Chapter 31: The Motor Unit and Muscle Action

Introduction

ANY ACTION—ASCENDING A FLIGHT of stairs, typing on a keyboard, even holding a pose—requires coordinating the movement of body parts. This is accomplished by the interaction of the nervous system with muscle. The role of the nervous system is to activate the muscles that provide the forces needed to move in a particular way. This is not a simple task. Not only must the nervous system decide which muscles to activate, how much to activate them, and the sequence in which they must be activated in order to move one part of the body, but it must also control the influence of the resultant muscle forces on other body parts and maintain the required posture.

This chapter examines how the nervous system controls muscle force and how the force exerted by a limb depends on muscle structure. We also describe how muscle activation changes to perform different types of movement.

The Motor Unit Is the Elementary Unit of Motor Control

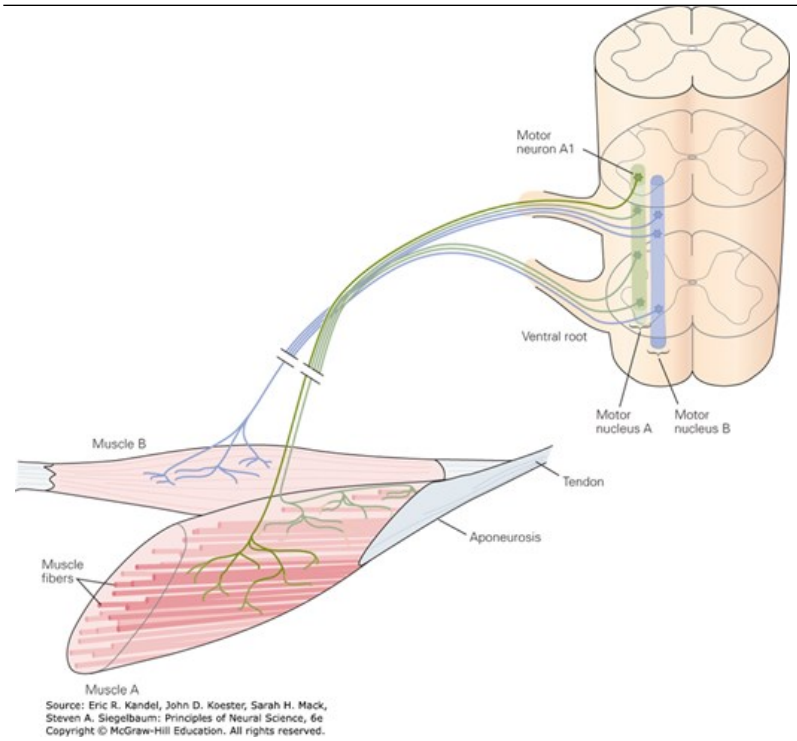
A Motor Unit Consists of a Motor Neuron and Multiple Muscle Fibers

The nervous system controls muscle force with signals sent from motor neurons in the spinal cord or brain stem to the muscle fibers. A motor neuron and the muscle fibers it innervates are known as a motor unit, the basic functional unit by which the nervous system controls movement, a concept proposed by Charles Sherrington in 1925.

A typical muscle is controlled by a few hundred motor neurons whose cell bodies are clustered in a motor nucleus in the spinal cord or brain stem. The axon of each motor neuron exits the spinal cord through the ventral root or through a cranial nerve in the brain stem and runs in a peripheral nerve to the muscle. When the axon reaches the muscle, it branches and innervates from a few to several thousand muscle fibers (Figure 31–1).

Figure 31–1

A typical muscle consists of many thousands of muscle fibers working in parallel and organized into a smaller number of motor units. A motor unit comprises a motor neuron and the muscle fibers it innervates, illustrated here by motor neuron A1. The motor neurons innervating one muscle are usually clustered into an elongated motor nucleus that may extend over one to four segments within the ventral spinal cord. The axons from a motor nucleus exit the spinal cord in several ventral roots and peripheral nerves but are collected into one nerve bundle near the target muscle. In the figure, motor nucleus A includes all those motor neurons innervating muscle A; likewise, motor nucleus B includes all the motor neurons that innervate muscle B. The extensively branched dendrites of each motor neuron (not shown in the figure) tend to intermingle with those of motor neurons from other nuclei.



Once synaptic input depolarizes the membrane potential of a motor neuron above threshold, the neuron generates an action potential that is propagated along the axon to its terminals in the muscle. The action potential releases acetylcholine at the neuromuscular synapse, triggering an action potential at the sarcolemma of the muscle fiber (Chapter 12). A muscle fiber has electrical properties similar to those of a large-diameter, unmyelinated axon, and thus, action potentials propagate along the sarcolemma, although more slowly due to the higher capacitance of the fiber resulting from the transverse tubules (see Figure 31–9). Because the action potentials in all the muscle fibers of a motor unit occur at approximately the same time, they contribute to extracellular currents that sum to generate a field potential near the active muscle fibers.

Most muscle contractions involve the activation of many motor units, whose currents sum to produce signals (*compound action potentials*) that can be detected by electromyography. The electromyogram (EMG) is typically large and can be easily recorded with electrodes placed on the skin over the muscle. The timing and amplitude of EMG activity, therefore, reflect the activation of muscle fibers by the motor neurons. EMG signals are useful for studying the neural control of movement and for diagnosing pathology (Chapter 57).

Each fiber in most mature vertebrate muscles is innervated by a single motor neuron. The number of muscle fibers innervated by one motor neuron, the *innervation number*, varies across muscles. In human skeletal muscles, the innervation number ranges from average values of 5 for an eye muscle to 1,800 for a leg muscle (Table 31–1). Because innervation number denotes the number of muscle fibers within a motor unit, differences in innervation number determine the differences in increments in force produced by activation of different motor units in the same muscle. Thus, the innervation number also indicates the fineness of control of the muscle at low forces; the smaller the innervation number, the finer the control achieved by varying the number of activated motor units.

Table 31–1

Innervation Numbers in Human Skeletal Muscles

Muscle	Alpha motor axons	Muscle fibers	Average innervation number
Biceps brachii	774	580,000	750
Brachioradialis	333	129,200	410
Cricothyroid	112	18,550	155
Gastrocnemius (medial)	579	1,042,000	1,800
Interossei dorsales (1)	119	40,500	340
Lumbricales (1)	96	10,269	107
Masseter	1,452	929,000	640
Opponens pollicis	133	79,000	595
Platysma	1,096	27,100	25
Posterior cricoarytenoid	140	16,200	116
Rectus lateralis	4,150	22,000	5
Temporalis	1,331	1,247,000	936
Tensor tympani	146	1,100	8
Tibialis anterior	445	272,850	613
Transverse arytenoid	139	34,470	247

Source: Adapted, with permission, from Enoka 2015. © Human Kinetics, Inc.

The differences in innervation numbers between motor units in the same muscle can be substantial. For example, motor units of the first dorsal interosseous muscle of the hand have innervation numbers ranging from approximately 21 to 1,770. The strongest motor unit in the hand's first dorsal interosseous muscle can exert approximately the same force as the average motor unit in the leg's medial gastrocnemius muscle due to different ranges of innervation numbers in the two muscles.

The muscle fibers of a single motor unit are distributed throughout the muscle and intermingle with fibers innervated by other motor neurons. The muscle fibers innervated by a single motor unit can be distributed across 8% to 75% of the volume in a limb muscle, with 2 to 5 muscle fibers belonging to the same motor unit among 100 muscle fibers. Therefore, the muscle fibers in a cross-section through the middle of an entire muscle are associated with 20 to 50 different motor units. This distribution and even the number of motor units change with age and with some neuromuscular disorders (Chapter 57). For example, muscle fibers that lose their innervation after the death of a motor neuron can be reinnervated by collateral sprouts from neighboring axons.

Some muscles comprise discrete compartments that are each innervated by a different primary branch of the muscle nerve. Branches of the median and ulnar nerves in the forearm, for example, innervate distinct compartments in three multitendon extrinsic hand muscles that enable the fingers to

be moved relatively independently. The muscle fibers belonging to each motor unit in such muscles tend to be confined to one compartment. A muscle can therefore consist of several functionally distinct regions.

The Properties of Motor Units Vary

The force exerted by a muscle depends not only on the number of motor units that are activated during a contraction but also on three properties of motor units: contraction speed, maximal force, and fatigability. These properties are assessed by examining the force exerted by individual motor units in response to variations in the number and rate of evoked action potentials.

The mechanical response to a single action potential is known as a *twitch contraction.* The time it takes the twitch to reach its peak force, the *contraction time,* is one measure of the contraction speed of the muscle fibers that compose a motor unit. The motor units in a muscle typically exhibit a range of contraction times from slow to fast contracting. The mechanical response to a series of action potentials that produce overlapping twitches is known as a *tetanic contraction* or *tetanus.*

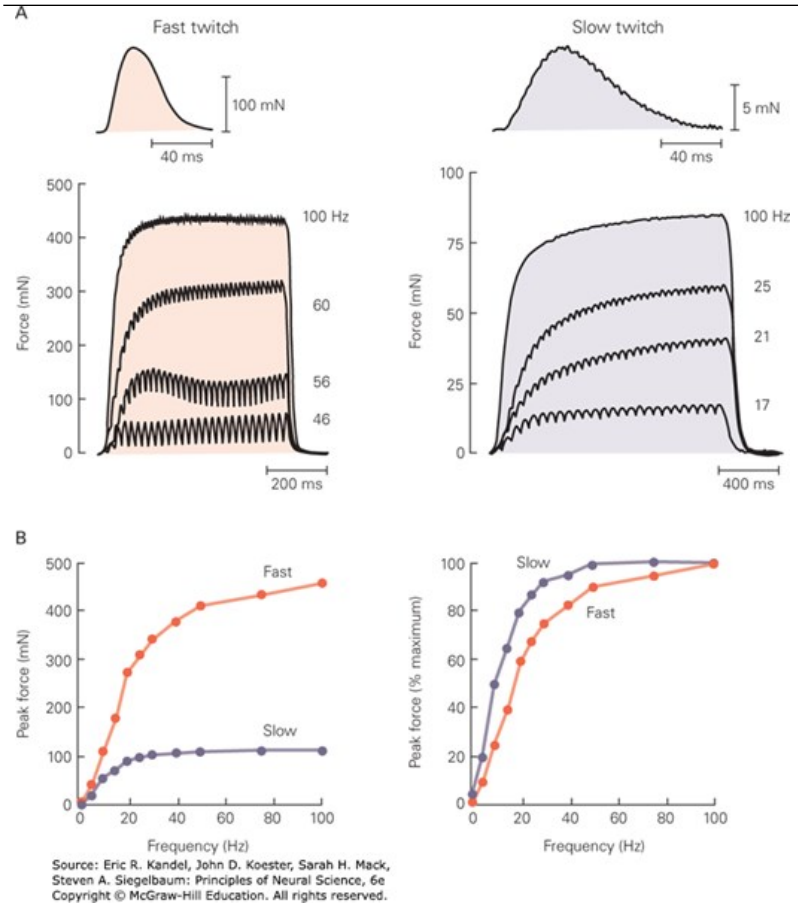
The force exerted during a tetanic contraction depends on the extent to which the twitches overlap and summate (ie, the force varies with the contraction time of the motor unit and the rate at which the action potentials are evoked). At lower rates of stimulation, the ripples in the tetanus denote the peaks of individual twitches (Figure 31–2A). The peak force achieved during a tetanic contraction varies as a sigmoidal function of action potential rate, with the shape of the curve depending on the contraction time of the motor unit (Figure 31–2B). Maximal force is reached at lower action potential rates for slow-contracting motor units than the rates needed to achieve maximal force in fast-contracting units.

Figure 31–2

The force exerted by a motor unit varies with the rate at which its neuron generates action potentials.

A. Traces show the forces exerted by fast- and slow-contracting motor units in response to a single action potential (**top trace**) and a series of action potentials (set of **four traces below**). The time to the peak twitch force, or contraction time, is briefer in the faster unit. The rates of the action potentials used to evoke the tetanic contractions range from 17 to 100 Hz in the slow-contracting unit to 46 to 100 Hz in the fast-contracting unit. The peak tetanic force evoked by 100-Hz stimulation is greater for the fast-contracting unit. Note the different force scales for the two sets of traces. (Adapted, with permission, from Botterman, Iwamoto, and Gonyea 1986; adapted from Fuglevand, Macefield, and Bigland-Ritchie 1999; and Macefield, Fuglevand, and Bigland-Ritchie 1996.)

B. Relation between peak force and the rate of action potentials for fast- and slow-contracting motor units. The absolute force (*left plot*) is greater for the fast-contracting motor unit at all frequencies. At lower stimulus rates (*right plot*), the force evoked in the slow-contracting motor unit (longer contraction time) sums to a greater relative force (percent of peak force) than in the fast-contracting motor unit (shorter contraction time).



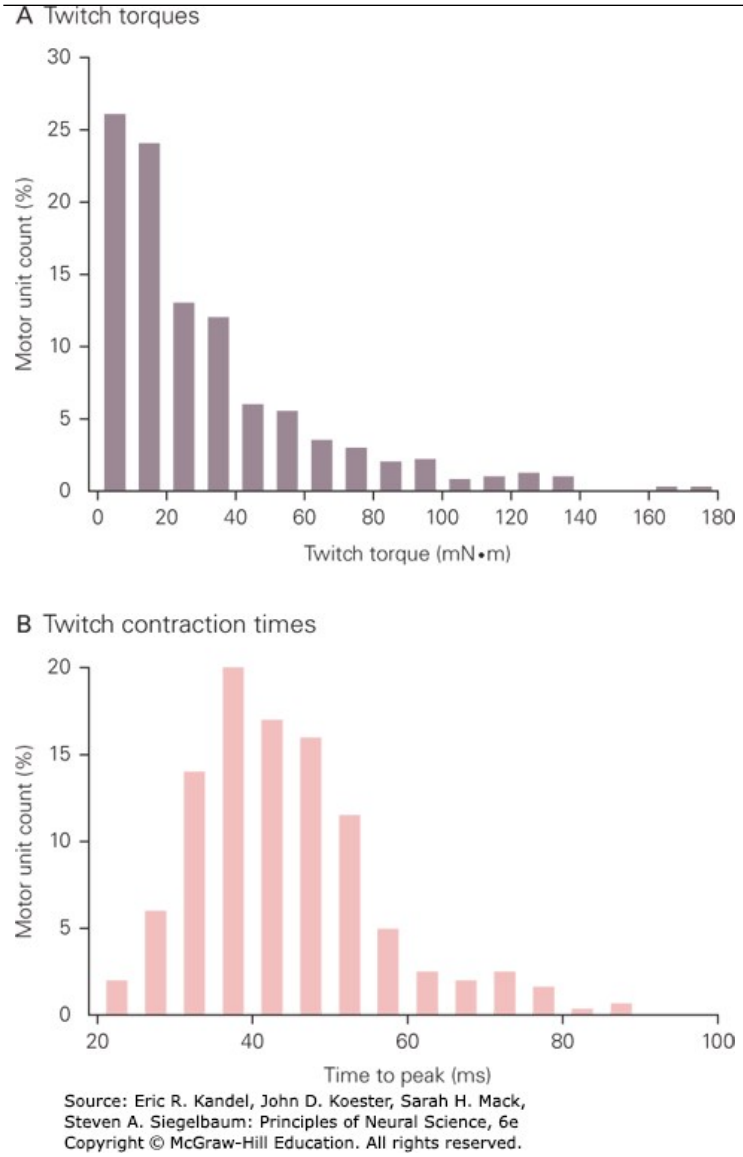
The functional properties of motor units vary across the population and between muscles. At one end of the distribution, motor units have long twitch contraction times and produce small forces, but are less fatigable. At the other end of the distribution, motor units have short contraction times, produce large forces, and are more fatigable. The order in which motor units are recruited during a voluntary contraction begins with the slow-contracting, low-force units and proceeds up to the fast-contracting, high-force units. As observed by Jacques Duchateau and colleagues, most motor units in humans produce low forces and have intermediate contraction times (Figure 31–3).

Figure 31–3

Most human motor units produce low forces and have intermediate contraction times. (Reproduced, with permission, from Van Cutsem et al. 1997. © Canadian Science Publishing.)

A. Distribution of twitch torques for 528 motor units in the tibialis anterior muscle obtained from 10 subjects.

B. Distribution of twitch contraction times for 528 motor units in the tibialis anterior muscle.

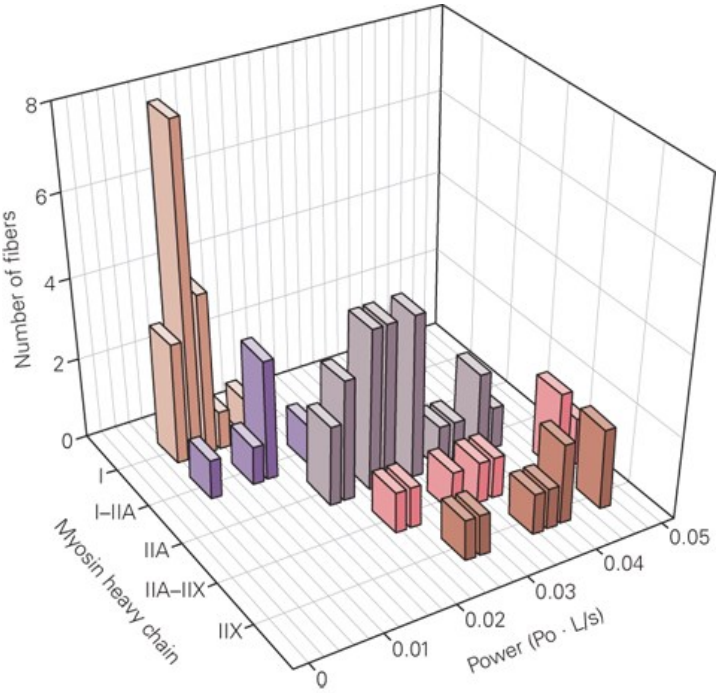


The range of contractile properties exhibited by motor units is partly attributable to differences in the structural specializations and metabolic properties of muscle fibers. One commonly used scheme to characterize muscle fibers is based on their reactivity to histochemical assays for the enzyme myosin adenosine triphosphatase (ATPase), which is used as an index of contractile speed. Histochemical stains for myosin ATPase can identify two types of muscle fibers: type I (low levels of myosin ATPase) and type II (high levels of myosin ATPase). Slow-contracting motor units contain type I muscle fibers, and fast-contracting units include type II fibers. The type II fibers can be further classified as being less fatigable (type IIa) or more fatigable (type IIb, IIx, or IId), due to the association between myosin ATPase content and the relative abundance of oxidative enzymes. Another commonly used scheme distinguishes muscle fibers on the basis of genetically defined isoforms of the myosin heavy chain (MHC). Muscle fibers in slow-contracting motor units express MHC-I, those in the less fatigable fast-contracting units express MHC-IIA, and those in the more fatigable fast-contracting units express MHC-IIX.

In actuality, the contractile properties of single muscle fibers are less distinct than the two classification schemes suggest (Figure 31–4). In addition to the variability in the contractile properties of each type of muscle fiber (MHC-I, -IIA, or -IIX), some muscle fibers co-express more than one MHC isoform. Such hybrid muscle fibers exhibit contractile properties that are intermediate between the muscle fibers that compose a single isoform. The relative proportion of hybrid fibers in a muscle increases with age. As with the distribution of contractile properties across motor units (Figure 31–3), the distribution across individual muscle fibers is also continuous, from slow to fast contracting and from least to most powerful (Figure 31–4).

Figure 31–4

The contractile properties of muscle fiber types are distributed continuously. Peak power produced by segments of single muscle fibers from the vastus lateralis muscle with different types of myosin heavy chain (MHC) isoforms. Two types of hybrid fibers (I-IIA and IIA-IIX) contain isoforms of both types of MHCs. Power is calculated as the product of peak tetanic force (P_o) and maximal shortening velocity (segment length per second [L/s]). (Adapted, with permission, from Bottinelli et al. 1996. Copyright © 1996 The Physiological Society.)



Physical Activity Can Alter Motor Unit Properties

Alterations in habitual levels of physical activity can influence the three contractile properties of motor units (contraction speed, maximal force, and fatigability). A decrease in muscle activity, such as occurs with aging, bed rest, limb immobilization, or space flight, reduces the maximal capabilities of all three properties. The effects of increased physical activity vary with the intensity and duration of the activity. Brief sets of strong contractions performed a few times each week can increase motor unit force (strength training); brief sets of rapid contractions performed a few times each week can increase motor unit discharge rate (power training); and prolonged periods of weaker contractions can reduce motor unit fatigability (endurance training).

Changes in the contractile properties of motor units involve adaptations in the structural specializations and biochemical properties of muscle fibers. The improvement in contraction speed caused by power training, for example, is associated with an increase in the maximal shortening velocity of a muscle fiber caused by an increase in the quantity of myosin ATPase in the fiber. Similarly, the increase in maximal force is associated with the enlarged size and increased intrinsic force capacity of the muscle fibers produced by an increase in the number and density of the contractile proteins.

In contrast, decreases in the fatigability of a muscle fiber can be caused by many different adaptations, such as increases in capillary density, number of mitochondria, efficiency of the processes involved in activating the contractile proteins (excitation-contraction coupling), and oxidative capacity of the muscle fibers. Although the adaptive capabilities of muscle fibers decline with age, the muscles remain responsive to exercise even at 90 years of age.

Despite the efficacy of strength, power, and endurance training in altering the contractile properties of muscle fibers, these training regimens have little effect on the composition of a muscle's fibers. Although several weeks of exercise can change the relative proportion of type IIA and IIX fibers, it produces no change in the proportion of type I fibers. All fiber types adapt in response to exercise, although to varying extents depending on the type of exercise. For example, strength training of leg muscles for 2 to 3 months can increase the cross-sectional area of type I fibers by 0% to 20% and of

type II fibers by 20% to 60%, increase the proportion of type IIa fibers by approximately 10%, and decrease the proportion of type IIx fibers by a similar amount. Furthermore, endurance training may increase the enzyme activities of oxidative metabolic pathways without noticeable changes in the proportions of type I and type II fibers, but the relative proportions of type IIa and IIx fibers do change as a function of the duration of each exercise session. Conversely, although several weeks of bed rest or limb immobilization do not change the proportions of fiber types in a muscle, they do decrease the size and intrinsic force capacity of muscle fibers. Adaptations in fiber type properties and proportions in turn alter the distribution of contractile properties in muscle fibers (Figure 31–4) and motor units (Figure 31–3).

Although physical activity has little influence on the proportion of type I fibers in a muscle, more substantial interventions can have an effect. Space flight, for example, exposes muscles to a sustained decrease in gravity that reduces the proportion of type I fibers in some leg muscles and decreases contractile properties. Similarly, surgically changing the nerve that innervates a muscle alters the pattern of activation and eventually causes the muscle to exhibit properties similar to those of the muscle that was originally innervated by the transplanted nerve. Connecting a nerve that originally innervated a rapidly contracting leg muscle to a slowly contracting leg muscle, for example, will cause the slower muscle to become more like a faster muscle. In contrast, a history of performing powerful contractions with leg muscles is associated with a modest reduction in the proportion of type I fibers, a marked increase in the proportion of type IIx fibers, and a huge increase in the power that can be produced by the type IIa and IIx fibers.

Muscle Force Is Controlled by the Recruitment and Discharge Rate of Motor Units

The force exerted by a muscle during a contraction depends on the number of motor units that are activated and the rate at which each of the active motor neurons discharges action potentials. Force is increased during a muscle contraction by the activation of additional motor units, which are recruited progressively from the weakest to the strongest (Figure 31–5). A motor unit's recruitment threshold is the force during the contraction at which the motor unit is activated. Muscle force decreases gradually by terminating the activity of motor units in the reverse order from strongest to weakest.

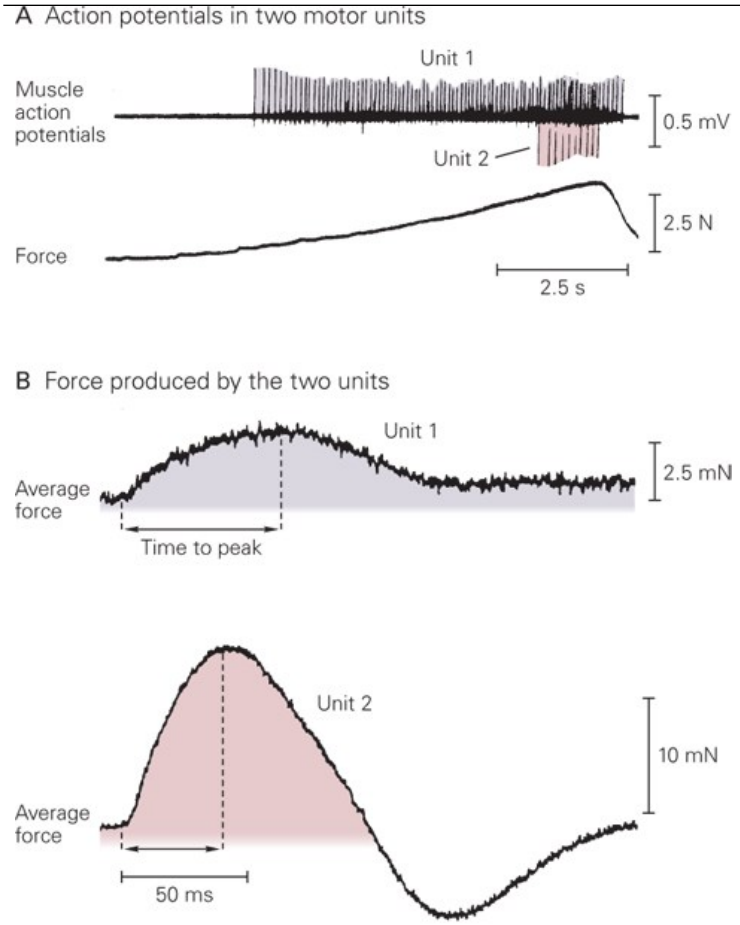
Figure 31–5

(Left) **Motor units that exert low forces are recruited before those that exert greater forces.** (Adapted, with permission, from Desmedt and Godaux 1977; Milner-Brown, Stein, and Yemm 1973. Copyright © 1973 The Physiological Society.)

A. Action potentials in two motor units were recorded concurrently with a single intramuscular electrode while the subject gradually increased muscle force. Motor unit 1 began discharging action potentials near the beginning of the voluntary contraction, and its discharge rate increased during the contraction. Motor unit 2 began discharging action potentials near the end of the contraction.

B. Average twitch forces for motor units 1 and 2 as extracted with an averaging procedure during the voluntary contraction.

C. The plot shows the net muscle forces at which 64 motor units in a hand muscle of one person were recruited (recruitment threshold) during a voluntary contraction relative to the twitch forces of the individual motor units.



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

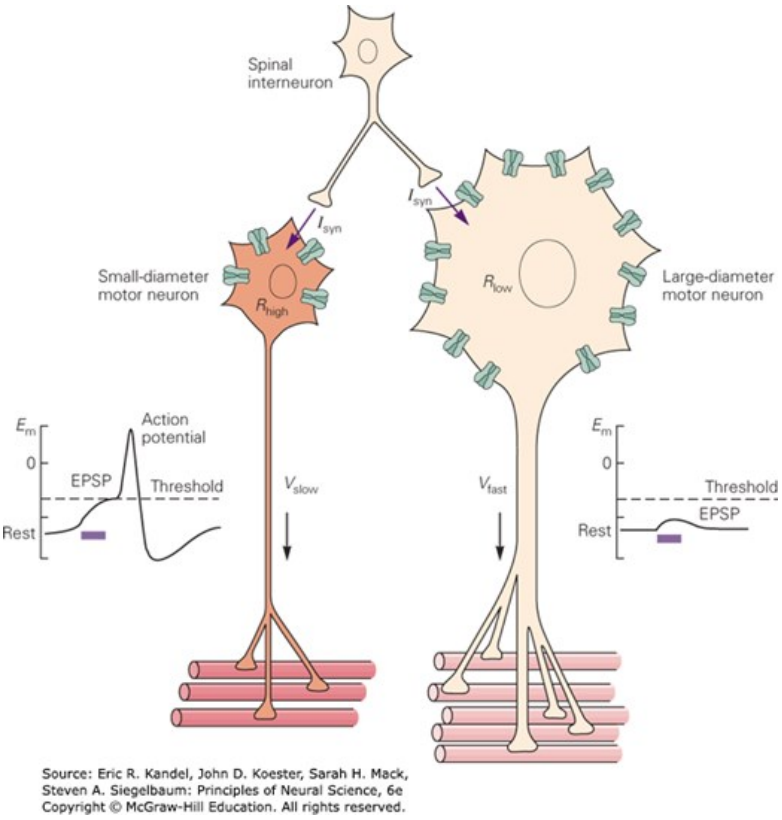
The order in which motor units are recruited is highly correlated with several indices of motor unit size, including the size of the motor neuron cell bodies, the diameter and conduction velocity of the axons, and the amount of force that the muscle fibers can exert. Because individual sources of synaptic input are broadly distributed across most neurons in a motor nucleus, the orderly recruitment of motor neurons is not accomplished by the

sequential activation of different sets of synaptic inputs that target specific motor neurons. Rather, recruitment order is determined by intrinsic differences in the responsiveness of individual motor neurons to relatively uniform synaptic input.

One of these factors is the anatomical size of a neuron's soma and dendrites. Smaller neurons have a higher input resistance (R_{in}) to current and, due to Ohm's law ($\Delta V_m = I_{syn} \times R_{in}$), experience a greater change in membrane potential (ΔV_m) in response to a given synaptic current (I_{syn}). Consequently, increases in the net excitatory input to a motor nucleus cause the levels of depolarization to reach threshold in an ascending order of motor neuron size: Contraction force is increased by recruiting the smallest motor neuron first and the largest motor neuron last (Figure 31–6). This effect is known as the size principle of motor neuron recruitment, a concept enunciated by Elwood Henneman in 1957.

Figure 31–6

The size principle of motor neuron recruitment. Two motor neurons of different sizes have the same resting membrane potential (V_r) and receive the same excitatory synaptic current (I_{syn}) from a spinal interneuron. Because the small motor neuron has a smaller surface area, it has fewer parallel ion channels and therefore a higher input resistance (R_{high}). According to Ohm's law ($V = IR$), I_{syn} in the small neuron produces a large excitatory postsynaptic potential (**EPSP**) that reaches threshold, resulting in the discharge of an action potential. However, the axon of the small motor neuron has a small diameter and thus conducts the action potential at a relatively low velocity (V_{slow}) and to fewer muscle fibers. In contrast, the large motor neuron has a larger surface area, which results in a lower transmembrane resistance (R_{low}) and a smaller EPSP that does not reach threshold in response to I_{syn}; however, when synaptic input does reach threshold, the action potential is conducted relatively rapidly (V_{fast}) (Chapter 9).



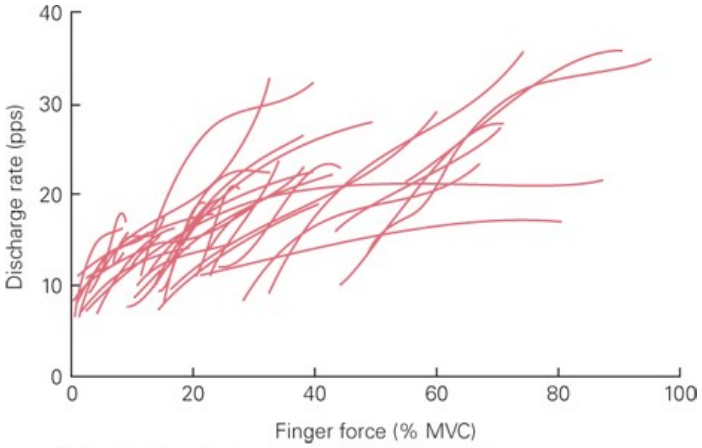
The size principle has two important consequences for the control of movement by the nervous system. First, the sequence of motor neuron recruitment is determined by the properties of the spinal neurons and not by supraspinal regions of the nervous system. This means that the brain cannot selectively activate specific motor units. Second, the axons arising from small motor neurons are thinner than those associated with large motor neurons and innervate fewer muscle fibers. Because the number of muscle fibers innervated by a motor neuron is a key determinant of motor unit force, motor units are activated in order of increasing strength, so the earliest recruited motor units are the weakest ones.

As suggested by Edgar Adrian in the 1920s, the muscle force at which the last motor unit in a motor nucleus is recruited varies between muscles. In

some hand muscles, all the motor units have been recruited when the force reaches approximately 60% of maximum during a slow muscle contraction. In the biceps brachii, deltoid, and tibialis anterior muscles, recruitment continues up to approximately 85% of the maximal force. Beyond the upper limit of motor unit recruitment, changes in muscle force depend solely on variations in the rate at which motor neurons generate action potentials. Over most of the operating range of a muscle, the force it exerts depends on concurrent changes in discharge rate and the number of active motor units (Figure 31–7). Except at low forces, however, variation in discharge rate has a greater influence on muscle force than does changes in the number of active motor units.

Figure 31–7

Muscle force can be adjusted by varying the number of active motor units and their discharge rate. Each line shows the discharge rate (pulses per second [**pps**]) for a single motor unit in a hand muscle over a range of finger forces (maximal voluntary contraction [**MVC**]). The finger force was produced by the action of a single hand muscle. The leftmost point of each line indicates the threshold force at which the motor unit is recruited, whereas the rightmost point corresponds to the peak force at which the motor unit could be identified. The range of discharge rates was often less for motor units with lower recruitment thresholds. Increases in finger force were produced by concurrent increases in discharge rate and the number of activated motor units. (Adapted, with permission, from Moritz et al. 2005.)



The order in which motor units are recruited does not change with contraction speed. Due to the time involved in excitation-contraction coupling, faster contractions require the action potential for each motor unit to be generated earlier than during a slow contraction. As a result of this adjustment, the upper limit of motor unit recruitment during the fastest muscle contractions is approximately 40% of maximum. Consequently, it is possible to manipulate the rate at which motor units are recruited by varying contraction speed.

The Input–Output Properties of Motor Neurons Are Modified by Input From the Brain Stem

The discharge rate of motor neurons depends on the magnitude of the depolarization generated by excitatory inputs and the intrinsic membrane properties of the motor neurons in the spinal cord. These properties can be profoundly modified by input from monoaminergic neurons in the brain stem (Chapter 40). In the absence of this input, the dendrites of motor neurons passively transmit synaptic current to the cell body, resulting in a modest depolarization that immediately ceases when the input stops. Under these conditions, the relation between input current and discharge rate is linear over a wide range.

The input–output relation becomes nonlinear, however, when the monoamines serotonin and norepinephrine induce a huge increase in conductance by activating L-type Ca^{2+} channels that are located on the dendrites of the motor neurons. The resulting inward Ca^{2+} currents can enhance synaptic currents by three- to five-fold (Figure 31–8). In an active motor neuron, this augmented current can sustain an elevated discharge rate after a brief depolarizing input has ended, a behavior known as *self-sustained firing*. A subsequent brief inhibitory input, such as from a spinal reflex pathway, can terminate such self-sustained firing.

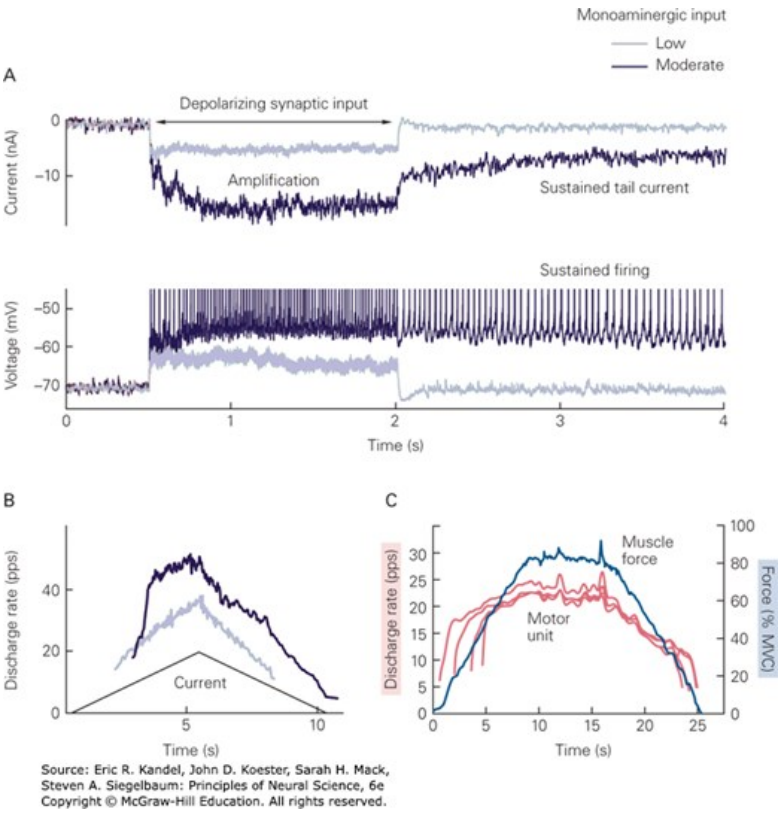
Figure 31–8

Monoaminergic input enhances the excitability of motor neurons. (Part A, adapted, with permission, of Heckman et al. 2009. Copyright © 2009 International Federation of Clinical Neurophysiology; Part B, data from CJ Heckman; Part C, adapted, with permission, from Erim et al. 1996. Copyright © 1996 John Wiley & Sons, Inc.)

A. Membrane currents and potentials in spinal motor neurons of adult cats that were either deeply anesthetized (low monoaminergic drive) or decerebrate (moderate monoaminergic drive). When monoaminergic input is absent or low, a brief excitatory input produces an equally brief synaptic current during voltage clamp (**upper record**). This current is not sufficient to bring the membrane potential of the neuron to threshold for generating action potentials in the unclamped condition (**lower record**). The same brief excitatory input during moderate levels of monoaminergic input activates a persistent inward current in the dendrites, which amplifies the excitatory synaptic current and decays slowly following cessation of synaptic input (**upper record**). This persistent inward current causes a high discharge rate during the input and sustains a lesser discharge rate after the input ceases (**lower record**). A brief inhibitory input will return the neuron to its resting state.

B. High levels of monoaminergic input to a motor neuron give rise to a persistent inward current in response to injected current, resulting in a much greater discharge rate for a given amount of current.

C. The **blue** trace represents the force exerted by the dorsiflexor muscle during a contraction that gradually increased to 80% of maximal voluntary isometric contraction (**MVC**) force in a human subject. Each of the four **pink** traces indicates the change in the rate at which a single motor unit discharged action potentials during the contraction. The leftmost point (start) of each of these four traces shows the time when the motor unit was recruited, and the rightmost point (end) denotes the time at which the motor neuron stopped discharging action potentials. The rapid increase in discharge rate during the increase in muscle force is similar to the change in rate observed in the presence of moderate levels of monoaminergic input (see part **B**).



Because the properties of motor neurons are strongly influenced by monoamines, the excitability of the pool of motor neurons innervating a single muscle is partly under control of the brain stem. In the awake state, moderate levels of monoaminergic input to the motor neurons of slowly contracting motor units promote self-sustained firing. This is probably the source of the sustained force exerted by slower motor units to maintain posture (Chapter 36). Conversely, the withdrawal of monoaminergic drive during sleep decreases excitability and helps ensure a relaxed motor state. Thus, monoaminergic input from the brain stem can adjust the gain of the motor unit pool to meet the demands of different tasks. This flexibility does not compromise the size principle of orderly recruitment because the threshold for activation of the persistent inward currents is lowest in the motor

neurons of slower contracting motor units, which are the first recruited even in the absence of monoamines.

Muscle Force Depends on the Structure of Muscle

Muscle force depends not only on the amount of motor neuron activity but also on the arrangement of the fibers in the muscle. Because movement involves the controlled variation of muscle force, the nervous system must take into account the structure of muscle to achieve specific movements.

The Sarcomere Is the Basic Organizational Unit of Contractile Proteins

Individual muscles contain thousands of fibers that vary from 1 to 50 mm in length and from 10 to 60 µm in diameter. The variation in fiber dimensions reflects differences in the quantity of contractile protein. Despite this quantitative variation, the organization of contractile proteins is similar in all muscle fibers. The proteins are arranged in repeating sets of thick and thin filaments, each set known as a *sarcomere* (Figure 31–9). The in vivo length of a sarcomere, which is bounded by Z disks, ranges from 1.5 to 3.5 µm within and across muscles. Sarcomeres are arranged in series to form a *myofibril,* and the myofibrils are aligned in parallel to form a muscle fiber (myocyte).

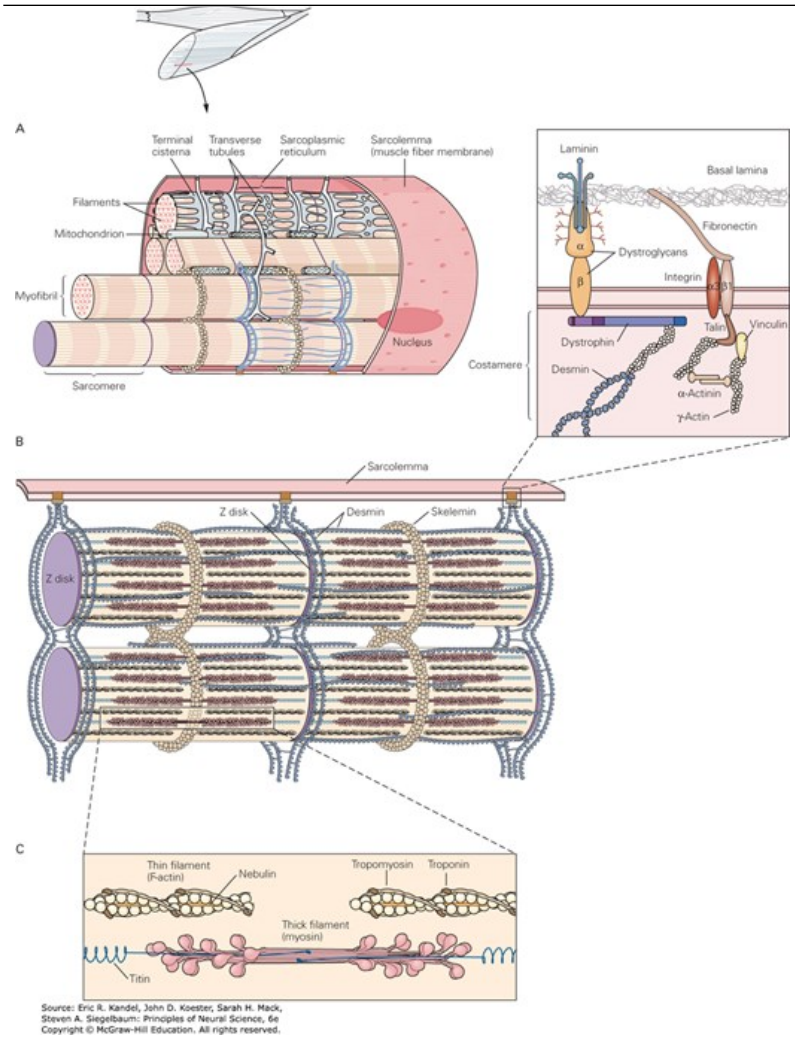
Figure 31–9

The sarcomere is the basic functional unit of muscle. (Adapted from Bloom and Fawcett 1975.)

A. This section of a muscle fiber shows its anatomical organization. Several myofibrils lie side by side in a fiber, and each myofibril is made up of sarcomeres arranged end to end and separated by Z disks (see part **B**). The myofibrils are surrounded by an activation system (the transverse tubules, terminal cisternae, and sarcoplasmic reticulum) that initiates muscle contraction.

B. Sarcomeres are connected to one another and to the muscle fiber membrane by the cytoskeletal lattice. The cytoskeleton influences the length of the contractile elements, the thick and thin filaments (see part **C**). It maintains the alignment of these filaments within a sarcomere, connects adjacent myofibrils, and transmits force to the extracellular matrix of connective tissue through costameres. One consequence of this organization is that the force generated by the contractile elements in a sarcomere can be transmitted along and across sarcomeres (through desmin and skelemin), within and between sarcomeres (through nebulin and titin), and to the sarcolemma through the costameres. The Z disk is a focal point for many of these connections.

C. The thick and thin filaments comprise different contractile proteins. The thin filament includes polymerized actin along with the regulatory proteins tropomyosin and troponin. The thick filament is an array of myosin molecules; each molecule includes a stem that terminates in a pair of globular heads. The protein titin maintains the position of each thick filament in the middle of the sarcomere.



The force that each sarcomere can generate arises from the interaction of the contractile thick and thin filaments. The thick filament consists of several hundred myosin molecules arranged in a structured sequence. Each myosin molecule comprises paired coiled-coil domains that terminate in a pair of globular heads. The myosin molecules in the two halves of a thick filament point in opposite directions and are progressively displaced so that the heads, which extend away from the filament, protrude around the thick filament (Figure 31–9C). The thick filament is anchored in the middle of the sarcomere by the protein titin, which connects each end of the thick filament with neighboring strands of actin in the thin filament and with the Z-disc. To maximize the interaction between the globular heads of myosin and the thin filaments, six thin filaments surround each thick filament.

The primary components of the thin filament are two helical strands of fibrous F-actin, each of which contains approximately 200 actin monomers. Superimposed on F-actin are tropomyosin and troponin, proteins that control the interaction between actin and myosin. Tropomyosin consists of two coiled strands that lie in the groove of the F-actin helix; troponin is a small molecular complex that is attached to tropomyosin at regular intervals (Figure 31–9C).

The thin filaments are anchored to the Z disk at each end of the sarcomere, whereas the thick filaments occupy the middle of the sarcomere (Figure 31–9B). This organization accounts for the alternating light and dark bands of striated muscle. The light band contains only thin filaments, whereas the dark band contains both thick and thin filaments. When a muscle is activated, the width of the light band decreases but the width of the dark band does not change, suggesting that the thick and thin filaments slide relative to one another during a contraction. This led to the *sliding filament hypothesis* of muscle contraction proposed by A. F. Huxley and H. E. Huxley in the 1950s.

The sliding of the thick and thin filaments is triggered by the release of Ca^{2+} from within the sarcoplasm of a muscle fiber in response to an action potential that travels along the fiber's membrane, the sarcolemma. Varying the amount of Ca^{2+} in the sarcoplasm controls the interaction between the thick and thin filaments. The Ca^{2+} concentration in the sarcoplasm is kept low under resting conditions by active pumping of Ca^{2+} into the sarcoplasmic

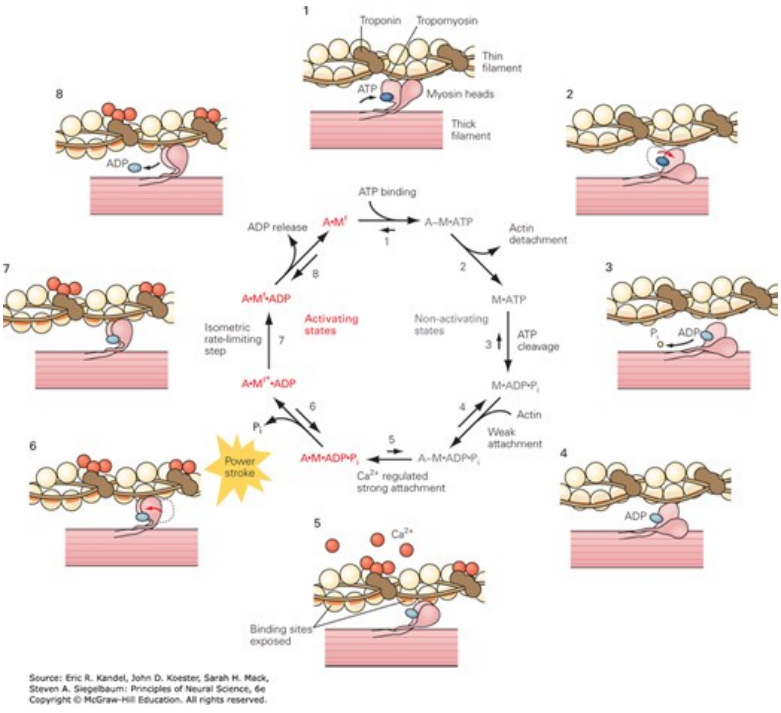
reticulum, a network of longitudinal tubules and chambers of smooth endoplasmic reticulum. Calcium is stored in the terminal cisternae, which are located next to intracellular extensions of the sarcolemma known as transverse tubules (T-tubules). The transverse tubules, terminal cisternae, and sarcoplasmic reticulum constitute an activation system that transforms an action potential into the sliding of the thick and thin filaments (Figure 31–9A).

As an action potential propagates along the sarcolemma, it invades the transverse tubules and causes the rapid release of Ca^{2+} from the terminal cisternae into the sarcoplasm. Once in the sarcoplasm, Ca^{2+} diffuses among the filaments and binds reversibly to troponin, which results in the displacement of the troponin–tropomyosin complex and enables the sliding of the thick and thin filaments. Because a single action potential does not release enough Ca^{2+} to bind all available troponin sites in skeletal muscle, the strength of a contraction increases with the action potential rate.

The sliding of the filaments depends on mechanical work performed by the globular heads of myosin, work that uses chemical energy contained in adenosine triphosphate (ATP). The actions of the myosin heads are regulated by the *cross-bridge cycle*, a sequence of detachment, activation, and attachment (Figure 31–10). In each cycle, a globular head undergoes a displacement of 5 to 10 nm. Contractile activity continues as long as Ca^{2+} and ATP are present in the cytoplasm in sufficient amounts.

Figure 31–10

The cross-bridge cycle. Several nonactivating states are followed by several activating states triggered by Ca^{2+}. The cycle begins at the top (**step 1**) with the binding of adenosine triphosphate (**ATP**) to the myosin head. The myosin head detaches from actin (**step 2**), ATP is cleaved to phosphate (P_i) and adenosine diphosphate (**ADP**) (**step 3**), and the myosin becomes weakly bound to actin (**step 4**). The binding of Ca^{2+} to troponin causes tropomyosin to slide over actin and enables the two myosin heads to close (**step 5**). This results in the release of P_i and the extension of the myosin neck, the power stroke of the cross-bridge cycle (**step 6**). Each cross-bridge exerts a force of approximately 2 pN during a structural change (**step 7**) and the release of ADP (**step 8**). (•, strong binding; ~, weak binding; M^f, cross-bridge force of myosin; and M^{f*}, force-bearing state of myosin.) (Adapted, with permission, from Gordon, Regnier, and Homsher 2001.)



Once the contractile proteins have been activated by the release of Ca^{2+}, sarcomere length may increase, remain the same, or decrease depending on the magnitude of the load against which the muscle is acting. The force generated by an activated sarcomere when its length does not change or decreases can be explained by the cross-bridge cycle involving the thick and thin filaments. When the length of the activated sarcomere increases, however, the force developed by the extension of titin adds significantly to the sarcomere force. The force produced by titin during the stretch of an

activated sarcomere is augmented by its ability to increase stiffness, which is accomplished when titin binds Ca^{2+} and then attaches at specific locations on actin to reduce the length that it can be stretched. The force produced by activated sarcomeres therefore depends on the interactions of three filaments (actin, myosin, and titin).

Noncontractile Elements Provide Essential Structural Support

Structural elements of the muscle fiber maintain the alignment of the contractile proteins within the fiber and facilitate the transmission of force from the sarcomeres to the skeleton. A network of proteins (nebulin, titin) maintains the orientation of the thick and thin filaments within the sarcomere, whereas other proteins (desmin, skelemins) constrain the lateral alignment of the myofibrils (Figure 31–9B). These proteins contribute to the elasticity of muscle and maintain the appropriate alignment of cellular structures when the muscle acts against an external load.

Although some of the force generated by the cross bridges is transmitted along the sarcomeres in series, most of it travels laterally from the thin filaments to an extracellular matrix that surrounds each muscle fiber, through a group of transmembrane and membrane-associated proteins called a *costamere* (see inset for Figure 31–9B). The lateral transmission of force follows two pathways through the costamere, one through a dystrophin–glycoprotein complex and the other through vinculin and members of the integrin family. Mutations of genes that encode components of the dystrophin–glycoprotein complex cause muscular dystrophies in humans, which are associated with substantial decreases in muscle force.

Contractile Force Depends on Muscle Fiber Activation, Length, and Velocity

The force that a muscle fiber can exert depends on the number of cross bridges formed and the force produced by each cross bridge. These two factors are influenced by the Ca^{2+} concentration in the sarcoplasm, the amount of overlap between the thick and thin filaments, and the velocity with which the thick and thin filaments slide past one another.

The influx of Ca^{2+} that activates formation of the cross bridges is transitory because continuous pump activity quickly returns Ca^{2+} to the sarcoplasmic reticulum. The release and reuptake of Ca^{2+} in response to a single action potential occurs so quickly that only some of the potential cross bridges are formed. This explains why the peak force of a twitch is less than the maximal force of the muscle fiber (see Figure 31–2A). Maximal force can be achieved only with a series of action potentials that sustains the Ca^{2+} concentration in the sarcoplasm, thus maximizing cross bridge formation.

Although Ca^{2+} activates formation of the cross bridges, cross bridges can be formed only when the thick and thin filaments overlap. This overlap varies as the filaments slide relative to one another (Figure 31–11A). The amount of overlap between actin and myosin is optimal at an intermediate sarcomere length (L_o), and the relative force is maximal. Increases in sarcomere length reduce the overlap between actin and myosin and the force that can be developed. Decreases in sarcomere length cause the thin filaments to overlap, reducing the number of binding sites available to the myosin heads. Although many muscles operate over a narrow range of sarcomere lengths (approximately 94 ± 13% L_o, mean ± standard deviation), among muscles, there is considerable diversity in sarcomere lengths during movement.

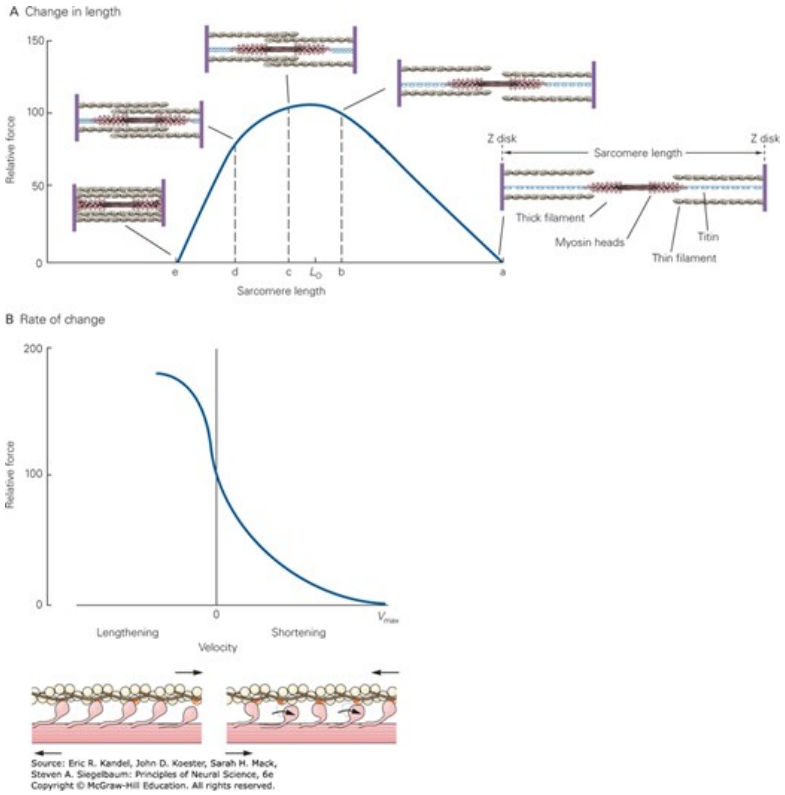
Figure 31–11

Contractile force varies with the change in sarcomere length and velocity.

A. At an intermediate sarcomere length, L_o, the amount of overlap between actin and myosin is optimal and the relative force is maximal. When the sarcomere is stretched beyond the length at which the thick and thin filaments overlap (length **a**), cross bridges cannot form and no force is exerted. As sarcomere length decreases and the overlap of the thick and thin filaments increases (between lengths **a** and **b**), the force increases because the number of cross bridges increases. With further reductions in length (between lengths **c** and **e**), the extreme overlap of the thin filaments with each other occludes potential attachment sites and the force decreases.

B. Contractile force varies with the rate of change in sarcomere length. Relative to the force that a sarcomere can exert during an isometric contraction (zero velocity), the peak force declines as the rate of shortening increases. Muscle force reaches a minimum at the maximal shortening velocity (V_{max}). In contrast, when the sarcomere is lengthened while being activated, the peak force increases to values greater than those during an isometric contraction. Shortening causes the myosin heads to spend more time near the end of their power stroke, where they produce less contractile force, and more time detaching, recocking, and reattaching, during which they produce no force. When the muscle is actively lengthened, the myosin heads

spend more time stretched beyond their angle of attachment and little time unattached because they do not need to be recocked after being pulled away from the actin in this manner. Titin also contributes significantly to sarcomere force during lengthening contractions.



Because structures that connect the contractile proteins to the skeleton also influence the force that a muscle can exert, muscle force increases with length over its operating range. This property enables muscle to function like a spring and to resist changes in length. Muscle stiffness, which corresponds to the slope of the relation between muscle force and muscle length (N/m), depends on the structure of the muscle. A stiffer muscle, similar to a stronger spring, is more resistant to changes in length.

Once activated, cross bridges perform work and cause the thick and thin filaments to slide relative to one another. Due to the elasticity of intracellular cytoskeletal proteins and the extracellular matrix, sarcomeres will shorten when the cross bridges are activated and the length of the muscle fiber is held fixed (*isometric contraction*). When the length of the muscle fiber is not kept constant, the direction and rate of change in sarcomere length depend on the amount of muscle fiber force relative to the magnitude of the load against which the fiber acts. Sarcomere length decreases when the muscle fiber force exceeds the load (*shortening contraction*) but increases when the force is less than the load (*lengthening contraction*). The maximal force that a muscle fiber can exert decreases as shortening velocity increases but increases as lengthening velocity increases (Figure 31–11B).

The maximal rate at which a muscle fiber can shorten is limited by the peak rate at which cross bridges can form. The variation in fiber force as contraction velocity changes is largely caused by differences in the average force exerted by each cross bridge. For example, the decrease in force during a shortening contraction is attributable to a reduction in cross-bridge displacement during each power stroke and the failure of some myosin heads to find attachment sites. Conversely, the increase in force during a lengthening contraction reflects the stretching of incompletely activated sarcomeres, the more rapid reattachment of cross bridges after they have been pulled apart, and the attachment of Ca^{2+} to titin.

The rate of cross-bridge cycling depends not only on contraction velocity but also on the preceding activity of the muscle. For example, the rate of cross-bridge cycling increases after a brief isometric contraction. When a muscle is stretched while in this state, such as would occur during a postural disturbance, muscle stiffness is enhanced, and the muscle is more effective at resisting the change in length. This property is known as *short-range stiffness.* Conversely, the cross-bridge cycling rate decreases after shortening contractions, and the muscle does not exhibit short-range stiffness.

Muscle Torque Depends on Musculoskeletal Geometry

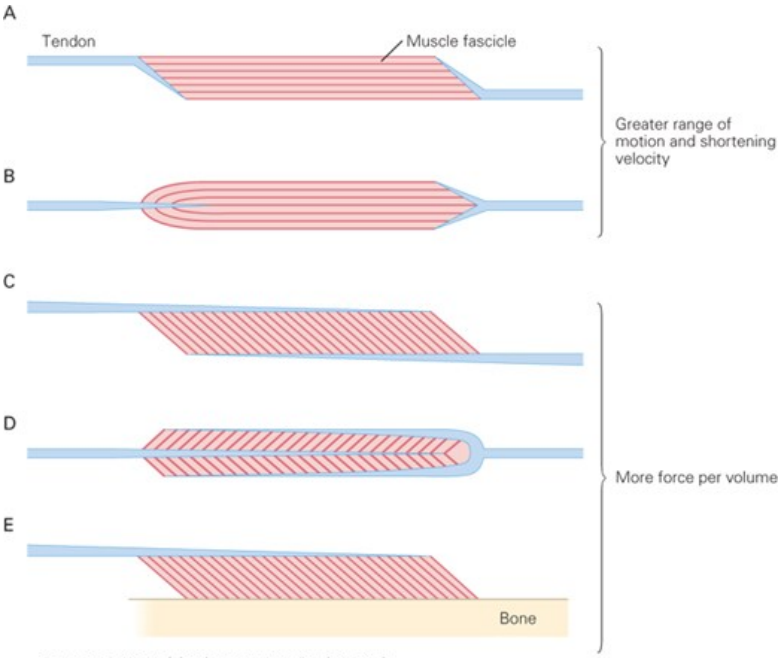
The anatomy of a muscle has a pronounced effect on its force capacity, range of motion, and shortening velocity. The anatomical features that

influence function include the arrangement of the sarcomeres in each muscle fiber, the organization of the muscle fibers within the muscle, and the location of the muscle's attachments on the skeleton. These features vary widely among muscles.

At the level of a single muscle fiber, the number of sarcomeres in series and in parallel can vary. The number of sarcomeres in series determines the length of the myofibril and thus the length of the muscle fiber. Because one sarcomere can shorten by a certain length with a given maximal velocity, both the range of motion and the maximal shortening velocity of a muscle fiber are proportional to the number of sarcomeres in series. The force that a myofibril can exert is equal to the average sarcomere force and is not influenced by the number of sarcomeres in series. Rather, the force capacity of a fiber depends on the number of sarcomeres in parallel and hence on the diameter or cross-sectional area of the fiber. At the level of the muscle, the functional attributes of the fibers are modified by the orientation of the fascicles (bundles of muscle fibers) to the line of pull of the muscle and the length of the fiber relative to the muscle length. In most muscles, the fascicles are not parallel to the line of pull but fan out in feather-like (pennate) arrangements (Figure 31–12).

Figure 31–12

Five common arrangements of tendon and muscle. The fundamental distinction between these arrangements is whether or not the muscle fascicles are aligned with the line of pull of the muscles. The fascicles in muscles A and B are parallel to the line of pull (longitudinal axis of the muscle), whereas the fascicles in muscles C, D, and E are rotated away from the line of pull. The magnitude of this rotation is expressed as the pennation angle. (Reproduced, with permission, from Alexander and Ker 1990.)



The relative orientation, or pennation angle of the fascicles, ranges from close to 0° (biceps brachii, sartorius) to approximately 30° (soleus). Because more fibers can fit into a given volume as the pennation angle increases, muscles with large pennation angles typically have more fascicles in parallel and hence large cross-sectional areas when measured perpendicular to the long axis of individual muscle fibers. Given the linear relation between cross-sectional area (quantity of contractile proteins in parallel) and maximal force (~22.5 N • cm^{-2}), these muscles are capable of a greater maximal force. However, the fibers in pennate muscles are generally short and have a lesser maximal shortening velocity than those in nonpennate muscles.

The functional consequences of this anatomical arrangement can be seen by comparing the contractile properties of two muscles with different numbers of fibers and fiber lengths. If the two muscles have identical fiber lengths but one has twice as many fibers, the range of motion of the two muscles will be similar because it is a function of fiber length, but the maximal force capacity will vary in proportion to the number of muscle fibers. If the two muscles have identical numbers of fibers but the fibers in one muscle are twice as long, the muscle with the longer fibers will have a greater range of motion and a greater maximal shortening velocity, even though the two muscles have a similar force capacity. Because of this effect, the muscle with longer fibers is able to exert more force and produce more power (the product of force and velocity) at a given absolute shortening

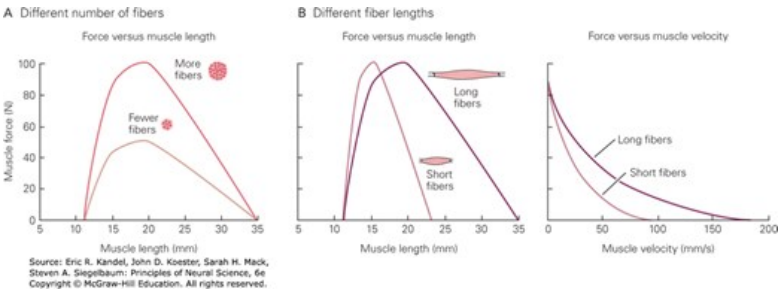
velocity (Figure 31–13).

Figure 31–13

Muscle dimensions influence the peak force and maximal shortening velocity. (Reproduced, with permission, from Lieber and Fridén 2000. Copyright © 2000 John Wiley & Sons, Inc.)

A. Muscle force at various muscle lengths for two muscles with similar fiber lengths but different numbers of muscle fibers (different cross-sectional area). The muscle with twice as many fibers exerts greater force.

B. Muscle force at various muscle lengths for two muscles with the same cross-sectional area but different fiber lengths. The muscle with longer fibers (approximately twice as long as those of the other muscle) has an increased range of motion (left plot). It also has a greater maximal shortening velocity and exerts greater force at a given absolute velocity (right plot).



Muscle fiber lengths and cross-sectional areas vary substantially throughout the human body, which suggests that the contractile properties of individual muscles also differ markedly (Table 31–2). In the leg, for example, pennation angle ranges from 1° (sartorius) to 30° (vastus medialis), fiber length ranges from 4 mm (soleus) to 40 mm (sartorius), and cross-sectional area ranges from 2 cm^2 (sartorius) to 52 cm^2 (soleus). In addition, the fact that muscle fiber length is usually less than muscle length indicates that muscle fibers are connected serially within a muscle. Functionally coupled muscles tend to have complementary combinations of these properties. For example, the three vasti muscles have similar muscle fiber lengths (10 cm), but they differ in pennation angle (intermedius is the smallest) and cross-sectional area (lateralis is the largest). A similar relation exists for soleus and the two heads (medial and lateral) of gastrocnemius.

Table 31–2

Average Architectural Properties for Some Human Skeletal Leg Muscles

Muscle	Mass (g)	Muscle length (cm)	Fiber length (cm)	Pennation angle (°)	Cross-sectional area (cm^2)
Thigh					
Sartorius	78	45	40	1	2
Rectus femoris	111	36	8	14	14
Vastus lateralis	376	27	10	18	35
Vastus intermedius	172	41	10	5	17
Vastus medialis	239	44	10	30	21
Gracilis	53	29	23	8	2
Adductor longus	75	22	11	7	7

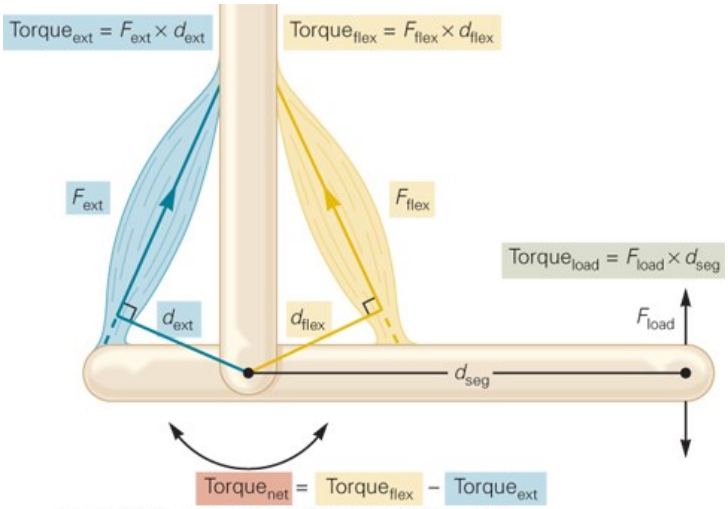
Adductor brevis	55	15	10	6	5
Adductor magnus	325	38	14	16	21
Biceps femoris (long)	113	35	10	12	11
Biceps femoris (short)	60	22	11	12	5
Semitendinosus	100	30	19	13	5
Semimembranosus	134	29	7	15	18
Lower leg					
Tibialis anterior	80	26	7	10	11
Extensor hallucis longus	21	24	7	9	3
Extensor digitorum longus	41	29	7	11	6
Peroneus longus	58	27	5	14	10
Peroneus brevis	24	24	5	11	5
Gastrocnemius (medial)	113	27	5	10	21
Gastrocnemius (lateral)	62	22	6	12	10
Soleus	276	41	4	28	52
Flexor hallucis longus	39	27	5	17	7
Flexor digitorum longus	20	27	4	14	4
Tibialis posterior	58	31	4	14	14

Source: Adapted, with permission, from Ward et al. 2009.

Movement involves the muscle-controlled rotation of adjacent body segments, which means that the capacity of a muscle to contribute to a movement also depends on its location relative to the joint that it spans. The rotary force exerted by a muscle about a joint is referred to as *muscle torque* and is calculated as the product of the muscle force and the *moment arm,* the shortest perpendicular distance from the line of pull of the muscle to the joint's center (Figure 31–14).

Figure 31–14

Muscle torque varies over the range of motion about a joint. A muscle's torque about a joint is the product of its contractile force (F) and its moment arm relative to the joint (d). The moment arm is the shortest perpendicular distance from the line of pull of the muscle to the center of rotation of the joint. Because the moment arm changes when the joint rotates, muscle torque varies with angular displacement about the joint. The net torque about a joint, which determines the mechanical action, is the difference in the torques exerted by opposing muscles, such as extensors (ext) and flexors (flex). Similarly, a force applied to the limb (F_{load}) will exert a torque about the joint that depends on F_{load} and its distance from the joint (d_{seg}).



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

The moment arm usually changes as a joint rotates through its range of motion; the amount of change depends on where the muscle is attached to the skeleton relative to the joint. If the force exerted by a muscle remains relatively constant throughout the joint's range of motion, muscle torque varies in direct proportion to the change in the moment arm. For many muscles, the moment arm is maximal in the middle of the range of motion, which usually corresponds to the position of maximal muscle force and hence greatest muscle torque.

Different Movements Require Different Activation Strategies

The human body has approximately 600 muscles, each with a distinct torque profile about one or more joints. To perform a desired movement, the nervous system must activate an appropriate combination of muscles with adequate intensity and timing of activity. The activation must be appropriate for the contractile properties and musculoskeletal geometry of many muscles, as well as the mechanical interactions between body segments. As a result of these demands, activation strategies differ with the details of the movement.

Contraction Velocity Can Vary in Magnitude and Direction

Movement speed depends on the contraction velocity of a muscle. The only ways to vary contraction velocity are to alter either the number of motor units recruited or the rates at which they discharge action potentials. The velocity of a contraction can vary in both magnitude and direction (see Figure 31–11B). To control the velocity of a contraction, the nervous system must scale the magnitude of the net muscle torque relative to the load torque (Figure 31–14), which includes both the weight of the body part and any external load acting on the body.

When muscle torque exceeds load torque, the muscle shortens as it performs a shortening contraction. When muscle torque is less than load torque, the muscle lengthens as it performs a lengthening contraction. For the example shown in Figure 31–14, the load is lifted with a shortening contraction of the flexor and lowered with a lengthening contraction of the flexor. Both types of contractions are common in daily activities.

Shortening and lengthening contractions are not simply the result of adjusting motor unit activity so that the net muscle torque is greater or less than the load torque. When the task involves lifting a load with a prescribed trajectory, activation of the motor units must be aligned so that the sum of the rise times produce the appropriate torque so as to match the desired trajectory while lifting (shortening contractions), whereas while lowering the load (lengthening contractions), the sum of the decay times must be similarly controlled. The nervous system accomplishes this with different descending input and sensory feedback during the two types of contractions. Because of these differences in required motor unit activity, the control of the two types of contraction respond differently to stresses imposed on the system. Declines in the capacity to control motor unit activity, such as observed in older adults and persons performing rehabilitation exercises after an orthopedic procedure, are associated with greater difficulty in performing lengthening contractions.

The amount of motor unit activity relative to the load also influences the contraction velocity. This effect depends on both the number of motor units recruited and the maximal rates at which the motor units can discharge action potentials. As described previously, physical training with rapid

contractions, such as power training, increases the rate at which motor units can discharge trains of action potentials, which can be mimicked by step injections of current into a motor neuron. Changes in the maximal shortening velocity of a muscle after a change in the habitual level of physical activity are the result, at least partly, of factors that influence the ability of motor neurons to discharge action potentials at high rates.

Movements Involve the Coordination of Many Muscles

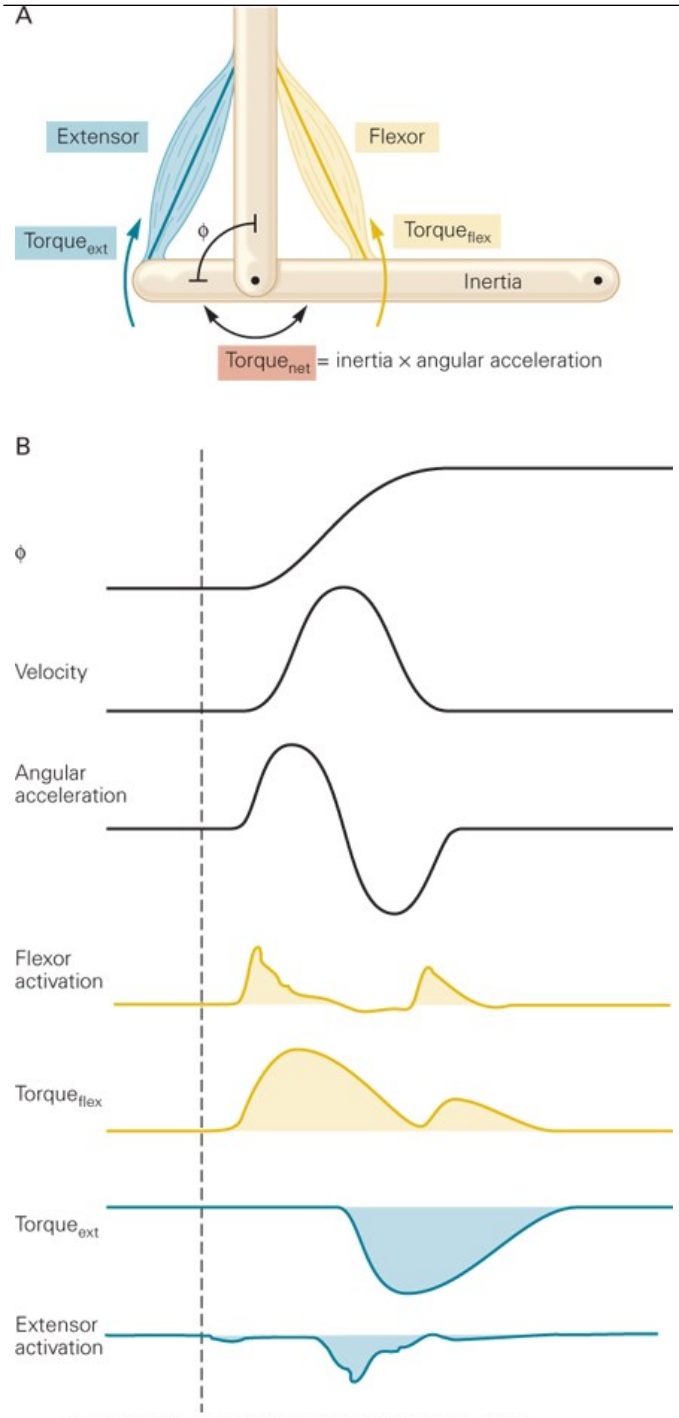
In the simplest case, muscles span a single joint and cause the attached body segments to accelerate about a single axis of rotation. Because muscles can exert only a pulling force, motion about a single axis of rotation requires at least two muscles or groups of muscles when the action involves shortening contractions (Figure 31–15A).

Figure 31–15

(Left) Antagonist muscles spanning a single joint control movement of a limb about a single axis of rotation.

A. According to Newton's law of acceleration (force = mass × acceleration), force is required to change the velocity of a mass. Muscles exert a torque to accelerate the inertial mass of the skeletal segment around a joint. For angular motion, Newton's law is written as torque = rotational inertia × angular acceleration.

B. The angular velocity for movement of a limb from one position to another has a bell-shaped profile. Acceleration in one direction is followed by acceleration in the opposite direction—the flexor and extensor muscles are activated in succession. The records here show the activation profiles and associated muscle torques for a fast elbow flexion movement. Because contractile force decays relatively slowly, the flexor muscle is usually activated a second time to counter the prolonged acceleration generated by the extensor muscle and to stop the limb at the intended joint angle.



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

Because most muscles attach to the skeleton slightly off center from the axis of rotation, they can cause movement about more than one axis of rotation. If one of the actions is not required, the nervous system must activate other muscles to control the unwanted movement. For example, activation of the radial flexor muscle of the wrist can cause the wrist to flex and abduct. If the intended action is only wrist flexion, then the abduction action must be opposed by another muscle, such as the ulnar flexor muscle, which causes wrist flexion and adduction. Depending on the geometry of the articulating surfaces and the attachment sites of the muscles, the multiple muscles that span a joint are capable of producing movements about one to three axes of rotation. Furthermore, some structures can be displaced linearly (eg, the scapula on the trunk), adding to the degrees of freedom about a joint.

The off-axis attachment of muscles enhances the flexibility of the skeletal motor system; the same movement can be achieved by activating different combinations of muscles. However, this additional flexibility requires the nervous system to control the unwanted actions. A solution used by the nervous system is to organize relations among selected muscles to produce specific actions. A particular sequence of muscle activations is known as a *muscle synergy,* and movement is produced through the coordinated activation of these synergies. For example, EMG recordings of human subjects suggest that variations of movements with the same general purpose, such as grasping various objects with the hand, reaching and pointing in different directions, or walking and running at several speeds, are controlled by approximately five muscle synergies.

The number of muscles that participate in a movement also varies with the speed of the movement. For example, slow lifting of a load requires only that the muscle torque slightly exceed the load torque (see Figure 31–14), and thus, only the flexor muscle is activated. This strategy is used when lifting a handheld weight with the elbow flexor muscles. In contrast, to perform this movement rapidly with an abrupt termination at an intended joint angle, both the flexor and extensor muscles must be activated. First, the flexor muscle is activated to accelerate the limb in the direction of flexion, followed by activation of the extensor muscle to accelerate the limb in the direction of extension, and finally a burst of activity by the flexor muscle to increase the angular momentum of the limb and the handheld weight in the direction of flexion so that it arrives at the desired joint angle (Figure 31–15B). The amount of extensor muscle activity increases with the speed of the movement.

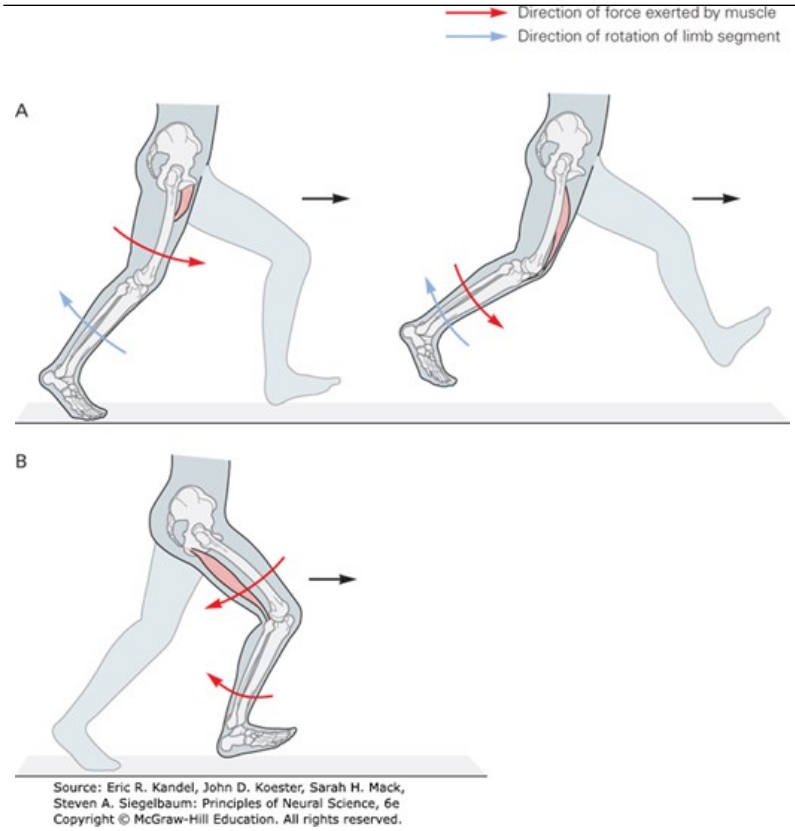
Increases in movement speed introduce another factor that the nervous system must control: unwanted accelerations in other body segments. Because body parts are connected to one another, motion in one part can induce motion in another. The induced motion is often controlled with lengthening contractions, such as those experienced by thigh muscles during the swing phase of running (Figure 31–16A).

Figure 31–16

A single muscle can influence the motion about many joints.

A. Muscles that cross one joint can accelerate an adjacent body segment. For example, at the beginning of the swing phase while running, the hip flexor muscles are activated to accelerate the thigh forward (**red arrow**). This action causes the lower leg to rotate backward (**blue arrow**) and the knee joint to flex. To control the knee joint flexion during the first part of the swing phase, the knee extensor muscles are activated and undergo a lengthening contraction to accelerate the lower leg forward (**red arrow**) while it continues to rotate backward (**blue arrow**).

B. Many muscles cross more than one joint to exert an effect on more than one body segment. For example, the hamstring muscles of the leg accelerate the hip in the direction of extension and the knee in the direction of flexion (**red arrows**). During running, at the end of the swing phase, the hamstring muscles are activated and undergo lengthening contractions to control the forward rotation of the leg (hip flexion and knee extension). This strategy is more economical than activating individual muscles at the hip and knee joints to control the forward rotation of the leg.



Muscles that span more than one joint can be used to control these motion-dependent interactions between body parts. At the end of the swing phase in running, activation of the hamstring muscles causes both the thigh and lower leg to accelerate backward (Figure 31–16B). If a hip extensor muscle is used to accelerate the thigh backward instead of the hamstring muscles, the lower leg would accelerate forward, requiring activation of a knee flexor muscle to control the unwanted lower leg motion so that the foot could be placed on the ground. Use of the two-joint hamstring muscles is a more economical strategy, but one that can subject the hamstrings to high stresses during fast movements, such as sprinting. The control of such motion-dependent interactions often involves lengthening contractions, which maximize muscle stiffness and the ability of muscle to resist changes in length.

For most movements, the nervous system must establish rigid connections between some body parts for two reasons. First, as expressed in Newton's law of action and reaction, a reaction force must provide a foundation for the acceleration of a body part. For example, in a reaching movement performed by a person standing upright, the ground must provide a reaction force against the feet. The muscle actions that produce the arm movement exert forces that are transmitted through the body to the feet and are opposed by the ground. Different substrates provide different amounts of reaction force, which is why ice or sand can influence movement capabilities.

Second, uncertain conditions are usually accommodated by stiffening the joints through concurrent activation of the muscles that produce force in opposite directions. Coactivation of opposing muscles occurs often when a support surface is unsteady, when the body might experience an unexpected perturbation, or when lifting a heavy load. Because coactivation increases the energetic cost of performing a task, one characteristic of skilled performance is the ability to accomplish a task with minimal activation of muscles that produce opposing actions.

Muscle Work Depends on the Pattern of Activation

Limb muscles in healthy young adults are active 10% to 20% of the time during waking hours. For much of this time, the muscles perform constant-length (*isometric*) contractions to maintain a variety of static body postures. In contrast, muscle length has to change during a movement so that the muscle can perform work to displace body parts. A muscle performs positive work and produces power during a shortening contraction, whereas it performs negative work and absorbs power during a lengthening contraction. The capacity of muscle to do positive work establishes performance capabilities, such as the maximal height that can be jumped.

The nervous system can augment the positive work capacity of muscle by commanding a brief period of negative work before performing positive

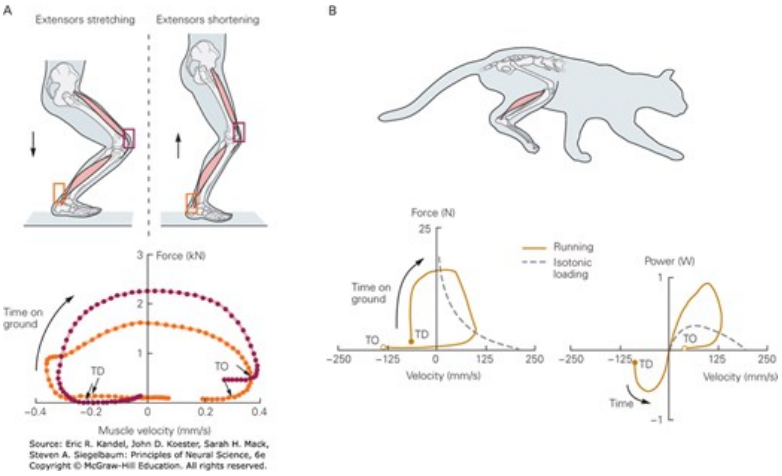
work. This activation sequence, the *stretch–shorten cycle,* occurs in many movements. When a person jumps in place on two feet, for example, the support phase involves an initial stretch (lengthening) and subsequent shortening of the ankle extensor and knee extensor muscles (Figure 31–17A). The forces in the Achilles and patellar tendons increase during the stretch of the lengthening contraction and reach a maximum at the onset of the shortening phase. As a result, the muscles can perform more positive work and produce more power during the shortening contraction (Figure 31–17B).

Figure 31–17

An initial phase of negative work augments subsequent positive work performed by the muscle. (Reproduced, with permission, from Finni, Komi, and Lepola 2000. Copyright © 2000, Springer-Verlag; Gregor et al. 1988.)

A. The force in the Achilles tendon (**orange**) and patellar tendon (**purple**) vary during the ground-contact phase of two-legged hopping. The feet contact the ground at touchdown (**TD**) and leave the ground at toe-off (**TO**). For approximately the first half of the movement, the quadriceps and triceps surae muscles lengthen, performing negative work (negative velocity). The muscles perform positive work when they shorten (positive velocity). The sites of force transducer measurements are indicated by rectangles.

B. The force exerted by the soleus muscle of a cat running at moderate speed varies from the instant the paw touches the ground (**TD**) until it leaves the ground (**TO**). The force exerted by the muscle during the shortening contraction (positive velocity) is greater than the peak forces measured when the muscle contracts maximally against various constant loads (isotonic loading). Negative velocity reflects a lengthening contraction in the soleus muscle. The power produced by the soleus muscle of the cat during running is greater than that produced in an isolated-muscle experiment (**dashed line**). The phase of negative power corresponds to the lengthening contraction just after the paw is placed on the ground (TD), when the muscle performs negative work.



Although negative work involves an increase in the length of the muscle, the length of the fascicles in the muscle often remains relatively constant, which indicates that the connective tissue structures are stretched prior to the shortening contraction. Thus, the capacity of the muscle to perform more positive work comes from strain energy that can be stored in the elastic elements of muscle and tendon during the stretch phase and released during the subsequent shortening phase. More strain energy can be stored in long tendons, but short tendons are more advantageous when the movement requires the rapid release of strain energy.

Highlights

1. The basic functional unit for the control of movement by the nervous system is the motor unit, which comprises a motor neuron and the muscle fibers it innervates.

2. The force exerted by a muscle depends in part on the number and properties of the motor units that are activated and the rates at which they discharge action potentials. The key motor unit properties include contraction speed, maximal force, and fatigability, all of which can be altered by physical activity. Motor unit properties vary continuously across the population that innervates each muscle; that is, there are not distinct types of motor units. Due to technological advances, it is becoming possible to characterize the adaptations exhibited by populations of motor units in

response to different types of changes in physical activity.

3. Motor units tend to be activated in a stereotypical order that is highly correlated with motor neuron size. The rate at which motor units are recruited during a voluntary contraction increases with contraction speed.

4. The rate at which a motor unit discharges action potentials in response to a given synaptic input can be modulated by descending inputs from the brain stem. The modulatory input is likely critical for establishing the level of excitation in spinal pathways, but this has been difficult to demonstrate in humans.

5. Except at low muscle forces, variation in discharge rate has a greater influence on muscle force than does the number of activated motor units. Moreover, the variability in discharge rate of the motor unit population influences the level of fine motor control.

6. The sarcomere is the smallest element of muscle to include a complete set of contractile proteins. A transient connection between the contractile proteins myosin and actin, known as the cross-bridge cycle, enables muscle to exert a force. The organization of the sarcomeres within a muscle varies substantially and, in addition to motor unit activity, has a major effect on the contractile properties of the muscle.

7. For a given arrangement of sarcomeres, the force a muscle can exert depends on the activation of the cross bridges by Ca^{2+}, the amount of overlap between the thick and thin filaments, and the velocity of the moving filaments. Sarcomere force during lengthening contractions is augmented by a Ca^{2+}-mediated increase in titin stiffness. The force produced by activated sarcomeres depends on the interactions of three filaments: actin, myosin, and titin.

8. Most of the force generated by activated sarcomeres is transmitted laterally through a network of noncontractile proteins that maintains the alignment of the thick and thin filaments.

9. The functional capability of a muscle depends on the torque that it can exert, which is influenced both by its contractile properties and by the location of its attachments on the skeleton relative to the joint that it spans.

10. To perform a movement, the nervous system activates multiple muscles and controls the torque exerted about the involved joints. The nervous system can vary the magnitude and direction of a movement by altering the amount of motor unit activity, and hence muscle torque, relative to the load acting on the body.

11. Although muscle exerts only a pulling force on the skeleton, it can do so whether the activated muscle shortens or is lengthened by a load torque that exceeds the muscle torque. The force capacity of muscle is greater during lengthening contractions. Motor unit activity differs during shortening and lengthening contractions, but little is known about how the synaptic inputs to motor neurons differ during these two types of contractions.

12. Faster movements elicit motion-dependent interactions between body parts that produce unwanted accelerations. These actions must be controlled by the nervous system to produce an intended movement.

13. The nervous system must coordinate the activity of multiple muscles to provide a mechanical link between moving body parts and the required support from the surroundings. The muscles engaged for each action, such as grasping, reaching, running, and walking, are organized into a few sets that exhibit a stereotypical pattern of activation, but it is not known why particular patterns are preferred.

14. The patterns of muscle activity vary substantially between movements and often include strategies that augment the work capacity of muscles. The patterns can be modified by experience, but little is known about the locus of the adaptations other than that both spinal and supraspinal pathways are involved.

Roger M. Enoka

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Chapter 34: Voluntary Movement: Motor Cortices

Introduction

IN THIS CHAPTER, WE DESCRIBE HOW the cerebral cortex uses sensory information from the external world to guide motor actions that allow the individual to interact with the surrounding environment. We begin with a general description of what we mean by the term voluntary movement and some theoretical frameworks for understanding its control, followed by the basic anatomy of the cortical circuits involved in voluntary motor behavior. We then consider how information related to the body, external space, and behavioral goals is combined and processed in parietal cortical regions. This is followed by a discussion of the role of premotor cortical regions in selecting and planning motor actions. Finally, we examine the role played by the primary motor cortex in motor execution.

Voluntary Movement Is the Physical Manifestation of an Intention to Act

Animals, including humans, have a nervous system not just so that they can sense their world or think about it, but primarily to interact with it to survive and reproduce. Understanding how purposeful actions are achieved is one of the great challenges in neuroscience. We focus here on the cerebral cortical control of voluntary motor behavior, in particular voluntary arm and hand movements in primates.

In contrast to stereotypical fixed-latency reflexive responses that are automatically triggered by incoming sensory stimuli (Chapter 32), voluntary movements are purposeful, intentional, and context-dependent, and are typically accompanied, at least in humans, by a sense of "ownership" of the actions, the sense that the actions have been willfully caused by the individual. Decisions to act are often made without an external trigger stimulus. Moreover, the continuous flux of events and conditions in the world presents changing opportunities for action, and thus voluntary action involves choices between alternatives, including the choice not to act. Finally, the same object or event can evoke different actions at different times, depending on the current context.

Throughout evolution, these features of voluntary behavior have become increasingly prominent in higher primates, especially in humans, indicating that the neural circuits controlling voluntary behavior in primates are adaptive. In particular, evolution has resulted in an increasing degree of dissociation of the physical properties of sensory inputs from their behavioral salience to the individual. Adaptation of the control circuits also enhances the repertoire of voluntary motor actions available to a species by allowing individuals to remember and learn from prior experience, to predict the future outcomes of different action choices, and to adopt new strategies and find new solutions to attain their desired goals. Volitional self-control over how, when, and even whether to act endows primate voluntary behavior with much of its richness and flexibility and prevents behavior from becoming impulsive, compulsive, or even harmful.

Voluntary behavior is the physical manifestation of an individual's intention to act on the environment, usually to achieve a goal immediately or at some point in the future. This may require single nonstereotypical movements or sequences of actions tailored to current conditions and to the longer-term objectives of the individual. The ability to use fingers, hands, and arms independent of locomotion further helps primates, and especially humans, exploit their environment. Most animals must search their environment for food when hungry. In contrast, humans can "forage" by using their hands to cook a meal or simply enter a few numbers on a cellphone to order food for delivery. Because large areas of the cerebral cortex are implicated in various aspects of voluntary motor control, the study of the cortical control of voluntary movement provides important insights into the purposive functional organization of the cerebral cortex as a whole.

Theoretical Frameworks Help Interpret Behavior and the Neural Basis of Voluntary Control

The neural processes by which individuals acquire information about their environment and the relationship of their body to it, decide how to interact with the environment to achieve short- or long-term goals, and organize and execute the voluntary movement(s) that will fulfill their goals are traditionally partitioned into three analytic components: Perceptual mechanisms generate an internal representation of the external world and the

individual within it, cognitive processes use this internal model of the world to select a course of action to interact with its environment, and the chosen plan of action is then relayed to the motor systems for implementation. This serial view of the brain's overall functional organization has long dominated neuroscience; this textbook, for example, has separate sections dedicated to perception, cognition, and movement.

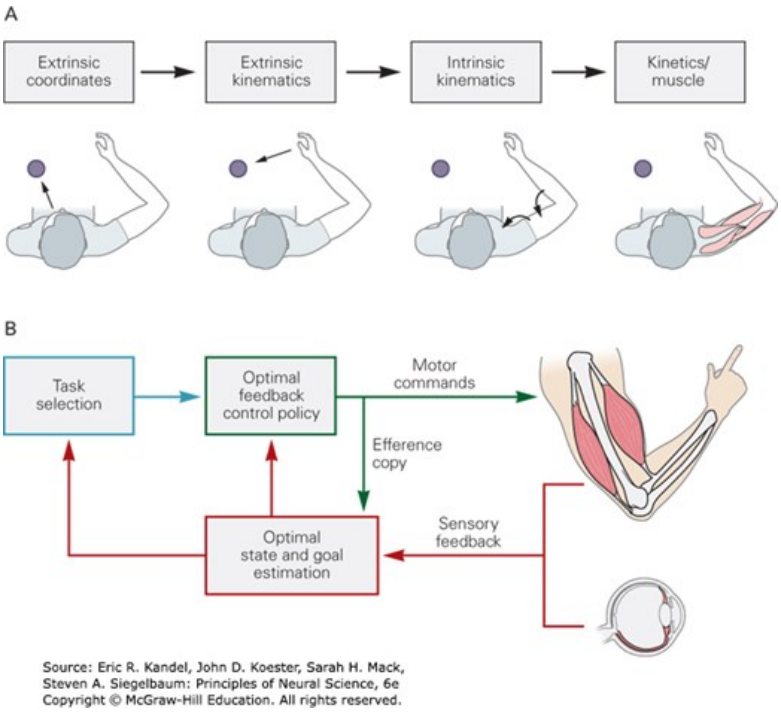
The brain must transform a goal into motor commands that realize the goal. For example, taking a sip of coffee requires the brain to convert visual information about the coffee cup and somatic information about the current posture and motion of your arm and hand into a pattern of muscle contractions that moves your hand to the cup, grasps it, and then lifts it to your mouth. Many behavioral and modeling studies suggest that this could be accomplished by a series of transformations of sensorimotor coordinates that convert the retinal image of the cup into motor commands (Figure 34–1A).

Figure 34–1

Theoretical frameworks for interpreting neural processing during voluntary motor actions.

A. The concept of sensorimotor transformations addresses the basic problem that tasks such as reaching to a visual target require the brain and spinal cord to convert sensory information about the spatial location of the target, initially represented in retinal coordinates, into patterns of muscle activity to move the limb to the target object. It is assumed that this sensorimotor transformation involves the use of intermediary representations—representation of the location of the target object relative to the body, the spatiotemporal trajectory of the hand (extrinsic kinematics), and motion of the joints (intrinsic kinematics) necessary to reach and grasp the object—before generating the patterns of neural activity that specify the causal forces (kinetics) or muscle activity.

B. Optimal feedback control recognizes three key processes for control. Optimal state and goal estimation (**red box**) integrates sensory feedback from various modalities along with an efference copy of motor commands to estimate the present position and motion of the body and objects in the world. Task selection (**blue box**) involves processes that identify behavioral goals based on internal desires and information about the state of the body and the world. Control policy (**green box**) determines the feedback gains, operations, and processes necessary to generate motor commands to control movement.



Variants of this sensorimotor transformation model have guided the design and interpretation of many studies on the control of voluntary arm movements. Neural recording studies, including many that will be described here, have found possible neural correlates of the motor parameters and sensorimotor transformations presumed to underlie movement planning and execution. This conceptual framework is an example of a *representational model* of brain function. Just as the activity of neurons in primary sensory areas appears to encode specific physical properties of

stimuli, the sensorimotor transformation model assumes that the activity of neurons in the motor system explicitly encodes or represents specific properties and parameters of the intended movement.

However, the sensorimotor transformation model has important limitations. Among them, the parameters and coordinate systems typically used in such models were imported from physics and engineering, rather than derived from the physiological properties of biological sensors and effectors. Furthermore, the model places all emphasis on strictly serial feedforward computations and relegates feedback circuits primarily to the detection and correction of performance errors after they are committed. The model also requires that every temporal detail of a movement be explicitly calculated before the motor system can generate any motor commands. Another limitation is its rigidity; it assumes that the same sequence of computations controls every movement in every context. Finally, this approach has not addressed how the proposed sensorimotor transformations could be implemented by neurons.

In recent years, theoretical studies of the motor system have been moving away from strictly representational models to more dynamical causal models. This approach begins with the premise that the functional architecture of motor control circuits evolved to generate movements, not to represent their parameters. These circuit properties were acquired by evolutionary changes in neural circuitry and by experience-dependent adaptive processes during postnatal development that produce the patterns of synaptic connectivity within the neural circuits that are necessary to generate the desired movements. Spinal and supraspinal motor circuits ensure that spinal motor neurons generate the appropriate muscle contraction signals across task conditions without relying on computational formalisms such as coordinate transformations.

One such theoretical framework is optimal feedback control (Figure 34–1B; and see Chapter 30). There are many different forms of optimal control, and each captures important aspects of control. Optimal feedback control, as the name implies, emphasizes the importance of feedback signals for the planning and control of movements. It is optimal in the sense that it emphasizes the importance of the behavioral goal and the current context in determining how best to plan and control movements. This flexibility can explain how human motor performance can be both highly variable and yet successful.

The optimal feedback control framework also divides the control of voluntary movements into three key processes: state estimation, task selection, and control policy (Figure 34–1B). State estimation involves forward internal models that use efference copies of motor commands and external sensory feedback to provide the best estimate of the present state of the body and the environment (Chapter 30). Task selection involves the neural processes by which the brain chooses a behavioral goal in the current context and what motor action(s) might best attain that goal. This selection can be based on the sensory evidence supporting alternative actions and alternate options to attain the goal, and on other factors that influence the optimal response such as motivational state, task urgency, preferences, relative benefits versus risks, the mechanical properties of the body and environment, and even the biomechanical costs of different action choices. Finally, the control policy provides the set of rules and computations that establish how to generate the motor commands to attain the behavioral goal given the present state of the body and the environment. Importantly, the control policy process in optimal feedback control is not a series of pure feedforward computations to calculate every instantaneous detail of a desired movement trajectory and associated muscle activity patterns before movement onset. Instead, it involves context- and time-dependent adjustments to feedback circuit gains that allow the spatiotemporal form of muscle activity to emerge dynamically in real time as part of the control process underlying movement generation.

The sensorimotor transformation and optimal feedback control models are not mutually incompatible hypotheses. Optimal feedback control explains certain features of motor behavior but is largely agnostic as to the neural implementation for control. It assumes that motor circuits are dynamical systems that attain desired goals under varying task constraints. As a result, a given neuron may contribute to sensorimotor control in different task conditions, but its activity may not correspond to a specific movement parameter in a definable coordinate framework. In contrast, sensorimotor transformation models do not fully explain how real-time movement control is implemented by motor circuits, but emphasize the need to convert information from sensory signals to motor commands.

Even if the neural control system is dynamical, the system it controls—the musculoskeletal plant—is a physical object that must obey the universal physical laws of motion. Thus, neural activity should show correlations with those physical parameters and laws that will help to infer how those neurons are contributing to voluntary motor control, even if they are not attempting to encode those terms. Indeed, experimental tasks that dissociate different types of movement-related information have revealed important differences in how neural activity in different cortical motor regions correlates with different movement properties and different aspects of movement planning and execution. Finally, we can impose arbitrary volitional control on how we move. For example, we can choose to make an unobstructed reaching movement efficiently along a straight path to the target or whimsically along a complex curved path even though there is no obstacle to avoid and the movement is energetically costly. The experimental

challenge is to reveal how the brain can implement this willful control with neurons and neural circuits.

Many Frontal and Parietal Cortical Regions Are Involved in Voluntary Control

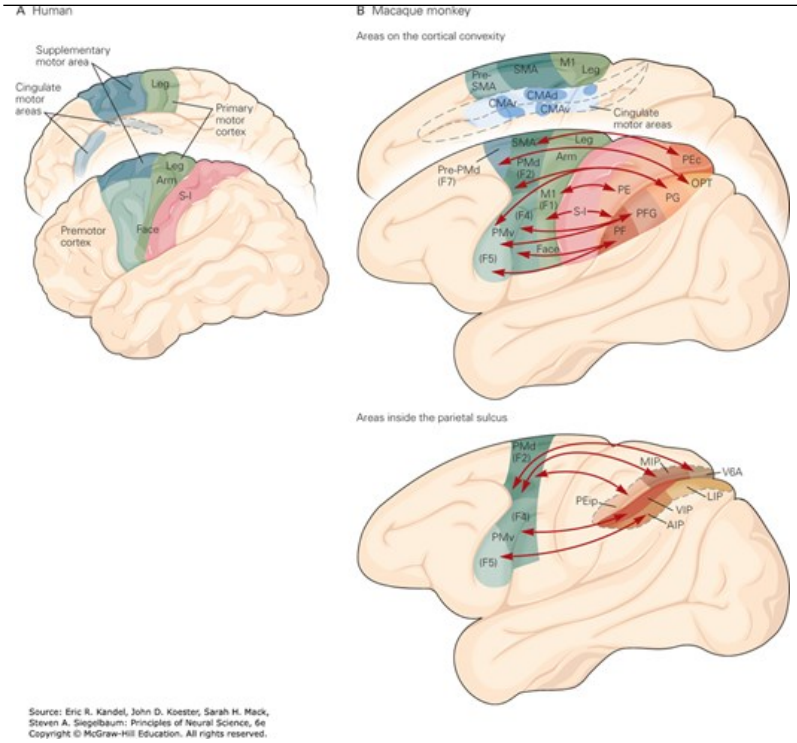
Here we describe the regions of frontal and parietal cortex that convert sensory inputs into motor commands to produce voluntary movement. We then examine the neural circuits involved in the voluntary control of arm and hand movements that are prominent components of the motor repertory of primates. We focus on studies in the rhesus monkey (*Macaca mulatta*), as much of our knowledge of the cortical control of the arm and hand comes from this species and the neural circuity underlying human voluntary control appears to have a similar organization. Many other neural structures, including the prefrontal cortex, the basal ganglia, and cerebellum, also play critical roles in the global organization of goal-directed voluntary behavior (Chapters 37 and 38).

Several different nomenclatures have been used in partitioning the precentral, postcentral, and parietal cortex, based on regional differences in cytoarchitectonic and myeloarchitectonic details, cortico-cortical connectivity, the distribution of different marker molecules, and regional differences in neural response properties. Here we will use some of the more widely accepted terminology without describing approximate homologies among the various nomenclatures.

Based on the pioneering cytoarchitectonic studies of humans by Brodmann, the different lobes of the monkey's cerebral cortex were divided into smaller regions, including two in precentral cortex (areas 4 and 6), four in the postcentral cortex (areas 1, 2, 3a, and 3b), and at least two in the superior and inferior parietal cortex (areas 5 and 7). While these cytoarchitectonic divisions persist in the literature, subsequent anatomical and functional studies have radically changed the view of how the precentral and parietal cortices are organized (Figure 34–2).

Figure 34–2

Parietal and frontal motor areas that support voluntary control. For illustration purposes, the intraparietal sulcus is opened in the bottom panel. The parietal areas are designated in Constantin von Economo's terminology by the letter **P** (parietal), followed by letters instead of numbers to indicate the cytoarchitectonically different areas. Areas PF and PFG roughly correspond to Brodmann's area 7b, and areas PG and OPT to Brodmann's area 7a. Areas inside the intraparietal sulcus include the anterior, lateral, medial, and ventral intraparietal areas (**AIP**, **LIP**, **MIP**, **VIP**, respectively), as well as the PE intraparietal area (**PEip**) and visual area 6A (**V6A**). **Arrows** show the patterns of the principal reciprocal connections between functionally related parietal and frontal motor areas. (Abbreviations: **CMAr**, rostral cingulate motor area; **CMAv**, ventral cingulate motor area; **CMd**, dorsal cingulate motor area; **F**, frontal; **M1**, primary motor cortex; **OPT**, occipito-parieto-temporal; **P**, parietal; **PE**, **PF**, and **PFG** are parietal areas according to the nomenclature of von Economo; **PMd**, dorsal premotor cortex; **PMv**, ventral premotor cortex; **Pre-PMd**, predorsal premotor cortex; **S-I**, primary somatosensory cortex; **SMA**, supplemental motor area.)



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e
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Current maps usually place the *primary motor cortex* (M1), the cortical region most directly involved in motor execution in primates, in Brodmann's area 4. Brodmann's area 6 is now typically divided into five or six functional areas that are principally involved in different aspects of the planning and control of motor actions of different parts of the body. Arm-control regions include the *dorsal premotor cortex* (PMd) and *predorsal premotor cortex* (pre-PMd), in the caudal and rostral parts of the dorsal convexity of lateral area 6, respectively. Hand-control regions include the *ventral premotor cortex* (PMv), found on the ventral convexity of area 6, which has been further divided into two or three smaller subregions. A variety of functions related to motor selection, sequencing, and initiation have been found in medial premotor cortical regions. These include a region on the medial surface of the cortical hemisphere that was originally called the secondary motor cortex by Woolsey and colleagues, who discovered it, but is now called the *supplementary motor area*. This region is in turn split into two regions, a *supplementary motor area proper* (SMA) in the caudal part and a *presupplementary motor area* (pre-SMA) in the rostral part. Outside of Brodmann's area 6, three additional motor areas, the dorsal, ventral, and rostral cingulate motor areas (CMAd, CMAv, and CMAr, respectively), are also involved in motor selection but have not been as well studied as more lateral premotor areas.

The *primary somatosensory cortex* (S-I; including areas 1, 2, 3a, and 3b) is located in the anterior postcentral gyrus. It processes cutaneous and muscle mechanoreceptor signals from the periphery and transmits that information to other parietal and precentral cortical regions (Chapter 19). Like area 6, Brodmann's parietal areas 5 and 7 are now divided into several regions within and adjacent to the intraparietal sulcus (IPS), each of which integrates various types of sensory information about the body or spatial goals for voluntary motor control. These include parietal lobe areas PE and PEc on the rostral or superior bank, and PF, PFG, PG, and OPT on the caudal, inferior bank. Areas inside the IPS include the anterior, lateral, medial, and ventral intraparietal areas (AIP, LIP, MIP, and VIP, respectively) as well as intraparietal area PEip and higher visual area V6A.

These precentral, postcentral, and parietal cortical regions are interconnected by complex patterns of reciprocal, convergent, and divergent projections. The SMA, PMd, and PMv have somatotopically organized reciprocal connections not only with M1 but also with each other. Both the SMA and M1 receive somatotopically organized input from S-I and the dorsorostral parietal cortex, whereas PMd and PMv are reciprocally connected with progressively more caudal, medial, and lateral parts of the parietal cortex. These somatosensory and parietal inputs provide the primary motor and caudal premotor regions with sensory information related to behavioral goals, target objects, and the position and motion of the body that is used to plan and guide motor acts.

In contrast, pre-SMA and pre-PMd project to SMA and PMd but do not project to M1 and are only weakly connected with the parietal lobe. They instead have reciprocal connections with prefrontal cortex and so may impose more arbitrary context-dependent control over voluntary behavior. Prefrontal cortex is also connected with other premotor cortical regions.

The control of hand and arm motor actions is implemented by partially segregated parallel circuits distributed across several parietal and precentral motor areas. Hand motor function is generally supported by frontoparietal circuits that are located more laterally, notably AIP and PMv. In contrast, proximal arm motor function is supported by circuits that are more medial, notably parietal areas PE and MIP and precentral areas PMd, SMA, and pre-SMA.

Descending Motor Commands Are Principally Transmitted by the Corticospinal Tract

Older textbooks often referred to the primary motor cortex (M1) as the "final common path." Other cortical motor areas were thought to influence voluntary movements via their projections to M1, which then formulated the descending motor command that was transmitted to the spinal cord. This is not correct.

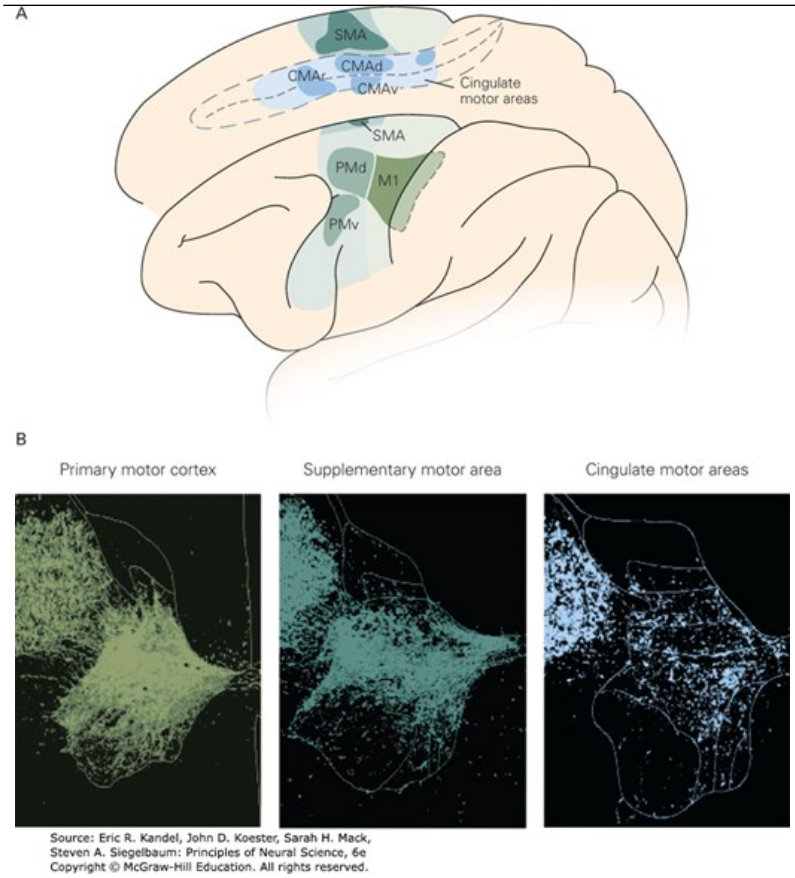
Several cortical motor regions outside of M1 project to subcortical areas of the brain as well as to the spinal cord in parallel with the descending projections from M1. The key descending pathway for voluntary control is the *pyramidal tract*, which originates in cortical layer V in a number of precentral and parietal areas. The pyramidal tract contains axons that terminate in brain stem motor structures (the *corticobulbar tract*) and axons that project down to the spinal cord (*corticospinal tract*). Precentral areas include not only M1 but also SMA, PMd, PMv, and the cingulate motor areas (Figure 34–3). Descending fibers from S-I and parietal areas, including PE and PFG, also travel in the pyramidal tract. The pre-SMA and pre-PMd do not send axons directly to the spinal cord; instead, their descending outputs reach the spinal cord indirectly through projections to other subcortical structures.

Figure 34–3

Cortical origins of the corticospinal tract. (Reproduced, with permission, from Dum and Strick 2002. Copyright © 2002 Elsevier Science Inc.)

A. Corticospinal neurons that modulate muscle activity in the contralateral arm and hand originate in the parts of the primary motor cortex (**M1**) motor map and many subdivisions of the premotor cortex (**PMd**, **PMv**, **SMA**) that are related to arm and hand movements (indicated by the darker zones). The axons from these areas project into the spinal cord cervical enlargement (see part **B**). Corticospinal fibers projecting to the leg, trunk, and other somatotopic parts of the brain stem and spinal motor system originate in the other parts of the motor and premotor cortex, indicated by the lighter zones. (Abbreviations: **CMAd**, dorsal cingulate motor area; **CMAr**, rostral cingulate motor area; **CMAv**, ventral cingulate motor area; **M1**, primary motor cortex; **PMd**, dorsal premotor cortex; **PMv**, ventral premotor cortex; **SMA**, supplementary motor area.)

B. Transverse sections of the spinal cord at the level of the cervical enlargement in monkeys after injection of the anterograde tracer horseradish peroxidase into different arm-related cortical motor regions to label the distribution of corticospinal axons arising from each cortical region. The corticospinal axons from the primary motor cortex (*left*), supplementary motor area (*middle*), and cingulate motor areas (*right*) all terminate on interneuronal networks in the intermediate laminae (V–VIII) of the spinal cord. Only the primary motor cortex contains corticospinal neurons (corticomotoneuronal cells) whose axons terminate directly on spinal motor neurons in the most ventral and lateral part of the spinal ventral horn (Rexed's lamina IX). Rexed's laminae I to IX of the dorsal and ventral horns are shown in faint outline in each section. The dense cluster of labeled axons adjacent to the dorsal horn (*upper left*) in each section are corticospinal axons descending in the dorsolateral funiculus, before entering the spinal intermediate and ventral laminae.



Most corticospinal tract axons originating in one hemisphere cross to the other side of the midline (decussate) at the pyramid in the caudal medulla, and from there project to the spinal cord itself, forming the lateral corticospinal tract. A small portion does not decussate and forms the ventral corticospinal tract. Many corticospinal axons in primates, and virtually all corticospinal axons in other mammals, terminate only on spinal interneurons and exert their influence on voluntary movement indirectly through spinal interneuronal and reflex pathways. In monkeys, all corticospinal axons from premotor cortical areas and many from M1 terminate on interneurons in the spinal intermediate zone, whereas postcentral and parietal areas target interneurons in the dorsal horn. The terminal endings of a sizeable portion of the corticospinal axons arising from M1 in primates, but not other mammals, arborize at their targets and synapse directly on spinal alpha motor neurons that in turn innervate muscles; these M1 neurons with direct monosynaptic projections to spinal motor neurons are called *corticomotoneuronal cells*.

Any voluntary arm movement can have destabilizing effects on the rest of the body due to mechanical interactions between body segments. Thus, control of voluntary arm movements requires coordination with neural circuits responsible for the control of posture and balance. This is mediated by descending projections from cortical motor areas to the reticular formation, which in turn project to the spinal cord via the reticulospinal tract (Chapters 33 and 36).

Imposing a Delay Period Before the Onset of Movement Isolates the Neural Activity Associated With Planning From That Associated With Executing the Action

Voluntary movement requires the intervention of a number of neural processes between the arrival of salient sensory inputs and the initiation of an appropriate motor response. With the development in the 1960s of single-cell recording in the cerebral cortex of awake animals, tasks that experimentally manipulate different attributes of movements have been used to study every cortical area involved in the control of arm and hand movements to try to identify neural correlates of the presumed control processes in each area.

In “reaction-time” tasks, animals make a prespecified response when they detect a particular stimulus, such as reaching to a target when it appears (Figure 34–4A). The stimulus informs the animal both what movement to make and when to make it. However, reaction times in such tasks are typically short, often less than 300 ms, and most or all putative planning stages leading up to the initiation of the movement are accomplished within that brief time. This makes it very difficult to discern what kinds of information are represented in the activity of the neurons at each given moment and thus to

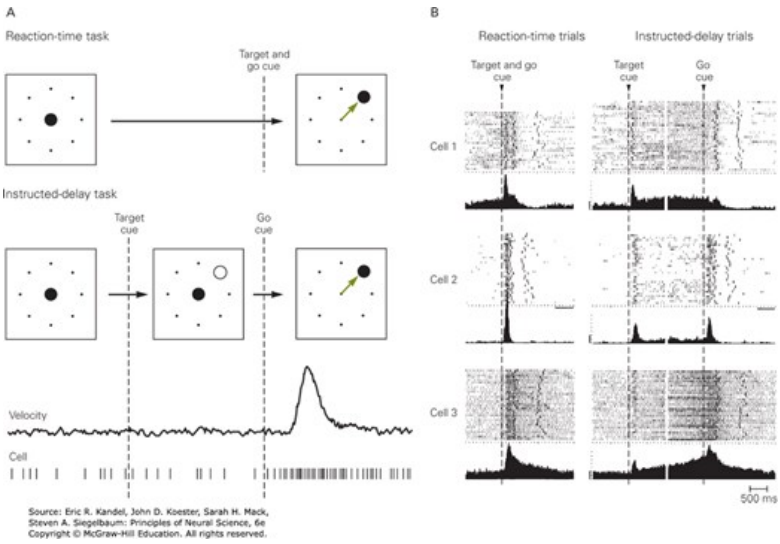
what processes they are contributing (Figure 34–4B).

Figure 34–4

Neural processes related to movement planning and movement execution can be dissociated in time. (Reproduced, with permission, from Crammond and Kalaska 2000.)

A. In a *reaction-time task*, a sensory cue instructs the subject both where to move (target cue) and when to move (go cue). All neural operations required to plan and initiate the execution of the movement are performed in the brief time between the appearance of the cue and the onset of movement. In an *instructed-delay task*, an initial cue tells the subject where to move, and only later is the go cue given. The knowledge provided by the first cue permits the subject to plan the upcoming movement. Any changes in activity that occur after the first cue but before the second are presumed to be neural correlates of the planning stage.

B. Movement planning and execution are not completely segregated at the level of single neurons or neural populations in a given cortical area. Raster plots and cumulative histograms show the responses of three premotor cortex neurons to movements in each cell's preferred direction during reaction-time trials and instructed-delay trials. In the raster plots, each row represents activity in a single trial. The thin tics in each raster row represent action potentials, and the two thicker tics show the onset and end of movement. In reaction-time trials, the monkey does not know in which direction to move until the target appears. In contrast, in instructed-delay trials, an initial cue informs the monkey where the target lies well in advance of the appearance of a second signal to initiate the movement. During the delay period, activity in many premotor cells shows directionally tuned changes that signal the direction of the impending delayed movement. The activity in cell 1 appears to be strictly related to the planning phase of the task, for there is no execution-related activity after the go signal in the instructed-delay task. The other two cells show different degrees of activity related to both planning and execution.



However, a critical feature of voluntary behavior is that movement initiation is not obligatory the instant an intention to act is formed. This volitional control over the timing of movement has been exploited by so-called "instructed-delay" motor tasks (Figure 34–4A), in which an instructional cue informs the animal about specific aspects of an impending movement such as the location of a target, but the animal must withhold the response until a delayed stimulus signals when to make the movement. This protocol allows researchers to dissociate in time the neural processes associated with the early stages of planning the intended act from those that are directly coupled in real time to the initiation and control of the movement.

As expected, neurons in all the movement-related cortical areas discharge prior to and during movement execution in reaction-time tasks (Figure 34–4B), and their activity correlates systematically with different properties of movements, such as their direction, velocity, spatial trajectory, and causal forces and muscle activity. Critically, however, many neurons in the same areas also signal information about an intended motor act during an instructed-delay period long before its initiation (Figure 34–4B). Thus, even though planning and execution are distinct serial stages in voluntary motor control, they are not implemented by distinct neural populations in different cortical areas. Moreover, even a well-trained monkey will occasionally make the wrong movement in response to an instructional cue. In those trials, the activity during the delay period generally predicts the erroneous motor response that the monkey will eventually make. This is compelling evidence that the activity is a neural correlate of the monkey's motor

intentions, not a passive sensory response to the instructional cues.

Parietal Cortex Provides Information About the World and the Body for State Estimation to Plan and Execute Motor Actions

Sensory information is essential for selecting appropriate and effective actions. Before drinking from a cup, the brain uses visual input to identify which object is the cup, where it is located relative to the body, and its physical properties such as size, shape, and handle orientation. In addition, information about the current posture and motion of the arm and hand is provided by integrating proprioceptive signals from the limb with efference copies of motor commands (Chapter 30). Finally, cutaneous signals are critical when interacting manually with objects, such as grasping and lifting the cup.

Several lines of evidence implicate the parietal cortex as a key brain region in sensory processing for motor action. The parietal lobe, especially PE, PEip, and MIP, receives strong somatic sensory inputs about body posture and movement from S-I. Several parietal regions along and within the IPS are major components of the dorsal visual pathway, which processes visuospatial information about objects that guides arm and hand movements while reaching to, grasping, and manipulating them. The parietal lobe is also reciprocally interconnected with precentral cortical motor areas to provide the precentral cortex with signals for the sensory guidance of movement and to receive efference copies of motor commands from those same precentral areas. Finally, human subjects with lesions of the posterior parietal cortex often demonstrate specific impairments in using sensory information to guide motor action (Box 34–1).

Box 34–1 Lesion Studies of Posterior Parietal Cortex Lead to Deficits in the Use of Sensory Information to Guide Action

Naturally occurring or experimentally induced lesions have long been used to infer the roles of different neural structures. However, the effects of lesions must always be interpreted with caution. It is often incorrect to conclude that the function perturbed by an insult to a part of the motor system resides uniquely in the damaged structure or that the injured neurons explicitly perform that function. Furthermore, the adverse effects of lesions can be masked or altered by compensatory mechanisms in remaining, intact structures. Nevertheless, lesion experiments have been fundamental in differentiating the functional roles of brain regions.

Behavioral studies by Goodale, Milner, Rossetti, and others on patients with parietal cortical damage have led to the conclusion that a primary function of the parietal lobe is to extract sensory information about the external world and one's own body for the planning and guidance of movements. Such studies have shown that patients with lesions of certain parts of the parietal lobe suffer specific deficits in the ability to direct their arm and hand accurately to the spatial location of objects and to shape the orientation and grip aperture of the hand prior to grasping it.

They have also shown a particularly severe deficit in the ability to make rapid adjustments to their ongoing reach and grasping actions in response to unexpected changes in the location or orientation of the target object. This visual guidance of action is provided by visual signals that are routed through the dorsal visual stream and may operate in parallel with and independently of perceptual processes evoked by the visual inputs that are routed simultaneously through the ventral visual stream in the temporal lobe. For instance, whereas our visual perception of the size and orientation of objects can be deceived by certain perceptual illusions, the motor system often behaves as if it is not fooled and makes accurate movements.

The Parietal Cortex Links Sensory Information to Motor Actions

We experience the space that surrounds us as a single unified environment within which objects have specific locations relative to each other and to ourselves. Classical neurology suggested that the parietal lobe constructed a unified multimodal neural representation of the world by integration of inputs from different sensory modalities. This single map of space was assumed to provide all the information necessary both for spatial perception and for the sensory guidance of movement, and so was shared by the different motor circuits that controlled different parts of the body, such as the eyes, arm, and hand.

However, the idea that the parietal cortex contains a single topographically organized representation of space is incorrect. Instead, the posterior parietal cortex contains several distinct functional areas that work in parallel and receive different combinations of sensory and motor inputs related

to the guidance of movement of different effectors, such as the eyes, arm, and hand. Neurons in these areas are often multimodal, with both visual and somatic sensory receptive fields, and also discharge preferentially prior to and during movements of a specific effector. Each functional area is connected to frontal motor regions involved in control of the same effectors. Finally, each region is not topographically organized in the familiar sense of a faithful point-to-point representation of surrounding space, but rather comprises a complex mixture of neurons with different sensory inputs that may contribute to the multisensory integration required to guide motor actions with the environment.

Body Position and Motion Are Represented in Several Areas of Posterior Parietal Cortex

The S-I and adjacent superior parietal cortex regions PE, MIP, and PEip are a major source of proprioceptive and tactile sensory information about the position and motion of body parts. Neurons in S-I areas 1 and 2 typically respond to tactile input from a limited part of the contralateral body or to movements of one or a few adjacent joints in specific directions.

In contrast, many PE and MIP neurons discharge during passive and active movements of multiple joints. Some cells also respond during combined movements of multiple body parts, including bilateral movements of both arms. Many PE and MIP neurons also have large tactile receptive fields whose responses are modulated by context during limb movement or posture. For instance, a neuron with a tactile receptive field that covers the entire glabrous (palmar) surface of the hand may only respond to physical contact with an object when the hand is close to the body and not when it touches the object with the arm fully extended.

These findings indicate that while area 1 and 2 neurons encode the positions and movements of specific body parts, superior parietal neurons integrate information on the positions of individual joints as well as the positions of limb segments with respect to the body. This integration creates a neural “body schema” that provides information on where the arm is located with respect to the body and how different arm segments are positioned and moving with respect to one another. This body schema is critical for selecting how to attain behavioral goals and for ongoing control of movement.

For instance, a key requirement for efficient reaching is knowledge of where the arm is before and during the reach. Monkeys with experimental lesions in Brodmann’s area 2 and the adjacent superior parietal lobule (area 5 or PE) show deficits in reaching to and manipulating objects under proprioceptive and tactile guidance without vision. Human patients with similar lesions show the same deficit, without the spatial neglect that is a common consequence of more lateral lesions in the inferior parietal lobe.

Spatial Goals Are Represented in Several Areas of Posterior Parietal Cortex

Functional areas within the IPS are strongly implicated in the processing of spatial, especially visual, information relevant to action. Each of these areas has unique ways of representing objects and spatial goals relative to the body and contributes to controlling motor actions of different parts of the body. For instance, many neurons in the lateral intraparietal area (LIP) receive visual input from extrastriate cortical areas. Their receptive fields are fixed in retinal coordinates and shift to new spatial locations whenever the monkey changes its direction of gaze. Neural responses also often increase when the animal attends to a stimulus within the receptive field even without looking at it, and they often discharge prior to a saccade that is directed toward a visual stimulus in their receptive field (Figure 34–5A; and see Chapter 35).

Figure 34–5

Neurons in the parietal cortex of the monkey are selective for the location of objects in the visual field relative to particular parts of the body. Each histogram represents the firing rate of a representative neuron as a function of time following presentation of a stimulus. In each diagram, the line emanating from the eyes indicates where the monkey is looking.

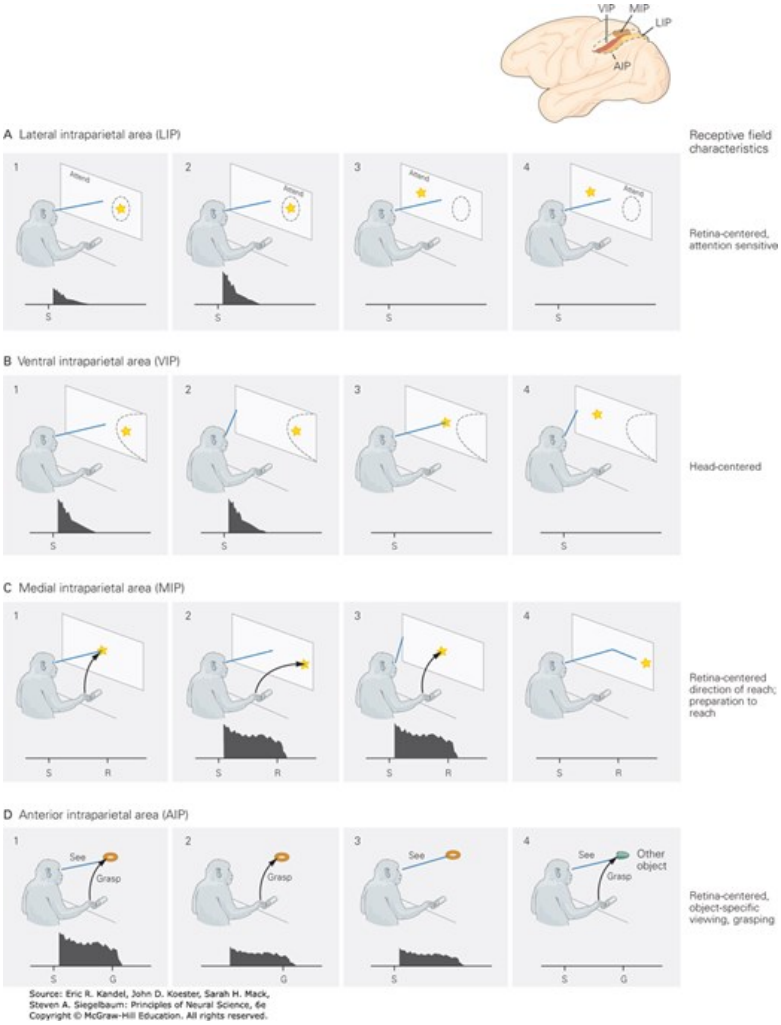
A. Neurons in the lateral intraparietal area have *retina-centered* receptive fields. The strength of the visual response depends on whether the monkey is paying attention to the stimulus (**S**). The neuron fires when a light is flashed inside its receptive field (**dotted circle**) (**1**). The response is more robust if the monkey is instructed to attend to the location of the stimulus (**2**). The neuron does not fire if the stimulus is presented outside the receptive field, regardless of where attention is directed (**3**, **4**).

B. In the ventral intraparietal area, some neurons have *head-centered* receptive fields. This is determined by keeping the head in a fixed position while the monkey is instructed to shift its gaze to various locations. This neuron fires when a light appears to the right of the midline of the head (**1**, **2**). It does not fire when the light appears at another location relative to the head, such as the midline or to the left. (**3**, **4**). The critical contrast is between situations 1 and 4. The retinal location of the light is the same in both (slightly to the right of the fixation point), yet the neuron fires in 1, when the

stimulus is to the right of the head, but not in 4, when the stimulus is to the left of the head.

C. In the medial intraparietal area, neurons are selective for the retina-centered direction of the reach (**R**) and fire when the monkey is preparing to reach for a visual target. This neuron fires when the monkey reaches for a target to the right of where he is looking (**2**, **3**). It does not fire when he reaches for a target at which he is looking (**1**) or when he moves only his eyes to the target at the right (**4**). The physical direction of the reach is not a factor in the neuron's firing: It is the same in 1 and 3, and yet, the neuron fires only in 3.

D. In the anterior intraparietal area, neurons are selective for objects of particular shapes and fire when the monkey is looking at or preparing to grasp (**G**) an object. This neuron fires when the monkey is viewing a ring (**3**) or making a memory-guided reach to it in the dark (**2**). It fires especially strongly when the monkey is grasping the ring under visual guidance (**1**). It does not fire during viewing or grasping of other objects (**4**).



Several parietal regions are preferentially implicated in the control of arm and hand movements. For instance, the most medial regions of the superior parietal cortex, areas V6A and PEc, receive input from extrastriate visual areas V2 and V3. Many V6A and PEc neurons have visual receptive fields in retinal coordinates, but their activity is also frequently modulated by the direction of gaze, the current arm posture, and the direction of reaching movements.

The ventral intraparietal area (VIP) in the fundus of the IPS receives inputs from two components of the dorsal visual stream, the medial temporal cortex and medial superior temporal cortex, which are involved in the analysis of optic flow and visual motion. Many VIP neurons respond to visual stimuli and somatosensory stimuli with receptive fields on the face or head and, in some cases, on the arm or trunk. Neural activity is in head-centered coordinates, as somatosensory and visual information remains in register even if the eyes move to fixate different spatial locations (Figure 34–5B). Some VIP neurons respond to both visual and tactile stimuli moving in the same direction, whereas others are strongly activated by visual stimuli that move toward their tactile receptive field but only if the path of motion will eventually intersect the tactile receptive field. These neurons may allow the

monkeys to link the location and motion of objects in their immediate peripersonal space with different parts of their body.

Another area of parietal cortex related to reaching is the parietal reach region (PRR). The PRR likely corresponds to the medial intraparietal cortex (MIP) and adjacent arm-control parts of the superior and inferior parietal cortex. The activity of many PRR neurons varies with the location of reach targets relative to the hand. However, this signal is not fixed to the current location of the hand or target but rather on the current direction of gaze (Figure 34–5C). Each time the monkey looks in a different direction, the reach-related activity of PRR neurons changes, even if the location of the target and hand and the required reach trajectory do not change. In contrast, the reach-related activity of many neurons in areas PE and PEip is less related to gaze and more strongly related to the current hand position and arm posture. PE and PEip neurons thus provide a more stable signal about the location of the reach target relative to the current position of the hand compared to PRR.

Finally, neurons in the anterior intraparietal area (AIP) are primarily implicated in object grasping and manipulation by movements of the hand. Many AIP neurons are preferentially active while reaching for and grasping objects of particular shapes, sizes, and spatial orientations, and often even while viewing those objects before grasping them (Figure 34–5D). There is a broad range of neural response properties, from neurons that respond almost exclusively to visual input about the objects but not to the grasping actions to neurons that discharge only during the hand movements themselves even in the dark. This suggests that the AIP contains neural circuits that begin to transform visual information about the physical properties of an object that are relevant to how it could be handled—what James Gibson has called the object's *affordances*—into appropriate hand actions (Chapter 56).

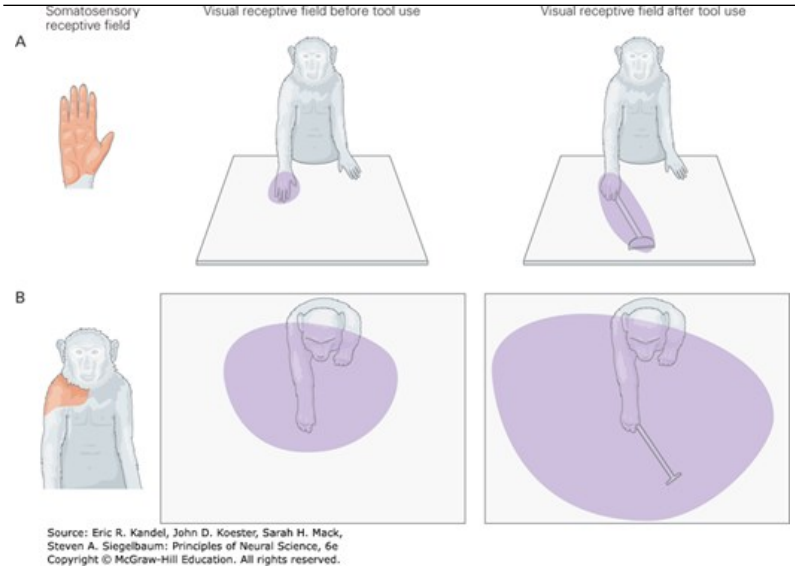
A fascinating discovery about the parietal cortex is that the receptive fields of neurons can be altered by individual experience, such as tool use. Monkeys were trained to retrieve food pellets that were out of normal reach of the arm and hand by using a rake-shaped tool. Many VIP neurons normally respond to visual objects when they are either located near the current position of the hand or anywhere within reach with the arm. After training, their visual receptive fields transiently expand to incorporate the tool when the monkey grasps it, as if the distal end of the tool had become a functional extension of the monkey's own hand and arm (Figure 34–6).

Figure 34–6

Some neurons in the parietal cortex of the monkey have receptive fields that dynamically expand once a tool is grasped. (Adapted from Maravita and Iriki, 2004.Copyright © 2003 Published by Elsevier Ltd.)

A. The **orange** area on the hand (*left*) indicates the somatosensory receptive field for a neuron. The **purple** area (*middle*) indicates the neuron's visual receptive field (vRF) region around the hand. The vRF is anchored to the hand and changes spatial location whenever the monkey moves its arm. The vRF expands when the monkey grasps a rake after it has learned how to use the rake to reach for objects in the workspace (*right*).

B. A single neuron that has a shoulder-centered bimodal somatosensory (**orange**) and visual (**purple**) receptive field is illustrated. The vRF for this neuron (*middle*) is larger than the one shown in part **A**, possibly reflecting the potential workspace related to whole-arm function. The vRF also expands to incorporate the extended workspace permitted by use of a rake (*right*).



Internally Generated Feedback May Influence Parietal Cortex Activity

The delays involved in the transmission of visual and somatic feedback about arm movements from the periphery to cortical circuits can lead to oscillations or even instabilities in real-time sensorimotor control. One theoretical solution to this problem is to use a forward internal model to make predictive estimates of body motion based on internal efference copies of outgoing motor commands as well as from slower peripheral feedback signals (Chapter 30).

Several lines of evidence suggest that parietal cortex circuits, along with the cerebellum (Chapter 37), may implement a similar solution. Many reach-related neurons in PE, MIP, and PRR are active not only in response to passive sensory inputs but also before the onset of movement and during the instructed-delay period of delayed-reaching tasks. These responses suggest that these neurons process centrally generated signals about motor intentions prior to movement onset. This premovement activity is often interpreted as evidence that the parietal cortex generates feedforward signals that contribute to the early planning of movements. However, an alternate interpretation is that the premovement activity is driven by an efference copy of the motor command for the intended movement that is transmitted into the parietal cortex via its reciprocal connections with precentral motor areas. This combination of peripheral sensory inputs and central efference copies could permit some parietal reach-related circuits to compute a continuously updated estimate of the current state of the arm and its position relative to the behavioral goal. This estimate could be used to make rapid corrections for errors in ongoing arm movements.

Whether the parietal circuits are primarily involved in the formation of a subject's motor intentions or in state estimation will depend on the origin of its premovement activity. If it is mainly generated within the parietal cortex itself, this will strongly implicate the parietal cortex in the planning of intended movements. In contrast, if it is primarily driven by an efference copy relayed from precentral motor areas, this would strongly implicate the parietal circuits in state estimation, including predicting how the arm should move in response to the motor command.

Premotor Cortex Supports Motor Selection and Planning

As outlined at the beginning of this chapter, a decision to act in a particular way in a given situation is shaped by many factors, including sensory information about objects, events, and opportunities for action from the environment, body position and motion, internal motivational states, prior experiences, reward preferences, and learned arbitrary rules and strategies linking sensory inputs to motor actions. There can be many reasons why you want to drink some coffee, and that desire can be fulfilled by actions ranging from simply reaching out to your full coffee cup to making coffee at home or going to a café.

Frontal premotor cortical regions just rostral to M1 play an important role in early movement planning or task-selection processes. Many neurons in those areas, such as the PMd neurons shown in Figure 34–4, generate activity during instructed-delay tasks that reflect the motor intentions of the monkey and even the factors that influenced those action choices. The different premotor cortical regions are presumed to make different but overlapping contributions to motor selection and planning. For instance, the lateral premotor cortex, including PMd and PMv, have traditionally been

implicated in actions initiated and guided by external sensory inputs. In contrast, medial premotor areas, including SMA, pre-SMA, and CMA, have been implicated in the control of self-initiated movements as well as the suppression of actions. However, the distinction between their respective contributions is not absolute.

Medial Premotor Cortex Is Involved in the Contextual Control of Voluntary Actions

Clinton Woolsey's pioneering electrical stimulation studies showed that, in addition to the motor map in M1, the medial wall of the frontal cortex contains an array of neurons that also regulate body movements. This medial motor map, now called the supplementary motor area (SMA), includes the entire contralateral body but is coarser than the detailed map in M1, as described later. Strong stimulus currents are required to evoke movements, which are often complex actions such as postural adjustments or stepping and climbing and can involve both sides of the body. Today, there is agreement that this region contains two areas that have distinct cytoarchitectonic characteristics, axonal connections, and functional properties: a more caudal SMA proper and a more rostral presupplementary motor area (pre-SMA), which we will collectively call the supplementary motor cortex (SMC).

The SMC has been implicated in many aspects of voluntary behavior, although its contribution remains controversial. Several lines of evidence support a role in self-initiated behavior. In humans, electrical stimulation of SMC below the threshold for movement initiation can evoke an introspective sense of an urge to move that does not arise during M1 stimulation. Lesions of SMC produce problems initiating desired movements or suppressing undesirable movements (Box 34–2). Moreover, recordings of slow cortical potentials at the surface of the skull during the execution of self-paced movements show that the initial potential arises in the frontal cortex as much as 0.8 to 1.0 second before the onset of movement. This signal, named the *readiness potential,* has its peak in the cortex centered in SMC. Because it occurs well before movement, the readiness potential has been widely interpreted as evidence that neural activity in this region is involved in forming the intention to move, not just in executing movement.

Box 34–2 Lesions of Premotor Cortex Lead to Impairments in the Selection, Initiation, and Suppression of Voluntary Behavior

Lesions of the supplementary motor area (SMA) and presupplementary motor area (pre-SMA) and the prefrontal areas connected with them produce deficits in the initiation and suppression of movements. Initiation deficits manifest themselves as loss of self-initiated arm movements, even though the patient can move when adequately prompted. This deficit can involve movement of parts of the body (*akinesia*) contralateral to the region and speech (*mutism*).

Deficits in movement suppression, in contrast, include the inability to suppress behaviors that are socially inappropriate. These include compulsive grasping of an object when the hand touches it (*forced grasping*), irrepressible reaching and searching movements aimed at an object that has been presented visually (*groping movements*), and impulsive arm and hand movements to grab nearby objects and even people without conscious awareness of the intention to do so (*alien-hand* or *anarchic-hand syndrome*).

Another striking syndrome is *utilization behavior*, in which a patient compulsively grabs and uses objects without consideration of need or the social context. Examples are picking up and putting on multiple pairs of glasses or reaching for and eating food when the patient is not hungry or when the food is clearly part of someone else's meal.

These deficits in the initiation and suppression of actions may represent opposite facets of the same functional role for SMA and especially pre-SMA in the conditional or context-dependent control of voluntary behavior.

Lesions affecting premotor cortex also lead to impairments in the selection of motor actions. For example, when a normal monkey sees a tasty food treat behind a small transparent barrier, it readily reaches around the barrier to grasp it. However, after a large premotor cortex lesion, the monkey may persistently try to reach directly toward the treat and so repeatedly strikes the barrier with its hand, rather than making a detour around the barrier.

More focal lesions or inactivation of the ventral premotor cortex perturbs the ability to use visual information about an object to shape the hand appropriately for the object's size, shape, and orientation before grasping it. Focal lesions of the dorsal premotor cortex affect the ability to learn and recall arbitrary sensorimotor mappings or conditional stimulus–response associations, whereas supplementary motor cortex lesions impede the ability to learn and recall temporal sequences of movement.

Neurons in both SMA and pre-SMA discharge before and during voluntary movements. Unlike M1 neurons, the activity of most SMA neurons is less tightly coupled to particular actions of a body part and appears instead to be associated with more complex, coordinated motor acts of the hand, arm, head, or trunk. Compared to SMA neurons, pre-SMA neurons often begin to discharge much earlier in advance of movement onset and are less tightly coupled to the execution of movements.

The SMC has been implicated in the so-called *executive control* of behavior, such as operations required to switch between different actions, plans, and strategies. For example, in monkeys, some SMC neurons discharge strongly when a subject is presented with a cue instructing it to change movement targets or to suppress a previously intended movement. The SMC may therefore contain a system that can override motor plans when they are no longer appropriate.

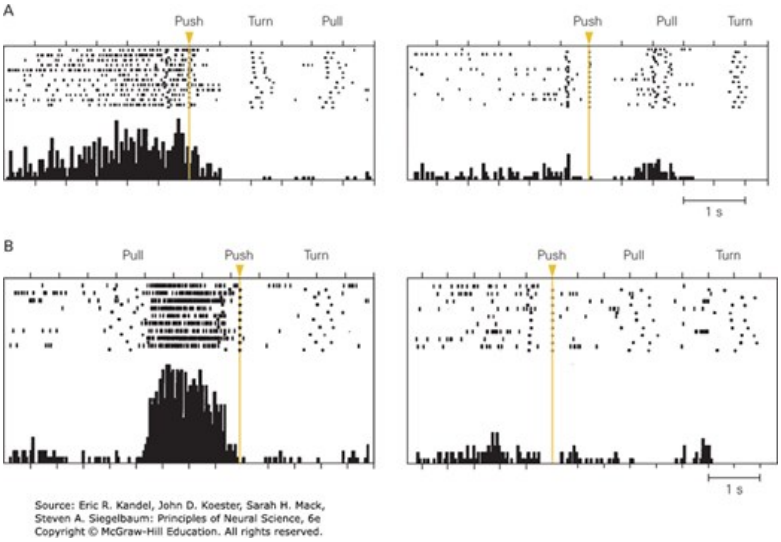
The SMC has also been implicated in the organization and execution of movement sequences. Some SMC neurons discharge before the start of a particular sequence of three movements but not before a different sequence of the same three movements (Figure 34–7). Other neurons discharge only when a particular movement occurs in a specific position in a sequence or when a particular pair of consecutive movements occurs regardless of their position in the sequence. In contrast, some other SMC neurons discharge only when the monkey makes the movement that occurs in a particular ordinal position of a sequence (eg, only the third) irrespective of its nature or how many movements remain to be executed in the sequence.

Figure 34–7

Some neurons in the supplementary motor complex of monkeys encode a specific sequence of motor acts. (Adapted, with permission, from Tanji 2001. Copyright © 2001 by Annual Reviews.)

A. A neuron discharges selectively during the waiting period before the first movement of the memorized sequence push-turn-pull (*left*). When the sequence is push-pull-turn (*right*), the cell remains relatively silent, even though the first movement in both sequences is the same (push). Triangles at the top of each raster plot indicate the start of the push movement.

B. Records of a neuron whose activity increases selectively during the interval between completion of one motor act, a pull, and the initiation of another act, a push. The cell is not active when a push is the first movement in the sequence or when pull is followed by turn.



These seemingly disparate functions may reflect a more general role of the SMC in *contextual control* of voluntary behavior. Contextual control involves selecting and executing those actions deemed appropriate on the basis of different combinations of internal and external cues as well as withholding inappropriate actions in a specific environmental or social context. It also can involve organizing the sequence of actions required to achieve a particular goal. Contextual control likely also involves contributions from other neural circuits such as regions of the prefrontal cortex and the basal ganglia.

The cingulate motor areas (CMA) may also contribute to the contextual control of behavior. CMA appears to be involved in selecting alternate actions following motor errors or in response to changing reward contingencies. For example, monkeys were trained to push or turn a handle in response to a

noninstructive trigger signal. Initially, the monkeys received a large reward if they made the same movement (pushing or turning the handle) in sequential trials. After several trials, the reward size began to decrease. If the monkeys then switched to the other movement, the reward size returned to maximum once that movement was repeated for several trials. The best strategy for the monkeys, therefore, was to switch between repetitions of either pushing or turning the handle as soon as they detected a reduction in reward size.

In this task, some neurons in the rostral CMA responded during the interval between the reception of reward and the start of the next trial. On trials with a reduced reward, task-related activity in these neurons did not change when the monkeys made the same movement in the next trial; their activity only changed when the monkeys switched to the other movement in the next trial. Importantly, those same neurons did not show the same response change when a visual cue instructed the monkeys to change movements in the next trial. This suggests that these rostral CMA neurons were preferentially involved in the voluntary decision to switch and move to the alternate goal based on action outcomes (reward size), but not by visual instructions to switch.

Dorsal Premotor Cortex Is Involved in Planning Sensory-Guided Movement of the Arm

Some of the first neural evidence that the lateral premotor cortex, including PMd and PMv, plays a crucial role in the selection and planning of sensory-guided motor actions came from recording studies by Ed Evarts, Steven Wise, and colleagues in the 1980s. These studies showed that many premotor neurons emitted brief short-latency discharge bursts in response to instructional cues that signaled specific movements, or sustained activity during the instructed-delay period between the appearance of the instructional cue and a second cue that permitted the instructed movement (Figure 34–4).

This activity reflects information about the intended act, including the spatial location of the target, the direction of arm movement, and other movement attributes. Importantly, PMd delay-period activity can reflect the intention to reach to a particular location with either the contralateral or ipsilateral arm, even though the biomechanical details of the two arm movements are very different. This suggests that PMd activity can signal the intention to generate a motor act independent of the effector used to generate the action, in an extrinsic spatial coordinate framework consistent with a prediction of the sensorimotor coordinate transformation model of motor planning. Imaging studies have likewise found evidence for an extrinsic spatial representation of finger-tapping sequences made with either hand in human premotor cortex.

Selection of an appropriate action from among multiple alternatives is a critical aspect of voluntary control. Delay-period activity in PMd can reflect that process. For example, in one experiment, recordings were made from PMd neurons in monkeys during a task in which the animals first received two colored spatial cues that identified two potential targets for reaching in opposite directions. After a memorized-delay period, a new centrally-located color cue informed the monkeys which of the spatial cues was the correct target. Following the first instruction, neural activity in PMd signaled both potential-reaching movements, but immediately after the second instruction, activity in PMd signaled only the monkeys' reaching choice (Figure 34–8A). This showed that PMd can prepare multiple potential motor actions prior to the final decision about which action to take. Subsequent studies suggest that this might be limited to no more than three to four simultaneous potential actions. Reach-related neurons in parietal area PRR also contribute to the preparation for two potential motor actions before the final action decision is made (Figure 34–8B), revealing how this process is distributed across multiple arm movement–related cortical neural populations.

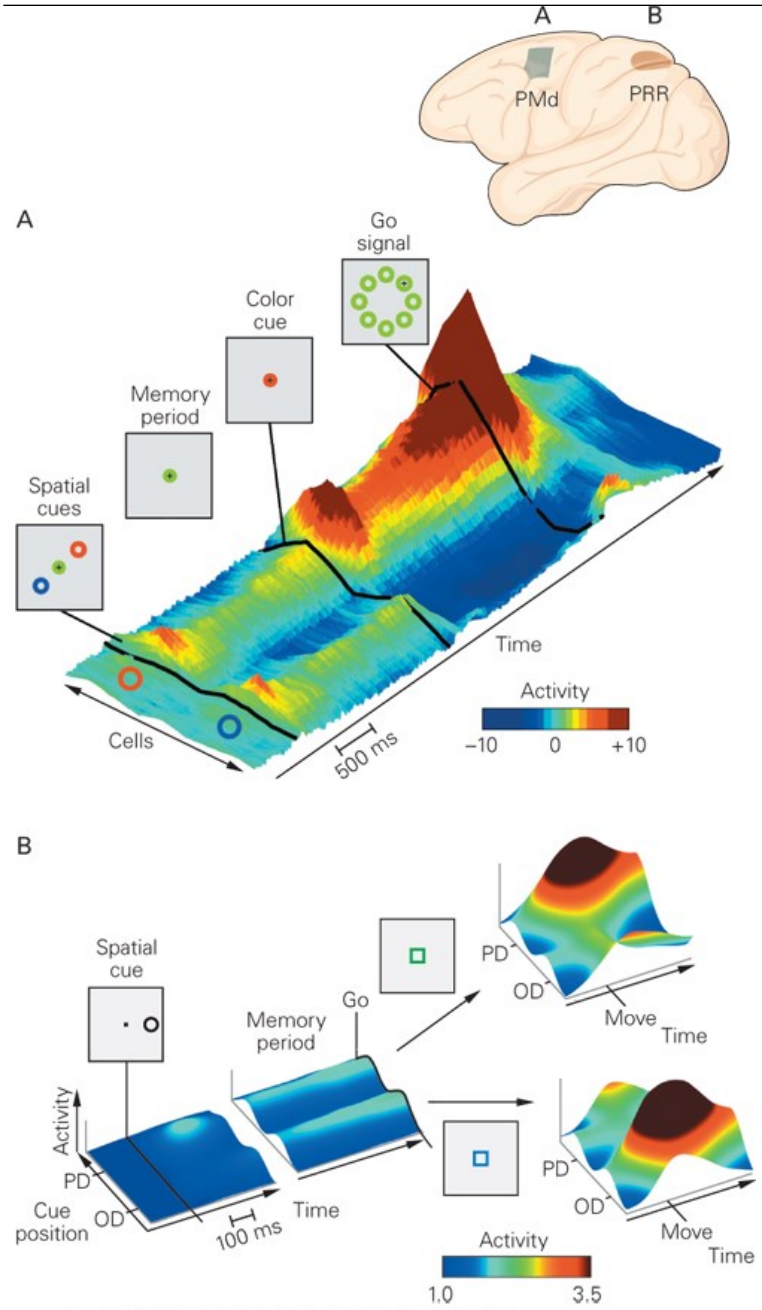
Figure 34–8

Activity of reach-related cortical neurons in monkeys during a target selection task reflects potential movements to different targets as well as the chosen direction of reach.

A. The three-dimensional colored surface depicts the mean level of activity of a population of dorsal premotor cortex (**PMd**) neurons with respect to baseline in a task in which a monkey must choose one of two color-coded reach targets in each trial. Cells are sorted along one axis (labeled "cells") based on their preferred movement direction (neurons located at the **red** and **blue circles** prefer movements at 45° and 215°, respectively). Diagrams beside the neural response profile display the stimuli presented to the monkey at different times during the trial. **Red** and **blue** cues provide information about potential actions; **green** cues guide the monkeys through different stages of each trial but provide no information about what reach to make. Shortly after the start of each trial, two potential reach targets (**blue** and **red** spatial cues) appear in opposite locations relative to the starting position of the arm (**green circle**) for 500 ms and then disappear. After a memorized delay period, the color of the starting circle changes to either **red** or **blue** (color cue), indicating to the monkey which is the correct target, in this case at 45°. After a further delay period, the go signal (**green circles** at all eight possible target locations) instructs the monkey to begin reaching to its chosen target. During the period of target uncertainty between the appearance of the two spatial cues and the central color cue, PMd neurons that prefer the two potential reach movements (**red** and **blue**

circles) are simultaneously activated, whereas neurons that prefer other movements are inactive or suppressed, so that the entire PMd population encodes the two potential reach actions. As soon as the color cue appears to identify the correct target, the PMd neural activity changes rapidly to signal the reach movement chosen by the monkey. Had the color cue designated the target at 215°, the neurons preferring that target (**blue circle**) would increase their activity, and the neurons preferring the target at 45° (**red circle**) would decrease their activity (not shown). (Reproduced, with permission, from Cisek and Kalaska 2010. Copyright © 2010 by Annual Reviews.)

B. In a second study of neural activity in the parietal reach region (**PRR**), the format of data is the same as in part **A**. In this study, the monkey is presented with a single spatial cue that instructs it to prepare to reach either to the cue's location (**PD**) or in the opposite direction (**OD**). After a random memorized delay period, a color cue specifies whether the reach should be to the remembered location of the spatial cue (**green**; PD) or in the OD (**blue**). PRR neural activity is sorted according to the preferred movement direction of each neuron, as in part **A**. Population activity initially specifies the spatial cue location but then reflects both potential movement directions during the remainder of the memorized delay period. Shortly after the color cue appears, the activity quickly shifts to reflect the chosen reach direction, either the PD or OD. (Reproduced, with permission, from Klaes et al. 2011. Copyright © 2011 Elsevier Inc.)



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

PMd neurons can also signal a deliberate decision not to move. Many PMd neurons generate directionally tuned activity during an instructed-delay period when a colored visual cue at a target location instructs a monkey to reach to the target, but decrease their activity when a different colored cue at the same location instructs the monkey to refrain from reaching to it. This differential activity is an unequivocal signal, seconds before the action is executed, about the monkey's intention to reach in a particular direction or not to move in response to an instructional cue (Figure 34–9). Interestingly, many neurons in the parietal area PE/MIP studied in the same task continue to generate directionally tuned activity during the delay period even after the instructional cue to withhold reaching, suggesting that the parietal cortex retains a representation of potential actions that ultimately are not executed.

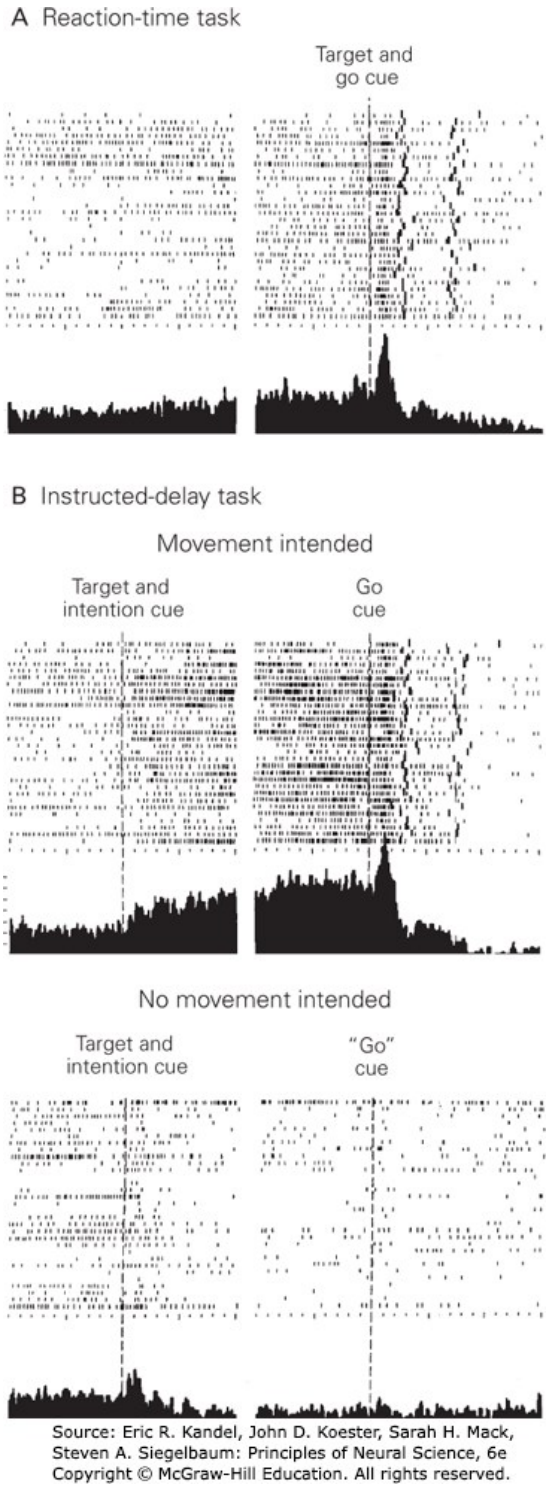
Figure 34–9

Decisions about response choices are evident in the activity of premotor cortex neurons in the monkey. (Reproduced, with permission,

from Crammond and Kalaska 2000.)

A. In a reaction-time task (reaching), a cell exhibits gradually increasing tonic firing while waiting for the appearance of a target. When the target appears (go cue), the cell generates a directionally tuned response.

B. In an instructed-delay task, when a monkey is shown the target and instructed to move once the go cue appears, the cell generates a strong directionally tuned signal for the duration of the delay period before the go cue (**top**). When the monkey is shown the target and instructed not to move when the go cue appears, the cell's activity decreases (**bottom**).



Many neurons in premotor cortex also discharge during movement execution. Given this close proximity of planning- and execution-related activity, even at the level of individual neurons, a major question is why planning-related neural activity does not immediately initiate a movement. What prevents the movement from being executed prematurely? It does not appear that planning-related activity simply fails to exceed a minimum threshold required to initiate the movement or that there is a separate overt braking mechanism that must be released to allow the movement to begin.

A different way to interpret neural processing during the planning and execution of reaching that might provide answers to such questions comes from a dynamical-systems perspective. The idea is that cortical motor circuits form a dynamical system whose distributed activity patterns evolve in time as a function of their initial state, input signals, and stochastic neural response variability ("noise"). Activity patterns during different stages of planning and execution thus reflect different states of the network, including a specific state during the delay period that can prepare the movement but not activate muscles (Figure 34–10). The overall similarity of the population-level activity patterns during repetitions of the same movement shows that the entire population undergoes a coordinated pattern of co-modulation of activity during the planning and execution of the movement, determined by the synaptic connectivity within the neural circuit.

Figure 34–10

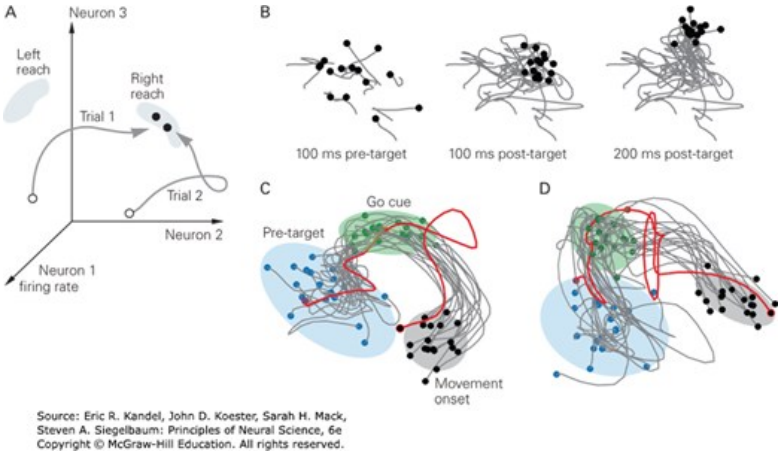
The time-varying neural activity in the dorsal premotor cortex of monkeys during different stages of the planning and execution of a movement can be viewed as transitions between different activation states. (Adapted, with permission, from Churchland MM et al. 2010. Stimulus onset quenches neural variability: a widespread cortical phenomenon. Nat Neurosci 13:369-378. Copyright © Springer Nature.)

A. A schematic illustration of how the simultaneous activity of neurons can be viewed as a trajectory through a multi-neuron activity "state space." The time-varying activity level of three simultaneously recorded neurons is represented along three axes, which defines a three-neuron state space. A specific plan (reach left or reach right) requires different combinations of preparatory firing rates for the three neurons (**gray zones**). Prior to the formation of the intention to move left or right, the baseline activity of the three neurons occupies a region in state space that is associated with holding the arm in its current position (**open circles**, for two different trials). When an instruction appears to make a reach to the right, the combined activity of the three neurons changes in a coordinated fashion, creating time-varying "neural trajectories" (**gray arrows**) that converge on the region of state space that is associated with generating a rightward movement (**filled circles** within the "right reach" gray zone).

B. Projection of the simultaneous activity of a large population of dorsal premotor cortex (PMd) neurons onto a two-dimensional state space shortly before (pre-target) and after (post-target) the appearance of a reach target cue in a task in which the reach movement must be delayed until a subsequent go cue is presented. **Gray lines** show the temporal evolution of the neural trajectories during the earliest part of movement preparation from 200 ms before target cue until the specified pre- or post-target time (**black dots**) in 15 different trials to the same target location. Neural activity initially meanders randomly within the region of state space associated with the starting posture of the arm (*left*). It then begins to converge onto a smaller region of the state space shortly after the reach target instruction appears (*center*) and begins to evolve along the neural trajectory associated with entering the preparatory state for the reach (*right*).

C. A more complete illustration of the neural trajectories recorded during 18 different repeated trials to the same target in this delayed reaching task from the initial pre-target postural state to the onset of movement. **Blue dots** indicate activity while holding the arm in the starting posture 100 ms before appearance of the target instruction onset. Once the target instruction appears, the neural trajectories evolve toward a region of state space associated with the preparatory activity state during the delay period (**green zone**), where it dwells until a go cue appears that allows the monkey to initiate the withheld movement (**green dots**). While in this reach-preparatory part of the state space during the delay period, the arm stays at the start position because PMd activity in that part of state space is not capable of activating muscles (ie, it is "output-null"). When the go cue appears, the neural trajectories unfold toward a different region of state space associated with the initiation of the intended reach movement (**gray zone** and **black dots**). The neural activity can only cause the muscle activity for the intended movement when it enters this "output-potent" zone of state space. The trial-to-trial variability of the neural trajectories can account for intertrial variability in movement kinematics and reaction times. One outlier trial (**red**) had a long reaction time and followed a more complex and time-consuming neural trajectory from the **green** to the **gray** zone. The output-null preparatory (**green**) and output-potent movement-initiation (**gray**) zones for reaches to different target locations occupy different regions of the total population state space distinct from those associated with this reach target.

D. Data are for the same target location as in part **C** but were recorded on a different day. The neural trajectory structure is fundamentally similar for the same movements between recording sessions. Differences in the overall pattern of activity can be explained by interday differences in the activity of individual neurons and differences in the composition of the recorded neural population between sessions.



Dorsal Premotor Cortex Is Involved in Applying Rules (Associations) That Govern Behavior

Behavior is often guided by arbitrary rules that link specific symbolic cues to particular actions. When driving your car, you must perform different actions depending on whether a traffic light is green, amber, or red. In monkeys that have learned to associate arbitrary cues with specific movements, many cells in premotor areas respond selectively to specific cues. For instance, in order to select the correct target in the two-target study in Figure 34–8, the monkeys had to apply a rule that mapped color to target location provided by the two sequential instructional cues.

The PMd is implicated in the acquisition of new movement-related associations or rules. In one experiment, recordings from PMd neurons were made while the monkeys learned the association between four unfamiliar visual cues and four different movement directions. Although the monkeys' choices were initially random, they learned the rules within a few dozen trials. The monkeys made an arm movement in response to each cue; during the early "guessing" phase of learning, the activity of many PMd neurons was weak but gradually increased in strength and directional tuning as the monkeys learned which cue signaled which movement. Other neurons showed a reciprocal decline in activity as the rules were acquired. These changes in activity during learning reflected both the movement choices and the rising level of knowledge of the rules linking cues with actions.

The nature of the rule can also have a strong effect on neural responses. In monkeys that have been trained to choose between several possible movements based on a spatial rule (a visual cue's location) or a semantic rule (a cue's arbitrarily designated meaning independent of its location), many prefrontal and PMd neurons are preferentially active when the animal chooses a movement using one rule but not the other. This shows that the neural activity is related not just to a particular cue or action but also to the association between them.

Premotor areas are involved in the implementation of even abstract rules. For example, monkeys were trained in a task that required two decisions, one perceptual and the other behavioral, that had no prior association. In each trial, the monkeys first had to decide whether two sequentially presented visual images were the same or different (a *match/nonmatch perceptual decision*). In some trials, a *rule cue* presented at the same time as the sample visual image instructed the monkeys to move their hand if the two images were identical and to refrain from moving if they differed (a *go/no-go motor decision*); in other trials, the rule was reversed—move if the images differ and do not move if they match. Neural activity in PMd after the test visual images were presented was correlated more strongly to the motor decision than the perceptual decision in each trial, but both decisions were expressed in PMd. More strikingly, PMd activity was also correlated with the match/non-match *behavioral rule* during the delay period between the two visual images that guided the motor decision after the test image appeared (Figure 34–11). These results suggest that PMd has a major role in applying rules that govern the appropriateness of a behavior and in making behavioral decisions according to the prevailing rules. Neural recordings in prefrontal cortex during the same task (not shown) found a strong representation of the physical identity of the visual images, but weaker and later correlates of the behavioral rule and the motor decision than in PMd.

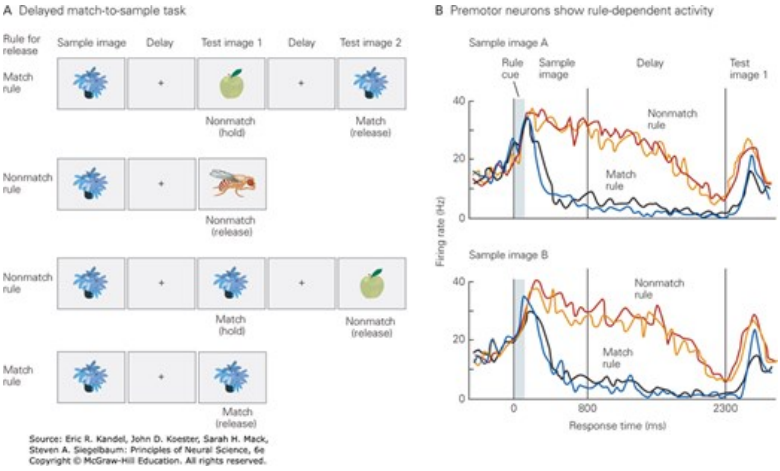
Figure 34–11

Premotor cortex neurons in the monkey choose particular voluntary behaviors based on decisional rules. (Reproduced, with permission, from Wallis and Miller 2003.)

A. A monkey must make a decision about whether to release a lever or keep holding it based on two prior decisions: a perceptual choice, whether a test

image is the same as or different from a sample image presented earlier, and a behavioral choice, whether the current rule is to release the lever when the test image is the same as the sample (match rule) or when it is different (nonmatch rule). The monkey is informed of the behavioral rule that applies in each trial by a rule cue, such as an auditory tone or juice drops, which is presented for 100 ms at the same time as the onset of the sample image at the start of the trial.

B. A neuron in the dorsal premotor cortex has a higher discharge rate whenever the nonmatch rule is in effect during the delay between the presentation of the first and second images. The responses to two different sample images (upper and lower plots) were recorded from the same cell, indicating that the rule-dependent activity is not altered by changing the images. Nor, as shown by the pairs of curves associated with each rule, does activity depend on the type of rule cue (auditory tone or juice drops). (Tone cue trials: **orange** and **blue curves**; juice cue trials: **red** and **black curves**). Other dorsal premotor cortex cells (not shown) respond preferentially to the match rule over the nonmatch rule. The differential activity of the neuron up to presentation of the test image reflects the rule that will guide the animal's motor response to the test image, not the physical properties of the visual stimuli or the motor response.



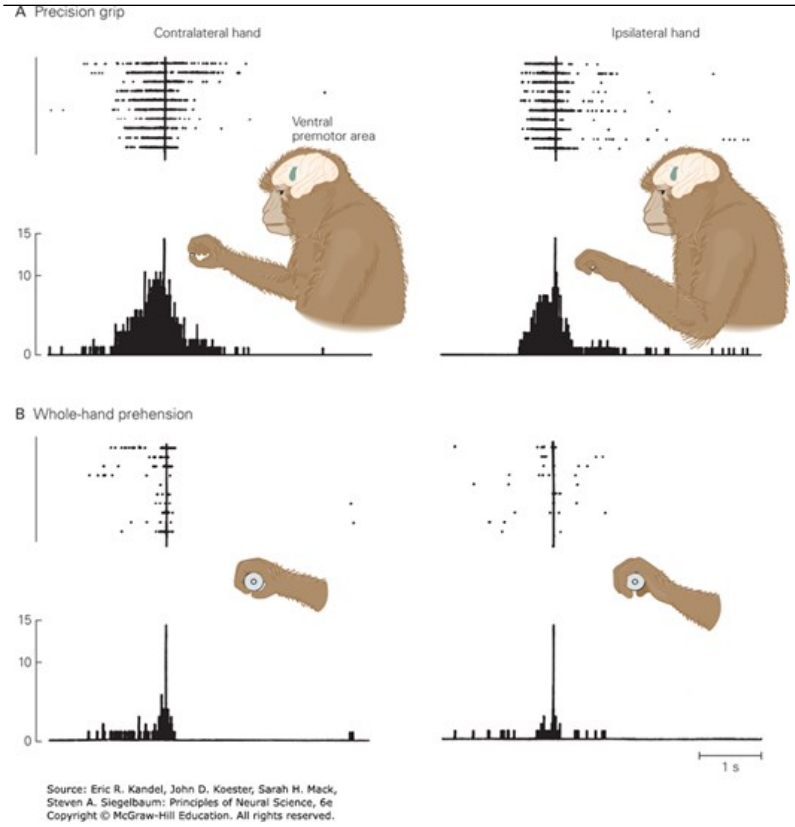
Ventral Premotor Cortex Is Involved in Planning Motor Actions of the Hand

The most lateral part of the premotor cortex, area PMv, is reciprocally connected with parietal cortex areas AIP, PF, and PFG and the secondary somatosensory area. Electrical stimulation shows that PMv contains extensively overlapping circuits that control hand and mouth movements.

Like AIP neurons, many PMv neurons appear to contribute to the control of hand actions based on the physical affordances offered by target objects. These neurons tend to fire preferentially during certain stereotypical hand actions, such as grasping, holding, tearing, or manipulating objects. Many neurons discharge only if the monkey uses a specific type of grip, such as a precision grip, whole-hand prehension, or finger prehension (Figure 34–12). Precision grip is the type most often represented. Some PMv neurons discharge throughout the entire action, while others discharge selectively at particular stages of one type of prehension, such as during the opening or closing of the fingers.

Figure 34–12

Some neurons in the ventral premotor cortex of a monkey discharge selectively during one type of grasping. This neuron discharges vigorously during a precision grip with the thumb and index finger of either the right or the left hand but very weakly during whole-hand prehension with either hand. Raster plots and histograms are aligned (**vertical line**) with the moment the monkey touches the food (**A**) or grasps the handle (**B**). (Reproduced, with permission, from Rizzolatti et al. 1988. Copyright © Springer-Verlag 1988.)



Another striking property of PMv neurons is that their discharge often correlates with the goal of a motor act and not with the individual movements forming it. Thus, many PMv neurons discharge when grasping an object is executed with effectors as different as the right hand, the left hand, and even the mouth. Conversely, a PMv neuron may be active when an index finger is flexed to grasp an object but not when the animal flexes the same finger to scratch itself.

Premotor Cortex May Contribute to Perceptual Decisions That Guide Motor Actions

A series of studies provide evidence that cortical motor areas not only represent the sensory information that guides voluntary movements but also express the neural operations necessary to make and act on perceptual decisions. Monkeys were trained to discriminate the difference in frequency between two brief vibratory stimuli applied to one finger and separated in time by a few seconds. The animals had to decide whether the frequency of the second stimulus was higher or lower than the first and to report their perceptual decision by reaching out to push one of two buttons with the other hand.

The decision-making process in this task can be conceived as a chain of neural operations: (1) encode the first stimulus frequency (f1) when it is presented; (2) maintain a representation of f1 in working memory during the interval between the two stimuli; (3) encode the second stimulus frequency (f2) when it is presented; (4) compare f2 to the memory trace of f1; (5) decide whether the frequency of f2 is higher or lower than that of f1; and finally, (6) use that decision to choose the appropriate movement of the other hand. Everything prior to the last step would appear to fall entirely within the domain of sensory discriminative processing.

While the monkeys performed the task, neurons in the primary (S-I) and secondary (S-II) somatosensory cortices encoded the frequencies of the stimuli while they were presented. During the interval between f1 and f2, there was no sustained activity in S-I representing the memorized f1 and only a transient representation in S-II, which vanished before f2 was presented.

Strikingly, however, the activity of many neurons in the prefrontal cortex, SMC, and PMv scaled with the frequencies of f1 and f2 while they were being delivered. Furthermore, some prefrontal and premotor neurons showed sustained activity proportional to the frequency of f1 during the delay period between f1 and f2. Most remarkably, many neurons in those areas, especially in PMv, encoded the *difference* in frequency between f2 and f1 independently of their actual frequencies when f2 was delivered (Figure 34–13). This centrally generated signal is appropriate to mediate the perceptual discrimination that determines which button to push. Neurons that encoded the f2–f1 difference were absent in S-I and were far more

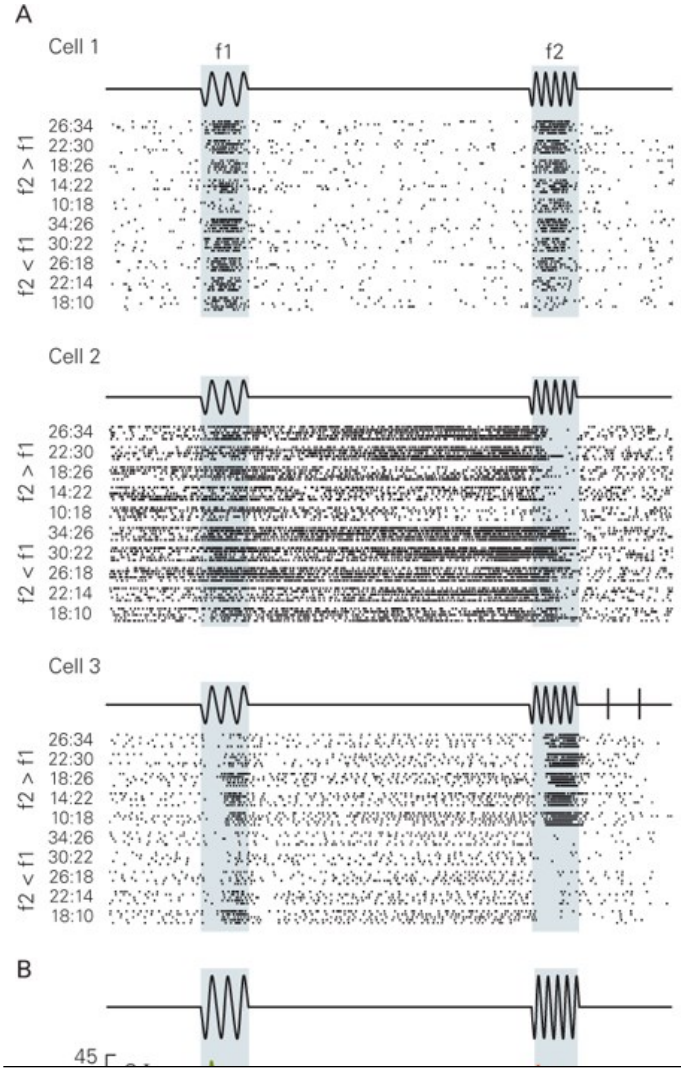
common in SMC and PMv than in S-II.

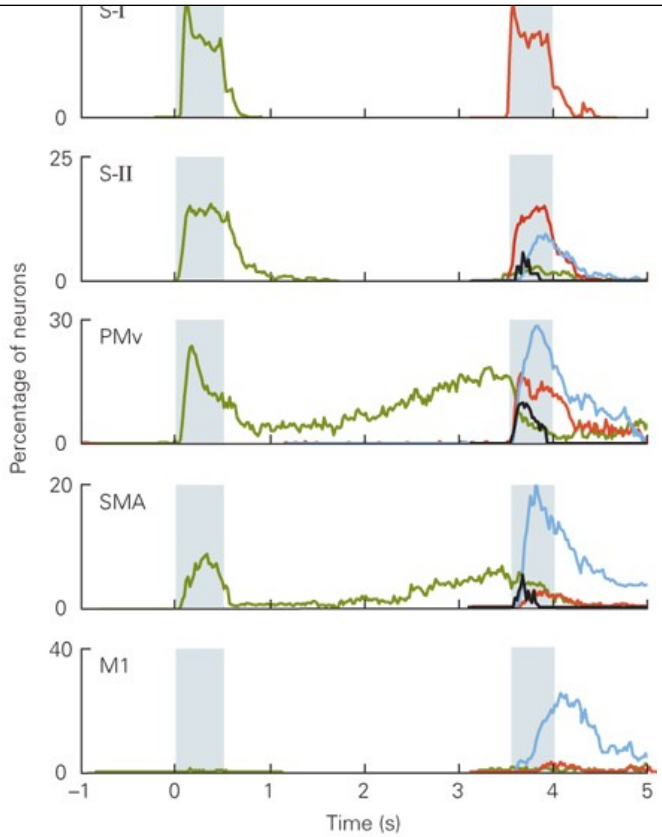
Figure 34–13

(Right) Neural activity in ventral premotor cortex in monkeys expresses the operations required to choose a motor response based on sensory information. (Adapted, with permission, from Romo, Hernández, and Zainos 2004. Copyright © 2004 Cell Press.)

A. These records of three neurons in the ventral premotor cortex of a monkey were made while the animal performed a task in which it had to decide whether the second of two vibration stimuli (**f1** and **f2**, applied to the index finger of one hand) was of higher or lower frequency than the first. The choice was signaled by pushing one of two buttons with the nonstimulated hand. The frequencies of f1 and f2 are indicated by the numbers on the left of each set of raster plots. Cell 1 encoded the frequencies of both f1 and f2 while the stimuli were being presented but was not active at any other time. This response profile resembles that of many neurons in the primary somatosensory cortex. Cell 2 encoded the frequency of f1 and sustained its response during the delay period. During the presentation of f2, the neuron's response was enhanced when f1 was higher than f2 and suppressed when it was lower. Cell 3 responded to f1 during stimulation and was weakly active during the delay period. However, during exposure to f2, the cell's activity robustly signaled the difference f2–f1 independently of the specific frequencies f1 and f2.

B. Histograms show the percentage of neurons in different cortical areas whose activity correlated at each instant with different parameters during the tactile discrimination task. **Green** shows the correlation with f1, **red** the correlation with f2, **black** the interaction between f1and f2, and **blue** the correlation with the difference between f2–f1. (Abbreviations: **M1**, primary motor cortex; **PMv**, ventral premotor cortex; **S-I**, primary somatosensory cortex; **S-II**, secondary somatosensory cortex; **SMA**, supplementary motor area.)





Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

Several Cortical Motor Areas Are Active When the Motor Actions of Others Are Being Observed

Some premotor and parietal areas can be activated when no overt action is intended, such as when an individual is asked to imagine performing a certain motor act. This phenomenon, termed *motor imagery,* has been demonstrated in humans using functional brain imaging. The neural activity evoked by motor imagery presumably reflects brain mechanisms associated with motor planning and preparation that have been disassociated from its overt execution.

A second condition in which cortical motor circuits are activated without intending overt action is when an individual observes another individual performing motor acts that are part of her own motor repertoire. The control of behavior and social interaction depends greatly on the ability to recognize and understand what others are doing and why they are doing it. Such understanding could result from a high-order visual perceptual analysis of the nature of the observed behavior and by drawing inferences about the motivation and purpose of the behavior based on one's own experience. An alternative explanation is the *direct-matching hypothesis*, the idea that observation of the actions of others activates motor circuits in the observer that control similar motor actions. According to this hypothesis, empathetic activation of motor circuits could provide a link between the observed actions and the observer's stored knowledge of the nature, motives, and consequences of similar actions that they had performed in the past.

Striking evidence in support of the direct-matching hypothesis was provided by the discovery of a remarkable population of neurons called mirror neurons, first in PMv and later in the parietal AIP of monkeys. Mirror neurons discharge both when the monkey actively grasps and manipulates objects and when it observes similar actions performed by another monkey or the experimenter (Figure 34–14). Mirror neurons typically do not respond when a monkey simply observes a potential target object or when it observes mimed arm and hand actions without a target object. Some parietal mirror neurons can even differentiate the ultimate goal of similar observed actions, such as grasping and picking up food to eat it versus putting it into a cup.

Figure 34–14

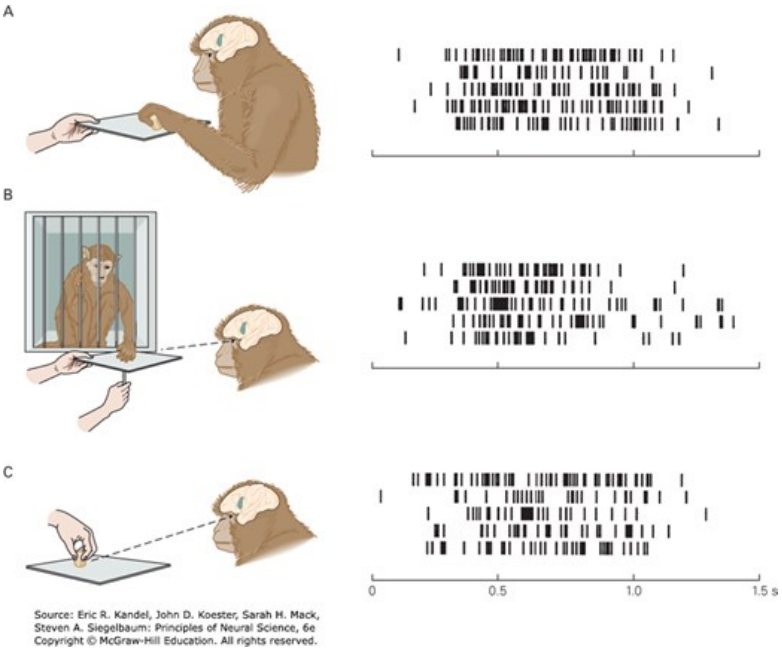
A mirror neuron in the ventral premotor cortex (area F5) of a monkey. (Reproduced, with permission, from Rizzolatti et al. 1996. Copyright © 1996 Elsevier Science B.V.)

A. The neuron is active when the monkey grasps an object.

B. The same neuron is also excited when the monkey observes another monkey grasping the object.

C. The neuron is similarly activated when the monkey observes the human experimenter grasping the object.

Time zero in the cell activity rasters corresponds approximately to the time of presentation of the object to grasp (panel A) or the onset of the observed grasping actions (panels B and C).



Neural-recording and brain-imaging studies show that humans are also endowed with a mirror-like mechanism to match observed actions with actions encoded in their motor system. This activity arises in various areas of cortex, including the rostral inferior parietal lobule, IPS, PMv, and posterior sector of the inferior frontal gyrus.

Cortical motor circuits appear to be involved in understanding and predicting the outcomes of observed events. In one experiment, PMd neurons implicated in the selection of reaching targets using visual cues (Figure 34–8) also discharged when monkeys simply watched the same cues and cursor motions on the monitor while an unseen party performed the task. The monkeys received a free juice reward when the cursor moved to the correct target but not if it moved to the wrong target. The monkeys began to lick the juice tube shortly after the cursor started to move to the correct target well before the juice was actually delivered, but quickly removed their mouth from the tube when the cursor moved toward the wrong target. This behavior showed that the monkeys correctly interpreted what they saw and accurately predicted its consequences.

Remarkably, the activity of most of the task-related PMd neurons was strikingly similar whether the monkeys used visual cues to plan and make arm movements or simply observed the visual events and predicted their outcome. Those neurons stopped responding during observation if no reward was delivered after correct trials or if the animal was sated and not interested in drinking juice. This showed that the neurons were not simply responding to the sensory inputs, but instead were processing the observed sensory events to predict their ultimate outcome for the monkey, namely the likelihood of a free juice reward.

This activation in connection with passive observation supports the idea that activation of premotor circuits in nonmotor contexts may contribute to understanding the nature and consequences of observed events in the environment. It has also been implicated in the ability of human subjects to learn new motor skills simply by observing a skilled person perform the same actions. Moreover, dysfunction of the mirror-neuron system in young children may contribute to some of the symptoms of autism.

Many Aspects of Voluntary Control Are Distributed Across Parietal and Premotor Cortex

While we have described the roles of premotor areas in parietal and precentral cortex separately, it must be emphasized that major sensorimotor control processes are shared across multiple cortical regions via their reciprocal interconnections.

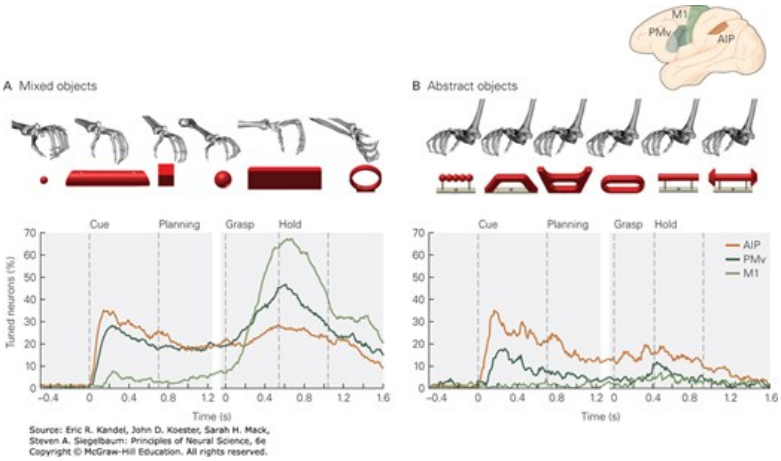
For instance, the neural processes that link the physical affordances of target objects to appropriate hand actions are distributed across parietal area AIP, premotor area PMv, and M1, with visuospatial aspects of the process more prominent in AIP and motor components more prevalent in precentral cortex (Figure 34–15). Likewise, as already noted, neural correlates of reach target selection in PRR (Figure 34–8B) strikingly resemble those reported in PMd (Figure 34–8A).

Figure 34–15

Visuomotor processing of object shape is distributed across several cortical areas in the monkey. (Reproduced, with permission, from Schaffelhofer and Scherberger 2016.)

A. A set of "mixed" objects elicit different visual responses and require different motor responses to grasp them. The plots show the percentages of neurons in the anterior intraparietal areas (**AIP**; **orange**), ventral premotor cortex (**PMv**; F5; **dark green**), and primary motor cortex (**M1**; **light green**) that significantly modulated their response as a function of object identity across time. Monkeys were first shown the object to grasp (cue and planning periods) and then allowed to reach to, grasp, and hold the object (grasp and hold periods). The proportion of neurons that varied their activity across object types (tuned neurons) during the cue and planning periods was greatest in AIP and least in M1, indicating that sensitivity to object visual shape was most prominent in AIP. During motor action (grasp and hold periods), the reverse pattern was observed, with many neurons in PMv and especially M1 displaying a strong dependence on the different grasping actions required to hold onto the different objects.

B. A set of "abstract" objects elicit different visual responses but require similar motor responses to grasp them. As with the "mixed" object set, many AIP neurons varied their activity as a function of object shape during the cue and planning periods, but fewer PMv and almost no M1 neurons showed sensitivity to observed object shape. During motor action (grasp and hold periods), very few PMv and M1 neurons showed any difference in activity as a function of the shape of the different objects, all of which required the same grasping action.



The Primary Motor Cortex Plays an Important Role in Motor Execution

Once an individual has decided on a behavioral goal, motor commands must then be communicated to muscles to move the body. The complexity of this problem cannot be underestimated as it requires precise control of the spatiotemporal patterns of activity of large numbers of muscles acting across many joints to achieve the behavioral goal, while also accounting for the complex, nonlinear mechanical properties of the musculoskeletal system and forces and loads imposed by the environment. These detailed patterns of muscle activity are coordinated by spinal motor neurons and interneuronal circuits (Chapter 32). However, the primary motor cortex (M1) plays an important role in generating the motor commands that control that spinal activity, including essential information necessary to select and control the timing and magnitude of muscle activity.

The Primary Motor Cortex Includes a Detailed Map of the Motor Periphery

The idea that a local region of the cerebral cortex contains a motor map of the body dedicated to voluntary motor control dates back to the work of the English neurologist John Hughlings Jackson in the middle of the 19th century. He reached this conclusion while treating patients with epileptic seizures that were characterized by recurring spasmodic involuntary movements that sometimes resembled fragments of purposive voluntary actions and that progressed systematically to include different parts of the body during each seizure episode (Chapter 58). Later in the 19th century, improved anesthesia and aseptic surgical techniques allowed direct experimental study of the cerebral cortex in experimental animals. Using those new methods, Gustav Fritsch and Eduard Hitzig in Berlin and David Ferrier in England showed that electrical stimulation of the surface of a limited area of cortex in different anesthetized mammalian species evoked movements of parts of the contralateral body. In monkeys, the electric currents needed to evoke movements were lowest in a narrow strip along the rostral bank of the central sulcus, the same region now called primary motor cortex.

Their experiments demonstrated that within this strip of tissue stimulation of adjacent sites evoked movements in adjacent body parts, starting with the foot, leg, and tail medially, and proceeding to the trunk, arm, hand, face, mouth, and tongue more laterally. When they lesioned a cortical site at which stimulation had evoked movements of a part of the body, movement of that body part was perturbed or lost after the animal recovered from surgery. These early experiments showed that the motor cortex contains an orderly motor map of major parts of the contralateral body and that the integrity of the motor map is necessary for voluntary control of the corresponding body parts. Studies in the first half of the 20th century on many species by Clinton Woolsey and on humans undergoing surgery by Wilder Penfield demonstrated that the general topographic organization of the rostral bank of the central sulcus is conserved across many species (Figure 34–16). One important observation was that the motor map is not an exact point-to-point reproduction of the body's anatomical form. Instead, the most finely controlled body parts, such as the fingers, face, and mouth, are represented by disproportionately large areas, reflecting the larger number of neurons needed for fine motor control.

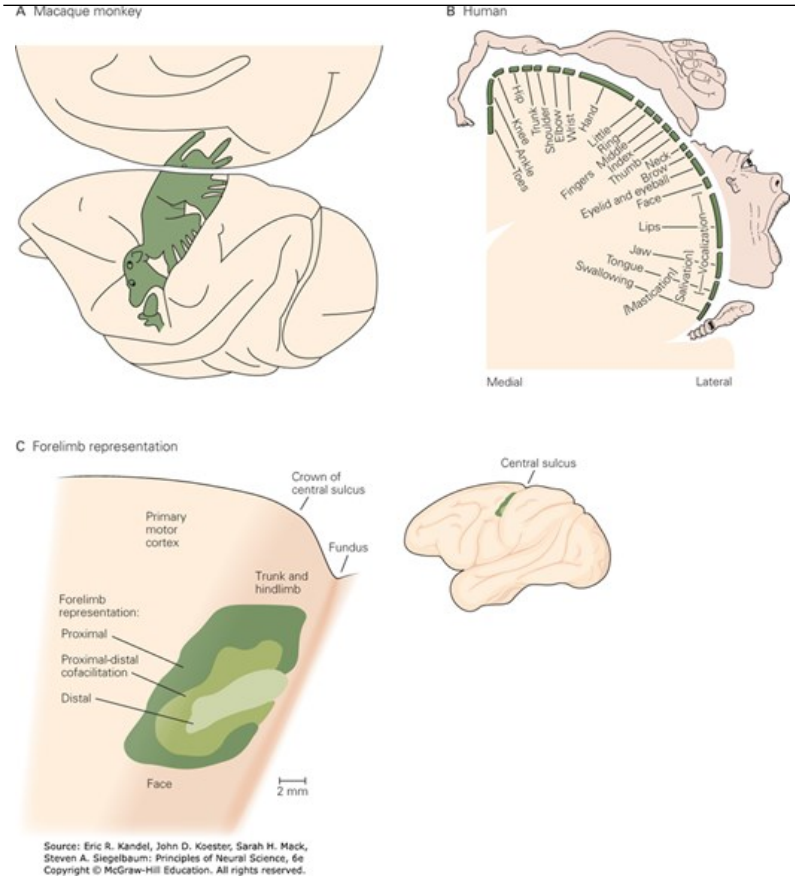
Figure 34–16

The motor cortex contains a topographic map of motor output to different parts of the body.

A. Studies by Clinton Woolsey and colleagues confirmed that the representation of different body parts in the monkey follows an orderly plan. Motor output to the foot and leg is medial, whereas the arm, face, and mouth areas are more lateral. The areas of cortex controlling the foot, hand, and mouth are much larger than the regions controlling other parts of the body.

B. Wilder Penfield and colleagues showed that the human motor cortex motor map has the same general mediolateral organization as in the monkey. However, the areas controlling the hand and mouth are even larger than in monkeys, whereas the area controlling the foot is much smaller. Penfield emphasized that this cartoon illustrated the relative size of the representation of each body part in the motor map; he did not claim that each body part was controlled by a single separate part of the motor map.

C. The arm motor map in monkeys has a concentric, horseshoe-shaped organization. Neurons that control the distal arm (digits and wrist) are concentrated in a central core (**pale green**) surrounded by neurons that control the proximal arm (elbow and shoulder; **dark green**). The neuron populations that control the distal and proximal parts of the arm overlap extensively in a zone of proximal-distal co-facilitation (**intermediate green**). (Reproduced, with permission, from Park et al. 2001. Copyright © 2001 Society for Neuroscience.)



Today the best-studied regions of the map are those parts controlling the arm and hand and reveal far more complexity than conveyed in the classic diagrams shown in Figure 34–16A,B. First, neurons controlling the muscles of the digits, hand, and distal arm tend to be concentrated within a central zone, whereas those controlling more proximal arm muscles are located in a horseshoe-shaped ring around the central core (Figure 34–16C). Second, stimulation sites overlap extensively, allowing control of muscles acting across different joints; conversely, each muscle can be activated by stimulating many sites dispersed across the arm/hand motor map. Finally, local horizontal axonal connections link different sites across the motor map, likely allowing coordination of activity across the map during the formation of motor commands.

Some Neurons in the Primary Motor Cortex Project Directly to Spinal Motor Neurons

As already noted, while many corticospinal axons in primates terminate only on spinal interneurons, others also synapse directly onto spinal motor neurons. These corticomotoneuronal (CM) cells are found only in the most caudal part of M1 that lies within the anterior bank of the central sulcus. There is extensive overlap in the distribution of the CM cells that project to the spinal motor neuron pools innervating different muscles (Figure 34–17A).

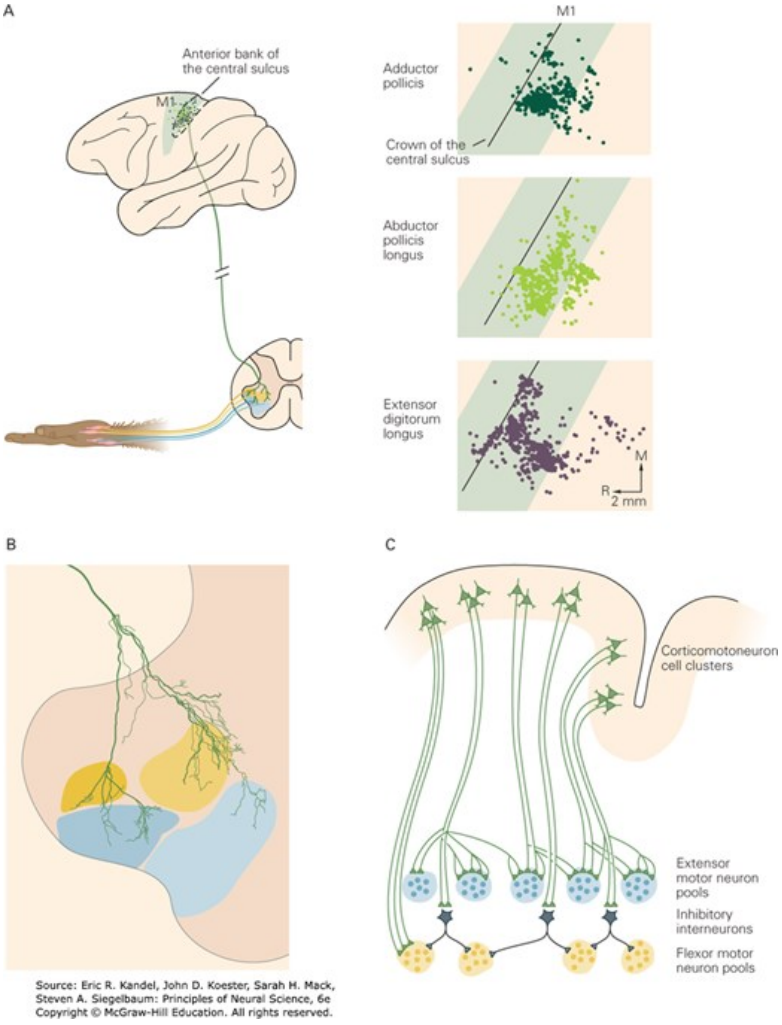
Figure 34–17

Corticomotoneuronal cells activate complex muscle patterns through divergent connections with spinal motor neurons that innervate different arm muscles.

A. Corticomotoneuronal (CM) cells, which project monosynaptically to spinal motor neurons, are located almost exclusively within the anterior bank of the central sulcus in the caudal part of the primary motor cortex (**M1**). The CM cells that control a single hand muscle are widely distributed throughout the arm motor map, and there is extensive overlap of the distribution of neurons projecting to different hand muscles. The distributions of the cell bodies of CM cells that project to the spinal motor pools that innervate the adductor pollicis, abductor pollicis longus, and extensor digitorum communis (shown on the right) illustrate this pattern of wide distribution and extensive overlap of CM cells projecting to different muscles. (Abbreviations: **M**, medial; **R**, rostral.) (Reproduced, with permission, from Rathelot and Strick 2006.)

B. A single CM axon terminal is shown arborized in the ventral horn of one segment of the spinal cord. It forms synapses with the spinal motor neuron pools of four different intrinsic hand muscles (**yellow** and **blue** zones), as well as with surrounding interneuronal networks. Each axon has several such terminal arborizations distributed along several spinal segments. (Reproduced, with permission, from Shinoda, Yokota, and Futami 1981.)

C. Different colonies of CM cells in the primary motor cortex terminate on different combinations of spinal interneuron networks and spinal motor pools, thus activating different combinations of agonist and antagonist muscles. Many other corticospinal axons terminate only on spinal interneurons (not shown). The figure shows CM projections largely onto extensor motor neuron pools. Flexor motor pools receive similar complex projections (not shown). (Adapted, with permission, from Cheney, Fetz, and Palmer 1985.)



CM cells are very rare or absent in nonprimate species and become a progressively larger component of the corticospinal tract in primate phylogeny from prosimians to monkeys, great apes, and humans. In monkeys, more CM cells project to the motor pools for muscles of the digits, hand, and wrist than to those for more proximal parts of the arm. The terminal of a CM cell axon often branches and terminates on spinal motor neurons for several different agonist muscles and can also influence the contractile activity of still more muscles through synapses on spinal interneurons (Figure 34–17B,C). This termination pattern is organized to produce coordinated patterns of activity in a *muscle field* of agonist and antagonist muscles. Most frequently, a CM cell axon directly excites the spinal motor neurons for several agonist muscles and indirectly suppresses the activity of some antagonist muscles through spinal inhibitory interneurons (Figure 34–17C). The fact that CM cells are more prominent in humans than in other species may be one of the reasons why lesions of M1 in humans have a more profound effect on voluntary motor control compared to other mammals (Box 34–3).

Box 34–3 Lesions in Primary Motor Cortex Lead to Impairments in Motor Execution

The effects of primary motor cortex (M1) lesions differ across species. Large lesions in cats do not cause paralysis; the animals can move and walk on a flat open surface. However, they have severe difficulties using visual information to navigate within a complex environment, avoid obstacles, or climb the rungs of a ladder. In cats, the pyramidal tract neurons in M1 are much more strongly activated when an animal must modify its normal stepping motion to clear an obstacle under visual guidance than during normal unimpeded locomotion over a flat, featureless surface (Chapter 33).

Large M1 lesions in monkeys have more drastic consequences, including initial paralysis and usually the permanent loss of independent movements of the thumb and fingers. Monkeys nevertheless recover some ability to make clumsy movements of the hands and arms and to walk and climb.

More focal lesions of M1 typically result in muscle weakness, slowing and imprecision of movements, and discoordination of multi-joint motions, perhaps as a result of selective perturbations of the control circuitry for specific muscles or muscle groups. Lesions limited to part of the motor map, such as the contralateral arm, leg, or face, lead to paralysis of that body part. There is diminished use of the affected body part, and movements of the distal extremities are much more affected than those of the proximal arm and trunk.

The severity of the deficits also depends on the level of required skill. Control of fine motor skills, such as independent movements of the fingers and hand and precision grip, is abolished. Any residual control of the fingers and the hand is usually reduced to clumsy, claw-like, synchronous flexion and extension motions of all fingers, not unlike the unskilled grasps of young infants. Remaining motor functions, such as postural activity, locomotion, reaching, and grasping objects with the whole hand, are often clumsy.

In humans, large motor cortex lesions are particularly devastating, resulting in severe motor deficits or complete paralysis of affected body parts, usually with limited potential for recovery. This presumably reflects the increased importance in humans of descending signals from M1 onto spinal interneuronal circuits and spinal motor neurons and a diminished capacity of other cortical and subcortical motor structures to compensate for the loss of those descending M1 signals.

The complexity of the motor map in M1—as revealed by short trains of electrical stimuli and anatomical and neurophysiological studies of direct and indirect M1 descending outputs targeting single muscles and small muscle groups—shows how motor commands from M1 to the spinal motor apparatus are able to control movements of every part of the body, with special focus on the fingers, hand, arm, face, and mouth in primates.

Activity in the Primary Motor Cortex Reflects Many Spatial and Temporal Features of Motor Output

As already noted, a given action such as reaching for an object can be described on many levels, ranging from the hand's spatial trajectory and velocity to its joint-centered causal forces and muscle activity (Figure 34–1A). Representational models assume that the motor system directly plans and controls specific parameters of movement. They predict that different neural populations encode the intended movement in a parameter space (ie, hand or joint motion or joint muscular torque) and perform the transformations between them. Dynamical models predict that neural circuits control movements through changes in their activation state from its current state to the desired final state. As their activity changes across time, correlates of various parameters and properties of the intended movement can be observed in the activity of single neurons and neural populations. However, the activity of most neurons reflects a combination of parameters that does not correspond to any identifiable parameter in any specific coordinate framework.

Despite their different assumptions, both perspectives suggest that one can infer the possible contribution of different neurons and different neural structures to motor control by studying how their activity correlates with different parameters of movements. The activity of M1 neurons has been intensively studied since the 1960s to try to reveal, for instance, whether M1 generates a high-level signal about the hand motion or a lower-level kinetic signal more related to the causal forces and muscle activity.

Knowledge about the nature of the control signals generated by M1 also helps to clarify the role of other motor structures, notably the spinal cord. If M1 encodes specific information about muscle activity patterns, less computational processing would be necessary at the spinal level. In contrast, if M1 mainly encodes higher-level information about the intended movement, the spinal cord would have to perform the processes that convert this global signal into detailed patterns of muscle activity.

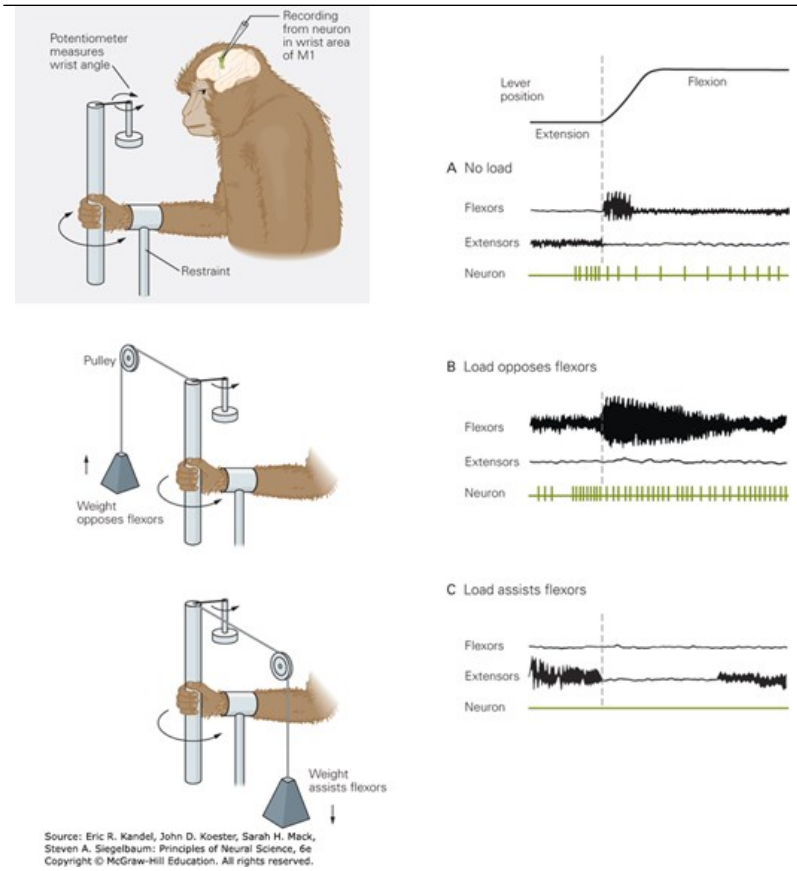
However, one of the major experimental challenges in identifying how M1 controls movement is the fact that virtually all movement-related parameters are intercorrelated through the laws of motion. As a consequence, a particular muscular force (kinetics) will cause a specific motion (kinematics) given an initial condition (posture, movement) of the body. As a result, if one recorded neural activity while a monkey makes reaching movements in different directions, a neuron that theoretically signals the spatial direction of movement will also inevitably show a correlation with the direction of causal forces. Likewise, the contractile activity of a muscle will co-vary systematically with the spatial direction of movement even though it is clearly generating the causal forces. Unless the task design adequately dissociates these different classes of parameters, it will yield ambiguous information about the functional role of each neuron.

Edward Evarts was the first to examine this issue in the 1960s, in pioneering single-neuron recordings in monkeys while they made simple flexion/extension movements of the wrist. Using a system of pulleys and weights, he applied a load to the wrist of the monkey that pulled the wrist in either the direction of flexion or extension in different trials. This required the monkey to alter the level of wrist muscle activity to compensate for the load while making the movements. As a result, the kinematics (direction and amplitude) of wrist movements remained constant, but the kinetics (forces and muscle activity) changed with the load.

Using a microelectrode, he located single neurons in the M1 motor map that modulated their activity when the monkey made movements of the wrist without the external load. In some neurons, their discharge increased during wrist flexion (*preferred movement direction*) and was suppressed during extension, whereas others displayed the opposite pattern. This movement-related activity typically began 50 to 150 ms before the onset of agonist muscle activity, supporting a causal link between M1 neural activity and movement. When a load was applied, many M1 neurons increased their activity when the load resisted movement in their preferred direction and decreased activity when the load assisted the movement (Figure 34–18). These changes in neural activity paralleled the changes in muscle activity required to compensate for the external load.

Figure 34–18

Activity of a motor cortex neuron correlates with changes in the direction and amplitude of muscle forces during wrist movements. The records are from an M1 neuron with an axon that projected down the pyramidal tract. The monkey flexes its wrist under three load conditions. When no load is applied to the wrist, the neuron fires before and during flexion (**A**). When a load opposing flexion is applied, the activity of the flexor muscles and the neuron increases (**B**). When a load assisting wrist flexion is applied, the flexor muscles and neuron fall silent (**C**). In all three conditions, the wrist displacement is the same, but the neural activity changes as the loads and compensatory muscle activity change. Thus, the activity of this motor cortex neuron is better related to the direction and level of forces and to muscle activity exerted during the movement than to the direction of wrist displacement. (Adapted from Evarts 1968.)



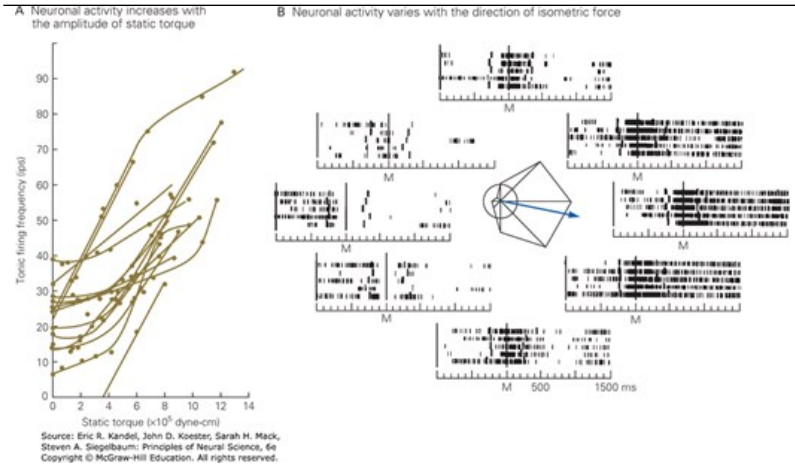
Subsequent studies have confirmed that the activity of many M1 neurons varies systematically with the magnitude of muscle force output. This is best shown in tasks in which monkeys generate isometric forces against immovable objects that prevent movement. The activity of many M1 neurons, including CM cells, varies with the direction and level of static isometric output forces generated across a single joint, such as the wrist or elbow, as well as during precise pinches using the thumb and index finger (Figure 34–19A). At least over part of the tested range, these responses vary linearly with the level of static force.

Figure 34–19

Activity in many primary motor cortex neurons correlates with the level and direction of force exerted in an isometric action.

A. The activity of many primary motor cortex neurons increases with the amplitude of static torque generated across a single joint. The plot shows the tonic firing rates of several different corticomotoneuronal cells at different levels of static torque exerted in the direction of wrist extension. Other motor cortex neurons show increasing activity with torque exerted in the direction of wrist flexion, and so would show response functions with the opposite slope (not shown). (Reproduced, with permission, from Fetz and Cheney 1980.)

B. When a monkey uses its whole arm to push on an immovable handle in its hand, the activity of some primary motor cortex neurons varies with the direction of isometric forces. Each of the eight raster plots shows the activity of the same primary motor cortex neuron during five repeated force ramps in one direction. Each row shows the pattern of spikes during a single trial of the task. The position of each raster of activity corresponds to the direction in which the monkey is generating isometric forces on the handle. The onset of the force ramp is indicated by the vertical line labeled **M**. The **thick ticks** on the left of that line in each row indicate when the target appeared on a computer monitor, telling the monkey the direction in which it should push on the handle. The central polar plot illustrates the directional tuning function of the neuron as a function of the direction of isometric forces. (Reproduced, with permission, from Sergio and Kalaska 2003.)



Most natural behaviors involve multi-joint, multi-muscle actions. For instance, reaching movements of the arm in different directions requires different patterns of coordinated motions at the shoulder and elbow. Proximal limb muscle activity during reaching shows a roughly cosine pattern of activity with maximal activity in a specific movement direction, its preferred movement direction, that gradually diminishes as the angle between the desired direction of reach and the muscle's preferred direction increases (Figure 34–20A). Like the proximal arm muscles, single neurons related to shoulder and elbow movements respond in a continuously graded fashion during movements in different reach directions centered on a preferred direction of maximal activity (Figure 34–20B). Different neurons have different preferred directions that cover the entire directional continuum around the circle, and during any given movement, neurons with a wide range of preferred directions discharge at different rates.

Figure 34–20

Limb muscles and primary motor cortical neurons are broadly tuned to the direction of reaching.

A. Plots show the activity of posterior deltoid of the right arm, a shoulder extensor, during arm movements in eight directions (see panel C) (central panel displays mean hand trajectories). The muscle is initially maximally active for movements at 270° (towards the body, preferred direction = 250°) and diminishes for movements in other directions. **Black lines** denote the mean activity of the muscle across multiple trials, and data are aligned on movement onset (**vertical thin line**). (Abbreviation: **EMG**, electromyography.)

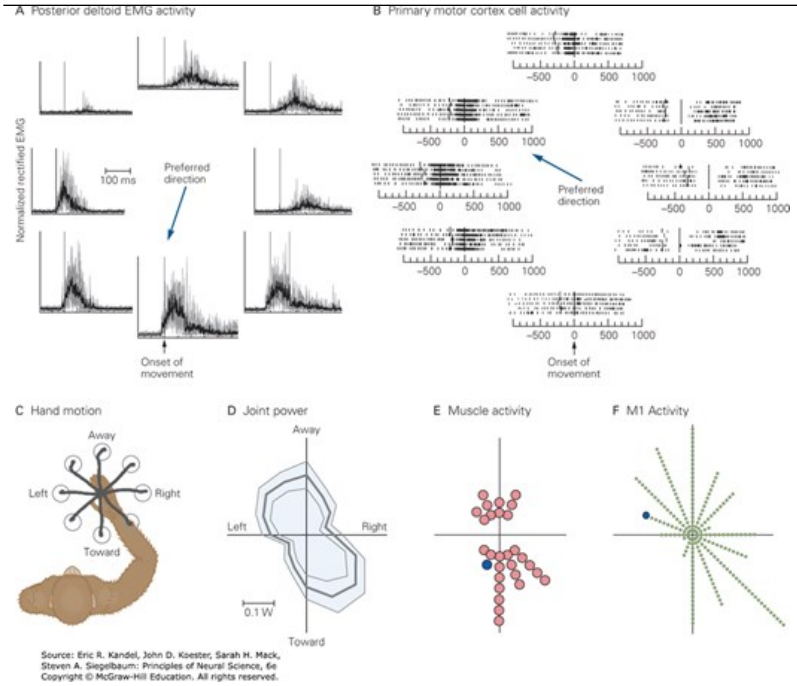
B. Raster plots show the firing pattern of a single primary motor cortex neuron during whole-arm movements in eight directions. The neuron discharges at the maximal rate for movements near 135° and 180° and at lesser intensities for movements in other directions. The cell's lowest firing rate is for movements opposite the cell's preferred direction. Each row of **thin tics** in each raster plot represents the activity in a single trial, aligned at the time of movement onset (time 0); **thick tics**, time of target appearance. (Reproduced, with permission, from Georgopoulos et al. 1982. Copyright © 1982 Society for Neuroscience.)

C. Hand trajectories when reaching from a central position in the horizontal plane.

D. Peak joint power (joint muscular torques multiplied by joint velocity) for movements performed in different spatial directions (shoulder and elbow power added together). A large amount of power is required to reach away from the body and to the upper left and to reach toward the body and to the lower right. (Right X-axis is at 0°.)

E. Preferred directions of proximal-limb muscles tend to be for movements that require greater muscular power, reflecting the obvious link between muscle use and the physical requirements of the motor task. Each **dot** represents an individual muscle binned into 22.5° sectors; the **blue dot** represents the preferred direction of the muscle displayed in panel **A**.

F. Distribution of preferred directions of neurons in primary motor cortex (**M1**). Each **dot** represents an individual neuron, and the **blue dot** represents the preferred direction of the neuron displayed in panel **B**. (Adapted, with permission, from Scott et al. 2001.)



As Ed Evarts had shown in single-joint tasks, much of the M1 activity during reaching is closely related to the causal kinetics. For instance, in monkeys trained to make reaching movements in eight directions while compensating for external loads that pulled the arm in different directions, the reach-related activity of both proximal-arm muscles and many M1 neurons changed systematically with the direction of the external loads and the corresponding corrective forces that the monkeys had to generate for each reach direction. Both muscle and neural activity increased when the load resisted movements in their preferred directions and decreased when the loads assisted those movements. In addition, when a monkey uses its whole arm to exert constant isometric force levels in different directions at the hand, the activity of many M1 neurons varies systematically with force direction, and the directional tuning curves for isometric force resemble those for activity during reaching movements (Figure 34–19B).

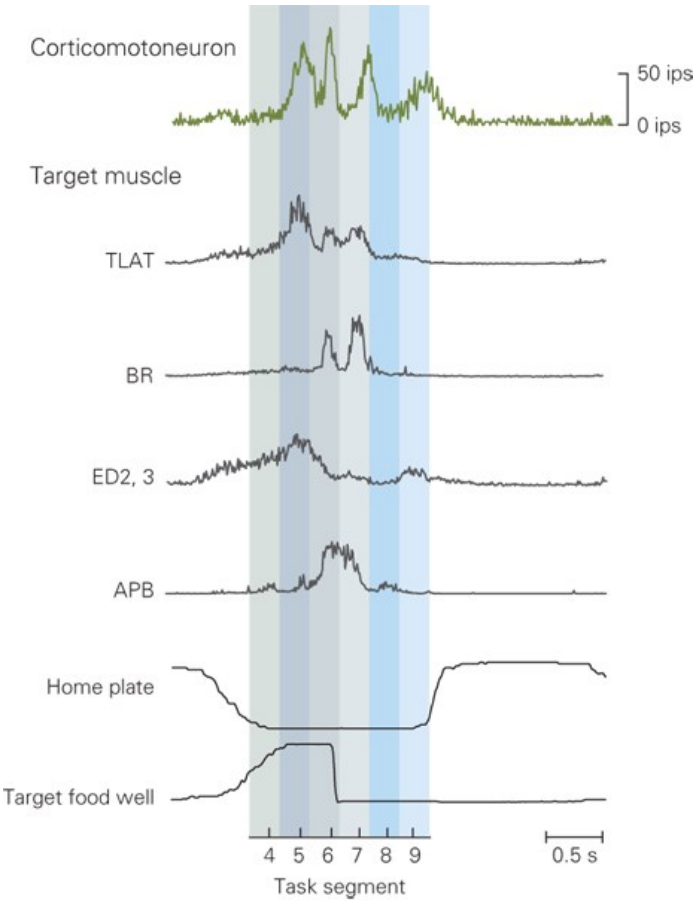
The complex and nonlinear properties of multi-segmented limbs present a major control problem for the motor system. For instance, one can make reaching movements with similar hand trajectories but different arm geometries that require changes in the causal joint-centered torques and muscle activity. In one experiment, when monkeys made horizontal reaching movements along the same planar spatial hand trajectories while holding the arm in different spatial orientations (ie, elbow raised versus lowered), the activity of proximal-arm muscles and many M1 neurons showed corresponding changes in the strength and directional tuning of their reach-related activity. This indicates that the M1 neurons generate signals that take into account the changes in intrinsic limb biomechanics during the reaching movements.

Similarly, arm movements toward or away from the body require much larger angular motion at the shoulder and elbow joints compared to movements to the right or left. In contrast, muscular torques tend to be larger for movements to the right and left. Both of these factors influence the amount of muscle activity required to move the limb, which can be quantified by a single term, joint muscular power (joint angular velocity multiplied by net muscular torque about that joint). With the limb in the horizontal plane, joint power is greatest for movements away from the body and slightly to the left, and toward the body and to the right (Figure 34–20C,D). This bias in the physics of limb movement leads to a bias in the preferred directions of shoulder and elbow muscles, which tend to be maximally active in these same directions (Figure 34–20E). Correspondingly, the distribution of preferred directions of neurons in M1 also parallels this bias, with neurons tending to have preferred directions either away and slightly to the left or toward and to the right (Figure 34–20F). Thus, the physics of the limb dictates the pattern of muscle activity needed to generate movement, and this in turn is reflected in the pattern of neural activity in M1.

The impact of limb physics on M1 activity extends to the level of muscle-related signals. The activity of some single M1 neurons, including CM cells, can be correlated with specific components of the contraction patterns of different muscles during such diverse tasks as isometric force generation, precision pinching of objects between the thumb and index finger, and complex reaching and grasping actions (Figure 34–21). These findings highlight how M1 contributes to the specification of muscle activity patterns for motor actions, including onset times and magnitudes. Nevertheless, the final pattern of muscle activity will only be generated by the spinal motor neurons since they alone take into account the additional influence of other descending supraspinal inputs and local spinal interneuronal processes.

Figure 34–21

The activity of some primary motor cortex neurons can be correlated with particular patterns of muscle activity. Bursts of activity in a single corticomotoneuron during a reach-and-grasp movement to retrieve food pellets from a small well are correlated with bursts of contractile activity in several of its target muscles at different times during the movement. (Abbreviations: **APB**, abductor pollicis brevis; **BR**, brachioradialis; **ED2, 3**, extensor digitorum 2, 3; **ips**, impulses per second;**TLAT**, lateral triceps.) (Reproduced, with permission, from Griffin et al. 2008.)



All the studies described so far related the activity of single M1 neurons to motor output. However, voluntary motor control is implemented by the simultaneous coordinated activity of many neurons throughout the motor system. Their activity is noisy, varying stochastically between repetitions of the same movement. Furthermore, their broad symmetrical movement-related tuning curves introduce a high level of uncertainty as to what the limb should do in response to the ambiguous signal generated by each neuron.

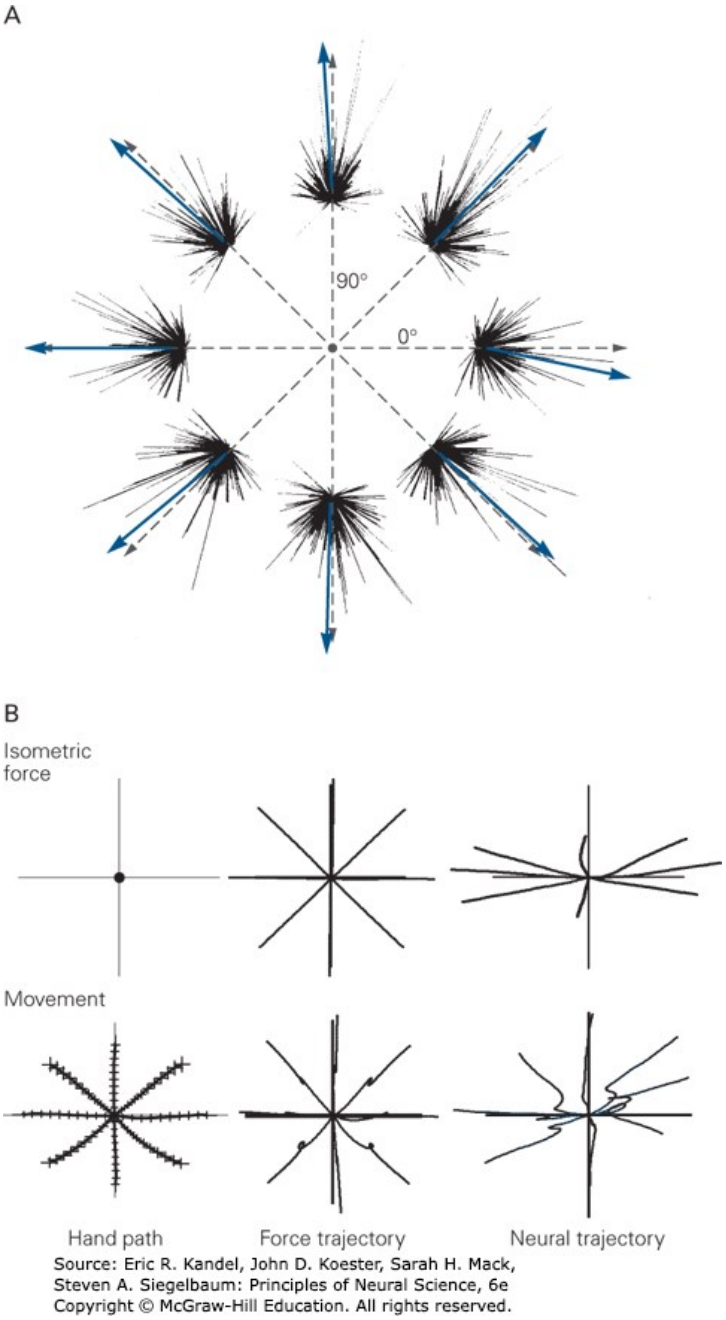
A simple computational approach was developed to extract a unique signal about each reaching movement by pooling the heterogeneous single-neuron activity of the recorded M1 population. The activity of each neuron is represented by a vector pointing in its preferred direction; the length of the vector varies as a function of its mean discharge rate during reaches in each direction. This vector notation implies that an increase in the activity of a given M1 neuron evokes changes in activity in the spinal motor apparatus and muscles that causes the arm to move along a path corresponding to the neuron's task-related preferred direction; the strength of that single-neuron influence varies systematically with the difference between the neuron's preferred direction and the desired movement (Chapter 39, Figure 39–6). When the reach-related activity of about 250 M1 neurons was represented by variable-length vectors for each of the eight reach directions and summed, the direction of the net resultant *population vectors* varied systematically with the actual reach directions (Figure 34–22A).

Figure 34–22

Population codes relate M1 activity to different properties of movement.

A. The eight single-neuron vector clusters (**thin black lines**) and the population vectors (**blue arrows**) represent the activity of the same population of cells during reaching movements in eight different directions. Each single-neuron vector points in the neuron's preferred movement direction, and its length is proportional to the discharge of the neuron during that movement. The population vectors were calculated by vectorial addition of all the single-cell vectors in each cluster; **dashed arrows** represent the direction of movement of the arm. (Reproduced, with permission, from Georgopoulos et al. 1983.)

B. Comparison of hand kinematics and kinetics and neural population activity in an isometric task and when moving a handle with a large mass. Force and neural trajectories were generated by linking sequences of 20-ms output force vectors or neural population vectors tip-to-tail for each direction of force or movement output. (Reproduced, with permission, from Sergio et al. 2005.)



The novel insights of this analysis were that the control of a given reach movement involves coordinated changes in the activity of M1 neurons

distributed throughout the M1 arm motor map and that their pooled activity clearly distinguishes the unique identity of each of the reach actions generated by the eight different distributed patterns of population activity. Subsequent studies demonstrated that "instantaneous" population vectors extracted from the pooled activity of large populations of M1 neurons during sequential 20-ms time bins from the start to the end of movement predicted the continually changing trajectory of the arm motions 100 to 150 ms into the future while monkeys made reaching movements or traced spirals on a computer monitor. This showed that the simple vector notation could be used to extract from the activity of populations of neurons a signal about intended motor output even on a moment-to-moment basis. These findings were anticipated by a prescient study in 1970 by Donald Humphrey and colleagues, who showed that the appropriately summed activity of three to five M1 neurons was better correlated to the temporal patterns of motor output during single-joint movements than was the signal of any of the single neurons.

Subsequent studies used the population-vector decoder algorithm to provide further insight into neural processing in M1. In one study, the activity of proximal arm–related M1 neurons was recorded while monkeys performed two tasks (Figure 34–22B). In the first task, they generated isometric force ramps in eight different spatial directions uniformly distributed at 45° intervals in a horizontal plane against a rigid handle that they held in their hand, without arm movements. A 20-ms population-vector decoder was used to extract the net directional bias of the pooled activity of many M1 neurons, and the result showed that these pooled signals varied systematically with the direction of output forces throughout the duration of the force-ramp generation, even though there were no movements. However, unlike the actual uniformly distributed directions of the forces generated by the monkey at the hand, the decoded population-vector signals were skewed toward the *x*-axis. This showed that the M1 activity reflected the nonlinear relationship between causal shoulder muscle torques and measured isometric forces at the hand resulting from the complex biomechanical properties of the arm (see Figure 34–20).

In the second task, the monkeys made reaching movements of the arm in the same eight directions to move a heavy handle. This required an initial accelerative force in the direction of movement and then a transient reversal of the direction of forces to decelerate the movement of their arm and the mass as it approached the target. The decoded M1 population-vector signals in this task varied dramatically through time. They were directed initially toward the target but then transiently reversed just before the peak of hand velocity. This showed once again that the M1 activity was more closely correlated with the time course of causal forces generating the reaching movements, including their transient directional reversal, than to the uninterrupted motion of the hand toward the target. They also found that correlates of the forces to generate reaching were strongest in M1, weaker in PMd, and largely absent in PE/MIP. This indicated that, unlike M1, reach-related neurons in area PE/MIP generated a reliable signal about stable arm postures and the kinematics of arm movements independent of the underlying causal forces and muscle activity.

Finally, one study has shown that reliable signals about the time-varying activity of proximal-arm muscles during reaching movements can be extracted from the activity of a population of simultaneously recorded M1 neurons. Another study found that the pooled activity of M1 neurons that fire selectively in connection with either shoulder or elbow movements can predict the changes in onset times and levels of contractile activity of the shoulder or elbow muscles during reaches in different directions.

These studies showed that the pooled activity of many M1 neurons is a rich and reliable source of signals about different time-varying attributes of whole-arm movements. This provided an important conceptual foundation for the development of more sophisticated decoder algorithms in brain–machine interfaces that make use of the movement-related information available in the simultaneous activity of many M1 neurons to allow subjects to control the actions of neuroprosthetic devices by covert modulations of M1 neuron activity without overt limb movements (Chapter 39).

Primary Motor Cortical Activity Also Reflects Higher-Order Features of Movement

Activity in M1 is not correlated only with causal forces and muscle activity. Many studies, beginning with those of Ed Evarts, that have attempted to dissociate kinematic from kinetic properties of motor outputs have found that the activity of some M1 neurons varies with the direction of movement but is only weakly influenced or not influenced at all by changes in output forces. Such neurons appear to preferentially signal the kinematic aspects of limb motion.

Changes in behavioral task can influence the relationship between M1 activity and motor output. One study has highlighted how contextual changes in an isometric force task altered the coding of force magnitude by M1 neurons. Either the order of forces or the range of expected forces results in changes in the activity in M1. They suggested that M1 neurons could dynamically adjust their relationship to output forces to optimize precision of control as a function of the range of forces that would be encountered in a given context. Another study found that many CM neurons may discharge intensely when monkeys performed precisely controlled force tasks with low force levels but are relatively inactive when the monkeys generate powerful contractions of the same muscles to make brisk, back-and-forth movements of the handle. Likewise, a study demonstrated that CM cells in

M1 could be very active when monkeys generated a precision-pinch grip of the thumb and index finger with relatively low force output, but were much less active or nearly silent when the animals generated much larger forces with a power grip involving the entire hand.

Still another study has shown that some M1 neurons that respond to loads applied to the limb during postural control can lose this load sensitivity as soon as the monkey makes a reaching movement to another spatial target, and vice versa. That is, those neurons can reflect output forces during postural control, but reflect only kinematics during movement. This change in the cell's response occurs quite abruptly, about 150 ms before the onset of movement. Importantly, any neurons that are sensitive to loads during both posture and movement will retain the same motor field across behaviors; that is, if the neuron responds only to shoulder flexor loads during postural control, it will respond only to shoulder flexor loads during reaching.

Even a simple change in the metrics of limb movement can have a large influence on M1 activity. In a study of monkeys making slow or fast reaching movements in different directions from a central target to peripheral targets, proximal limb muscles displayed relatively simple scaling of their activity patterns, reflecting increased forces for faster and longer reaches. In contrast, M1 neurons displayed a broad range of changes in their activity patterns that rarely paralleled the pattern of changes observed for muscles.

Activity in neurons can also correlate with higher-level features of movement such as the nature of an upcoming motor action. This was demonstrated in a study in which monkeys were trained to make wrist movements to three targets in a row starting from one extreme, stopping at a central position, and then finishing at the other extreme. Visual cues instructed the monkeys when to make each movement. Because the task used a predictable sequence of wrist movements, the monkeys knew before the visual cues appeared what would be the next direction of movement. While many M1 neurons signaled the current wrist posture or the direction of each movement while they were being performed, some M1 neurons reliably signaled the next movement in the sequence before the visual cue appeared. Many subsequent studies have confirmed that M1 neurons can signal impending intended movements, although these planning-like signals are not as prominent in M1 as in premotor cortical areas.

In summary, neural recording studies have revealed a diverse range of response properties within and across movement-related cortical areas, with stronger correlations to causal movement kinetics in M1 and to higher-order motor parameters in premotor and parietal cortex. However, these experimental findings have not yet led to a single unifying hypothesis about how cortical motor circuits control voluntary movements. Part of this uncertainty may result from inadequacies in experimental task design.

Representational motor-control models have interpreted these complex results as evidence of the transformations between different levels of representation of intended movements performed by neural populations distributed across different cortical motor areas. In contrast, nonrepresentational motor-control models such as optimal feedback control argue that these same results can only be interpreted as evidence of when and where neural correlates of different motor output parameters emerge in the dynamical activity distributed across cortical motor areas but do not shed much insight into the underlying neural computations. This illustrates the experimental challenges still confronting researchers as they try to reverse engineer the cortical motor circuitry to reveal its internal computational organization.

Sensory Feedback Is Transmitted Rapidly to the Primary Motor Cortex and Other Cortical Regions

Postcentral and posterior parietal cortex provide much of the sensory information related to the position and motion of the body and the location of spatial goals that is important in voluntary motor control, although the cerebellum is likely another important source (Chapter 37).

The type of afferent information transmitted to M1 differs between the proximal and distal portions of the limb. Afferent input from cutaneous and muscle sensory neurons is equally prevalent for hand-related neurons, reflecting the importance for both sources of sensory feedback when grasping and manipulating objects with the hand. Muscle afferents provide the major source of feedback from the proximal limb. Information from muscles is more prevalent in the rostral M1, whereas cutaneous input is more common in the caudal M1. Muscle afferent feedback to M1 is surprisingly rapid as it takes as little as 20 ms for M1 neurons to respond following a mechanical disturbance to the limb. Analogous to reaching, neural activity is broadly tuned to the direction of the mechanical disturbance.

Sensory feedback supports our ability to make rapid goal-directed corrections for motor errors that arise during movement planning and execution or are caused by unexpected disturbances of the limb. When a perturbing mechanical load is applied to the limb, the motor system generates a multipeaked compensatory electromyographic response, beginning with a short-latency stretch response (20–40 ms after the perturbation), followed by a long-latency response (50–100 ms) and then a so-called "voluntary" response (≥100 ms). The short latency of the initial response indicates that it is generated at the spinal level. The response is relatively small and stereotyped, and its intensity scales with the magnitude of the applied load. In

contrast, motor corrections beginning in the long-latency epoch (50–100 ms) are modulated by a broad range of factors necessary to attain a behavioral goal, including the physics of the limb and environment, the presence of obstacles in the environment, the urgency of the goal, and properties of the target, including alternate goals. These context-dependent features suggest the long-latency feedback epoch is an adaptive process in which the control policy (ie, feedback gains) is adjusted based on the behavioral goal, as predicted by the optimal feedback control model.

The ability of the motor system to rapidly generate these goal-directed long-latency motor responses is supported by a transcortical feedback pathway. Neural activity across frontoparietal circuits responds rapidly to mechanical disturbances to a limb, and the pattern of activity across the cortex depends on the behavioral context. Perturbation-related activity is observed in all cortical regions beginning at approximately 20 ms after the disturbance even if the monkey is distracted by watching a movie and does not have to respond to the disturbance (Figure 34–23A,B). If the monkey is actively maintaining its hand at a spatial goal, there is an immediate increase in the neural response in parietal area PE following the disturbance, followed shortly thereafter by changes in activity in other cortical regions (Figure 34–23A,B). If the disturbance is a cue that instructs the monkey to move to another spatial target, then M1 activity reflects the need for a more vigorous response if the disturbance knocks the hand away from the target compared to knocking the hand into the target (Figure 34–23C). In contrast, perturbation-related activity in PE remains similar regardless of target location.

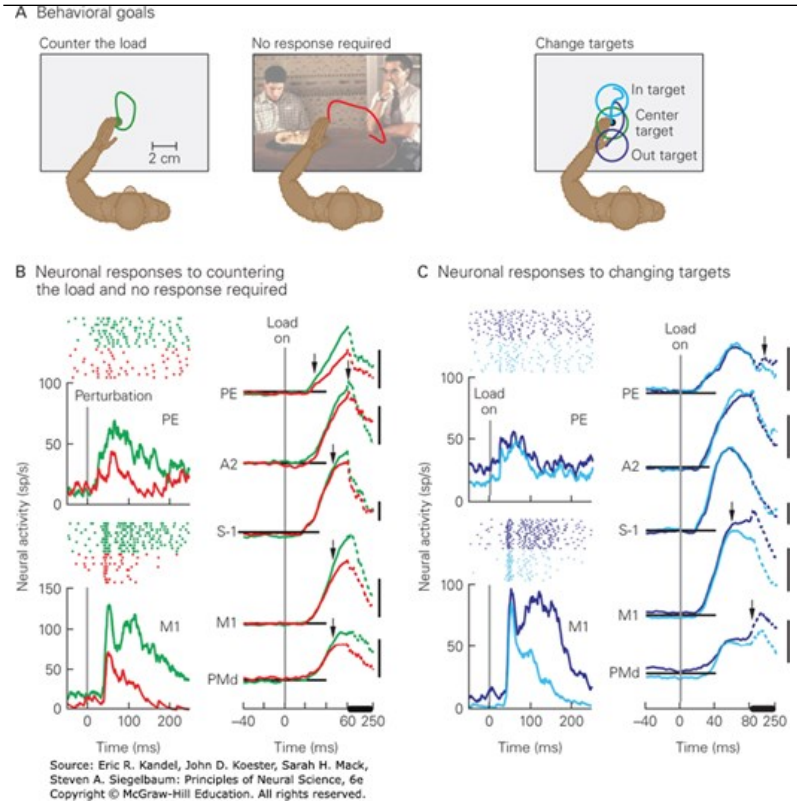
Figure 34–23

Changes in behavioral goals alter rapid sensory feedback to parietal and frontal motor cortices. (Reproduced, with permission, from Omrani et al. 2016. Part A photo is from the film American Pie and is reproduced, with permission, from Universal Studios. © 1999, Universal Pictures, All Rights Reserved.)

A. In the experiment described here, the responses of cortical regions to mechanical loads randomly applied to the arm are compared. In the *left* panel, motor corrections return the hand to the spatial goal following the disturbance (**green hand trajectory**). In the *middle* panel, the monkey watches a movie and does not have to respond to the disturbance, leading to the hand remaining to the right following the disturbance (**red hand trajectory**). In the *right* panel, the monkey places its hand at a central start target, and one of two other targets is also presented. The disturbance applied to the limb is a cue for the monkey to move to this second target with its position being either in the direction of the disturbance (**cyan** "in target" trajectory) or away from the disturbance (**blue** "out target" trajectory).

B. *Left:* Response of a neuron in PE and in M1 when a mechanical load was applied to the limb and the monkey had to counter the load and return the hand to a spatial target (**green**) or was not required to respond to the disturbance (**red**). *Right:* Population signals in each cortical region in response to perturbations. Note how all cortical areas show an increase in activity approximately 20 ms after the applied load. **Arrows** denote when activity was different when the monkey had to respond to the disturbance (**green curve**) as compared to not being required to respond to the disturbance (**red curve**). Note that PE is the first to show a difference in activity between the two conditions. Other cortical areas show changes at 40 ms or later. **A2** is a subregion of S-I. (For B and C: Vertical scale bars, 20/spikes/s); Activity between 60–250 ms (**thick horizontal line**) compressed for visualization purposes.)

C. *Left:* Responses of single neurons in PE and M1 when a mechanical load was a cue and instructed the monkey to move to another target. The disturbance either pushed the hand toward the target (**cyan**) or away from it (**blue**). *Right:* Population signals based on perturbation-related activity in each cortical region for the "in target" and "out target" conditions. The initial responses are similar for both "in target" and "out target" disturbances across all cortical areas, and **arrows** denote when there is a difference in activity between conditions. M1 is the first to display an increase in activity for the "out target" disturbance just prior to changes in muscle activity moving the hand to the spatial target.



The Primary Motor Cortex Is Dynamic and Adaptable

One of the most remarkable properties of the brain is the adaptability of its circuitry to changes in the environment—the capacity to learn from experience and to store the acquired knowledge as memories. When human subjects practice a motor skill, performance improves.

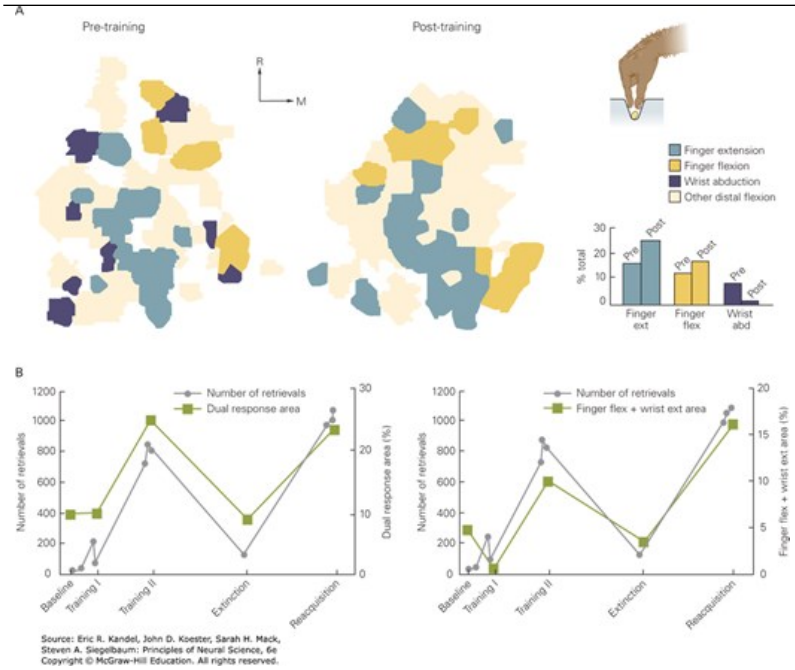
Motor experience can also modify the motor map. In monkeys trained to use precise movements of the thumb, index finger, and wrist to extract treats from a small well, the area of the motor map in which intracortical microstimulation (ICMS) could evoke movements at these joints was larger than before training (Figure 34–24). If a monkey did not practice the task for a lengthy period, its skill level decreased, as did the cortical area from which the trained movements could be elicited by ICMS. Similar modifications of the cortical representation of practiced actions in humans have been demonstrated by functional imaging and transcranial magnetic stimulation.

Figure 34–24

Learning a motor skill changes the organization of the M1 motor map. (Reproduced, with permission, from Nudo et al. 1996. Copyright © 1996 Society for Neuroscience.)

A. Motor maps for the hand in a monkey before and after training on retrieval of treats from a small well. Before training, areas of the motor map that generate index finger and wrist movements occupy less than half of a monkey's motor map. After training, the area from which the trained movements can be evoked by intracortical microstimulation expands substantially. The area of the map from which one could elicit individuated movements such as finger extension and flexion has expanded considerably, while the areas controlling wrist abduction, which this monkey used less in the new skill, became less prominent. (Abbreviations: **M**, medial; **R**, rostral.)

B. The areas of the motor output map parallel the level of performance (number of successful pellet retrievals) during acquisition of the motor skill and extinction (due to lack of practice). Two areas were tested: a "dual response" area (*left plot*), from which any combination of finger and wrist motions could be evoked, and an area from which the specific combination of finger flexion and wrist extension could be evoked (*right plot*). Both areas increased as the monkey's skill improved with practice and decreased as the monkey's skill was extinguished through lack of practice. These data are from a different monkey than the one in part **A** but trained for same task.



At least some of the processes contributing to these changes to the motor map are local to M1 itself. One of the mechanisms contributing to the cortical reorganization underlying improved reach-to-grasp performance in rodents involves changes in synaptic strength similar to long-term potentiation and depression within the local horizontal connections linking different parts of the arm motor map. It has been shown that spike-triggered ICMS could cause specific alterations to the M1 motor output map even without specific training. For instance, one study first identified two different cortical sites (A and B) that caused contractions of different muscles (muscle A and muscle B, respectively) when electrically stimulated. They then recorded the activity of a neuron at site A; whenever that neuron fired, they stimulated site B. Within a day or two of this ICMS conditioning at site B, electrical stimulation of site A was able to cause simultaneous contractions of both muscles A and B. The change likely resulted from a spike-timing dependent increase in synaptic strength that was limited to the horizontal cortical projection from site A to site B. Electromyographic responses elicited by ICMS at a third site that did not receive similar conditioning did not change, confirming that the effect was not generalized.

Motor adaptation to visual or mechanical disturbances has been studied extensively in human subjects (Chapter 30). Neural-recording studies have demonstrated that these alterations lead to changes in the activity of M1 neurons in monkeys as the animals adapt to the perturbations. For instance, when monkeys make reaching movements in a predictable external force field that pushes on the arm in a direction perpendicular to the direction of movement, their initially curved reach trajectories get straighter. As this adaptation evolves, large increases gradually arise in the activity of M1 cells whose preferred directional tuning is opposite to the applied force field. The magnitude of such adaptation-dependent changes in activity diminishes progressively as the angle between the force direction and cell preferred direction increases, following a cosine-like function. This shows that the adaptive changes were specific to the neurons that would make the greatest contribution to compensate for the external force field.

Another example of selective changes in M1 activity during motor learning comes from a visuomotor learning study in which visual feedback from a computer monitor is rotated 90° clockwise such that movements of a monkey's arm to the right result in downward movement of the cursor. Initially, the monkeys make arm movements in the original direction aimed at the visual target location, with corrections made online after movement onset. However, with practice, the monkeys begin to move in a new direction rotated counterclockwise to the visual target so that the cursor moves directly to the target. When training occurs for only one direction, learning generalizes poorly to other directions, suggesting that the adaptive changes occur only in neurons that evoke the adapted movement. The tuning curves of neurons with preferred directions near the learned direction were altered during training, whereas neurons with other preferred directions were not affected by the training. This confirmed that the adaptation was local, consistent with the findings of the force-field adaptation study, and explained why adaptation to the visuomotor rotation in one direction generalized poorly to other directions.

Motor-error signals in the precentral cortex also play an important role in trial-by-trial motor adaptation based on feedback learning. In one study with monkeys, an adjustable prism was used to displace the apparent location of the reach target in the environment. Visual feedback of the target and arm were blocked during the reaching movements, leading to systematic errors in touching the target. The monkeys were allowed to see visual feedback of the position of the hand relative to the target for a brief period of time at the end of movement (Figure 34–25). Activity in M1 and PMd during that brief

period of visual feedback after movement reflected the direction of reach end-point errors and could be involved in adapting reaching movements to correct these errors. To test that hypothesis, ICMS was then used in M1 and PMd to simulate those error responses and showed that the monkeys began to make adaptive changes in their reaching movements to compensate for the simulated errors even though no reaching error was actually made.

Figure 34–25

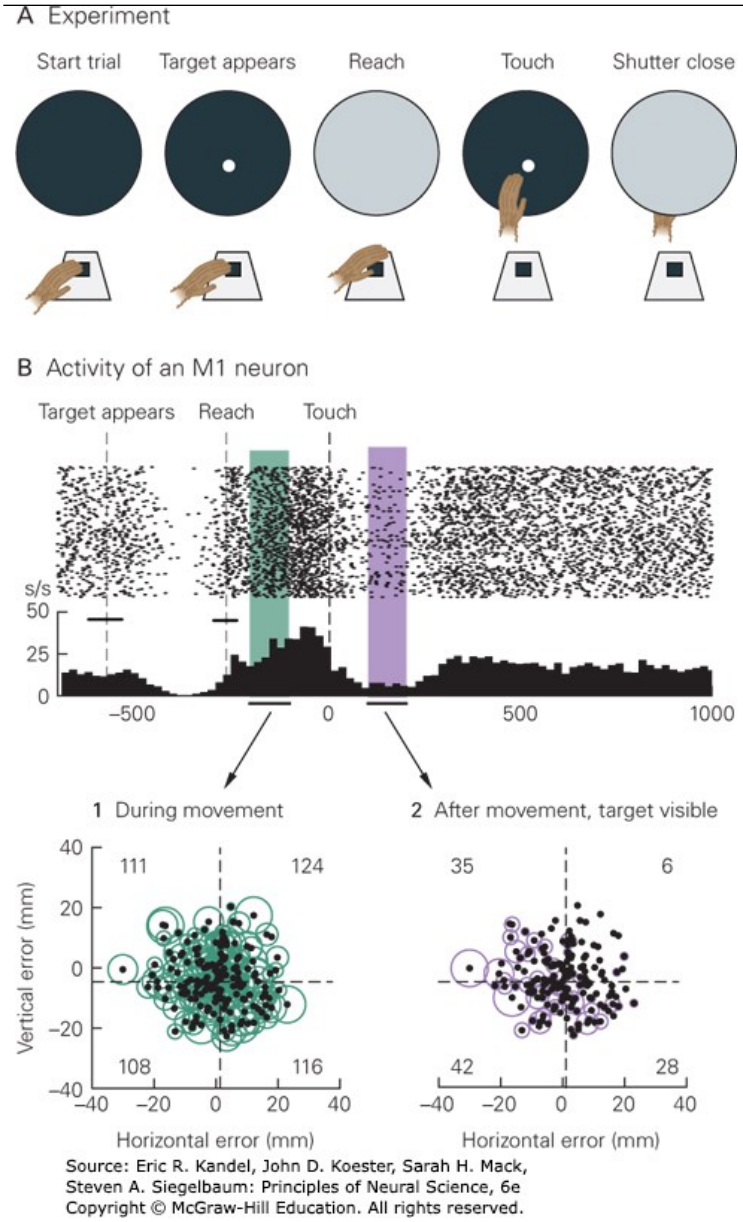
(right) Error signals in the primary motor cortex drive adaptation. After a movement is complete, M1 activity reflects the error between the spatial target and final hand position. (Reproduced, with permission, from Inoue, Uchimura, and Kitazawa 2016. Copyright © 2016 Elsevier Inc.)

A. Monkeys made reaching movements to spatial targets on a touch screen. On each trial, adjustable prism goggles shifted the viewed position of the spatial target by a variable amount during the movement, while a shutter blocked vision of the monkey's hand and the target. Feedback of the final hand position was only provided for 300 ms after contact with the touch screen at the end of movement.

B. Top: Discharge response of a typical M1 neuron. Raster plots and spike-timing histograms are aligned with the initial screen contact (touch).

1. Distribution of reach endpoint errors (**black dots**) where the origin represents the center of the target. **Diameters of green circles** denote the firing rate of the neuron during each movement (**green bar** in **B**); the firing rates were unrelated to the subsequent endpoint error. The numbers in each quadrant indicate the summed spike activity during movements that ended in the corresponding quadrant; they are all nearly equal.

2. Same as in part **B** except **purple circles** denote firing rate 100 to 200 ms after movement while the monkey can see its hand while touching the screen (**purple bar** in part **B**). The circles and spike counts show that the firing rate is greatest for endpoint errors down and to the left relative to the position of the target (0,0), revealing that that the neural activity during this postmovement period is strongly modulated by visual feedback of reach endpoint error.



Source: Eric R. Kandel, John D. Koester, Sarah H. Mack, Steven A. Siegelbaum: Principles of Neural Science, 6e

Some motor skills are relatively easy to learn, such as compensation for a visuomotor rotation. Others, however, are very difficult to learn. Recent studies examined this discrepancy by first measuring the activity of a population of M1 neurons as the monkey moved a cursor on a computer screen using a brain–machine interface and a neural activity decoder. This population-level mapping between M1 activity and cursor motion was then altered by changing the association between the directional tuning of each neuron and cursor motion in the decoder. When the altered decoder mapping retained the normal co-modulation structure of neural activity, as would be the case for instance if the mapping between the activity of all neurons and cursor motions was rotated clockwise by 45°, the monkeys showed significant adaptation to the perturbation within a few hundred trials during a single recording session. In contrast, when the perturbation required the monkeys to learn a more complex “unnatural” remapping, for instance, random clockwise and counterclockwise rotations of the apparent directional tuning of neurons by different amounts, the monkeys showed little ability to recover proficient cursor control over several hundred trials in a single recording session. Importantly, another study found that monkeys could eventually master an “unnatural” change in an M1 neural activity decoder mapping if they could practice with the same altered decoder over several days, indicating that they could learn a new neural co-modulation structure if allowed enough experience with it. These studies reinforce how neural circuits in these cortical motor regions are critical for motor skill learning.

The studies just described used brain–machine interfaces and neural decoders to explore how single neurons and neural populations contribute to motor skill learning. This technology promises to be an increasingly important research tool for developing new insights into the neural mechanisms

of voluntary motor control and motor skill learning (Chapter 39).

Highlights

1. Voluntary motor behavior implements an individual's intentional choice or decision to move within, and to interact physically with objects in, the environment. A hallmark of human motor action is the breadth of skills we possess and, when highly practiced, the ease and automaticity of these actions.

2. Voluntary motor control has long been separated into two stages—planning and execution—that can be dissociated in time. Neural recording studies have found correlates of these two stages differentially distributed across many movement-related cortical areas.

3. The overall computational problem that the motor system must resolve to control voluntary movement is to convert sensory information about the current state of the world and the body into plans for action and ultimately into patterns of muscle activity that generate the causal forces required to execute the desired movement(s), while avoiding or correcting for errors.

4. Representational models of voluntary motor control such as the sensorimotor coordinate transformation hypothesis assume that the motor system directly plans and controls specific features or parameters of intended movements. Single neurons and neural populations express those parameters in their activity and perform definable computations to effect the transformations between the controlled movement parameters in corresponding coordinate frameworks.

5. Dynamical systems models of voluntary motor control, in contrast, assume that motor circuits find empirical solutions for the computations underlying the planning and execution of movements by evolutionary and individual adaptive processes. One recent theory, optimal feedback control, proposes that planning and execution of voluntary movements involve three functional processes, namely, state estimation, task selection, and a control policy. Single neurons and neural populations contribute to voluntary motor control by participating in the computations underlying these three processes.

6. Distributed frontoparietal circuits in cerebral cortex play a pivotal role in voluntary control. There are substantial reciprocal axonal interconnections between frontal and parietal cortical regions, partially segregated based on body part (eg, hand, arm, eye). Frontal motor and parietal cortical regions both directly influence spinal processing through the corticospinal tract and indirectly through brain stem descending pathways.

7. Posterior parietal cortex plays a prominent role in identifying potential goals and objects in the environment, state estimation of the body, and sensory guidance of motor actions. Important sources of sensory signals are transmitted from visual cortex through the dorsal visual pathway and from primary somatosensory cortex. Behavioral goals and objects are represented in many parietal subregions, but how they are represented (relative to the orientation of the eye, head, or arm) varies across subregions. The presence of multiple representations provides a rich basis for defining the movement-relevant properties and the locations of objects in the world and relative to the body that can be used to select and guide movement.

8. Premotor and prefrontal cortices play a prominent role in task selection and motor planning. The dorsal and ventral premotor regions are often implicated when external sensory information plays a dominant role in selecting motor actions. In contrast, more medial premotor regions, such as the supplementary and cingulate motor areas, may play a more dominant role when internal desires are more critical in selecting and initiating a motor action. However, this dichotomy is not absolute, and multiple premotor and prefrontal cortical areas all contribute to the control of voluntary behavior in a broad range of contexts and conditions.

9. Primary motor cortex in primates has a representation of the entire body along its mediolateral axis, with larger cortical territories associated with the hand and face relative to other body parts. This cortical region also provides a large component of the corticospinal tract and has projections to both interneurons and alpha motor neurons in the spinal cord.

10. Neural activity that reflects the causal forces and the spatiotemporal features of muscle activity necessary to move the limb is particularly prominent in the primary motor cortex and can be rapidly altered to correct movement errors or to compensate for displacements of the limb away from the desired movement if the limb is perturbed. However, neural activity in primary motor cortex can also show more complex properties, reflecting changes based on the behavioral context, performance goals and constraints, and features such as movement kinematics. These

properties of primary motor cortex activity may reflect the formation of a task-specific control policy within the motor system.

11. Although parietal, premotor, and primary motor cortical regions play prominent roles in state estimation, motor planning, and motor execution, respectively, they are not uniquely responsible for any one aspect; they are instead distributed to some degree across most or all of these cortical regions.

12. The cortical motor system is adaptive and can undergo changes in its functional architecture to adapt to long-term changes in the physical properties of the world and the body, as well as acquire, retain, and recall new motor skills.

13. New technologies such as large-scale multi-neuron recording and imaging methods, enhanced multi-neuron activity decoding algorithms, and optogenetic control of the activity of specific neural populations will lead to deeper insights into the functional architecture of cortical motor circuits.

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