A3 are drawn. The jaw muscles consist primarily of the I3 muscle (dark gray structure with asterisk in left panel; two dark gray parallelogram-like figures in right panel); when the I3 muscles completely contract, they push the grasper (gray ball-like structure to the left in left panel; light gray oval in right panel) towards the esophagus (i.e., the I3 muscles retract the grasper). A2 and A3, b and d) Activation of two I3 motoneurons, B6 and B3, induce the I3 muscle to retract the closed grasper, pulling seaweed into the buccal cavity. A2 and A3, a and c) Activation of B38 during the protraction phase enhances the ingestion of seaweed by pinching the anterior of I3 and allowing I3 to hold the seaweed in place as the grasper protracts for the next swallow. As a consequence, the total inward amount that the seaweed has translated in panel d, A3, is greater than in panel d, A2 (compare right end of seaweed to vertical dashed lines in A2, A3). In all panels in A2 and A3, black arrows are grasper retractions and protractions; open arrows are seaweed movements towards and away from esophagus, and white cylindrical object with black border is the seaweed. Grasper closing on seaweed (b, d in A2, A3) is represented by “pinching” of grasper onto the seaweed. In A2 a, c, even though the grasper is not strongly pinching the seaweed, it is nonetheless somewhat egested during each grasper protraction (short open arrows). Modified from McManus et al. 2014.



acceleration depends on the torque about the ankle joint, whether achieved actively or passively (Fig. 12.5). By varying ankle torque from zero to the magnitude necessary to immobilize the joint, endpoint acceleration direction can be altered by over 90° in some cases. The whole-limb function of identical activations of the biceps femoris muscle therefore depends on the level of activation of ankle muscles. Similarly, power generated by a muscle at one joint often needs to be directed by a muscle at another joint to achieve a functional goal (Zajac 2002; Zajac et al. 2002).

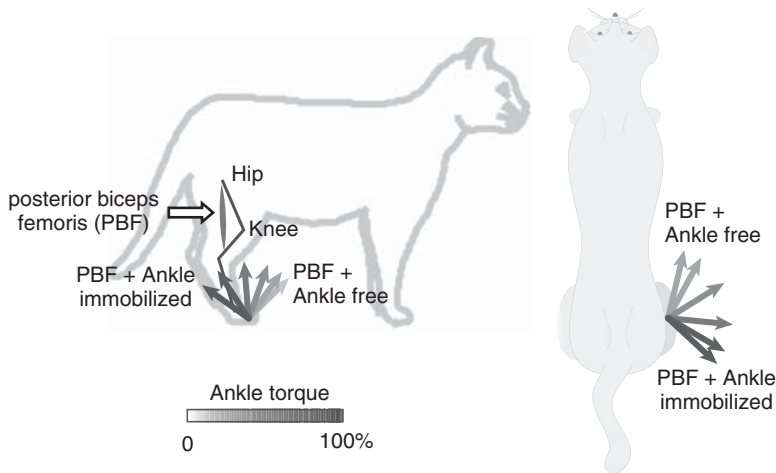


Figure 12.5 Direction of toe acceleration induced by activation of posterior biceps femoris (PBF) muscle differs across varying levels of ankle torque. In a musculoskeletal model of the cat hindlimb, the PBF was maximally activated simultaneously with ankle flexion/extension and ad/abduction torques that canceled 0 to 100% of their induced acceleration at the ankle, respectively. Total ankle torque levels required to functionally immobilize the joint were relatively low, and never exceeded 20% of the muscle torques produced by the PBF. Toe acceleration directions varied by over 90° in both the sagittal and dorsal planes. These results demonstrate how multi-muscle coordination or even the contributions of passive joint torques can dramatically alter the endpoint action of the limb when muscles are activated. Adapted from van Antwerp et al. 2007 with permission.

In soft tissue structures, expansion or contraction of one muscle can significantly affect surrounding muscles, as was described above for muscular hydrostats. For instance, changing one muscle's shape can alter the mechanical advantage of other muscles. A model of the *Aplysia* feeding grasper predicted that as the grasper closed, its shape would elongate and stretch the thin protractor muscle (I2) in the posterior of the feeding apparatus. This stretch would change I2's position on its length-tension curve, and its mechanical advantage, enhancing its ability to produce protraction (Novakovic et al. 2006). Experimental tests verified this prediction (Ye et al. 2006b) (Fig. 12.6). An important implication of these results is that activity of the grasper closer motorneurons (the B8a/b motorneurons) may strongly modulate the forces protractor motorneurons (B31/B32 and B61/B62) produce in I2 by altering I2 mechanics in the periphery.

12.3.3 Specialization of Biomechanical Structures Reflect Behavioral Repertoire

The data presented above suggest that the degree of specialization in organismal structures likely depends on behavioral context and repertoire. This observation allows us to expand our earlier principle to *the degree of specialization of muscle architecture and contractile properties may depend on the specialization of the biomechanical structure that contains it*. Structures that produce a limited repertoire of highly stereotyped and rapid motions are more likely to be associated with highly specialized muscle properties and biomechanical structures. In multi-functional biomechanical structures

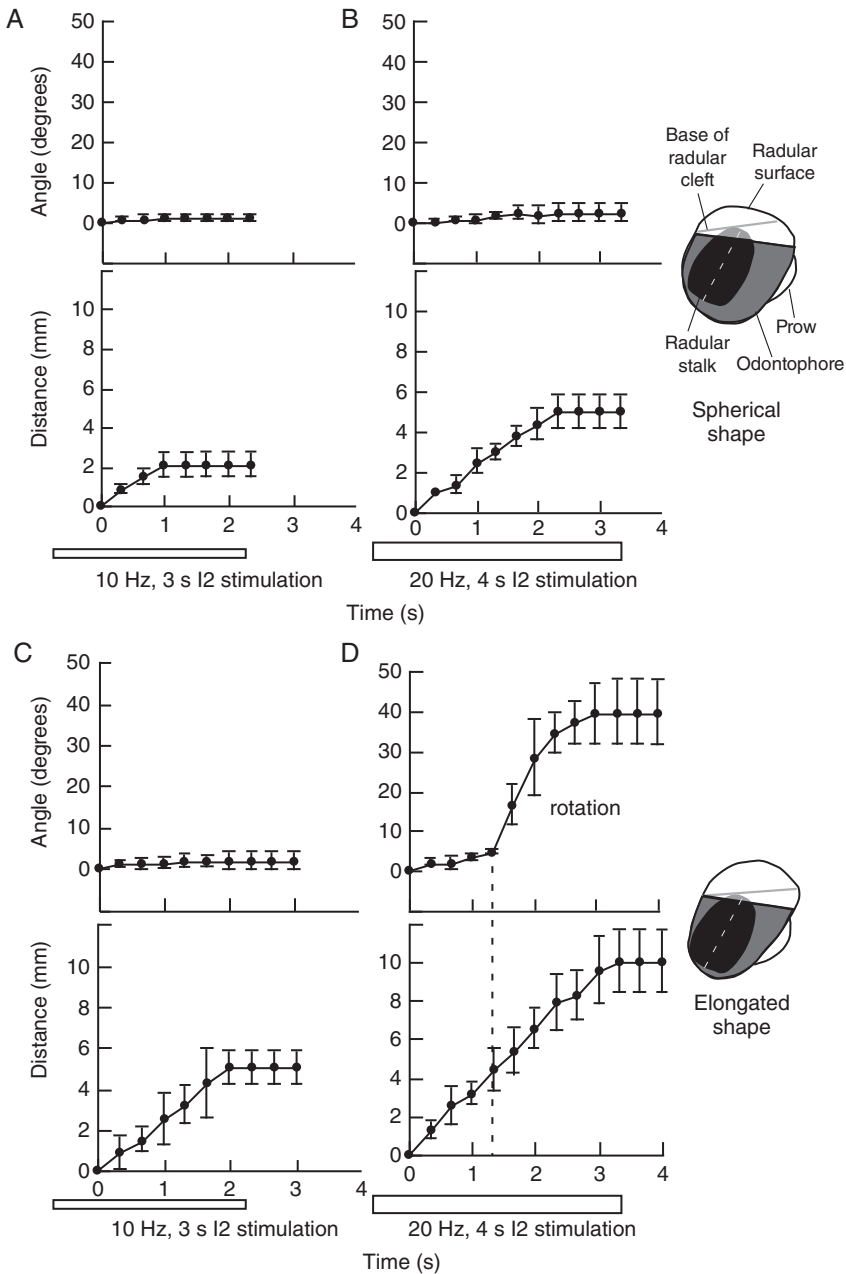


Figure 12.6 The shape of the grasper in *Aplysia californica* determines the effectiveness of the I2 protractor muscle. (A) When the grasper is open, it assumes a spherical shape. If I2 is activated at 10 Hz for 3 seconds, some translation but no rotation of the grasper is observed. (B) Higher and longer activation (20 Hz for 4 s) induces stronger translation, but no rotation, of the grasper. (C) When the grasper is closed, it assumes an elongated shape. If I2 is now activated at 10 Hz for 3 seconds, the resulting grasper translation is as large as that obtained in panel B when I2 was stimulated at twice the frequency and for a longer duration. Elongating the grasper thus significantly enhanced I2's ability to protract the grasper. (D) When the grasper is closed and I2 is activated at 20 Hz for 4 s, the resulting translation is much stronger and the grasper also rotates substantially. From Ye et al. 2006b with permission.

that produce a wide range of behaviors (slow, fast, multiple movement types such as different gaits or reaching trajectories), alternatively, muscle is likely less specialized, allowing more flexibility in the ways it can be used by the neural control system to produce this behavioral generality.

For example, the squid tentacle, specialized for extremely rapid striking, has unusual features: short thick filaments, oblique arrangements of muscle fibers, a precise arrangement of the muscles that elongate and shorten the tentacle. In contrast, in the same animals, the arms, which are used for grasping and manipulating objects, show none of these specializations. Similar specialization of muscle properties is observed in mantis shrimp depending on whether prey capture involves spearing or smashing (Blanco and Patek 2014). In terrestrial runners, variable muscle architecture specialization is present along the proximal–distal axis of the limb (Biewener and Daley 2007). To help mediate interactions with unpredictable variations in terrain, distal leg muscles have long elastic tendons with short muscle fibers; furthermore, the muscles tend to contract isometrically, allowing the tendon to absorb and return energy upon impact. More proximal leg muscles tend to have long fibers for operating at high velocities (Biewener and Daley 2007; Lieber and Ward 2011; Wilson and Lichtwark 2011). Similar specialization of leg muscles for posture versus locomotion is evident in the differences in the contractile properties in two ankle extensors: the gastrocnemius, which is almost all fast muscle, versus the soleus, which is all slow (Burke 1981; Kaya et al. 2003). Moreover, the weight-bearing ankle muscles have increased contraction relaxation time constants compared to ankle dorsiflexors and arm muscles (Burke 1981; Belanger and McComas 1985).

12.4 Biomechanics Defines Meaningful Patterns of Neural Activity

What patterns of neural activity are needed to generate a particular motor behavior? We have focused above on how behavioral context determines the mechanical effects of *single* muscles. We focus here on the coordination of *multiple muscles* to generate functional movements and address the broad question of motor control from the perspective of biomechanics. We do not attempt a comprehensive review, but provide an introduction to some of the key questions currently under study.

How do nervous systems harness the complex interactions between the motor system and the environment to produce flexible and robust motor outputs? In the previous sections, we discussed how identical patterns of neural activity or muscle activation can generate qualitatively different motor outputs (e.g., because of differences in body posture or environmental forces). But within a given context, one must also understand how ensembles of motoneurons can be activated in spatial and temporal patterns to produce meaningful behavior. One must also understand the many ways in which different patterns of neural activity or muscle activation can generate essentially identical motor outputs. With this understanding, one can begin to analyze variability in and between individuals, and the ways in which sensory feedback, exploration, and learning shape the variability in and across individuals to generate effective behavior (Ting et al. 2015).

A classical approach to studying motor behavior is to identify a canonical pattern of muscle activity that produces the forces and torques necessary to achieve a specific movement. The use of biomechanical models and optimization has been extremely important in identifying efficient patterns of movement that often resemble those observed experimentally. However, these approaches are based on three assumptions that do not account for the diversity of motor solutions and individual differences observed experimentally.

First, classical approaches assume there is a “correct” or “optimal” way of generating a movement, with optimality based on minimizing movement time, energy, or some other feature (Todorov and Jordan 2002; Scott 2004, 2008; Todorov 2004; Shadmehr and Krakauer 2008). However, biomechanical redundancy provides an abundance of motor solutions that may all be “good enough” to produce a desired action rapidly and robustly. These solutions may only be locally optimal, reflecting motor experience and competing costs and constraints (Loeb 2012; Tiel et al. 2015). Second, computing the “correct” trajectory requires an internal model or representation of the periphery for the nervous system to use. Finding the solution involves a computation of inverse kinematics or dynamics (see Chapter 11), similar to the computations needed to direct a robot limb (see Chapter 14). However, exploration and directed search guided by prior experience, biomechanical affordances, and the immediately prior movement, rather than exhaustive computation, may underlie motor movements and motor learning (Smith and Thelen 2003; Huang et al. 2008; Loeb 2012; Herzfeld and Shadmehr 2014; Wu et al. 2014). Third, it is also assumed that complex biomechanical computations are done quickly and efficiently and are readily instantiated by neural circuits. Recent studies, however, suggest that subjects prefer to use habitual movement patterns (Cohen and Sternad 2009) even when they have experienced more “optimal” ones (Ganesh et al. 2010; de Rugy et al. 2012).

Optimization approaches consider motor redundancy to be a problem for which a *single* solution must be found. In contrast, more recent approaches consider biomechanical *motor abundance* as providing a rich source of variation in how movements are learned, remembered, and recalled. Motor exploration and variability are considered essential to discovering novel useful movement patterns and do not necessarily follow rules of engineering approaches (Smith and Thelen 2003; Huang et al. 2008; Loeb 2012; Herzfeld and Shadmehr 2014; Wu et al. 2014). Moreover, when animals must rapidly respond, as when tracking prey or avoiding predators, there is very little time for elaborate computation. Rapid and reliable responses of “good enough” solutions allow animals to transition rapidly and seamlessly among different behaviors. Movement pattern variation is also observed in “don’t care” regions that do not affect critical aspects of motor performance. Individual patterns or styles of movement may emerge from interactions between the large motor solution space and individual differences in physical properties (e.g., size variations among animals of the same species) or how the motor space is explored (Loeb 2012; Furuya and Altenmuller 2013; Cullins et al. 2014). Indeed, sensory feedback may act to regulate the level of variability as an aid to motor movement. A recent study demonstrated that, in the presence of sensory feedback, animals varied less from one another, but showed more variation within their own behavior, suggesting that all of them were moved into a common solution space (Cullins et al. 2015; Hooper 2015).

12.4.1 Organismal Structures Are Multi-Functional

Coordination of Multiple Muscles Reconfigures the Body to Produce Different Behaviors Limb and body multi-functionality is critical to create a large motor repertoire, but requires understanding how muscles work together to generate movements. The ability to rapidly reconfigure a peripheral structure, flexibly adjusting motor responses as the environment changes, may confer selective advantages on animals. How are the same set of muscles and structures coordinated in different ways to produce different behaviors? Because, as discussed above, a muscle's function cannot be determined in isolation, movements cannot be constructed simply by adding the individual actions of each muscle. The coordinated actions of muscles over space and time instead need to be considered holistically. In thinking of the ways that muscles can work together to generate different actions of a limb or the body, the number of possible behaviors is immense. If one considers just simple on/off combinations of muscle activation across n muscles, one obtains 2^n possible joint torque patterns. This number of possibilities increases dramatically when one allows for different levels and timings of muscle activation, and becomes extremely large when the effects of changes in posture, environment, and movement that can modulate muscle function are factored in. The potential behavioral repertoire that a set of muscle can generate is thus much greater than the total number of muscles or even motor units.

In these complex systems, biomechanical constraints and affordances may reduce the set of viable combinations of muscle activity. For example, a neural pattern that would force the knee past its range of motion is clearly not functional. Certain patterns may harness the intrinsic biomechanical dynamics of the system and require less energy to produce, such as passive dynamic walking, and thus presumably be selected for. However, even with biomechanical constraints, the number of possible muscle coordination patterns that can achieve even a simple isometric force are extremely high (Bunderson et al. 2008, 2010). This number becomes much greater in more complex motor activities: it is possible to walk with many different gaits: slow, quick, smooth, sideways, skipping, backwards, or lurching (Cleese 1970). All these very different gaits, for each of which there will be many "good enough" patterns of muscle coordination, will reflect the biomechanical dynamics of the limb and environment. Indeed, a variety of multi-muscle patterns are recruited for walking and balance in animals and humans (Collins 1995; Ivanenko et al. 2004; Ting and Macpherson 2005; Cappellini et al. 2006; Torres-Oviedo et al. 2006; Clark et al. 2010; Yakovenko et al. 2011; Zelik et al. 2014).

Multi-functionality is not limited to muscle coactivation, but also applies to the timing and sequence of muscle activation. For example, the *Aplysia* feeding systems uses different muscle coordination patterns in various forms of swallowing and in rejection. During weak swallows, a grasper closer muscle (I4) acts purely to hold the food as other muscles push the grasper back into the buccal cavity; during stronger swallows, because of a change in grasper position, I4 both grasps food and pulls it inward, and a second muscle (the hinge) plays a critical role in grasper retraction (Ye et al. 2006a). During strong rejections, alternatively, the hinge muscle rotates the grasper ventrally and then dorsally; both capabilities are "unmasked" by a larger protraction phase (Ye et al. 2006b). These data suggest that multi-functionality emerges from mechanical structures in which flexible coalitions of muscles perform different functions in different

mechanical contexts and from neural circuitry that reorganizes itself to exploit these coalitions by changes in phasing, duration, and intensity of motorneuron activation.

Multi-Functionality May Be Mediated by Motor Modules Multiple lines of evidence indicate that muscle activation patterns at a given instant in time are constrained, reflecting consistent motor patterns that produce meaningful motor outputs (Ting et al. 2015). Several computational methods have demonstrated consistent structure underlying muscle activation patterns across multiple muscles and motor behaviors (d'Avella et al. 2003; Giszter et al. 2007; Ting 2007; Ting and McKay 2007; Bizzi et al. 2008). Using signal processing methods, such as principal components analysis, independent components analysis, and nonnegative matrix factorization (Lee and Seung 1999; Tresch et al. 1999, 2006; Ting and Chvatal 2010), motor signals can be decomposed into underlying *motor modules*, or *muscle synergies* that reflect consistent patterns of multi-muscle coordination that generate specific actions (see also Chapter 11). Motor modules have been associated with biomechanical outputs in both experimental and modeling studies (Neptune et al. 2009; Clark et al. 2010; Chvatal et al. 2011; Allen and Neptune 2012; Ting and Macpherson 2005; Safavynia and Ting 2013), and can be recruited across a variety of motor behaviors (Tresch et al. 1999; Torres-Oviedo et al. 2006; Chvatal et al. 2011; Roh et al. 2011; Chvatal and Ting 2013) suggesting that they form a repertoire of whole limb actions for movement (Fig. 12.7).

However, this underlying structure does not mean that actions are necessarily stereotyped. Motor modules may facilitate rapid adaptation by allowing meaningful motor actions to be flexibly combined, producing a wide range of different muscle activation patterns for movement. Variability observed across different types of behaviors, and trial-by-trial variability, can be accounted for by varying combinations of motor modules (Fig. 12.7) (Tresch et al. 1999; Hart and Giszter 2004; Cheung et al. 2005; Torres-Oviedo and Ting 2007; Roh et al. 2011). Variability across instances of movement may thus reflect differences in descending drive to stored movement patterns (Churchland et al. 2006) that could facilitate motor exploration (Huang et al. 2008; Wu et al. 2014) rather than random noise in individual muscles or trajectories. Indeed, learning to perform novel tasks is faster if it can be achieved by altering the recruitment of motor modules versus requiring activity incompatible with motor module coordination (Berger et al. 2013).

The computational methods used to analyze motor patterns have many limitations and may not be easily instantiated as neural mechanisms (Tresch and Jarc 2009; Ting and Chvatal 2010; Burkholder and van Antwerp 2013; Steele et al. 2013; Zelik et al. 2014), although they may still be useful in understanding motor coordination. Consistent structures in motor patterns are a hallmark of coordinated movement, whether they arise from specific neural structures (Saltiel et al. 2001; Lemay and Grill 2004; Hart and Giszter 2010; Overduin et al. 2012), reflect optimal coordination of biomechanics (Li et al. 2005; Kurtzer et al. 2006; Berniker et al. 2009; Kargo et al. 2010; Kutch and Valero-Cuevas 2012; Steele et al. 2013) or emerge from complex neural and biomechanical interactions (Ting and McKay 2007; Ting et al. 2009; McKay and Ting 2012; Giszter and Hart 2013).

The necessity of appropriate structure in neuromechanical interaction is highlighted in motor disorders, where current techniques can be used to evaluate different types and potential mechanisms of impairment (Cheung et al. 2009, 2012; Safavynia et al. 2011;

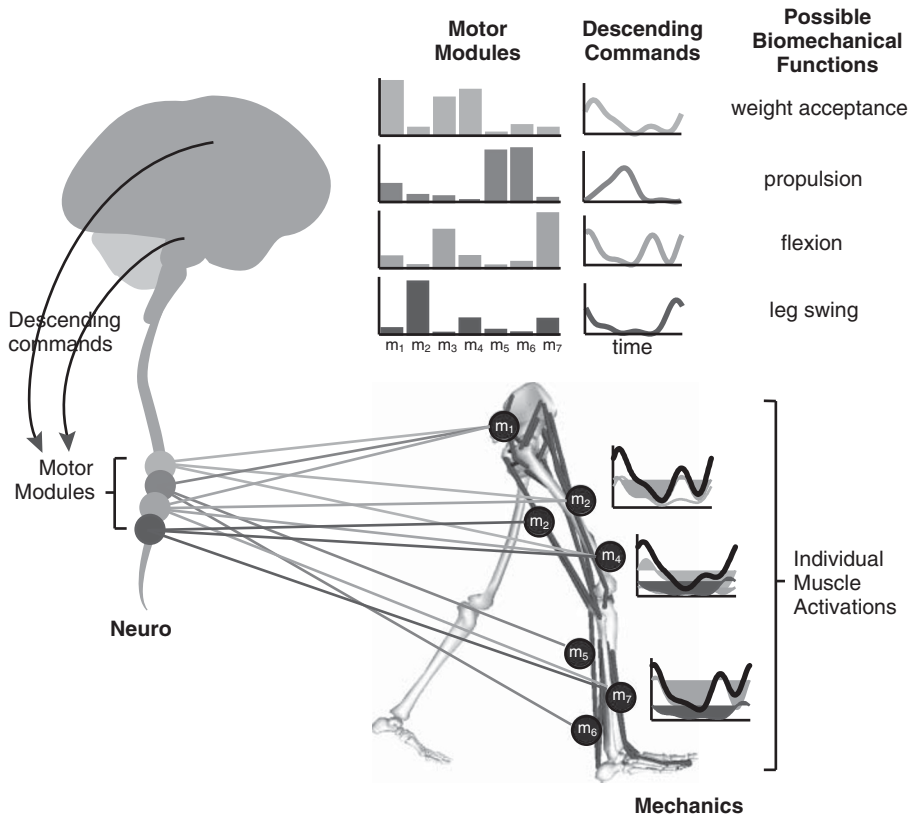


Figure 12.7 Multi-functionality of musculoskeletal systems is facilitated by motor modules. Motor modules reflect consistent, individual-specific patterns of multi-muscle activation that produce actions necessary for behavior. Each motor module can be recruited as a unit to modulate a given biomechanical output such as weight support, propulsion, and limb flexion. For example, the timing and amplitude of the recruitment, or descending command, to each module can be varied to generate a continuum of different muscle activation patterns appropriate for different gait speeds, as well as responses to perturbation during human walking.

Giszter and Hart 2013; Roh et al. 2013; Ting et al. 2015). For example, impairments in descending corticospinal drive in stroke are associated with a merging of motor modules in hemiplegic gait and a reduced ability to modulate motor module recruitment that limits leg motor capacity (Clark et al. 2010; Allen et al. 2013, 2014; Routson et al. 2014). In contrast, after spinal cord injury, motor patterns can lose all structure and become indistinguishable from random variation (Chvatal et al. 2013). In both cases, where motor patterns do exist, they may not be modulated appropriately in response to sensory feedback (Hayes et al. 2014; Routson et al. 2014).

Motor modules imply a reduction in dimensionality, and thus in the number of possible patterns. However, if one considers the very large number of different tasks that an animal or human may engage in over a lifetime, many different patterns are required (Zelik et al. 2014). It is thus not surprising that the number of possible muscle coordination patterns may far exceed the number of muscles (Chiel et al. 2009). This

combinatorial problem is also present in the neural coding of sensory information, in which large sets of so-called overcomplete representations are proposed to account for the ability to recognize visual features (Olshausen and Field 2004). As all existing algorithms necessarily reduce dimensionality, they are inherently limited in their ability to clarify the full complexity of motor systems.

Biomechanical models can be useful in identifying motor patterns that are compatible with and harness body affordances. Motor modules that reflect the natural dynamics of the peripheral motor system are similar to those measured experimentally and can be used to reproduce essential features of movement in frog leg (Berniker et al. 2009) and to drive simulations of human walking (Neptune et al. 2009; Allen and Neptune 2012; Allen et al. 2013). As a consequence, modules reflect an interaction between the neural and motor systems, and often align with coordination patterns that optimize energetic efficiency given biomechanical constraints (McKay and Ting 2012; Steele et al. 2013). Nonetheless, even among such solutions, variations in patterns exist. Including individual-specific motor structure constrains coordination patterns from among the many possible, and improves the accuracy of computer simulations of movement (Walter et al. 2014).

12.4.2 Many Functionally-Equivalent Solutions Exist for Sensorimotor Tasks

For any given motor behavior, there is an abundance of ways in which a wide variety of motor commands can generate similar or functionally-equivalent behaviors. Substantial redundancy exists at many levels, whether one examines joint torques, movement kinematics, or different behaviors that achieve the same goal (see also Chapter 11). While redundancy is usually considered a “problem” from the perspective of reverse-engineering a solution, the ability to choose from many solutions underlies the adaptability and robustness of biological systems. Indeed, the concept of *motor abundance* (Latash 2012) is one that should be celebrated and used to understand the many different ways in which variation in movement solutions (Loeb 2012; Ting et al. 2015) and variability in movements arises (Scholz and Schoner 1999; Scholz et al. 2000; Valero-Cuevas et al. 2009). Within these “motor equivalent” solutions, there may be some that are less desirable than others for any number of reasons, including energetics, stability, and generalizability across tasks. There may be solutions that are not optimal, but “good enough” to achieve the motor function. In the sections that follow, we provide evidence suggesting that biomechanics shapes the feasible ranges for variation in motor commands that generate a given motor task.

Motor Equivalents Exist at Many Levels of Organization Even at the level of generating joint torques, substantial variations in possible muscle activation patterns exist. Consider the problem of generating an isometric force with a simple arm model (Fig. 12.8). Even with only two antagonistic muscles spanning the joint, there are nonetheless an infinite number of muscle activation patterns that will generate a given magnitude of joint flexion torque at the elbow. A classical approach to find the minimum energy solution would predict that only the flexor muscle (m_1) would be activated, and its activation would increase with endpoint force magnitude (Fig. 12.8 m_1 plot, lower line labeled “Necessary”). If both muscles are activated, a feasible range of activity for each muscle can be found (shaded gray areas in m_1 and m_2 plots); the upper limit is limited by the

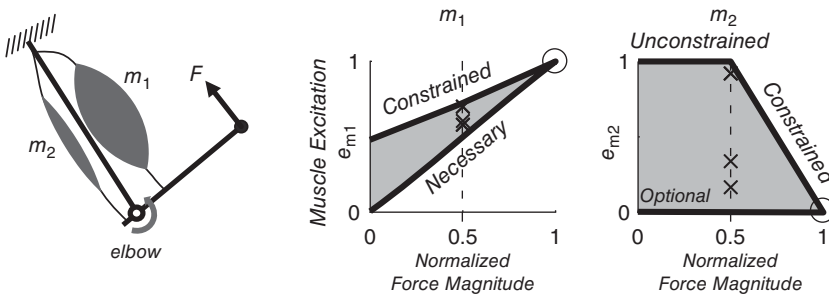


Figure 12.8 Muscle feasible ranges determine biomechanical constraints on goal-equivalent muscle activity. In a simple example of an elbow joint with an antagonistic muscle pair—flexor m_1 and extensor m_2 —the muscle activation level that can generate a force vector at the hand is illustrated. The line marked “Necessary” in the m_1 plot shows the minimum level of activation (that is, m_1 ’s activation when m_2 ’s activation is zero) necessary to generate normalized forces from 0 to 1. When producing any given level of normalized force (the “x”s on the plots show an example for producing a normalized force of 0.5) except for maximum normalized force, for which m_1 excitation must be 1 and m_2 excitation must be 0 (open circles on m_1 and m_2 plots), the normalized force can be produced across a range of m_2 activations by activating m_1 to a greater degree so as to cancel the opposing elbow torque caused by m_2 . In some cases, such co-activation of m_1 and m_2 may be desirable to provide limb stability. The upper limit of m_1 excitation (line marked “Constrained” on m_1 plot) is bounded by m_2 ’s strength, which in this case generates much less elbow torque. For example, to produce a normalized force of 0.5, m_1 amplitude varies along the dashed line in the m_1 plot as m_2 amplitude varies along the dashed line in the m_2 plot; the x’s in the m_1 plot show what m_1 amplitude must be to counteract the m_2 amplitudes marked by the x’s in the m_2 plot (upper m_1 plot x corresponds to upper m_2 plot x; middle m_1 to middle m_2 ; bottom m_1 to middle m_2). Because m_2 is the weaker muscle, for all normalized force values except 1 (for which m_2 excitation must be zero), m_2 has a much wider possible excitation range than m_1 . Only at maximal force is there a unique solution to the force generation problem, although this need not always be the case, particularly when there are multiple agonist and antagonists crossing a joint (Sohn et al. 2013).

strength of the opposing muscle. In this example, agonist (m_1) variations are relatively small at any given normalized force level, whereas the antagonist muscle (m_2) can be activated from 0 to 1 at all normalized force levels ≤ 0.5 . Only at the maximal force (open circles on m_1 and m_2 plots) can a unique solution for each muscle be defined. Using such techniques shows that the variation in muscle activity for isometric force production in the finger is relatively constrained, allowing little variability (Valero-Cuevas et al. 1998; Kutch and Valero-Cuevas 2012), whereas the possible variation is much greater in cat hindlimb (Sohn et al. 2013) and in human walking (Simpson et al. 2015). These appear to match the variability in muscle activity measured experimentally. However, different patterns that produce the same force may endow the limb with other characteristics that may or may not matter to the movement, such as limb stability (Franklin et al. 2004; Bunderson et al. 2008; Sohn and Ting 2013).

Considering a movement trajectory over time, Bernstein (1967) realized that the range of possible forces that could produce the trajectory depended on the initial conditions of the movement (Fig. 12.9). Variations in range indicate time points where the forces generating the movement could be highly variable. As predicted, different patterns of joint torques have been shown to produce similar kinematic outputs in arm movement (Gottlieb et al. 1995), and substantial variations in muscle activity that deviate from an optimal pattern have been observed in many movements, including human walking.

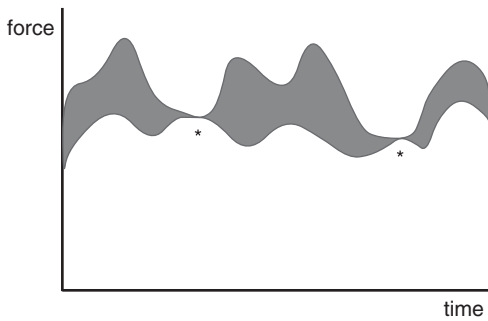


Figure 12.9 Range of possible forces that will generate a given kinematic trajectory. At only two times (asterisks) is a unique force required. Measurement of kinematic outputs thus does not uniquely define the forces necessary to generate the task. This lack of unique definition arises because forces must be integrated twice to determine the displacement of an organism or body and thus the required force will, in general, vary as a result of the prior displacement and velocity of the system. Further, due to biomechanical constraints and affordances, there may be times during a movement in which force variations have no impact on motor output, and thus can assume any value the muscles can produce. Figure is new but based on a classic, analogous figure in Bernstein (1967).

At other times, when the input force must be very precise, there is no room for variability. In a modeling study of single-legged locomotion, lowering and pushing backward the leg needed to be precisely coordinated to generate efficient locomotion, creating a biomechanical “bottleneck.” The highest fitness pattern generators for this model found by a genetic algorithm consequently produced precise timing at this phase of the pattern. In contrast, late in stance, the model leg continued to move backwards but could no longer exert force. During this “don’t care” region of the behavior, evolved pattern generators showed high variability (Beer et al. 1999).

Ultimately, the motor goal of an animal can rarely be characterized by a single kinematic or kinetic pattern. Rather, the fundamental question is “Did the animal meet a functionally-relevant goal?” Furthermore, movement kinematics and kinetics may vary and yet have the same adaptive fitness. If a squirrel monkey succeeds in plucking a breadfruit from various vantage points while climbing a tree, very different hand trajectories or force profiles may be adaptively equivalent. Limb stability may be increased by coactivating muscles (Franklin et al. 2004; Selen et al. 2009), or by changing arm configuration (Trumbower et al. 2009). Variations in responses and individuals have been found in animals ranging from insects (Hooper et al. 2006) to humans (Nussbaum and Chaffin 1997; Borzelli et al. 1999; Welch and Ting 2008; Torres-Oviedo and Ting 2010). People can walk with different gaits or recover balance using a wide range of strategies (Macpherson and Horak 2013).

12.4.3 Structure and Variability in Motor Patterns Reflect Biomechanics

A hallmark of biological behaviors is that they vary. Sources of noise that may cause variability exist at all levels of the neuromuscular transform. These include stochastic processes associated with synaptic communication between neurons, variation in neuron and muscle properties, and the effect of body mechanics and environmental forces discussed earlier. As a consequence, movements vary at every level studied: at the level of motor signals within a given motor task, during repetitions of the same task in the same

subject, across motor tasks, and across individuals. Such variations have been observed in insects, vertebrates, and humans, including those highly trained in movement such as musicians and athletes.

But variability in motor control is not random. Several different approaches use a biomechanical perspective to understand the structure and variability of motor behaviors. The goals of a task, and the biomechanical affordances and constraints defined by body structure, environment, and behavioral context all play a role in shaping variability. The effect of variations in muscle activity on motor output highly depends on biomechanical interactions. Many different biomechanical approaches have been used to understand “don’t care” regions of motor variability where there is little to no effect on motor output, versus defining sets of “task equivalent” outputs that all achieve the same goal “well enough” because their differences make little difference in task fulfillment. Taking an evolutionary perspective, how one learns to move is based on innate motor mechanisms, prior motor experience, and different motor goals. Not surprisingly, then, the need to rapidly recall reliable motor actions may lead to the individual movement styles that are found in invertebrates and vertebrates alike.

We will continue to use the simple example in Fig. 12.9 of combining two forces to generate a total net force to explain some key ideas and theories in the field related to variability, movement strategies, motor learning, and the role of experience in individual differences in movement. Assume two equivalent muscles that generate forces F_1 and F_2 and sum to generate a total desired force. To generate 4 N of force, any solution satisfying the equation $F_1 + F_2 = 4\text{N}$ is acceptable (Fig. 12.10, bold diagonal line). Thus, one muscle can be activated to 4 N while the other is kept off, or they can share the load, with the symmetric case being each muscle producing 2 N. This example can be directly mapped to questions of how muscles spanning the same joint should be activated to generate a desired joint torque (Herzog and Leonard 1991), or how two fingers together generate forces on an object (Latash et al. 2001; Scholz et al. 2002). However, it is also useful to think about this example in the context of controlling multiple muscles as described above, where muscle interaction might vary non-linearly, and is subject to movement context, environmental forces, and so on.

The Structure in Variability Depends on Biomechanical Task Relevance Evidence suggests that the nervous system allows greater variability in task-irrelevant “don’t care” dimensions, where large fluctuations in muscle activity do not affect motor goals. In our example, each of the two forces may fluctuate over time with similar dynamics, e.g., with a mean value of 2 N and variance of ± 1 N (Fig. 12.10, bars along axes). Total force will thus also fluctuate such that $F_{tot} = (F_1 + \Delta F_1) + (F_2 + \Delta F_2)$. If the fluctuations in F_1 and F_2 are independent, then the fluctuations in total force should be the vector sum of the F_1 and F_2 fluctuations, $\Delta F_{tot} = \sqrt{\Delta F_1^2 + \Delta F_2^2}$, and the F_{tot} fluctuations will appear as a circle when F_1 and F_2 are plotted against each other. Nonetheless, if the fluctuations in F_1 and F_2 are structured such that F_1 increases as F_2 decreases, i.e., $\Delta F_1 + \Delta F_2 = 0$, then the goal of generating $F_{tot} = 4\text{N}$ force can be perfectly maintained even as F_1 and F_2 fluctuate. Thus, different combinations of F_1 and F_2 , along the diagonal line of *equivalent solutions*, can be used. If the fluctuations in F_1 and F_2 do not precisely cancel each other out, then the variability in F_{tot} will be an ellipsoid oriented along the manifold

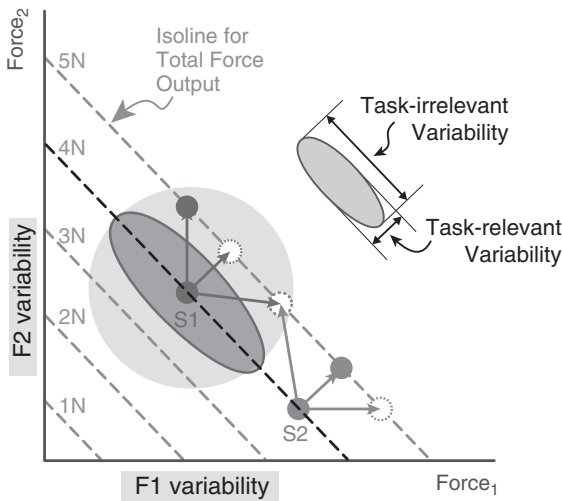


Figure 12.10 Simple example to illustrate different types of motor variability structures using a system where the total desired force $F_{tot} = F_1 + F_2$. Due to noise in biological systems, the levels of F_1 and F_2 can vary, in a range indicated by the bars along each axis. Dashed diagonal lines indicate combinations of F_1 and F_2 that generate a consistent level of F_{tot} , and denote goal-equivalent manifolds, “don’t care” dimensions, where fluctuations in F_1 and F_2 are task-irrelevant, i.e., do not change the total force. If F_1 and F_2 vary independently, the fluctuations will lie in the gray circular area, and total force will vary as a result. Structuring the fluctuations in F_1 and F_2 to reduce F_{tot} variation (i.e., making $F_1 + F_2 \approx 0$) results in greater variation along the task-irrelevant direction. In changing total force level, many different combinations of F_1 and F_2 can be selected (arrows going from 4 N isoline to 5 N isoline). The solution an individual chooses may depend on the initial state of force generation, e.g., S1 and S2, and a preferred ratio of changes in F_1 and F_2 used to increase F_{tot} (lines with different slopes leaving S1 and S2).

of equivalent solutions, with the variability being greater in the task-irrelevant versus task-relevant direction.

There are several theories that use biomechanics to explain structured variability in motor control, such as the uncontrolled manifold, theory of minimum intervention, and optimal feedback control (Bernstein 1967; Scholz and Schoner 1999; Todorov and Jordan 2002). Lower variability in task-relevant versus task-irrelevant dimension are predicted based on the idea that the nervous system only makes corrections to motor outputs that are relevant to task goals. Task-relevant and task-irrelevant variations can be identified in situations where explicit models of the biomechanical relationships between the goal and the measured components can be generated. Structured variability has been identified at the level of joint angles, joint torques, and muscles in a range of different experimental tasks. For example, the variability of finger location in space during pointing depends on the variability of arm joint angles and arm geometry and comparing the measured variability of finger location to that predicted by uncorrelated variations at each joint allows the degree of structure in the variability to be measured (Scholz et al. 2000). Leg joint torques similarly demonstrate structured variability in maintaining total vertical ground-reaction force in hopping (Yen et al. 2009). Muscle activity during isometric force production by the index finger also exhibits structured variability in maintaining endpoint force (Valero-Cuevas et al. 2009).

The computational metrics used may or may not reflect the actual goals and processes used by the nervous system. Representing variables in coordinate frames and units is useful for our understanding, but can influence the interpretation of variability (Sternad et al. 2010). Biomechanical models may not include all the constraints or affordances relevant to the behavior. However, the insights gained have real relevance to solving motor control problems. For example, in tennis serves, training that focuses on tight control of certain critical features of the movement, while allowing variability in others, is more effective than methods that emphasize consistency and repeatable movements (Handford 2006). Overconstraining movements in “don’t care” regions may actually be detrimental to expert performance.

Learning Is Simplified by an Abundance of Equivalent Motor Solutions Biomechanical redundancy also predicts that many different patterns in motor coordination can equivalently achieve the same task-level goal. In our example, consider the goal of increasing total force from 4 N to 5 N. In this case, the changes in F_1 and F_2 must be coordinated to achieve a net increase of 1 N. The most direct path is to increase forces perpendicular to the manifold of equivalent solutions, thus increasing both F_1 and F_2 by 0.5 N so that $\Delta F_1 + \Delta F_2 = 1\text{ N}$. This solution would be predicted by a minimum muscle stress criteria in which maximal muscle forces are avoided (Crowninshield and Brand 1981), or by minimizing signal-dependent noise in muscles (Harris and Wolpert 1998). However, F_1 and F_2 can be coordinated along *any* line that intersects with the 5 N solution manifold. In the extreme, either F_1 or F_2 would increase by 1 N, but all intermediate solutions are also viable (Fig. 12.10 arrows), each achieving 5 N in a slightly different way.

How does one select a particular “good enough” solution to achieve a task? Given the need to coordinate multiple muscles to control a limb, very specific coordination structures may be necessary to reliably move a limb in desired directions or to achieve a given force level (Ting and McKay 2007; Ting et al. 2015). Recent work suggests that movement variability is essential to motor learning (Huang et al. 2008; Shadmehr et al. 2010; Herzfeld and Shadmehr 2014; Wu et al. 2014), as it may help individuals explore the landscape of possible movement patterns (Loeb 2012).

The starting point of an individual and the exploration and refinement process can all affect the pattern an individual ultimately selects. In our example, consider two individuals, S_1 and S_2 , who use different F_1 and F_2 combinations to generate 4 N. In generating 5 N, a random search strategy would most likely result in solutions close to the starting point (Fig. 12.10). Because S_2 ’s solution for generating 4 N relies on high levels of F_1 and low levels of F_2 , S_2 ’s solution for generating 5 N would likely rely more on F_1 as well. In contrast, S_1 relies more equally on F_1 and F_2 . This example demonstrates how S_1 and S_2 may end up reaching the same solution starting from different initial conditions and using different movement strategies.

Evolutionary, developmental, and learning processes help identify “good enough” solutions that are critical for animal survival (Lacquaniti et al. 2013). Rather than searching exhaustively for optimal solutions, animals must rapidly and reliably generate movements in novel situations. Default movement patterns are established in the embryonic stage, where spontaneous motor activity such as kicking and flailing are observed (Bekoff 2001). These patterns, available at birth, rapidly adapt, allowing a fawn, for example, to run minutes after birth. Human infants are born with the capacity for stepping and kicking (Yang et al. 2004), and, through exploration

(Smith and Thelen 2003), existing movement patterns are refined and new ones created throughout development (Dominici et al. 2011), along with the ability to recruit them in task-specific manners (Angulo-Kinzler et al. 2002). Models of spinal circuitry and biomechanics suggest that stable “good enough” solutions can be found in just a few iterations of random searching (Tsianos et al. 2014). Movement strategies in adults may appear to rapidly optimize because they have been refined over time. Data suggest, however, that subjects do not optimize “online” but instead employ a range of different strategies leading to suboptimal performance (Ganesh et al. 2010; Snaterse et al. 2011; de Rugy et al. 2012). Similar challenges are faced in sports or the classroom in which stable, but non-optimal, and difficult-to-change, solutions are often learned (Chi and Roscoe 2002; Handford 2006).

Individuals Have Their Own Motor Styles The effects of movement history and experience lead to individual differences in movement and movement styles (Ting et al. 2015). A general principle is that individual—not averaged—solutions solve neuromotor problems (see also Fig. 5.1). In both invertebrates and vertebrates (including humans), individuals may have their own “motor program styles”; i.e., they show significant individual variations in motor outputs that are both consistent within a given animal and differ from one individual to another (Golowasch et al. 2002; Prinz et al. 2004; Marder and Goaillard 2006; Calabrese et al. 2011; Nussbaum and Chaffin 1997; Borzelli et al. 1999; Welch and Ting 2008; Torres-Oviedo and Ting 2010), although this variability can be reduced by training and is less in motor output components critical to producing the behavior. For example, when all feeding-related motorneurons in *Aplysia* are examined, the distribution of the durations of motorneuron activations varies across individuals (Fig. 12.11). However, the distributions of the motorneurons that play a critical role in feeding are similar across individuals (Cullins et al. 2014).

In humans, regulation of individual temporal variability in motor output enhances learning speed (Wu et al. 2014). Individual variation in the temporal patterns of motor response in reactive balance varies systematically in humans naive to the task (Welch and Ting 2008), but becomes smaller and closer to an energetically optimal solution in cats trained daily on the same task (Lockhart and Ting 2007). Individual-specific patterns of muscle activity associated with generating leg forces are also found in both cats (Torres-Oviedo et al. 2006, Fig. 12.12) and humans (Torres-Oviedo and Ting 2010). Consideration of individual movement patterns (Ting et al. 2012) also improves simulations of human movement (Walter et al. 2014).

Experience, social learning, and training play a strong role in shaping individual movement styles. Observing the actions of others activates neural circuitry similar to that used in self motion—so-called “mirror neurons”—and may help animals learn faster through mimicry (Rizzolatti and Strick 2013). Different movement patterns for grasping can be identified in musicians, shaped by their specific training (Gentner et al. 2010), and different musicians display different movement styles (Furuya and Altenmuller 2013). Context and interaction define how humans produce and perceive language, resulting in characteristic speech sounds specific to different languages, cultures, and individuals (Kuhl 2004).

Variability in movement styles may be subject to evolutionary selection. In *Drosophila melanogaster*, fast and slow larval feeding rates can be inherited, and adults from slower feeding larva live longer than adults from faster feeding larva

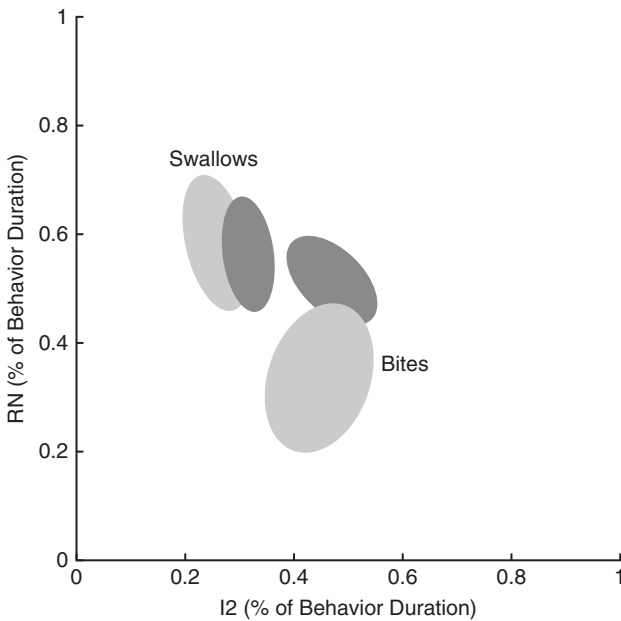


Figure 12.11 Individuality of motor pattern features is behavior-dependent. Durations of activity in the protractor muscle (I2) and the muscle closing the feeding grasper (I4) as a percentage of behavior duration are shown for bites and swallows in two different animals (light, dark ellipses). The distributions of the behavior percentages are represented by ellipses whose edges are iso-density contours bounding 50% of the density for bivariate Gaussian distributions fitted to each group of data. RN duration varies between individuals in bites but not swallows (bite ellipses are not aligned along the vertical axis but swallow ellipses are) because the duration of grasper closure is important for effectiveness in swallowing. In contrast, I2 duration correlates with motor output in both behaviors—bites have long I2 durations (stronger protractions), swallows have short I2 durations (weaker protractions). Consistent with I2's importance in both behaviors, in each behavior I2 duration is also similar in both animals. From Cullins et al. 2014 with permission.

(Foley and Luckinbill 2001). More generally, variation in behavior duration can distinguish individuals. For example, great tits (*Parus major*) vary in how quickly they explore their environment. These differences are correlated with other behavioral traits (e.g., aggressiveness), are heritable, and have differential effects on fitness depending on environmental factors (Dingemanse and Réale 2005).

12.4.4 Specialization of Neuromechanical Systems Reflect Behavioral Repertoire

Motor System Multi-Functionality Determines the Complexity of its Neural Control System The data presented above demonstrate that the relative importance of biomechanical specialization versus neural control complexity varies within and across animals. It thus seems reasonable to assert that the more multi-functional the motor system, the less the biomechanical specialization and the greater the complexity of the neural control.

Highly specialized biomechanical systems can produce very precise, rapid, and specialized behaviors, as in insect jumping or flight. Specialization of the motor periphery can tune interactions with the environment without need for complex neural control mechanisms. For example, the command neurons that cause the most rapid and

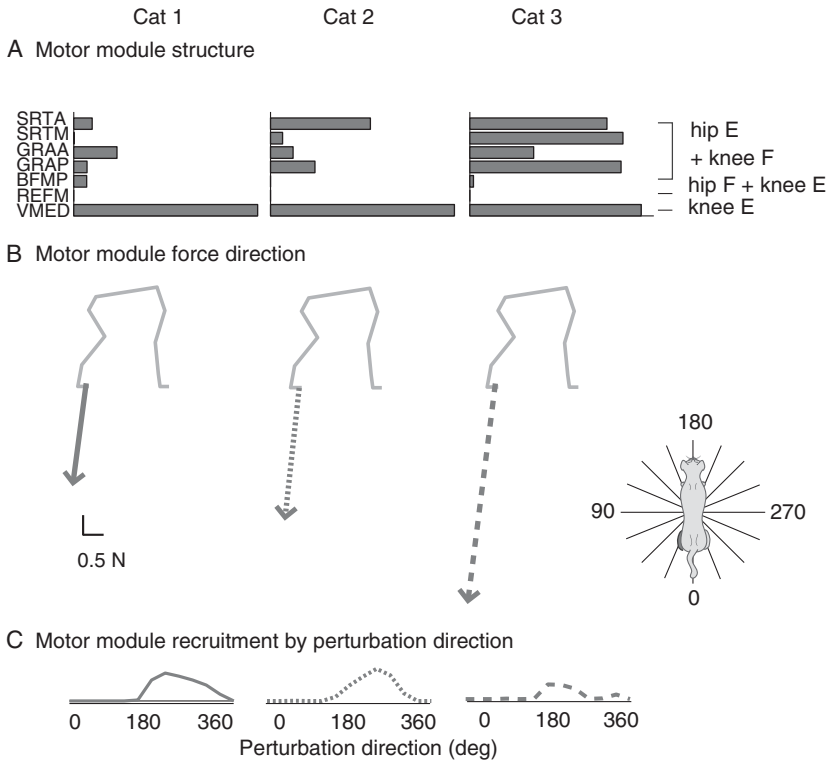


Figure 12.12 Individual-specific motor modules for achieving similar biomechanical function. (A) Motor modules that correspond to extensor force generation for postural control in cats vary across individuals. Open bars are muscles recorded in three animals. The motor modules for each animal include extensor muscles, reflecting biomechanical constraints on force generation. But the level of antagonistic muscle activity varies across individuals in each module. These modules were characteristic for each individual animal across a range of postural configurations and perturbation types. The different modules resulted in similar directions of ground-reaction forces (B) and the recruitment of motor modules with respect to the direction of postural disturbance was similar across individuals (C). Motor modules encoding common biomechanical functions across individuals may nonetheless reflect individual motor styles. From Torres-Oviedo et al. 2006 with permission.

invariant crayfish escape responses are highly reliable and may be critical to optimize performance for survival (Edwards et al. 1999). Similar specialization is seen in Mauthner neuron initiated escape responses in fish, in which tail stimuli rapidly generate a complex whole body movement (Korn and Faber 2005). The limited biomechanical affordances of specialized systems are key to their efficiency and reliability, and may help to optimize an essential motor behavior in evolution. Even these systems, however, are embedded in slower neural systems that can alter the rapid reflex responses through modulation, learning, or incorporation of social context (e.g., the effects of social dominance in crayfish on the escape response (Edwards et al. 1999), or of immediate environmental context on escape swim direction (Korn and Faber 2005)).

In contrast, structures serving multiple purposes have less specialized biomechanics, and more complex neural control systems, that allow the system to be multi-functional.

Increasing the biomechanical degrees of freedom and affordances allows for greater movement variability and richness in behavioral repertoire. For multi-functional systems, the key to survival is the ability to generate a variety of movements that rapidly and reliably reconfigure the body for different motor tasks, and this may be more important than optimal performance of any one task. Consider the highly developed nervous system in extremely reconfigurable animals such as octopuses. Not only do the neural control systems work to reconfigure the body to achieve desired motor goals (Hochner 2012), but additional motor functions can be achieved through tool use, communication, and social interactions (Hochner et al. 2006).

12.5 Conclusions

Throughout this chapter we have illustrated how biomechanical considerations are critical for understanding the neural control of movement at three levels: how neural activity is transformed into force in individual muscles, how organismal structure and environmental forces affect individual muscle function, and how motorneuron activity is structured to create, and the effects of motorneuron variability on, motor behavior. At each level, a biomechanical perspective is necessary to understand the extent to which a muscle's activity contributes to motor performance and whether different patterns of activity can equally well fulfill motor goals, which in turn can give rise to individual movement styles (Ting et al. 2015). The effects of neural signals on motor outputs is highly non-linear and context dependent, relying on the specific biomechanical constraints and affordances of the motor periphery. Consequently, there is similarly no direct mapping between a desired motor output and the neural signals necessary to generate the behavior.

Given that a given neural activity can generate multiple motor outputs, and that a given motor output can be generated by multiple neural activities, it seems unlikely that motor solutions are generated through explicit neural computation and optimization. Rather, they may arise from initial "default behaviors" created through evolutionary and developmental processes. During the lifetime of an individual, motor movements are adapted through exploration, guided by neuromechanical constraints. Individual motor styles are made possible by motor abundance, and are equally effective in achieving motor goals. As a general principle, we have seen that the level of specialization of the periphery has an inverse relation to the multi-functionality, neural control complexity, and thus the behavioral repertoire of an animal.

While there remain many open questions related to the structure and variability of motor systems, there are exciting prospects for future work as the ability to measure, manipulate, and simulate neuromechanical systems improves (Roth et al. 2014). Such approaches may facilitate the discovery of the essential features and components of neuromechanical systems, and make it possible to address the many open questions that remain. For example, how does ongoing sensory feedback shape motor activity during behavior (Shaw et al. 2014)? How are neuromechanical dynamics actively shaped by motor processes (Ting et al. 2009)? How can variability be used to enhance motor function (Wu et al. 2014)? What actual neural dynamics underlie motor behavior (Shaw et al. 2014)? Answering these challenging questions will provide deep insights into motor control across phylogeny.

Physical modeling and robotic approaches may also shed light on the complex and non-linear interactions that underlie movement, and provide principles for the development of autonomous robots with more complex motor capabilities (Ijspeert et al. 2007; Scrivens et al. 2008; Boxerbaum et al. 2012; Daltorio et al. 2013; Horchler et al. 2015). A biomechanical perspective also has translational implications for understanding motor deficits and the mechanisms of neural plasticity and for developing motor rehabilitation practices to help treat sensorimotor deficits. Understanding interactions between neural control and biomechanics may also provide insights and principles to guide the effective design of devices, such as artificial limbs, that interact with humans, and of assistive and rehabilitative robots.

Finally, the debates within the field of motor control about structure vs. variability and the roles of representation, environment, and context parallel more general debates in cognitive studies about how animals and humans interact with the world (Rosch 1999). Elenor Rosch stated that “Mind and world occur together in a succession of situations which are somewhat lawful and predictable. We want to be able to find those laws and to find a level of description which neither turns human action into something mechanical like engineering nor something mental like fantasy.” The interactions between animals and their environment create specific contexts in which animals need to generate reliable solutions. As a consequence, specific interactions between brain, body, and environment cannot be studied in isolation (Chiel and Beer 1997; Chiel et al. 2009) and shape how different individuals solve problems for moving, thinking, and learning. Engineering approaches have great power, but for this work to have relevance to biological systems it is important that it not be too prescriptive and take into account the natural variability, adaptability, and creativity in movement that are critical to survival in an instant, over a lifetime, and across evolutionary time.

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References

- Abbott BC, Aubert XM (1952) The force exerted by active striated muscle during and after change of length. *J Physiol* 117:77–86.
- Ahn AN (2012) How muscles function—the work loop technique. *J Exp Biol* 215:1051–1052.
- Ahn AN, Full RJ (2002) A motor and a brake: two leg extensor muscles acting at the same joint manage energy differently in a running insect. *J Exp Biol* 205:379–389.
- Ahn AN, Meijer K, Full RJ (2006) *In situ* muscle power differs without varying *in vitro* mechanical properties in two insect leg muscles innervated by the same motorneuron. *J Exp Biol* 209:3370–3382.

- Allen JL, Kautz SA, Neptune RR (2013) The influence of merged muscle excitation modules on post-stroke hemiparetic walking performance. *Clin Biomech* 28:697–704.
- Allen JL, Kautz SA, Neptune RR (2014) Forward propulsion asymmetry is indicative of changes in plantarflexor coordination during walking in individuals with post-stroke hemiparesis. *Clin Biomech* 29:780–786.
- Allen JL, Neptune RR (2012) Three-dimensional modular control of human walking. *J Biomech* 45:2157–2163.
- Amemiya Y, Iwamoto H, Kobayashi T, Sugi H, et al. (1988) Time-resolved X-ray diffraction studies on the effect of slow length changes on tetanized frog skeletal muscle. *J Physiol* 407:231–241.
- Angulo-Kinzler RM, Ulrich B, Thelen E (2002) Three-month-old infants can select specific leg motor solutions. *Motor Control* 6:52–68.
- Asakawa DS, Blemker SS, Gold GE, Delp SL (2002) *In vivo* motion of the rectus femoris muscle after tendon transfer surgery. *J Biomech* 35:1029–1037.
- Bartoo ML, Linke WA, Pollack GH (1997) Basis of passive tension and stiffness in isolated rabbit myofibrils. *Am J Physiol* 273:C266–276.
- Bayley TG, Sutton GP, Burrows M (2012) A buckling region in locust hindlegs contains resilin and absorbs energy when jumping or kicking goes wrong. *J Exp Biol* 215:1151–1161.
- Beer RD, Chiel HJ, Gallagher JC (1999) Evolution and analysis of model CPGs for walking: II. General principles and individual variability. *J Comput Neurosci* 7:119–147.
- Bekoff A (2001) Spontaneous embryonic motility: an enduring legacy. *Int J Dev Neurosci* 19:155–160.
- Belanger AY, McComas AJ (1985) A comparison of contractile properties in human arm and leg muscles. *Eur J Appl Physiol Occup Physiol* 54:326–330.
- Berger DJ, Gentner R, Edmunds T, Pai DK, d'Avella A (2013) Differences in adaptation rates after virtual surgeries provide direct evidence for modularity. *J Neurosci* 33:12384–12394.
- Berniker M, Jarc A, Bizzi E, Tresch MC (2009) Simplified and effective motor control based on muscle synergies to exploit musculoskeletal dynamics. *Proc Natl Acad Sci USA* 106:7601–7606.
- Bernstein N (1967) *The Coordination and Regulation of Movements*. Pergamon Press: New York.
- Biewener AA (2011) Muscle function in avian flight: achieving power and control. *Philos T Roy Soc B* 366:1496–1506.
- Biewener AA, Daley MA (2007) Unsteady locomotion: integrating muscle function with whole body dynamics and neuromuscular control. *J Exp Biol* 210:2949–2960.
- Binder-MacLeod S, Kesar T (2005) Catchlike property of skeletal muscle: recent findings and clinical implications. *Muscle Nerve* 31:681–693.
- Bizzi E, Cheung VC, d'Avella A, Saltiel P, Tresch M (2008) Combining modules for movement. *Brain Res Rev* 57:125–133.
- Blanco MM, Patek SN (2014) Muscle trade-offs in a power-amplified prey capture system. *Evolution* 68–5:1399–1414.
- Blemker SS, Pinsky PM, Delp SL (2005) A 3D model of muscle reveals the causes of nonuniform strains in the biceps brachii. *J Biomech* 38:657–665.
- Blickhan R (1986) Stiffness of an arthropod leg joint. *J Biomech* 19:375–384.

- Bobbert MF, van Ingen Schenau GJ (1988) Coordination in vertical jumping. *J Biomech* 21:249–262.
- Borzelli G, Cappozzo A, Papa E (1999) Inter- and intra-individual variability of ground reaction forces during sit-to-stand with principal component analysis. *Med Eng Phys* 21:235–240.
- Bowtell G, Williams TL (1994) Anguilliform body dynamics: a continuum model for the interaction between muscle activation and body curvature. *Journal Math Biol* 32:83–91.
- Boxerbaum AS, Shaw KM, Chiel HJ, Quinn RD (2012) Continuous wave peristaltic motion in a robot. *Int J Robot Res* 31:302–318.
- Boyle JH, Berri S, Cohen N (2012) Gait modulation in *C. elegans*: an integrated neuromechanical model. *Front Comput Neurosci* 6:10.
- Brezina V, Orekhova IV, Weiss KR (2000) Optimization of rhythmic behaviors by modulation of the neuromuscular transform. *J Neurophysiol* 83:260–279.
- Bunderson NE, Burkholder TJ, Ting LH (2008) Reduction of neuromuscular redundancy for postural force generation using an intrinsic stability criterion. *J Biomech* 41:1537–1544.
- Bunderson NE, McKay JL, Ting LH, Burkholder TJ (2010) Directional constraint of endpoint force emerges from hindlimb anatomy. *J Exp Biol* 213:2131–2141.
- Buneo CA, Soechting JF, Flanders M (1997) Postural dependence of muscle actions: implications for neural control. *J Neurosci* 17:2128–2142.
- Burke RE (1981) Motor units: anatomy, physiology and functional organization. *In Handbook of Physiology*. Brooks VB (ed). Washington, DC: Am Physiol Soc.
- Burkholder TJ, van Antwerp KW (2013) Practical limits on muscle synergy identification by non-negative matrix factorization in systems with mechanical constraints. *Med Biol Eng Comput* 51:187–196.
- Burrows M, Sutton G (2013) Interacting gears synchronize propulsive leg movements in a jumping insect. *Science* 341:1254–1256.
- Calabrese RL, Norris BJ, Wenning A, Wright TM (2011) Coping with variability in small neuronal networks. *Integr Comp Biol* 51:845–855.
- Campbell KS, Moss RL (2002) History-dependent mechanical properties of permeabilized rat soleus muscle fibers. *Biophys J* 82:929–943.
- Cappellini G, Ivanenko YP, Poppele RE, Lacquaniti F (2006) Motor patterns in human walking and running. *J Neurophysiol* 95:3426–3437.
- Chanaud CM, Macpherson JM (1991) Functionally complex muscles of the cat hindlimb III. Differential activation within biceps femoris during postural perturbations. *Exp Brain Res* 85:271–280.
- Chanaud CM, Pratt CA, Loeb GE (1991) Functionally complex muscles of the cat hindlimb V. The roles of histochemical fiber-type regionalization and mechanical heterogeneity in differential muscle activation. *Exp Brain Res* 85:300–313.
- Charles SK, Hogan N (2012) Stiffness, not inertial coupling, determines path curvature of wrist motion. *J Neurophysiol* 107:1230–1240.
- Cheung VC, d'Avella A, Tresch MC, Bizzi E (2005) Central and sensory contributions to the activation and organization of muscle synergies during natural motor behaviors. *J Neurosci* 25:6419–6434.
- Cheung VC, Piron L, Agostini M, Silvoni S, et al. (2009) Stability of muscle synergies for voluntary actions after cortical stroke in humans. *Proc Natl Acad Sci USA* 106:19563–19568.

- Cheung VCK, Turolla A, Agostini M, Silvoni S, et al. (2012) Muscle synergy patterns as physiological markers of motor cortical damage. *Proc Natl Acad Sci USA* 109:14652–14656.
- Chi MTH, Roscoe RD (2002) Reconsidering conceptual change: issues in theory and practice. *In* *The Processes and Challenges of Conceptual Change*. Limon M, Mason L (eds). Alphen aan den Rijn, The Netherlands: Kluwer.
- Chiel HJ, Beer RD (1997) The brain has a body: adaptive behavior emerges from interactions of nervous system, body and environment. *Trends Neurosci* 20:553–557.
- Chiel HJ, Crago P, Mansour JM, Hathi K (1992) Biomechanics of a muscular hydrostat: A model of lapping by a reptilian tongue. *Biol Cyber* 67:403–415.
- Chiel HJ, Ting LH, Ekeberg Ö, Hartmann MJ (2009) The brain in its body: motor control and sensing in a biomechanical context. *J Neurosci* 29:12807–12814.
- Churchland MM, Afshar A, Shenoy KV (2006) A central source of movement variability. *Neuron* 52:1085–1096.
- Chvatal SA, Macpherson JM, Torres-Oviedo G, Ting LH (2013) Absence of postural muscle synergies for balance after spinal cord transection. *J Neurophysiol* 110:1301–1310.
- Chvatal SA, Ting LH (2013) Common muscle synergies for balance and walking. *Front Comput Neurosci* 7:48.
- Chvatal SA, Torres-Oviedo G, Safavynia SA, Ting LH (2011) Common muscle synergies for control of center of mass and force in non-stepping and stepping postural behaviors. *J Neurophysiol* 106:999–1015.
- Clark DJ, Ting LH, Zajac FE, Neptune RR, Kautz SA (2010) Merging of healthy motor modules predicts reduced locomotor performance and muscle coordination complexity post-stroke. *J Neurophysiol* 103:844–857.
- Cleese J (1970) Memorandum from the Ministry of Silly Walks, BBC TV.
- Cohen RG, Sternad D (2009) Variability in motor learning: relocating, channeling and reducing noise. *Exp Brain Res* 193:69–83.
- Collins JJ (1995) The redundant nature of locomotor optimization laws. *J Biomech* 28:251–267.
- Collins S, Ruina A, Tedrake R, Wisse M (2005) Efficient bipedal robots based on passive-dynamic walkers. *Science* 307:1082–1085.
- Crowninshield RD, Brand RA (1981) A physiologically based criterion of muscle force prediction in locomotion. *J Biomech* 14:793–801.
- Cullins MJ, Gill JP, McManus JM, Lu H, et al. (2015) Sensory feedback reduces individuality by increasing variability within subjects. *Curr Biol* 25:2672–2676.
- Cullins MJ, Shaw KM, Gill JP, Chiel HJ (2014) Motorneuronal activity varies least among individuals when it matters most for behavior. *J Neurophysiol* 113:981–1000.
- d'Avella A, Saltiel P, Bizzi E (2003) Combinations of muscle synergies in the construction of a natural motor behavior. *Nat Neurosci* 6:300–308.
- Daley MA, Biewener AA (2006) Running over rough terrain reveals limb control for intrinsic stability. *Proc Natl Acad Sci USA* 103:15681–15686.
- Daley MA, Biewener AA (2011) Leg muscles that mediate stability: mechanics and control of two distal extensor muscles during obstacle negotiation in the guinea fowl. *Philos T Roy Soc Lond B* 366:1580–1591.
- Daltorio KA, Boxerbaum AS, Horchler AD, Shaw KM, et al. (2013) Efficient worm-like locomotion: slip and control of soft-bodied peristaltic robots. *Bioinspir Biomim* 8:035003.

- de Brito Fontana H, Roesler H, Herzog W (2014) *In vivo* vastus lateralis force–velocity relationship at the fascicle and muscle tendon unit level. *J Electromyogr Kinesiol* 24:934–940.
- de Ruyg A, Loeb GE, Carroll TJ (2012) Muscle coordination is habitual rather than optimal. *J Neurosci* 32:7384–7391.
- Delp SL, Loan JP (2000) A computational framework for simulating and analyzing human and animal movement. *Comput Sci Eng* 2:46–55.
- Delp SL, Loan JP, Hoy MG, Zajac FE, et al. (1990) An interactive graphics-based model of the lower extremity to study orthopaedic surgical procedures. *IEEE T Biomed Eng* 37:757–767.
- Deshpande AD, Gialias N, Matsuoka Y (2012) Contributions of intrinsic visco-elastic torques during planar index finger and wrist movements. *IEEE T Biomed Eng* 59:586–594.
- Dickinson MH, Farley CT, Full RJ, Koehl MAR, et al. (2000) How animals move: an integrative view. *Science* 288:100–106.
- Dingemanse NJ, Réale D (2005) Natural selection and animal personality. *Behavior* 142:1165–1190.
- Dominici N, Ivanenko YP, Cappellini G, d’Avella A, et al. (2011) Locomotor primitives in newborn babies and their development. *Science* 334:997–999.
- Duchateau J, Enoka RM (2011) Human motor unit recordings: origins and insight into the integrated motor system. *Brain Res* 1409:42–61.
- Dudek DM, Full RJ (2006) Passive mechanical properties of legs from running insects. *J Exp Biol* 209:1502–1515.
- Edman KA, Elzinga G, Noble MI (1982) Residual force enhancement after stretch of contracting frog single muscle fibers. *J Gen Physiol* 80:769–784.
- Edman KA, Tsuchiya T (1996) Strain of passive elements during force enhancement by stretch in frog muscle fibres. *J Physiol* 490:191–205.
- Edman KAP (2012) Residual force enhancement after stretch in striated muscle. A consequence of increased myofilament overlap? *J Physiol (London)* 590:1339–1345.
- Edwards DH, Heitler WJ, Krasne FB (1999) Fifty years of a command neuron: the neurobiology of escape behavior in the crayfish. *Trends Neurosci* 22:153–161.
- Elemans CP, Spierts IL, Müller UK, van Leeuwen JL, Goller F (2004) Bird song: superfast muscles control dove’s trill. *Nature* 431:146–146.
- Enoka RM, Baudry S, Rudroff T, Farina D, et al. (2011) Unraveling the neurophysiology of muscle fatigue. *J Electromyogr Kinesiol* 21:208–219.
- Enoka RM, Pearson KG (2013) The motor unit and muscle action. *In* Principles of Neural Science. Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ (eds). New York, NY: McGraw-Hill Medical.
- Finni T, Ikegawa S, Lepola V, Komi PV (2003) Comparison of force–velocity relationships of vastus lateralis muscle in isokinetic and in stretch-shortening cycle exercises. *Acta Physiol Scand* 177:483–491.
- Foley PA, Luckinbill LS (2001) The effects of selection for larval behavior on adult life-history features in *Drosophila melanogaster*. *Evolution* 55:2493–2502.
- Franklin DW, So U, Kawato M, Milner TE (2004) Impedance control balances stability with metabolically costly muscle activation. *J Neurophysiol* 92:3097–3105.
- Full RJ, Stokes DR, Ahn AN, Josephson RK (1998) Energy absorption during running by leg muscles in a cockroach. *J Exp Biol* 201:997–1012.

- Funabara D, Kanoh S, Siegman MJ, Butler TM, et al. (2005) Twitchin as a regulator of catch contraction in molluscan smooth muscle. *J Muscle Res Cell Motil* 26:455–460.
- Furuya S, Altenmuller E (2013) Flexibility of movement organization in piano performance. *Front Hum Neurosci* 7:173.
- Ganesh G, Haruno M, Kawato M, Burdet E (2010) Motor memory and local minimization of error and effort, not global optimization, determine motor behavior. *J Neurophysiol* 104:382–390.
- Gentner R, Gorges S, Weise D, aufm Kampe K, et al. (2010) Encoding of motor skill in the corticomuscular system of musicians. *Curr Biol* 20:1869–1874.
- Getz EB, Cooke R, Lehman SL (1998) Phase transition in force during ramp stretches of skeletal muscle. *Biophys J* 75:2971–2983.
- Giszter S, Patil V, Hart C (2007) Primitives, premotor drives, and pattern generation: a combined computational and neuroethological perspective. *Prog Brain Res* 165:323–346.
- Giszter SF, Hart CB (2013) Motor primitives and synergies in the spinal cord and after injury—the current state of play. *Ann NY Acad Sci* 1279:114–126.
- George NT, Irving TC, Williams C, Daniel, TL (2013) The cross-bridge spring: can cool muscles store elastic energy? *Science* 340:1217–1220.
- Golowasch J, Goldman MS, Abbott LF, Marder E (2002) Failure of averaging in the construction of a conductance-based neuron model. *J Neurophysiol* 87:1129–1131.
- Gordon AM, Huxley AF, Julian FJ (1966) The variation in isometric tension with sarcomere length in vertebrate muscle fibres. *J Physiol* 184:170–192.
- Gottlieb GL, Chen CH, Corcos DM (1995) Relations between joint torque, motion, and electromyographic patterns at the human elbow. *Exp Brain Res* 103:164–167.
- Gronenberg W (1996) Fast actions in small animals: springs and click mechanisms. *J Comp Physiol A* 178:727–734.
- Gunst SJ, Tang DD, Opazo Saez A (2003) Cytoskeletal remodeling of the airway smooth muscle cell: a mechanism for adaptation to mechanical forces in the lung. *Respir Physiol Neurobiol* 137:151–168.
- Haftel VK, Bichler EK, Nichols TR, Pinter MJ, Cope TC (2004) Movement reduces the dynamic response of muscle spindle afferents and motoneuron synaptic potentials in rat. *J Neurophysiol* 91:2164–2171.
- Handford C (2006) Serving up variability and stability. *In* *Movement System Variability*. Davids K, Bennet S, Newell K (eds). Champaign, IL: Human Kinetics.
- Harris CM, Wolpert DM (1998) Signal-dependent noise determines motor planning. *Nature* 394:780–784.
- Hart CB, Giszter SF (2004) Modular premotor drives and unit bursts as primitives for frog motor behaviors. *J Neurosci* 24:5269–5282.
- Hart CB, Giszter SF (2010) A neural basis for motor primitives in the spinal cord. *J Neurosci* 30:1322–1336.
- Hayes HB, Chvatal SA, French MA, Ting LH, Trumbower RD (2014) Neuromuscular constraints on muscle coordination during overground walking in persons with chronic incomplete spinal cord injury. *Clin Neurophysiol* 125:2024–2035.
- Heckman CJ, Hyngstrom AS, Johnson MD (2008) Active properties of motoneurone dendrites: diffuse descending neuromodulation, focused local inhibition. *J Physiol* 586:1225–1231.
- Henneman E (1957) Relation between size of neurons and their susceptibility to discharge. *Science* 126:1345–1347.

- Herzfeld DJ, Shadmehr R (2014) Motor variability is not noise, but grist for the learning mill. *Nat Neurosci* 17:149–150.
- Herzog W, Leonard TR (1991) Validation of optimization models that estimate the forces exerted by synergistic muscles. *J Biomech* 24:31–39.
- Herzog W, Leonard TR (2002) Force enhancement following stretching of skeletal muscle: a new mechanism. *J Exp Biol* 205:1275–1283.
- Herzog W, Leonard TR, Joumaa V, Mehta A (2008) Mysteries of muscle contraction. *J Applied Biomech* 24:1–13.
- Herzog W, Leonard TR, Wu JZ (2000) The relationship between force depression following shortening and mechanical work in skeletal muscle. *J Biomech* 33:659–668.
- Hicks JL, Schwartz MH, Arnold AS, Delp SL (2008) Crouched postures reduce the capacity of muscles to extend the hip and knee during the single-limb stance phase of gait. *J Biomech* 41:960–967.
- Higham TE, Biewener AA (2008) Integration within and between muscles during terrestrial locomotion: effects of incline and speed. *J Exp Biol* 211:2303–2316.
- Higham TE, Biewener AA (2011) Functional and architectural complexity within and between muscles: regional variation and intermuscular force transmission. *Philos T Roy Soc Lond B* 366:1477–1487.
- Hill AV (1938) The heat of shortening and the dynamic constants of muscle. *Proc Roy Soc Lond B* 126:136–195.
- Hill AV (1953) The mechanics of active muscle. *Proc R Soc Lond B Sci* 141:104–117.
- Hochner B (2012) An embodied view of octopus neurobiology. *Curr Biol* 22:R887–892.
- Hochner B, Shomrat T, Fiorito G (2006) The octopus: a model for a comparative analysis of the evolution of learning and memory mechanisms. *Biol Bull* 210:308–317.
- Hooper SL (2012) Body size and the neural control of movement. *Curr Biol* 22:R318–322.
- Hooper SL (2015) Sensory-motor integration: more variability reduces individuality. *Curr Biol* 20:R991–993
- Hooper SL, Guschlbauer C, Blumel M, Rosenbaum P, et al. (2009) Neural control of unloaded leg posture and of leg swing in stick insect, cockroach, and mouse differs from that in larger animals. *J Neurosci* 29:4109–4119.
- Hooper SL, Guschlbauer C, von Uckermann G, Buschges A (2006) Natural neural output that produces highly variable locomotory movements. *J Neurophysiol* 96:2072–2088.
- Hooper SL, Guschlbauer C, von Uckermann G, Büschges A (2007) Different motor neuron spike patterns produce contractions with very similar rises in graded slow muscles. *J Neurophysiol* 97:1428–1444.
- Hooper SL, Hobbs KH, Thuma JB (2008) Invertebrate muscles: thin and thick filament structure; molecular basis of contraction and its regulation, catch and asynchronous muscle. *Prog Neurobiol* 86:72–127.
- Hooper SL, Thuma JB (2005) Invertebrate muscles: muscle specific genes and proteins. *Physiol Rev* 85:1001–1060.
- Hooper SL, Weaver AL (2000) Motorneuron activity is often insufficient to predict motor response. *Curr Opin Neurobiol* 10:676–682.
- Horchler AD, Daltorio KA, Chiel HJ, Quinn RD (2015) Designing responsive pattern generators: stable heteroclinic channel cycles for modeling and control. *Bioinspir Biomim* 10:026001.
- Huang VS, Shadmehr R, Diedrichsen J (2008) Active learning: learning a motor skill without a coach. *J Neurophysiol* 100:879–887.

- Huijing PA (2003) Muscular force transmission necessitates a multilevel integrative approach to the analysis of function of skeletal muscle. *Exerc Sport Sci Rev* 31:167–175.
- Huxley AF (1957) Muscle structure and theories of contraction. *Prog Biophys and Biop Ch* 7:255–318.
- Ijspeert AJ, Crespi A, Ryczko D, Cabelguen JM (2007) From swimming to walking with a salamander robot driven by a spinal cord model. *Science* 315:1416–1420.
- Ivanenko YP, Poppele RE, Lacquaniti F (2004) Five basic muscle activation patterns account for muscle activity during human locomotion. *J Physiol* 556:267–282.
- Jindrich DL, Full RJ (2002) Dynamic stabilization of rapid hexapedal locomotion. *J Exp Biol* 205:2803–2823.
- Josephson RK (1985) Mechanical power output from striated-muscle during cyclic contraction. *J Exp Biol* 114:493–512.
- Joyce G, Rack PM, Ross H (1974) The forces generated at the human elbow joint in response to imposed sinusoidal movements of the forearm. *J Physiol* 240:351–374.
- Kargo WJ, Ramakrishnan A, Hart CB, Rome LC, Giszter SF (2010) A simple experimentally based model using proprioceptive regulation of motor primitives captures adjusted trajectory formation in spinal frogs. *J Neurophysiol* 103:573–590.
- Katz PS, Frost WN (1996) Intrinsic neuromodulation: altering neuronal circuits from within. *Trends Neurosci* 19:54–61.
- Kawakami Y, Fukunaga T (2006) New insights into *in vivo* human skeletal muscle function. *Exerc Sport Sci Rev* 34:16–21.
- Kawakami Y, Muraoka T, Ito S, Kanehisa H, Fukunaga T (2002) *In vivo* muscle fibre behaviour during counter-movement exercise in humans reveals a significant role for tendon elasticity. *J Physiol* 540:635–646.
- Kaya M, Leonard T, Herzog W (2003) Coordination of medial gastrocnemius and soleus forces during cat locomotion. *J Exp Biol* 206:3645–3655.
- Kier W, Leeuwen J (1997) A kinematic analysis of tentacle extension in the squid *Loligo pealei*. *J Exp Biol* 200:41–53.
- Kier WM (2012) The diversity of hydrostatic skeletons. *J Exp Biol* 215:1247–1257.
- Kier WM, Schachat FH (2008) Muscle specialization in the squid motor system. *J Exp Biol* 211:164–169.
- Kier WM, Smith KK (1985) Tongues, tentacles and trunks: the biomechanics of movement in muscular hydrostats. *Zool J Linnean Soc* 83:307–324.
- Kirsch RF, Boskov D, Rymer WZ (1994) Muscle stiffness during transient and continuous movements of cat muscle: perturbation characteristics and physiological relevance. *IEEE T Biomed Eng* 41:758–770.
- Korn H, Faber DS (2005) The Mauthner cell half a century later: a neurobiological model for decision-making? *Neuron* 47:13–28.
- Kristan WB, Skalak R, Wilson RJA, Skierczynski BA, et al. (2000) Biomechanics of hydroskeletons: studies of crawling in the medicinal leech. *In Biomechanics and Neural Control of Posture and Movement*. Winters JM, Crago PE (eds). New York, NY: Springer.
- Kuhl PK (2004) Early language acquisition: cracking the speech code. *Nat Rev Neurosci* 5:831–843.
- Kuo AD (2007) The six determinants of gait and the inverted pendulum analogy: a dynamic walking perspective. *Hum Mov Sci* 26:617–656.

- Kurtzer I, Pruszynski JA, Herter TM, Scott SH (2006) Primate upper limb muscles exhibit activity patterns that differ from their anatomical action during a postural task. *J Neurophysiol* 95:493–504.
- Kutch JJ, Valero-Cuevas FJ (2012) Challenges and new approaches to proving the existence of muscle synergies of neural origin. *PLoS Comput Biol* 8:e1002434.
- Lacquaniti F, Ivanenko YP, d'Avella A, Zelik KE, Zago M (2013) Evolutionary and developmental modules. *Front Comput Neurosci* 7:61.
- Latash ML (2012) The bliss (not the problem) of motor abundance (not redundancy). *Exp Brain Res* 217:1–5.
- Latash ML, Scholz JF, Danion F, Schoner G (2001) Structure of motor variability in marginally redundant multifinger force production tasks. *Exp Brain Res* 141:153–165.
- Lee DD, Seung HS (1999) Learning the parts of objects by non-negative matrix factorization. *Nature* 401:788–791.
- Lee RH, Heckman CJ (2000) Adjustable amplification of synaptic input in the dendrites of spinal motoneurons *in vivo*. *J Neurosci* 20:6734–6740.
- Lemay MA, Grill WM (2004) Modularity of motor output evoked by intraspinal microstimulation in cats. *J Neurophysiol* 91:502–514.
- Li W, Todorov E, Pan X (2005) Hierarchical optimal control of redundant biomechanical systems. *Proc 26th Annu Int Conf IEEE EMBS* 2:4618–4621.
- Lichtwark GA, Wilson AM (2008) Optimal muscle fascicle length and tendon stiffness for maximising gastrocnemius efficiency during human walking and running. *J Theor Biol* 252: 662–673.
- Lieber RL, Ward SR (2011) Skeletal muscle design to meet functional demands. *Philos T Roy Soc Lond B* 366:1466–1476.
- Lin DC, Rymer WZ (2001) Damping actions of the neuromuscular system with inertial loads: human flexor pollicis longus muscle. *J Neurophysiol* 85:1059–1066.
- Lockhart DB, Ting LH (2007) Optimal sensorimotor transformations for balance. *Nat Neurosci* 10:1329–1336.
- Loeb GE (2012) Optimal isn't good enough. *Biol Cybern* 106:757–765.
- Loram ID, Lakie M, Di Giulio I, Maganaris CN (2009) The consequences of short-range stiffness and fluctuating muscle activity for proprioception of postural joint rotations: the relevance to human standing. *J Neurophysiol* 102:460–474.
- Lu H, McManus JM, Cullins MJ, Chiel HJ (2015) Preparing the periphery for a subsequent behavior: motorneuronal activity during biting generates little force but prepares a retractor muscle to generate larger forces during swallowing in *Aplysia*. *J Neurosci* 35:5051–5066.
- Maas H, Sandercock TG (2010) Force transmission between synergistic skeletal muscles through connective tissue linkages. *J Biomed Biotechnol* 2010:575672.
- Macpherson JM (1988) Strategies that simplify the control of quadrupedal stance. II. Electromyographic activity. *J Neurophysiol* 60:218–231.
- Macpherson JM, Horak FB (2013) Posture. *In Principles of Neural Science*. Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ (eds). New York, NY: McGraw-Hill Medical.
- Marder E, Goaillard JM (2006) Variability, compensation and homeostasis in neuron and network function. *Nat Rev Neurosci* 7:563–574.
- Marechal G, Plaghki L (1979) Deficit of the isometric tetanic tension redeveloped after a release of frog muscle at a constant velocity. *J Gen Physiol* 73:453–467.

- McGowan C, Neptune R, Herzog W (2013) A phenomenological muscle model to assess history dependent effects in human movement. *J Biomech* 46:151–157.
- McKay JL, Ting LH (2012) Optimization of muscle activity for task-level goals predicts complex changes in limb forces across biomechanical contexts. *PLoS Comput Biol* 8:e1002465.
- McManus JM, Lu H, Cullins MJ, Chiel HJ (2014) Differential activation of an identified motoneuron and neuromodulation provide *Aplysia's* retractor muscle an additional function. *J Neurophysiol* 112:778–791.
- McMillen T, Williams T, Holmes P (2008) Non-linear muscles, passive viscoelasticity and body taper conspire to create neuromechanical phase lags in anguilliform swimmers. *PLoS Comput Biol* 4:e1000157.
- Meinertzhagen IA, Lemaire P, Okamura Y (2004) The neurobiology of the ascidian tadpole larva: recent developments in an ancient chordate. *Annu Rev Neurosci* 27:453–485.
- Minozzo FC, Lira CA (2013) Muscle residual force enhancement: a brief review. *Clinics (Sao Paulo)* 68:269–274.
- Morgan D (1977) Separation of active and passive components of short-range stiffness of muscle. *Am J Physiol* 232:C45–C49.
- Morgan DL (1990) New insights into the behavior of muscle during active lengthening. *Biophys J* 57:209–221.
- Morris LG, Hooper SL (1997) Muscle response to changing neuronal input in the lobster (*Panulirus interruptus*) stomatogastric system: spike number vs. spike frequency dependent domains. *J Neurosci* 17:5956–5971.
- Murphy RA, Rembold CM (2005) The latch-bridge hypothesis of smooth muscle contraction. *Can J Physiol Pharmacol* 83:857–864.
- Murray WM, Buchanan TS, Delp SL (2000) The isometric functional capacity of muscles that cross the elbow. *J Biomech* 33:943–952.
- Neptune RR, Clark DJ, Kautz SA (2009) Modular control of human walking: a simulation study. *J Biomech* 42:1282–1287.
- Nichols TR, Cope TC (2004) Cross-bridge mechanisms underlying the history-dependent properties of muscle spindles and stretch reflexes. *Can J Physiol Pharmacol* 82:569–576.
- Nishikawa K, Biewener AA, Aerts P, Ahn AN, et al. (2007) Neuromechanics: an integrative approach for understanding motor control. *Integr Comp Biol* 47:16–54.
- Novakovic VA, Sutton GP, Neustadter DM, Beer RD, Chiel HJ (2006) Mechanical reconfiguration mediates swallowing and rejection in *Aplysia californica*. *J Comp Physiol A* 192:857–870.
- Nussbaum MA, Chaffin DB (1997) Pattern classification reveals intersubject group differences in lumbar muscle recruitment during static loading. *Clin Biomech (Bristol, Avon)* 12:97–106.
- Olshausen BA, Field DJ (2004) Sparse coding of sensory inputs. *Curr Opin Neurobiol* 14:481–487.
- Overduin SA, d'Avella A, Carmena JM, Bizzi E (2012) Microstimulation activates a handful of muscle synergies. *Neuron* 76:1071–1077.
- Pai DK (2010) Muscle mass in musculoskeletal models. *J Biomech* 43:2093–2098.
- Pandy MG, Zajac FE (1991) Optimal muscular coordination strategies for jumping. *J Biomech* 24:1–10.
- Park J, Pažin N, Friedman J, Zatsiorsky VM, Latash ML (2014) Mechanical properties of the human hand digits: age-related differences. *Clin Biomech (Bristol, Avon)* 29:129–137.

- Perreault EJ, Heckman CJ, Sandercock TG (2003) Hill muscle model errors during movement are greatest within the physiologically relevant range of motor unit firing rates. *J Biomech* 36:211–218.
- Perreault EJ, Kirsch RF, Crago PE (2004) Multijoint dynamics and postural stability of the human arm. *Exp Brain Res* 157:507–517.
- Powers RK, Elbasiouny SM, Rymer WZ, Heckman CJ (2012) Contribution of intrinsic properties and synaptic inputs to motoneuron discharge patterns: a simulation study. *J Neurophysiol* 107:808–823.
- Prinz AA, Bucher D, Marder E (2004) Similar network activity from disparate circuit parameters. *Nat Neurosci* 7:1345–1352.
- Rack PM, Westbury DR (1969) The effects of length and stimulus rate on tension in the isometric cat soleus muscle. *J Physiol* 204:443–460.
- Rack PM, Westbury DR (1974) The short range stiffness of active mammalian muscle and its effect on mechanical properties. *J Physiol* 240:331–350.
- Riewald SA, Delp SL (1997) The action of the rectus femoris muscle following distal tendon transfer: does it generate knee flexion moment? *Dev Med & Child Neurol* 39:99–105.
- Ritzmann RE, Quinn RD, Fischer MS (2004) Convergent evolution and locomotion through complex terrain by insects, vertebrates and robots. *Arthropod Struct Dev* 33:361–379.
- Rizzolatti G, Strick PL (2013) Cognitive functions of the premotor system. *In* *Principles of Neural Science*. Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ (eds). New York, NY: McGraw-Hill Medical.
- Roberts TJ, Marsh RL, Weyand PG, Taylor CR (1997) Muscular force in running turkeys: the economy of minimizing work. *Science* 275:1113–1115.
- Roh J, Cheung VC, Bizzi E (2011) Modules in the brain stem and spinal cord underlying motor behaviors. *J Neurophysiol* 106:1363–1378.
- Roh J, Rymer WZ, Perreault EJ, Yoo SB, Beer RF (2013) Alterations in upper limb muscle synergy structure in chronic stroke survivors. *J Neurophysiol* 109:768–781.
- Rosch E (1999) Reclaiming concepts. *J Consciousness Stud* 6:61–77.
- Roth E, Sponberg S, Cowan NJ (2014) A comparative approach to closed-loop computation. *Curr Opin Neurobiol* 25:54–62.
- Routson RL, Kautz SA, Neptune RR (2014) Modular organization across changing task demands in healthy and poststroke gait. *Physiol Rep* 2:e12055.
- Safavynia SA, Ting LH (2013) Sensorimotor feedback based on task-relevant error robustly predicts temporal recruitment and multidirectional tuning of muscle synergies. *J Neurophysiol* 109:31–45.
- Safavynia SA, Torres-Oviedo G, Ting LH (2011) Muscle synergies: implications for clinical evaluation and rehabilitation of movement. *Top Spinal Cord Inj Rehabil* 17:16–24.
- Saltiel P, Wyler-Duda K, D'Avella A, Tresch MC, Bizzi E (2001) Muscle synergies encoded within the spinal cord: evidence from focal intraspinal NMDA iontophoresis in the frog. *J Neurophysiol* 85:605–619.
- Scholz JP, Danion F, Latash ML, Schoner G (2002) Understanding finger coordination through analysis of the structure of force variability. *Biol Cybern* 86:29–39.
- Scholz JP, Schoner G (1999) The uncontrolled manifold concept: identifying control variables for a functional task. *Exp Brain Res* 126:289–306.
- Scholz JP, Schoner G, Latash ML (2000) Identifying the control structure of multijoint coordination during pistol shooting. *Exp Brain Res* 135:382–404.

- Scott SH (2004) Optimal feedback control and the neural basis of volitional motor control. *Nat Rev Neurosci* 5:534–546.
- Scott SH (2008) Inconvenient truths about neural processing in primary motor cortex. *J Physiol* 586:1217–1224.
- Scrivens JE, Deweerth SP, Ting LH (2008) A robotic device for understanding neuromechanical interactions during standing balance control. *Bioinspir Biomim* 3:026002.
- Selen LP, Franklin DW, Wolpert DM (2009) Impedance control reduces instability that arises from motor noise. *J Neurosci* 29:12606–12616.
- Sensenig AT, Shultz JW (2003) Mechanics of cuticular elastic energy storage in leg joints lacking extensor muscles in arachnids. *J Exp Biol* 206:771–784.
- Shadmehr R, Krakauer JW (2008) A computational neuroanatomy for motor control. *Exp Brain Res* 185:359–381.
- Shadmehr R, Smith MA, Krakauer JW (2010) Error correction, sensory prediction, and adaptation in motor control. *Annu Rev Neurosci* 33:89–108.
- Shaw KM, Lyttle DN, Gill JP, Cullins MJ, et al. (2015) The significance of dynamical architecture for adaptive responses to mechanical loads during rhythmic behavior. *J Comput Neurosci* 38:25–51.
- Siebert T, Rode C, Herzog W, Till O, Blickhan R (2007) Non-linearities make a difference: comparison of two common Hill-type models with real muscle. *Biol Cybern* 98:133–143.
- Simpson CS, Sohn MH, Allen JL, Ting LH (2015) Feasible muscle activation ranges based on inverse dynamics analyses of human walking. *J Biomech* 48:2990–2997.
- Skierczynski BA, Wilson RJ, Kristan WB, Jr., Skalak R (1996) A model of the hydrostatic skeleton of the leech. *J Theor Biol* 181:329–342.
- Smith LB, Thelen E (2003) Development as a dynamic system. *Trends Cogn Sci* 7:343–348.
- Snaterse M, Ton R, Kuo AD, Donelan JM (2011) Distinct fast and slow processes contribute to the selection of preferred step frequency during human walking. *J Appl Physiol* 110:1682–1690.
- Sohn MH, McKay JL, Ting LH (2013) Defining feasible bounds on muscle activation in a redundant biomechanical task: practical implications of redundancy. *J Biomech* 46:1363–1368.
- Sohn MH, Ting LH (2013) The cost of being stable: a quantitative approach to examine trade-off between effort and stability. American Society of Biomechanics, Omaha, NB. <http://www.asbweb.org/conferences/2013/abstracts/369.pdf>.
- Sponberg S, Libby T, Mullens CH, Full RJ (2011a) Shifts in a single muscle's control potential of body dynamics are determined by mechanical feedback. *Philos T Roy Soc B* 366:1606–1620.
- Sponberg S, Spence AJ, Mullens CH, Full RJ (2011b) A single muscle's multi-functional control potential of body dynamics for postural control and running. *Philos T Roy Soc Lond B* 366:1592–1605.
- Stahl VA, Nichols TR (2014) Short-term effect of crural fasciotomy on kinematic variability and propulsion during level locomotion. *J Mot Behav* 46:339–349.
- Steele KM, Seth A, Hicks JL, Schwartz MS, Delp SL (2010) Muscle contributions to support and progression during single-limb stance in crouch gait. *J Biomech* 43:2099–2105.
- Steele KM, Tresch MC, Perreault EJ (2013) The number and choice of muscles impact the results of muscle synergy analyses. *Front Comput Neurosci* 7:105.

- Sternad D, Park SW, Muller H, Hogan N (2010) Coordinate dependence of variability analysis. *PLoS Comput Biol* 6:e1000751.
- Thuma JB, Hooper SL (2010) Direct evidence that stomatogastric (*Panulirus interruptus*) muscle passive responses are not due to background actomyosin cross-bridges. *J Comp Physiol A* 196:649–657.
- Ting LH (2007) Dimensional reduction in sensorimotor systems: a framework for understanding muscle coordination of posture. *Prog Brain Res* 165:299–321.
- Ting LH, Chiel HJ, Trumbower RD, Allen JL, et al. (2015) Neuromechanical principles underlying movement modularity and their implications for rehabilitation. *Neuron* 86:38–54.
- Ting LH, Chvatal SA (2010) Decomposing muscle activity in motor tasks: methods and interpretation. In *Motor control: Theories, Experiments, and Applications*. Danion F, Latash ML (eds). Oxford, UK: Oxford University Press.
- Ting LH, Chvatal SA, Safavynia SA, Lucas McKay J (2012) Review and perspective: neuromechanical considerations for predicting muscle activation patterns for movement. *Int J Numer Method Biomed Eng* 28:1003–1014.
- Ting LH, Macpherson JM (2005) A limited set of muscle synergies for force control during a postural task. *J Neurophysiol* 93:609–613.
- Ting LH, McKay JL (2007) Neuromechanics of muscle synergies for posture and movement. *Curr Opin Neurobiol* 17:622–628.
- Ting LH, van Antwerp KW, Scrivens JE, McKay JL, et al. (2009) Neuromechanical tuning of non-linear postural control dynamics. *Chaos* 19:026111.
- Todorov E (2004) Optimality principles in sensorimotor control. *Nat Neurosci* 7:907–915.
- Todorov E, Jordan MI (2002) Optimal feedback control as a theory of motor coordination. *Nat Neurosci* 5:1226–1235.
- Torres-Oviedo G, Macpherson JM, Ting LH (2006) Muscle synergy organization is robust across a variety of postural perturbations. *J Neurophysiol* 96:1530–1546.
- Torres-Oviedo G, Ting LH (2007) Muscle synergies characterizing human postural responses. *J Neurophysiol* 98:2144–2156.
- Torres-Oviedo G, Ting LH (2010) Subject-specific muscle synergies in human balance control are consistent across different biomechanical contexts. *J Neurophysiol* 103:3084–3098.
- Tresch MC, Cheung VC, d'Avella A (2006) Matrix factorization algorithms for the identification of muscle synergies: evaluation on simulated and experimental data sets. *J Neurophysiol* 95:2199–2212.
- Tresch MC, Jarc A (2009) The case for and against muscle synergies. *Curr Opin Neurobiol* 19:601–607.
- Tresch MC, Saltiel P, Bizzi E (1999) The construction of movement by the spinal cord. *Nat Neurosci* 2:162–167.
- Trimmer BA, Lin HT (2014) Bone-free: soft mechanics for adaptive locomotion. *Integr Comp Biol* 54:1122–1135.
- Trumbower RD, Krutky MA, Yang B-S, Perreault EJ (2009) Use of self-selected postures to regulate multi-joint stiffness during unconstrained tasks. *PloS One* 4:e5411.
- Tsianos GA, Goodner J, Loeb GE (2014) Useful properties of spinal circuits for learning and performing planar reaches. *J Neural Eng* 11:056006.

- Tytell ED, Hsu CY, Williams TL, Cohen AH, Fauci LJ (2010) Interactions between internal forces, body stiffness, and fluid environment in a neuromechanical model of lamprey swimming. *Proc Natl Acad Sci USA* 107:19832–19837.
- Valero-Cuevas FJ (2005) An integrative approach to the biomechanical function and neuromuscular control of the fingers. *J Biomech* 38:673–684.
- Valero-Cuevas FJ, Jae-Woong Y, Brown D, McNamara RV, et al. (2007) The tendon network of the fingers performs anatomical computation at a macroscopic scale. *IEEE T Biomed Eng* 54:1161–1166.
- Valero-Cuevas FJ, Venkadesan M, Todorov E (2009) Structured variability of muscle activations supports the minimal intervention principle of motor control. *J Neurophysiol* 102:59–68.
- Valero-Cuevas FJ, Zajac FE, Burgar CG (1998) Large index-fingertip forces are produced by subject-independent patterns of muscle excitation. *J Biomech* 31: 693–703.
- van Antwerp K, Burkholder T, Ting L (2007) Inter-joint coupling effects on muscle contributions to endpoint force and acceleration in a musculoskeletal model of the cat hindlimb. *J Biomech* 40:3570–3579.
- van Ingen Schenau GJ (1994) Proposed action of bi-articular muscles and the design of hindlimbs of bi- and quadrupeds. *Hum Mov Sci* 13:665–681.
- Van Leeuwen J, Kier WM (1997) Functional design of tentacles in squid: linking sarcomere ultrastructure to gross morphological dynamics. *Philos T Roy Soc Lond B* 352:551–571.
- Vandenboom R, Gittings W, Smith IC, Grange RW, Stull JT (2013) Myosin phosphorylation and force potentiation in skeletal muscle: evidence from animal models. *J Muscle Res Cell Motil* 34:317–332.
- Vogel S (1988) *Life's Devices: the Physical World of Animals and Plants*. Princeton University Press: Princeton, NJ.
- Voigt M, Simonsen EB, Dyhre-Poulsen P, Klausen K (1995) Mechanical and muscular factors influencing the performance in maximal vertical jumping after different prestretch loads. *J Biomech* 28:293–307.
- Wadepuhl M, Beyn W (1989) Computer simulation of the hydrostatic skeleton. The physical equivalent, mathematics and application to worm-like forms. *J Theor Biol* 136:379–402.
- Wakeling JM (2009) The recruitment of different compartments within a muscle depends on the mechanics of the movement. *Biol Lett* 5:30–34.
- Walter JP, Kinney AL, Banks SA, D'Lima DD, et al. (2014) Muscle synergies may improve optimization prediction of knee contact forces during walking. *J Biomech Eng* 136:021031.
- Welch TD, Ting LH (2008) A feedback model reproduces muscle activity during human postural responses to support-surface translations. *J Neurophysiol* 99:1032–1038.
- Welch TD, Ting LH (2009) A feedback model explains the differential scaling of human postural responses to perturbation acceleration and velocity. *J Neurophysiol* 101:3294–3309.
- Wilson A, Lichtwark G (2011) The anatomical arrangement of muscle and tendon enhances limb versatility and locomotor performance. *Philos T Roy Soc Lond B* 366:1540–1553.
- Wu HG, Miyamoto YR, Gonzalez Castro LN, Olveczky BP, Smith MA (2014) Temporal structure of motor variability is dynamically regulated and predicts motor learning ability. *Nat Neurosci* 17:312–321.

- Yakovenko S, Krouchev N, Drew T (2011) Sequential activation of motor cortical neurons contributes to intralimb coordination during reaching in the cat by modulating muscle synergies. *J Neurophysiol* 105:388–409.
- Yang JF, Lam T, Pang MY, Lamont E, et al. (2004) Infant stepping: a window to the behaviour of the human pattern generator for walking. *Can J Physiol Pharmacol* 82:662–674.
- Ye H, Morton DW, Chiel HJ (2006a) Neuromechanics of coordination during swallowing in *Aplysia californica*. *J Neurosci* 26:1470–1485.
- Ye H, Morton DW, Chiel HJ (2006b) Neuromechanics of multi-functionality during rejection in *Aplysia californica*. *J Neurosci* 26:10743–10755.
- Yen JT, Auyang AG, Chang YH (2009) Joint-level kinetic redundancy is exploited to control limb-level forces during human hopping. *Exp Brain Res* 196:439–451.
- Young RP, Scott SH, Loeb GE (1992) An intrinsic mechanism to stabilize posture—joint-angle-dependent moment arms of the feline ankle muscles. *Neurosci Lett* 145:137–140.
- Yu SN, Crago PE, Chiel HJ (1997) A nonisometric kinetic model for smooth muscle. *Am J Physiol* 272:C1025–C1039.
- Zahalak GI (1986) A comparison of the mechanical behavior of the cat soleus muscle with a distribution-moment model. *J Biomech Eng* 108:131–140.
- Zahalak GI, Ma SP (1990) Muscle activation and contraction: constitutive relations based directly on cross-bridge kinetics. *J Biomech Eng* 112:52–62.
- Zajac FE (1989) Muscle and tendon: properties, models, scaling, and application to biomechanics and motor control. *Crit Rev Biomed Eng* 17:359–411.
- Zajac FE (2002) Understanding muscle coordination of the human leg with dynamical simulations. *J Biomech* 35:1011–1018.
- Zajac FE, Gordon ME (1989) Determining muscle's force and action in multi-articular movement. *Exerc Sport Sci Rev* 17:187–230.
- Zajac FE, Neptune RR, Kautz SA (2002) Biomechanics and muscle coordination of human walking. Part I: introduction to concepts, power transfer, dynamics and simulations. *Gait Posture* 16:215–232.
- Zaniolo G, Lane NJ, Burighel P, Manni L (2002) Development of the motor nervous system in ascidians. *J Comp Neurol* 443:124–135.
- Zelik KE, La Scaleia V, Ivanenko YP, Lacquaniti F (2014) Can modular strategies simplify neural control of multidirectional human locomotion? *J Neurophysiol* 111:1686–1702.
- Zucker RS, Regehr WG (2002) Short-term synaptic plasticity. *Annu Rev Physiol* 64:355–405.