Movement

- Movement is the planning, coordination & execution of a motor program that relies on information provided by the sensory system
- Movement is controlled by the motor systems of the spinal cord and the brain
- Motor systems translate neural signals into contractile force in muscles
- Allows us to maintain balance and posture, move our body, limbs, eyes, tongue & communicate through speech

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Speaker notes

No notes on this slide.

Types of movement

- Reflex responses– knee jerk, withdrawal from pain, swallowing. Muscle contractions and relaxations that are rapid, stereotyped, involuntary and coordinated
- Rhythmic motor patterns– walking, running, chewing. Typically initiation and termination are voluntary and triggered by peripheral stimuli
- Voluntary movements– initiated movements to accomplish a specific goal (e.g. piano playing, writing). These are goal directed and largely learned movements that improve with practice, as one learns to anticipate and correct for environmental obstacles

Speaker notes

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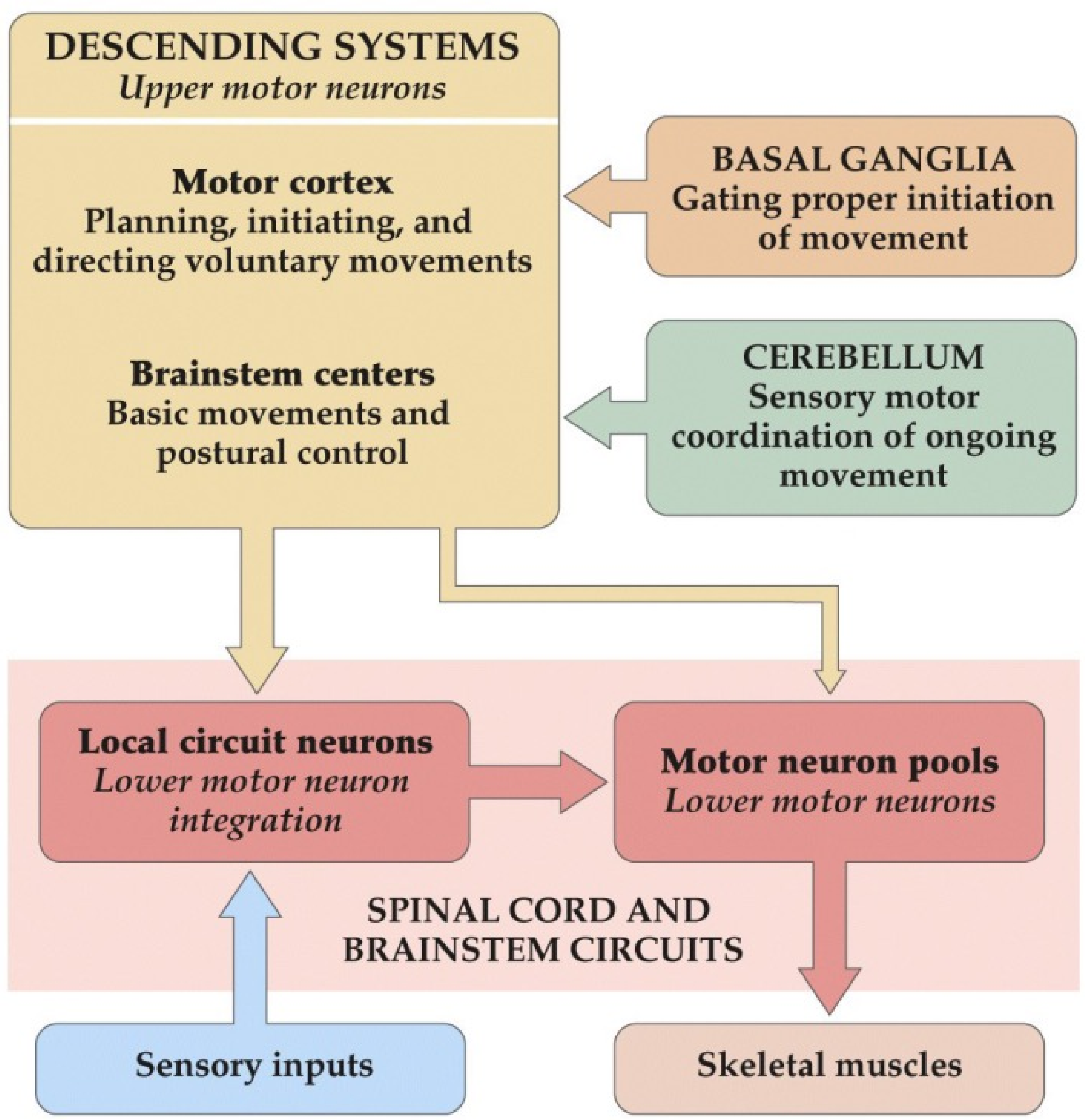
Overall organization of neural structures that control movement



Upper motor system

Gating

Motor learning

Lower motor system

Execute movement

State of muscle contraction

Output system

Neuroscience 5e Fig. 16.1

Speaker notes

No notes on this slide.

Control of movement

- Motor systems responsible for the control of movement can be divided into four distinct but highly interactive subsystems
- Lower motor system– Gray matter of spinal cord and brainstem- contain lower motor neurons and lower circuit neurons. The final common path of all motor output
- Upper motor systems– Send information to spinal cord and brain stem, initiate voluntary movements. Contains motor cortex and some brainstem centers
- Cerebellum– No direct access to lower motor systems. Connects to upper motor systems. Responsible for motor learning
- Basal ganglia– Suppresses unwanted movements and primes neurons for the initiation of movements. Parkinson’s and Huntington’s diseases affect the basal ganglia

Speaker notes

No notes on this slide.

Muscles

- Relaxation and contraction
- Muscles can pull but not push. Thus separate sets of muscles at the opposite sides of joints must mediate flexion or extension
- Movements at a joint engage two opposing sets of muscles

Speaker notes

Muscles only pull they do not push, therefore we have opposing/antagonistic muscles

EMG– electromyograph, measures electrical activity in muscles. Bicep/tricep figure with EMG histogram around elbow joint.

Coupling of excitation and contraction

- Action potential in motor axon
- End plate potential at neuromuscular junction
- Action potential in muscle fiber
- The AP in the muscle fiber is followed by a twitch in the muscle fiber
- Twitch– transient all-or-none contraction

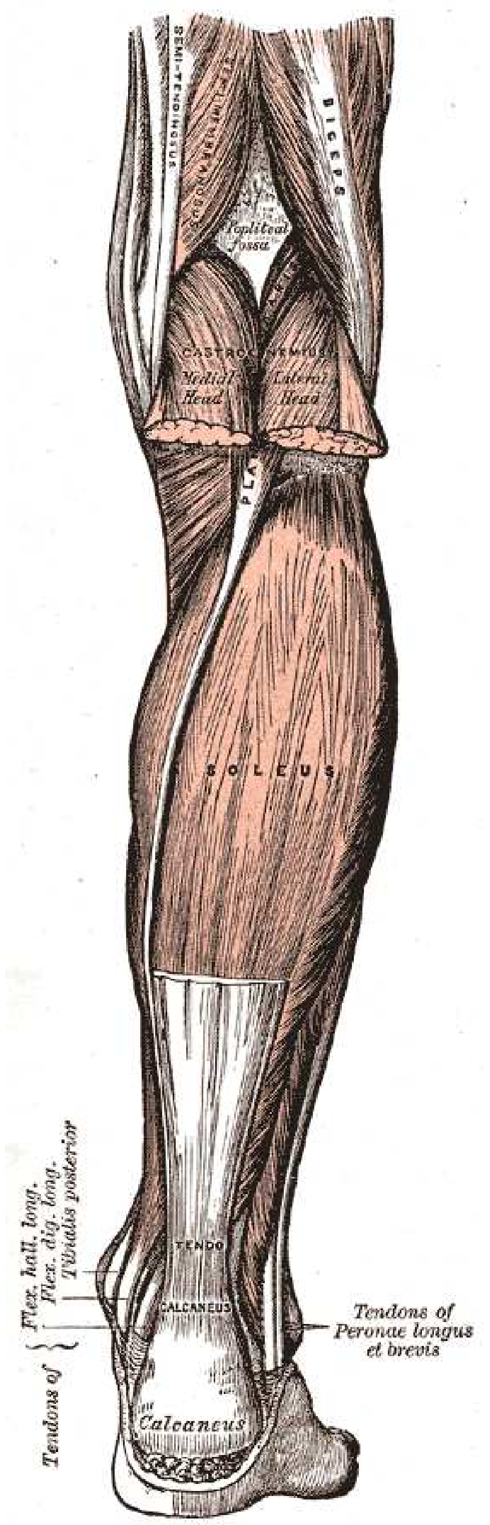
Speaker notes

- Each muscle fiber is innervated by only one motor neuron. Group of muscle fibers in a muscle innervated by a single motor neuron is a motor unit
- twitch happens after small small latency, 5-10 ms

todo: motor neuron AP --> muscle fiber EPP --> muscle fiber AP. AP and Vm in muscle fiber, latency, and muscle tension rise and decay

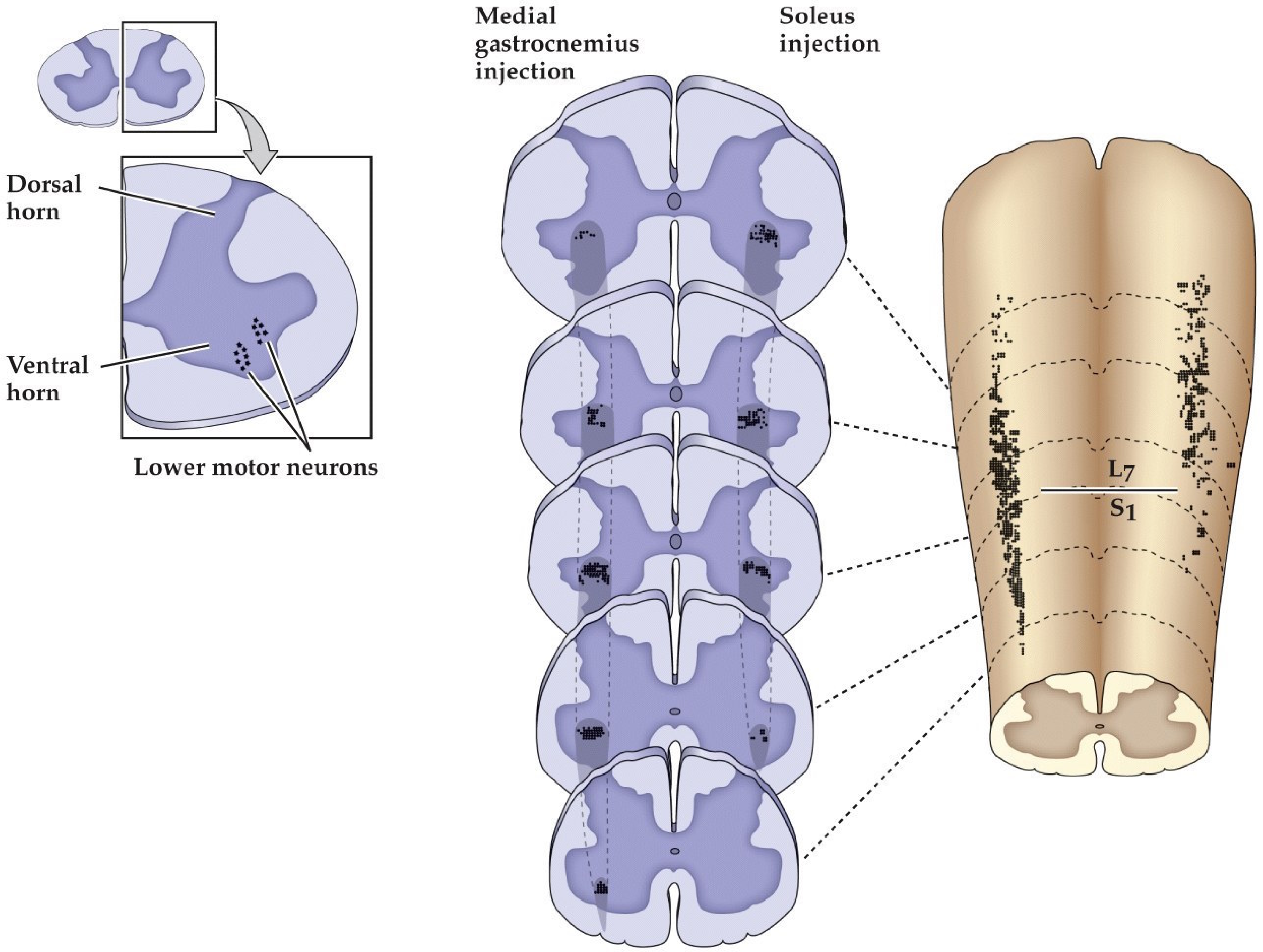
Organization of lower motor neurons in the ventral horn of the spinal cord

gastrocnemius, soleus muscle



Gray's Anatomy

retrograde motor neuron labeling



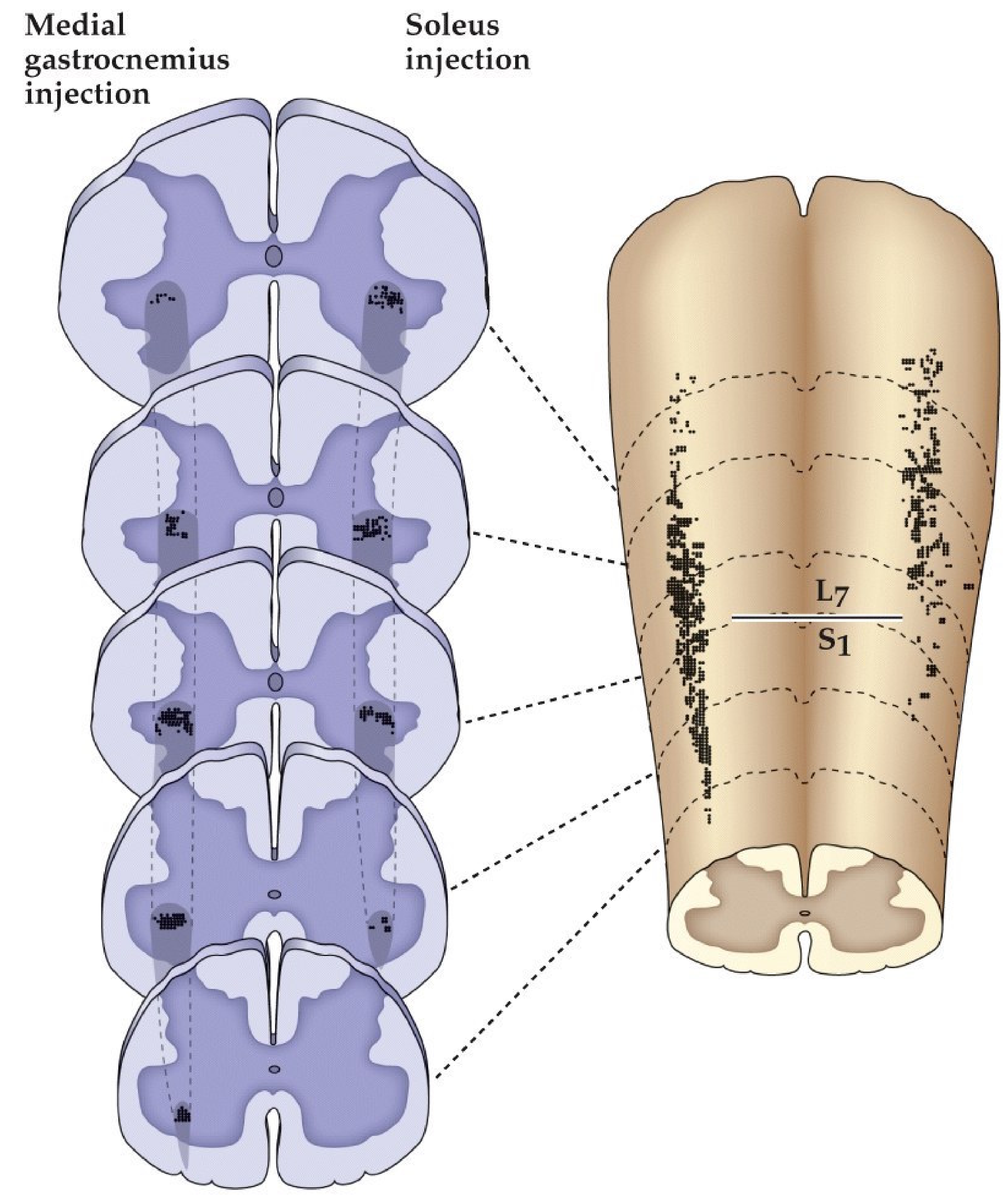
Neuroscience 5e Fig. 16.2, Burke et al., 1977

Speaker notes

- Motor neurons id. by injecting a retrograde tracer into medial gastrocnemius or soleus muscle of cat. Labels neuronal cell bodies and their spatial distribution
- Lower motor neurons form distinct clusters (motor pools)

Motor pools

- Retrograde labeling of muscles show that the cell bodies of motor neurons are found in ventral horn of the spinal cord
- Each motor neuron innervates muscle fibers within a single muscle
- All the motor neurons innervating a single muscle are grouped together in clusters called motor pools
- Motor pools are located with a slight spread along the A-P axis
- There is topography along medial-lateral axis of the spinal cord. Neurons that innervate axial musculature (trunk) are located medially, neurons that innervate distal muscles are located laterally



Neuroscience 5e Fig 16.2

Speaker notes

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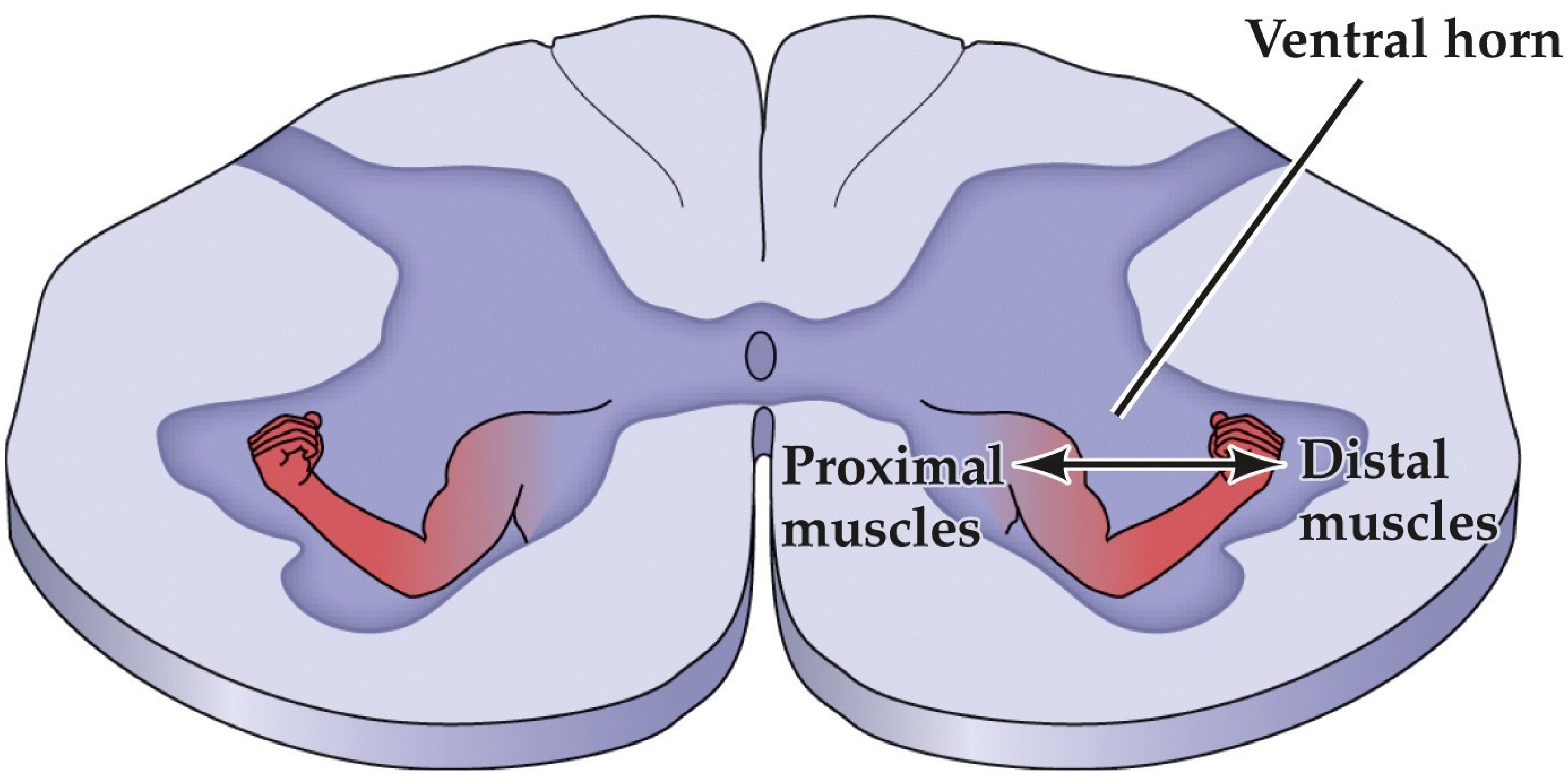
Somatotopic organization of lower motor neurons in the ventral horn



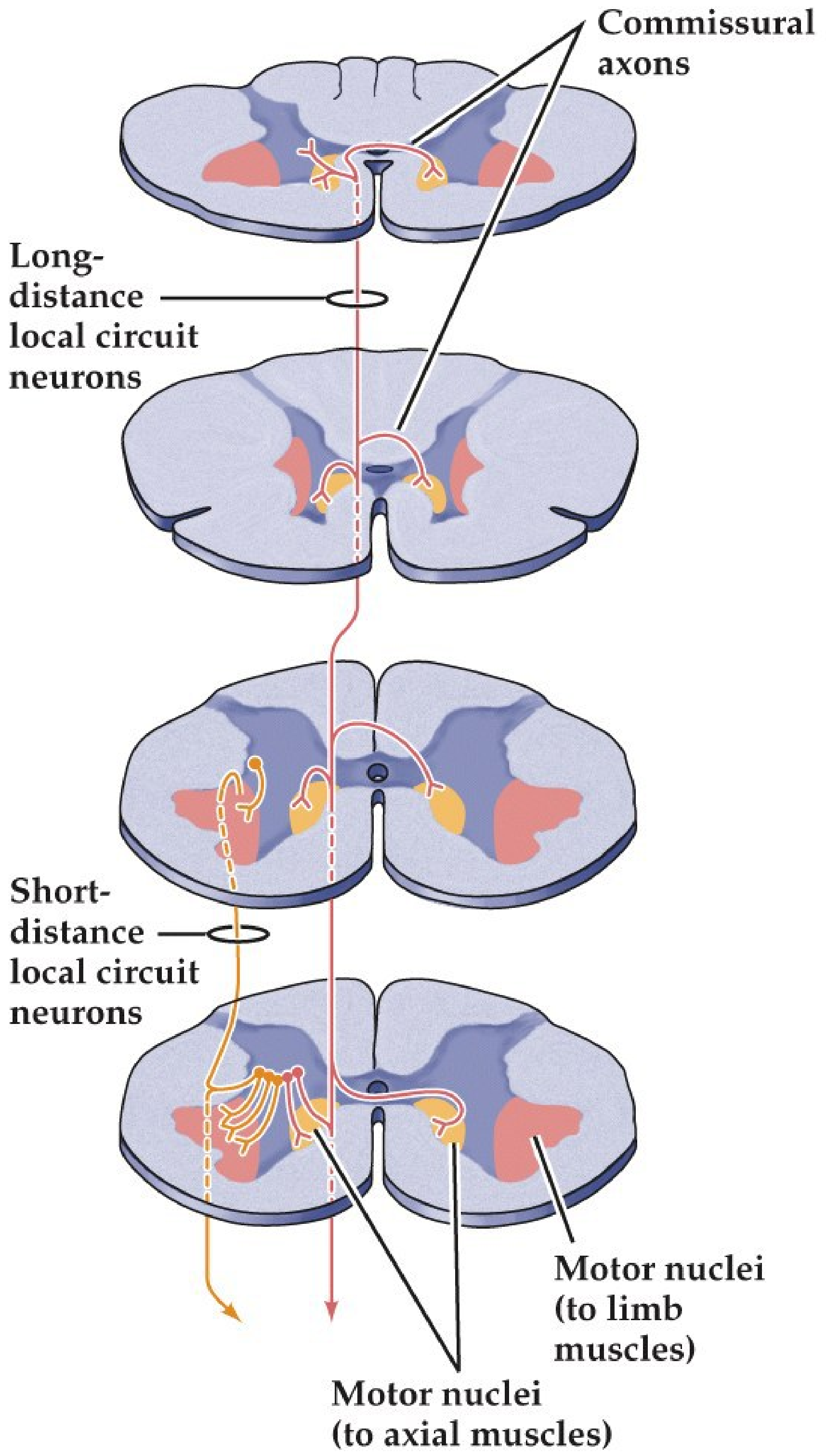
Neuroscience 5e Fig. 16.3

Speaker notes

somatotopic mapping of body parts

Location of local circuit neurons that supply the medial region of the ventral horn

- Medially localized local circuit motor neurons deal with posture, project over a few segments both contra and ipsilaterally
- Lateral circuit motor neurons deal with fine movements, project ipsilaterally



Neuroscience 5e Fig. 16.4

Speaker notes

No notes on this slide.

Types of motor neurons

- α motor neurons– innervate the extrafusal muscle fibers, the striated muscle fibers that generate the forces needed for movement
- γ motor neurons– innervate specialized muscle fibers in the muscle spindles that are embedded within connective tissue in the muscle, known as intrafusal muscle fibers. These fibers are also innervated by sensory axons that send info to the brain and spinal cord about the length and tension of muscle

Speaker notes

No notes on this slide.

Amyotrophic lateral sclerosis (ALS)

- 'Lou Gehrig's disease'
- A disease of α- motor neurons and upper motor neurons
- 30,000 Americans have it at any given time
- Both genetic and spontaneous mechanisms to contract ALS
- Superoxide dismutase (SOD1) is a gene that when mutated leads to ALS (autosomal dominant)

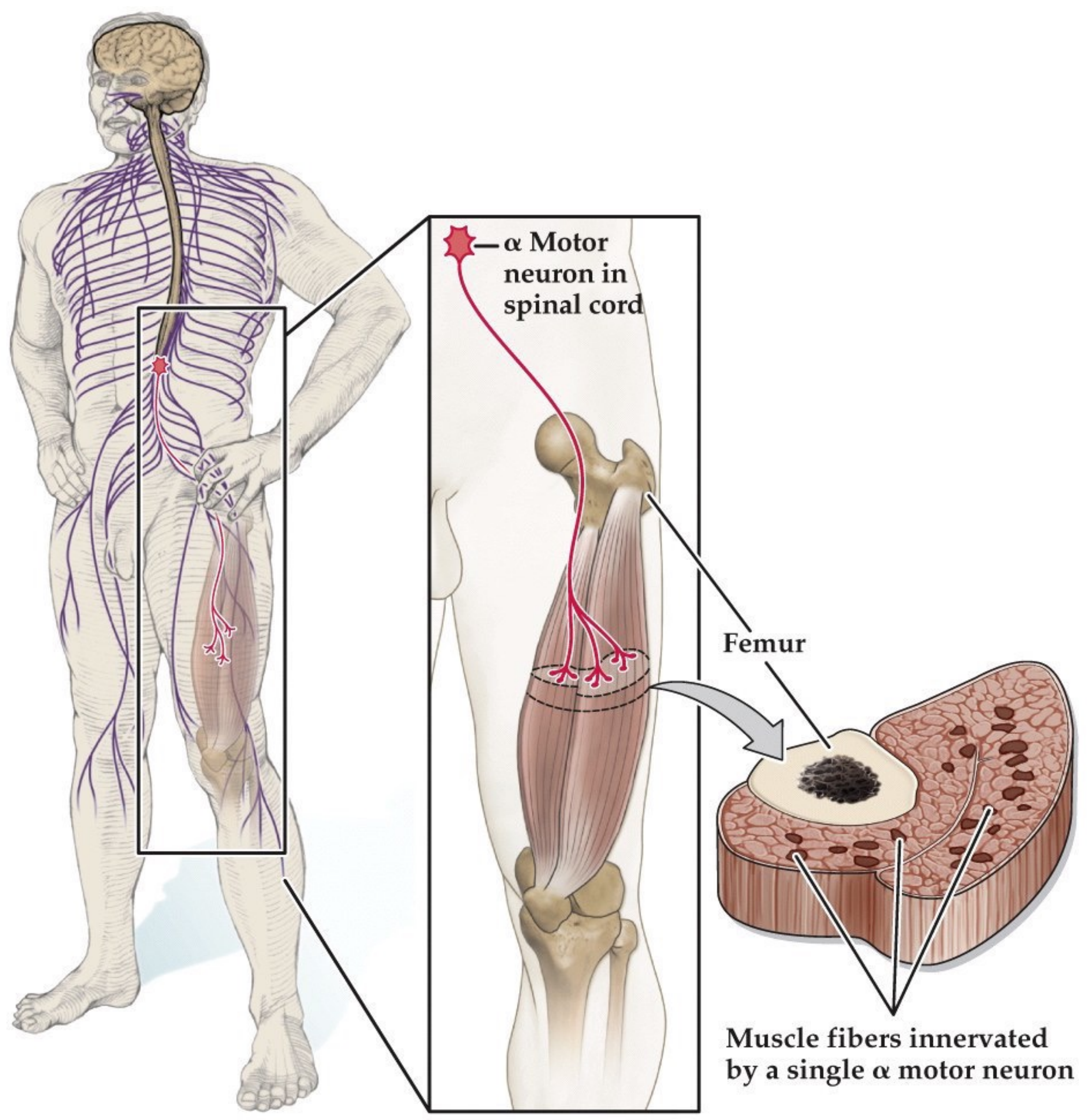
Speaker notes

axon transport disease in neurons with long axons

Superoxide dismutase
: enzyme
: helps break down potentially harmful oxygen molecules in cells

The motor unit

- A motor unit is the sum total of extrafusal skeletal muscle fibers within a muscle that are innervated by a single α motor neuron
- An action potential normally brings to threshold all muscle fibers it contacts



Neuroscience 5e Fig. 16.5

Speaker notes

motor unit

- motor unit in soleus (important for posture) has ~180 muscle fibers/per motor neuron
- gastrocnemius has large and small motor units with 1000-2000 muscle fibers per motor neuron. Generates forces for sudden changes in body position.
- extraocular motor units very small (~3 fibers/unit). High proportion of fibers that can contract at max velocity
- but lots of use dependent motor unit plasticity (athletes, hypogravity conditions)

Types of motor units

- Slow (S) motor unit– Small motor neurons innervate relatively few muscle fibers and generate small forces. They innervate small “red” muscle fibers that contract slowly but are relatively resistant to fatigue. These are rich in mitochondria and myoglobin, and are important for activities that require sustained muscular contraction such as posture
- Fast fatigable (FF) motor unit– Large motor neurons innervate larger, more powerful units. Larger α motor neurons innervate larger pale muscle fibers that generate more force, have sparse mitochondria and are easily fatigued
- Fast fatigue-resistant (FR) motor unit– are of intermediate size, not as fast as FF units but less fatigable

Speaker notes

- oxidative metabolism in slow type I to generate ATP, more mitochondria, greater capillary density
- type II are less oxidative more glyolytic by storing glycogen, white due to low myoglobin.
  - muscles have short term energy store in creatine phosphate that is used to regenerate ATP from ADP with creatine kinase
  - Glucose used for glycolysis anaerobically forming 2ATP and 2 lactic acid molecules. Fat globules during anaerobic excercise. For aerobic conditions lactate not formed, pyruvate and citric acid instead

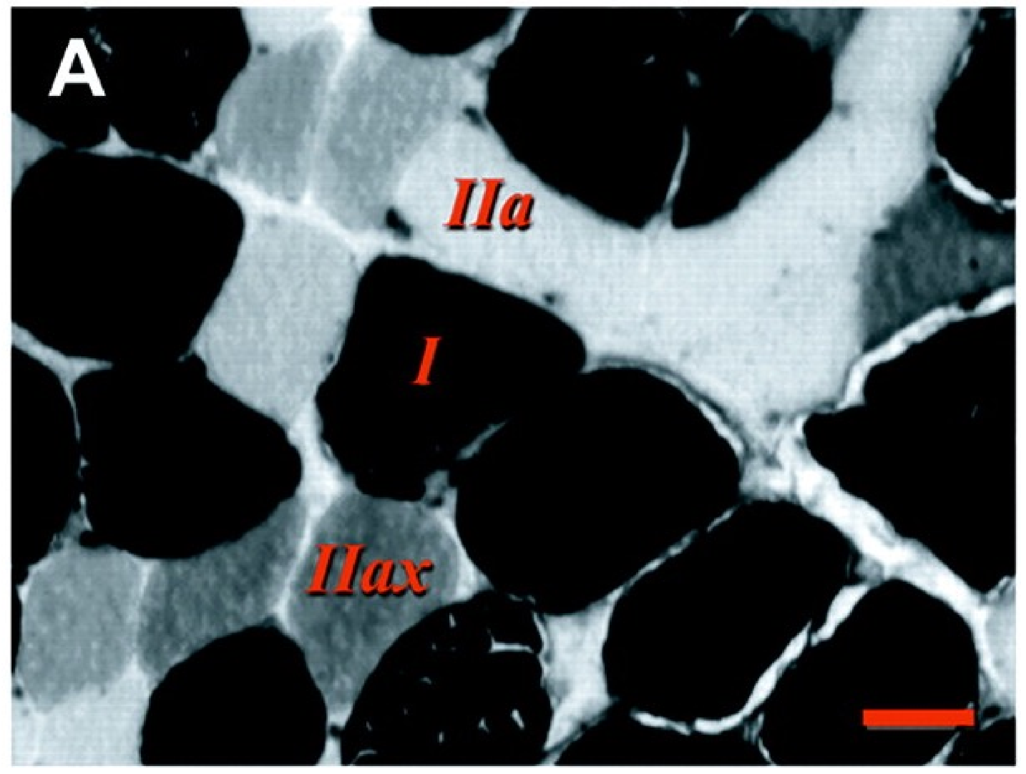
myoglobin
: related to hemoglobin
: iron and O2 binding pigment protein in muscle tissue
: cetaceans have particular high abundance of myoglobin
: not found as much in smooth muscle

neuroglobin
: present in neurons, maybe astrocytes
: seals
: CSF
: structure determined for human in 2003 and mouse soon after
: NO dynamics, neuron survival under reduced O2 conditions?

Skeletal muscle fiber types

- Histochemical staining for myosin ATPase at different shows the different fiber types
  - Type I slow (innervated by S pools) are darkest at low pH
  - Type IIa fast fatigable are lightest
  - Type IIx (IIb in other mammals) fast fatigue-resistant are light to intermediate in staining

human diaphragm myofiber myosin ATPase histology, pH 4.60



Levine et al., *J Applied Physiol* 2002 Fig. 1a. 50 µm scalebar

Speaker notes

Variation in histochemical staining for myosin ATPase activity at different pHs for the fiber types due to different Myosin heavy chain (MHC) type in the type I, IIa, IIx (formerly IIb) fibers.

IIb not actually expressed humans, but in other mammals. Human MHC IIb is actually IIx [Smerdu-1994]

Type II includes IIa, IIax, IIx, IIc (other species)

Muscles made up of fascicles, which are multiple bands of cells called muscle fibers. During development muscle fibers form from fusion of several myoblasts into long multinucleated cells. Cell size can then be regulated thereafter (e.g. with excercise). But no new muscle cells are added.

Myosatellite cells are between basemente membrane and sarcolemma of muscle fibers. Normally quiescient, but can become activated by exercise or pathology and provide extra myonuclei for muscle growth and repair[#Zammit-2006].

- Sexually dimorphic muscles include the perineal, masticatory, laryngeal muscles [#Berchtold-2000]
- hypogravity conditions affects mostly postural muscles. Body core [#Berchtold-2000]
- hypogravity conditions induced by walking on crutches or hindlimb suspension results in reduced muscle mass and strength [#Berchtold-2000]
  - reduction more pronounced in extensors than in flexors [#Berchtold-2000]

[Smerdu-1994]: Smerdu, V; Karsch-Mizrachi, I; Campione, M; Leinwand, L; Schiaffino, S (Dec 1994). "Type IIx myosin heavy chain transcripts are expressed in type IIb fibers of human skeletal muscle.". The American journal of physiology. 267 (6 Pt 1): C1723–8. PMID 7545970.

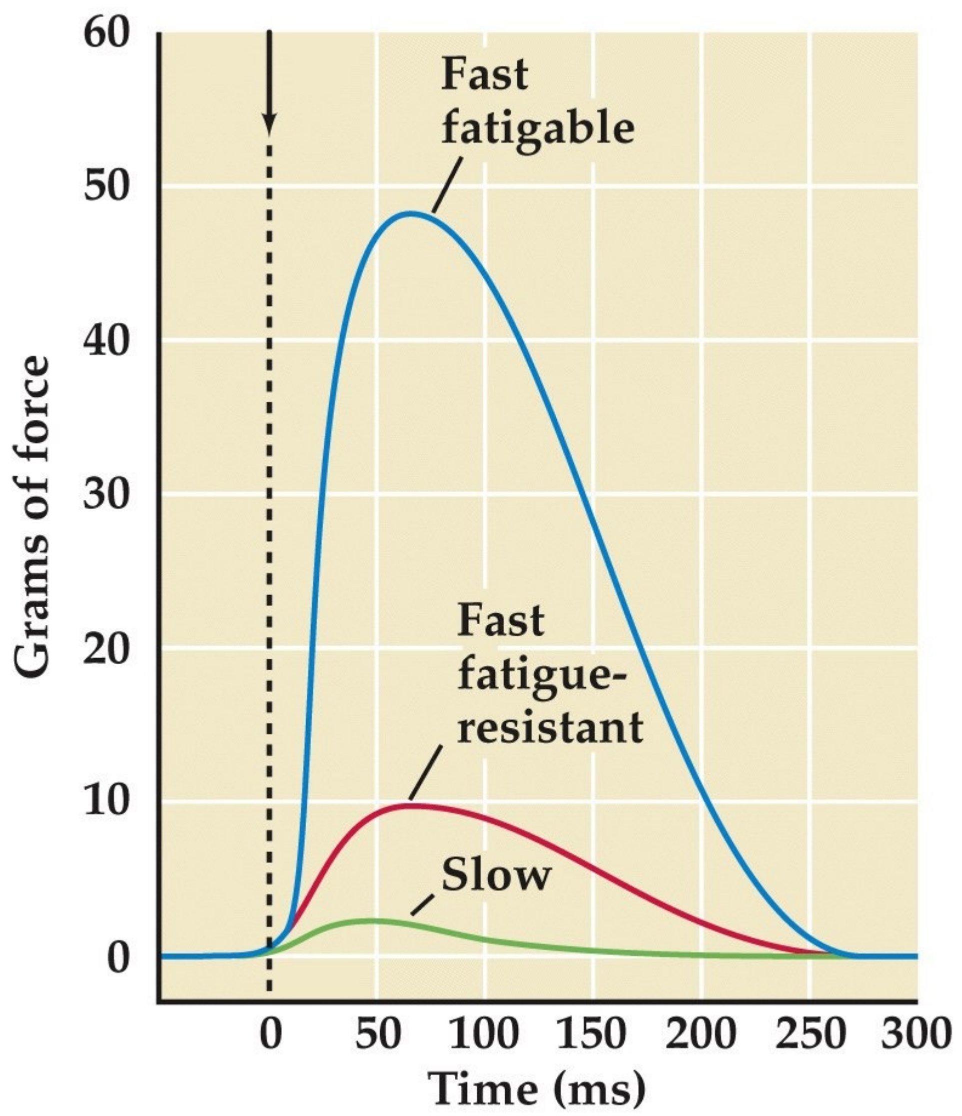
[#Zammit-2006]: Zammit, PS; Partridge, TA; Yablonka-Reuveni, Z (November 2006). "The skeletal muscle satellite cell: the stem cell that came in from the cold.". Journal of Histochemistry and Cytochemistry. 54 (11): 1177–91. doi:10.1369/jhc.6r6995.2006. PMID 16899758.

[#Berchtold-2000]: Berchtold, M. W., Brinkmeier, H., and Müntener, M. (2000). Calcium ion in skeletal muscle: its crucial role for muscle function, plasticity, and disease, Physiol Rev, 80(3), 1215-65. PMID 10893434

Force and fatiguability of the three different types of motor units

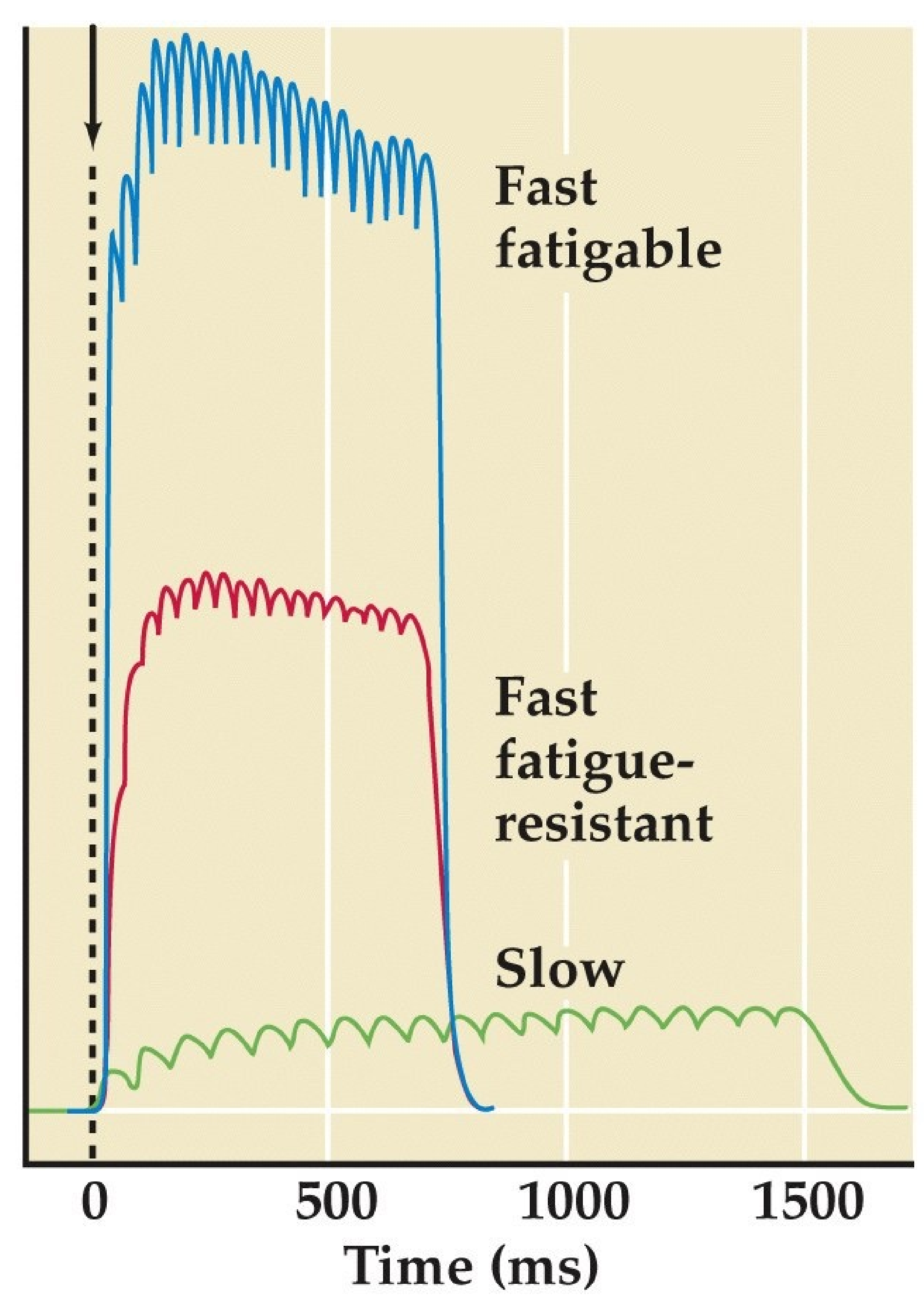
Stimulation of single α motor neurons from different classes

Single stimulation

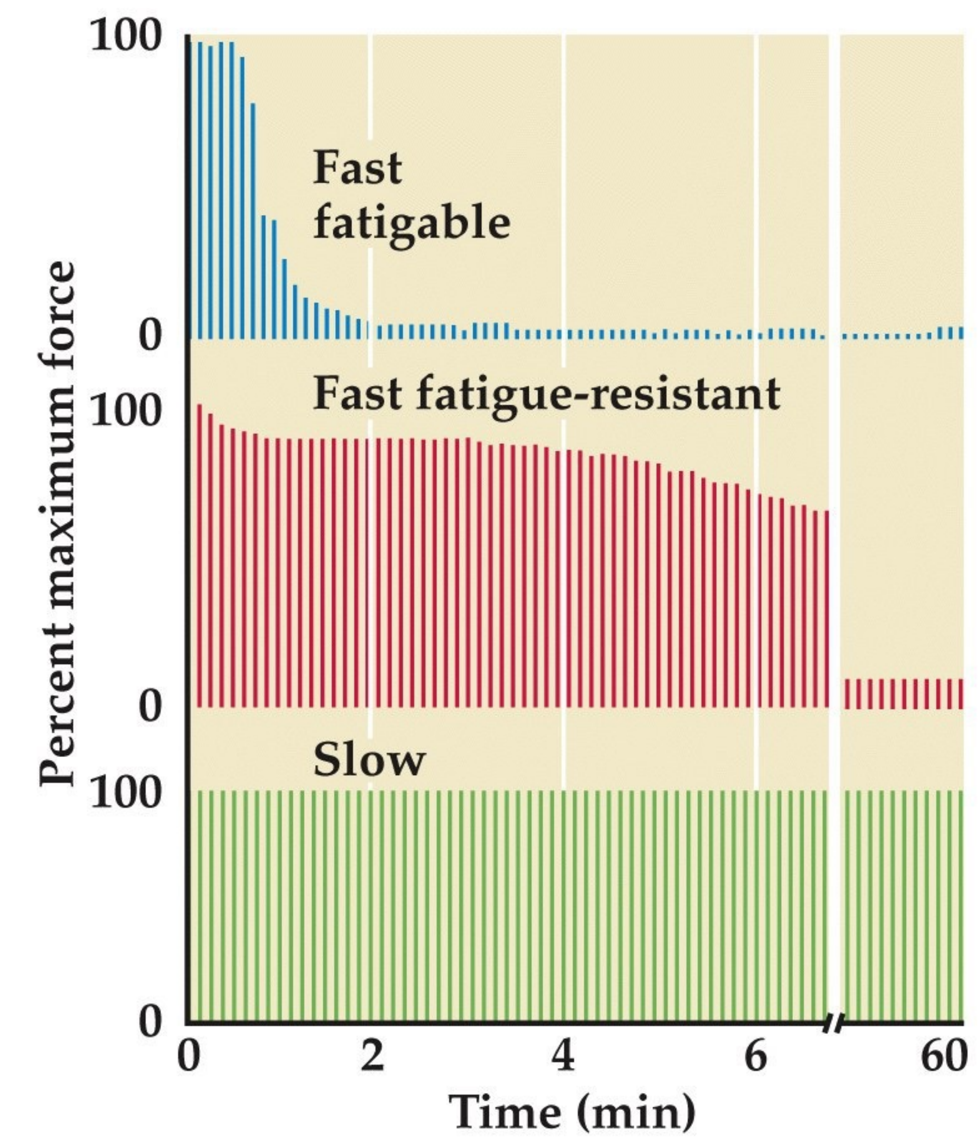


Neuroscience 5e Fig. 16.6, after Burke et al, 1974

Repetitive stimulations



Time to fatigue (minutes)



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Speaker notes

-muscle tension in resp to single AP -change in tension in resp to repetitive stimulation. Notice summation

- notice time axes in right

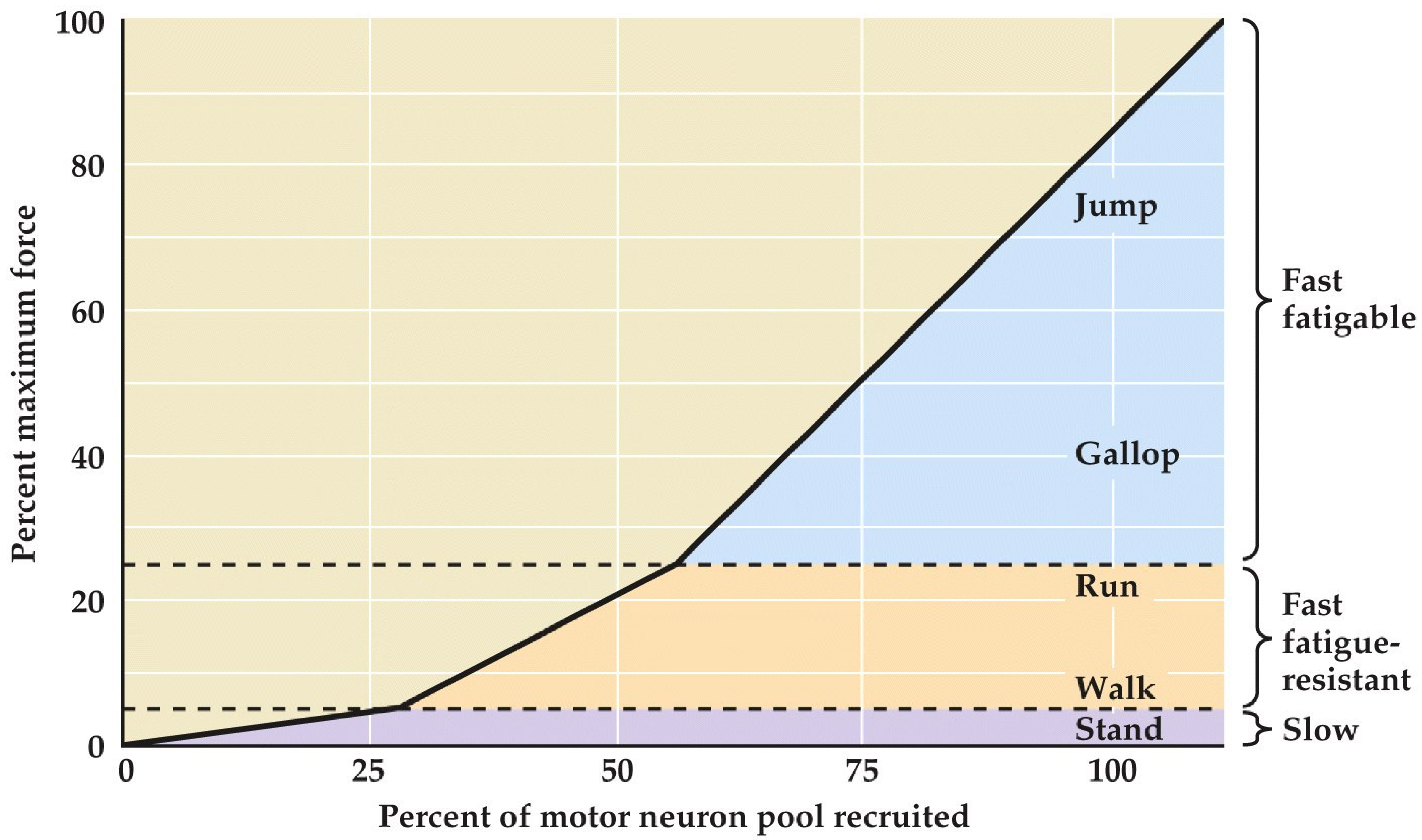
Contributions to muscle tension

- Size principle– more stimulation leads to more contraction (force produced) by the muscle
- At low stimulation, only slow groups are recruited. Additional stimulation recruits FR, while FF are recruited by the highest stimulation
- Provides a range of forces to perform different motor tasks
- Frequency of action potentials also plays a role in muscle tension. If muscle fibers are activated by a new action potential before they have had time to fully relax from the previous time, they produce more force

Speaker notes

No notes on this slide.

Recruitment of motor neurons to medial gastrocnemius (leg muscle)



Neuroscience 5e Fig. 16.7, after Walmsley et al., 1978

Speaker notes

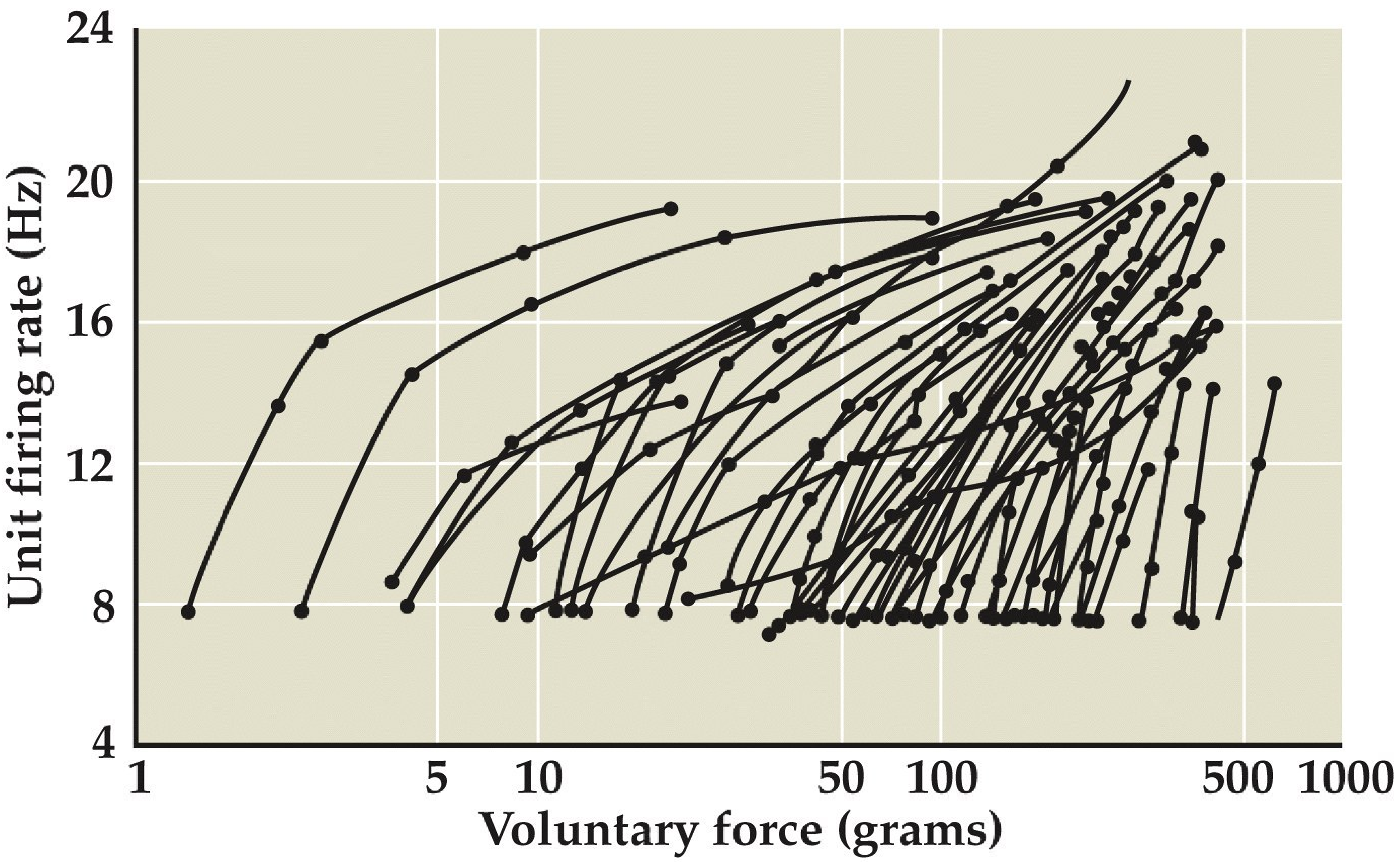
slow for standing

FR for walking or running

FF for sprinting, jumping

Motor unit activity as voluntary force is increased

small motor units ----> large motor units

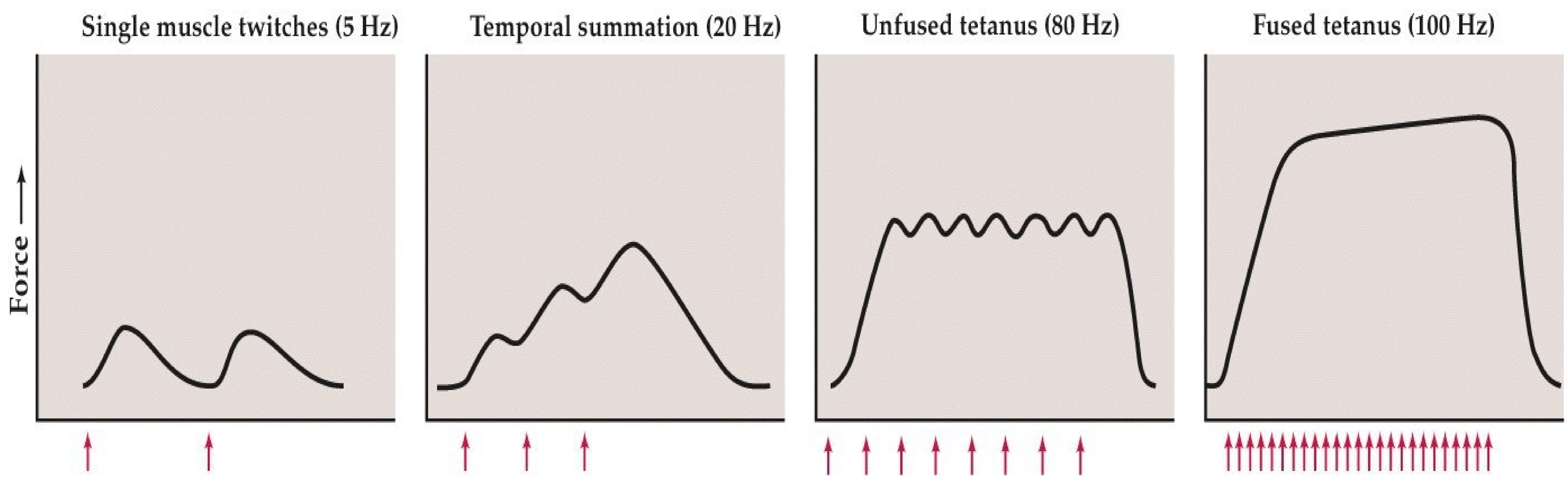


Neuroscience 5e Fig. 16.9, after Monster and Chan 1977

Speaker notes

- This is in the human hand
- low threshold motor units gen least amount of force and are first

Summation of force as a function of stimulation rate



Neuroscience 5e Fig. 16.8

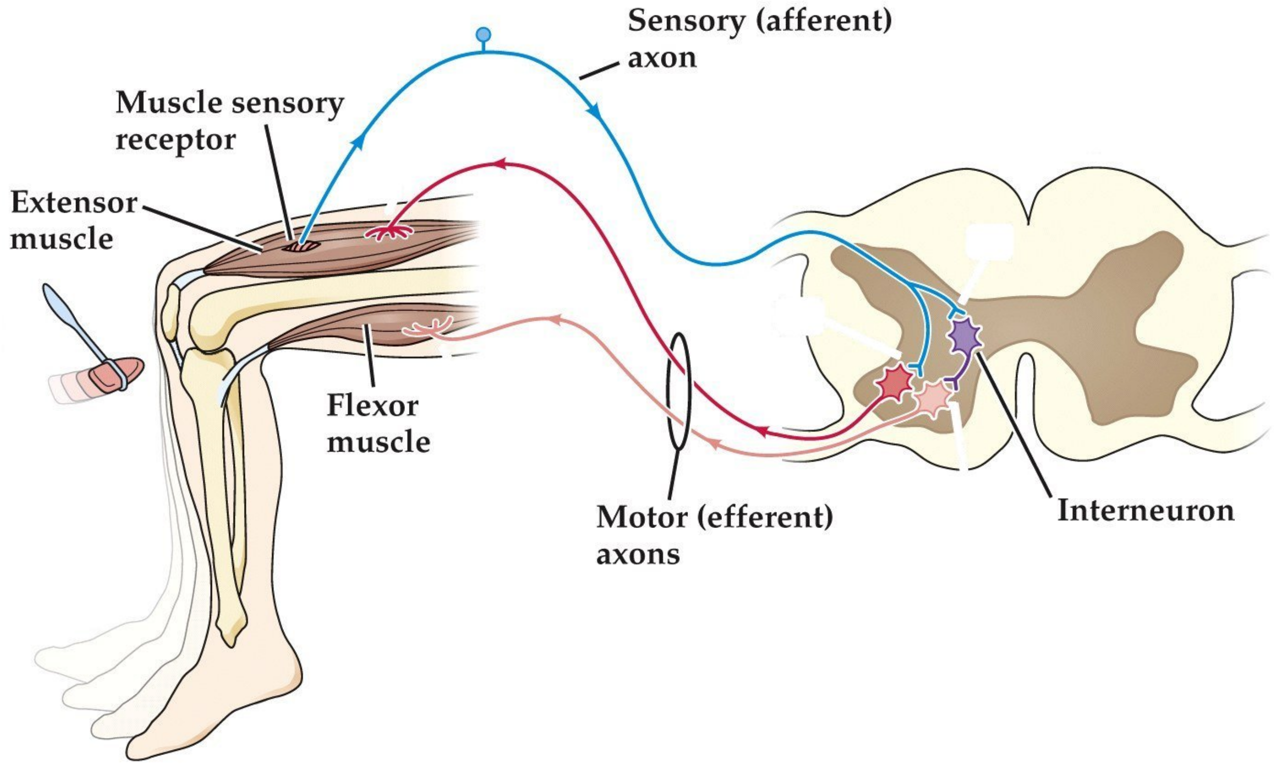
Speaker notes

-id. twitches

- higher freq, tet stim gives sum of twitches to produce greater force

Spinal reflexes

- Simple reflexes are stereotyped movements elicited by the activation of skin or muscle receptors, and are the basic unit of movements (Charles Sherrington, 1906)
- Complex sequences of movements can be produced by combining simple reflexes

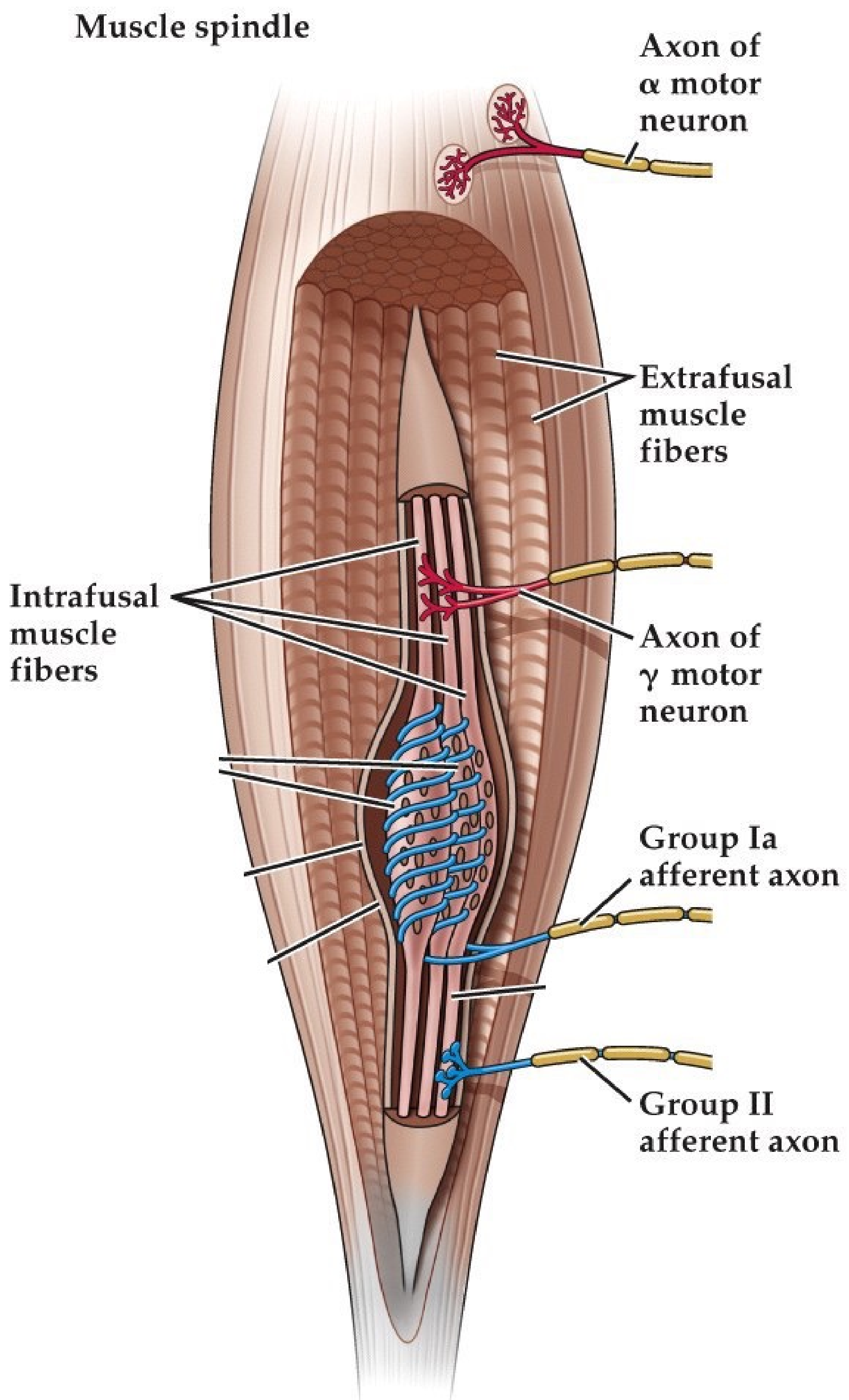


Neuroscience 5e Fig. 1.7

Speaker notes

myotactic reflex, first lecture.

The muscle spindle: a sensory organ for determining muscle length and stretch



Neuroscience 5e Fig. 16.10

Speaker notes

- spindle is organ for stretch
- spindles comprise 8-10 intrafusal fibers
  - nuclear bag fibers
    - dynamic subclass
    - static subclass
    - most spindles have 2-3 bag fibers
  - nuclear chain fibers
    - most spindles have 4-6+ chain fibers

Ia afferent activity
: mostly from dynamic type of nuclear bag fiber
: phasic response
: emphasize velocity of stretch

II afferents
: innervate static nuclear bag fibers and nuclear chain fibers
: signal sustained fiber stretch by firing tonically, little dynamic sensitivity
: muscle tone

There are also dynamic and static classes of gamma motor neurons

The muscle spindle helps form negative feedback circuit through its connectivity with spinal neurons.

Types of somatosensory afferents

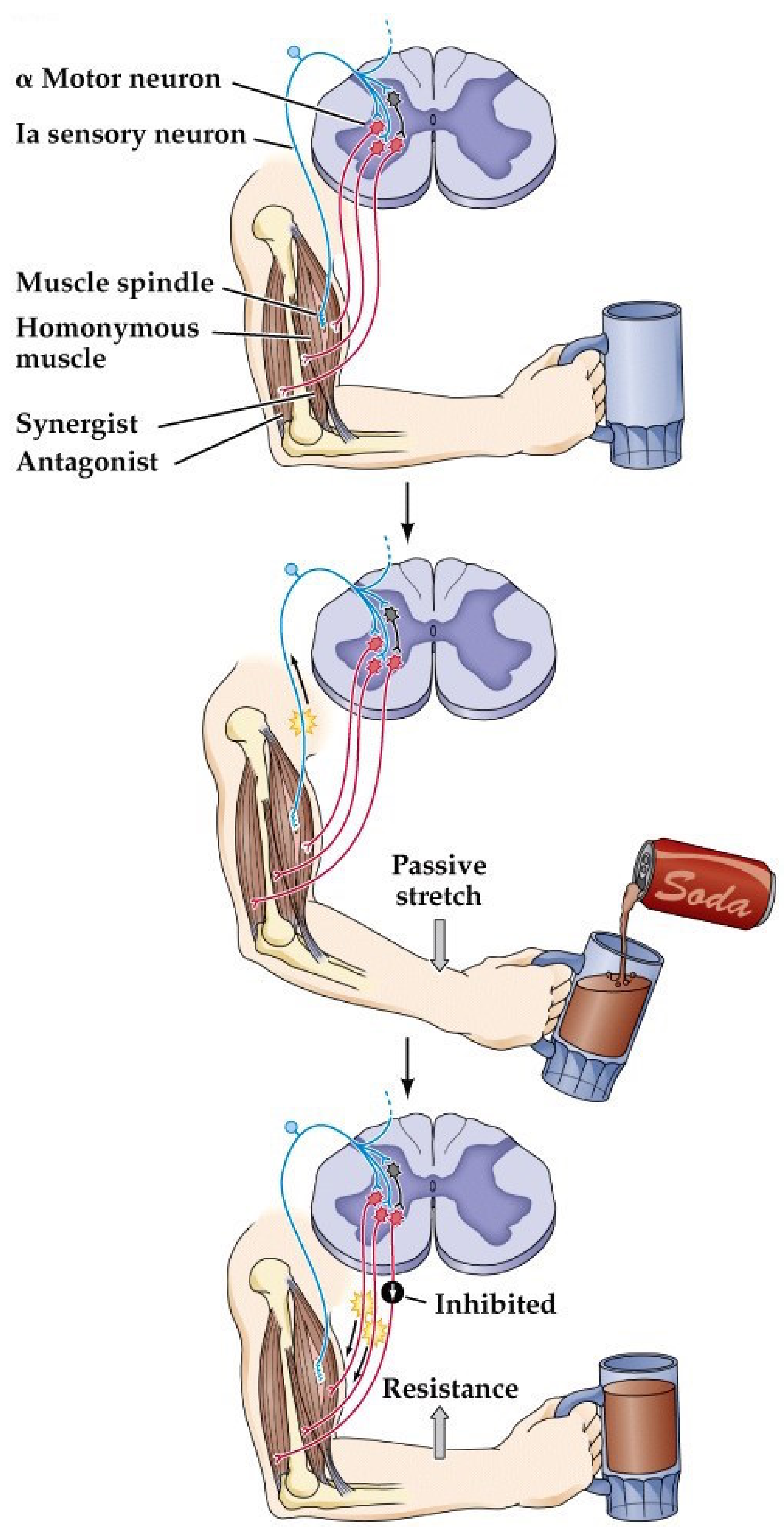
sensory function	**receptor type**	**afferent axon type (alt name)**	**axon diameter (μm)**	**conduction velocity (m/s)**
proprioception	muscle spindle	Aα (Ia + Ib), **myelinated**	13–20	80–120
touch	Merkel, Meissner, Pacinian, and Ruffini cells	Aβ (II), **myelinated**	6–12	35–75
pain, temperature	free nerve endings	Aδ (III), **myelinated**	1–5	5–30
pain, temperature, itch	free nerve endings	C, **unmyelinated**	0.2–1.5	0.5–2

Speaker notes

This table summarizes the somatosensory afferents types, and variety in their functions, morphologies, and AP conduction velocities.

Tab. 1 after Rosenzweig 2005

The stretch reflex



Neuroscience 5e Fig. 16.10

Speaker notes

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The stretch reflex

- Large diameter sensory fibers (Ia afferents, fast) are coiled around muscle spindles
- Stretch imposed on a muscle stretches intrafusal muscle fibers, which in turn initiates action potentials by activating mechanically gated ion channels in Ia axons
- Ia sensory neurons synapse with motor neurons in the ventral horn of the spinal cord that innervate the same muscle (homonymous muscle) or synergistic muscles
- Ia sensory neurons activate local inhibitory connections for the antagonistic muscles

Speaker notes

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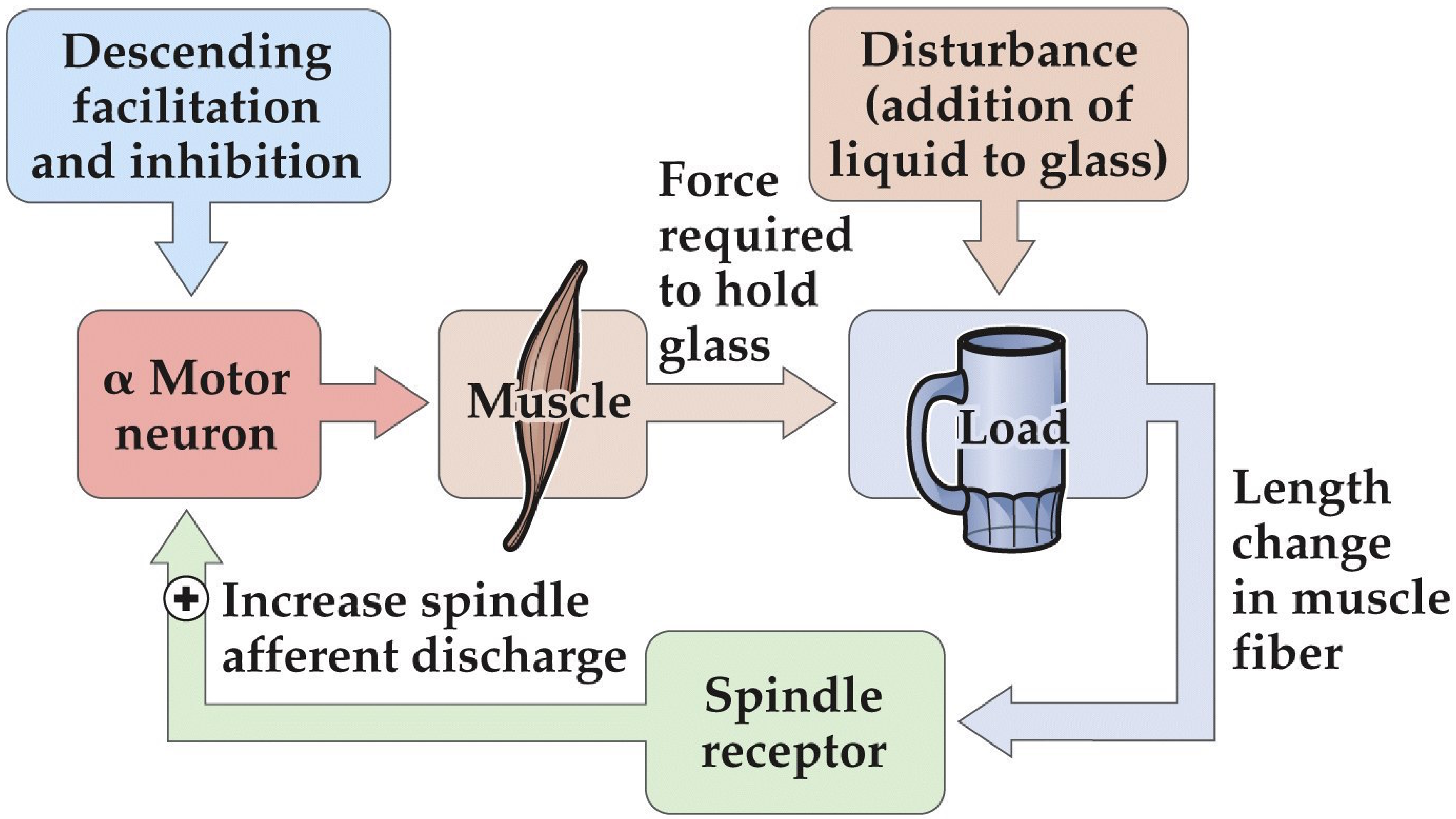
The stretch reflex



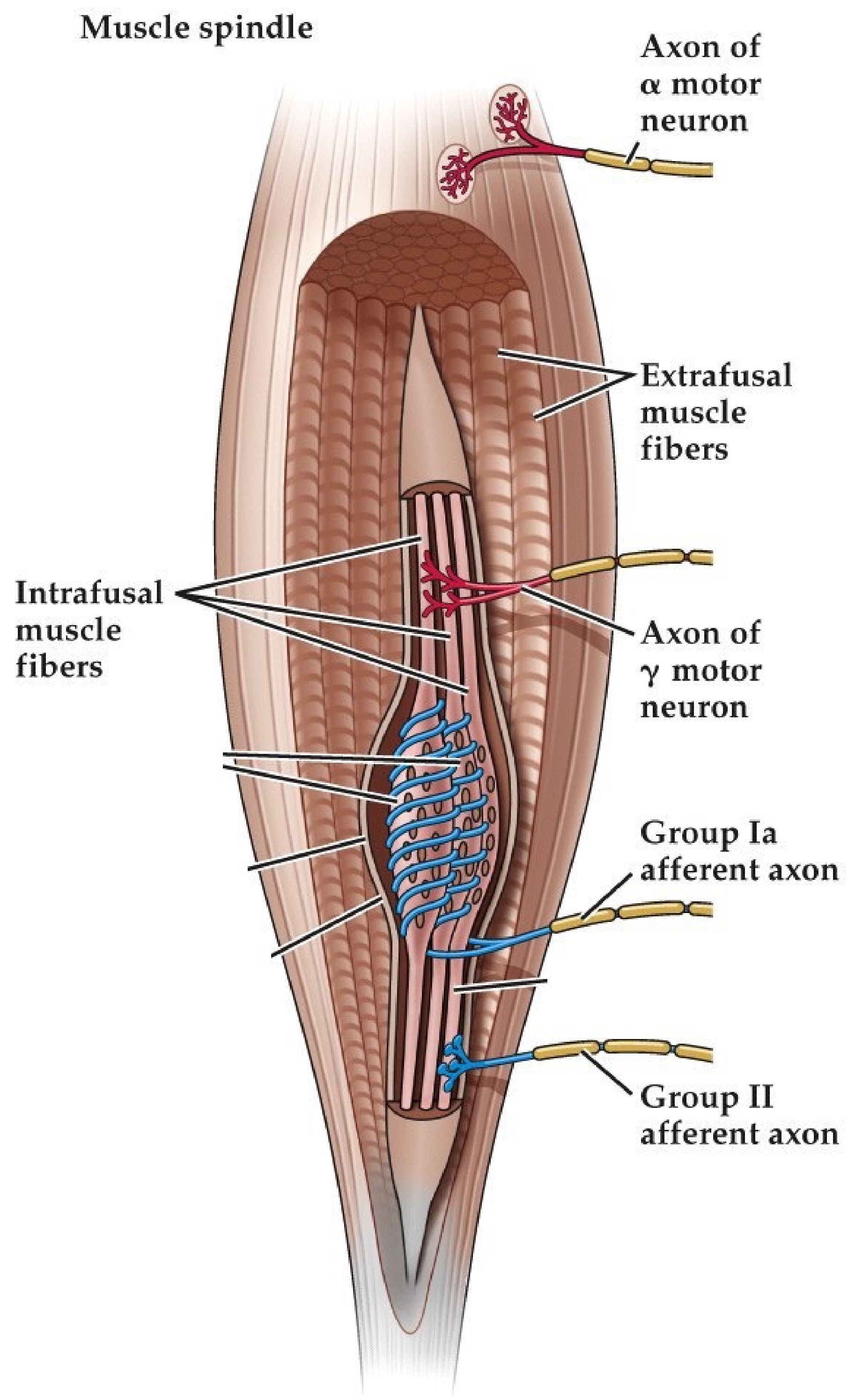
Neuroscience 5e Fig. 16.10

Speaker notes

- So next time your boss says why are you standing around doing nothing, just say that you're busy utilzing your lower motor neurons and type Ia sensory afferents ;)

γ motor neurons

- γ motor neurons control the functional characteristics of the muscle spindles
- When muscles contract, spindle afferents do not fall silent. Instead γ neurons that terminate at spindle poles cause intrafusal fiber contraction at the poles, and lead to tension across the fiber in the presence of muscle contraction. This allows spindles to function at all muscle lengths and tensions
- Gain or γ bias refers to the fact that spindles can adjust how much output will happen when they are stretched. Large gain means a small amount of stretch applied to the intrafusal fibers will produce a large increase in the number of motor neurons recruited and an increase in firing rates. Gain is continually adjusted to meet circumstances



Neuroscience 5e Fig. 16.10

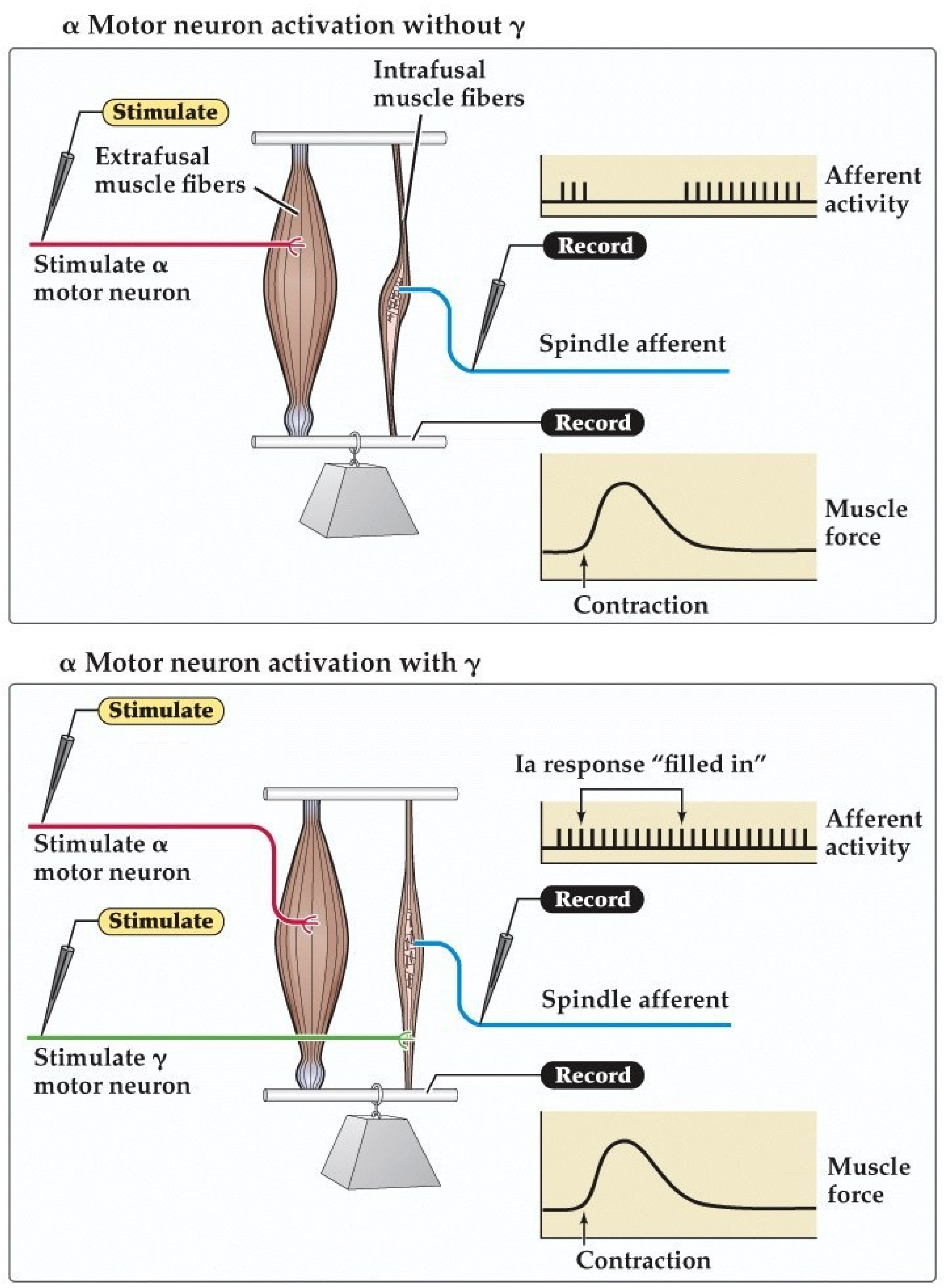
Speaker notes

But the infrafusal muscle fibers are muscle-- why not just have the muscle spindle feedback and be done with it...

Need to adjust the muscle spindles so that they can provide useful feedback across a range of muscle lengths. Provide gain to keep muscle spindles active at all lengths.

piezo1 and piezo2 https://pubmed.ncbi.nlm.nih.gov/20813920/

γ motor neuron activity affects responses of muscle spindles



Neuroscience 5e Fig. 16.11

Speaker notes

No notes on this slide.

Stretch reflex video summary

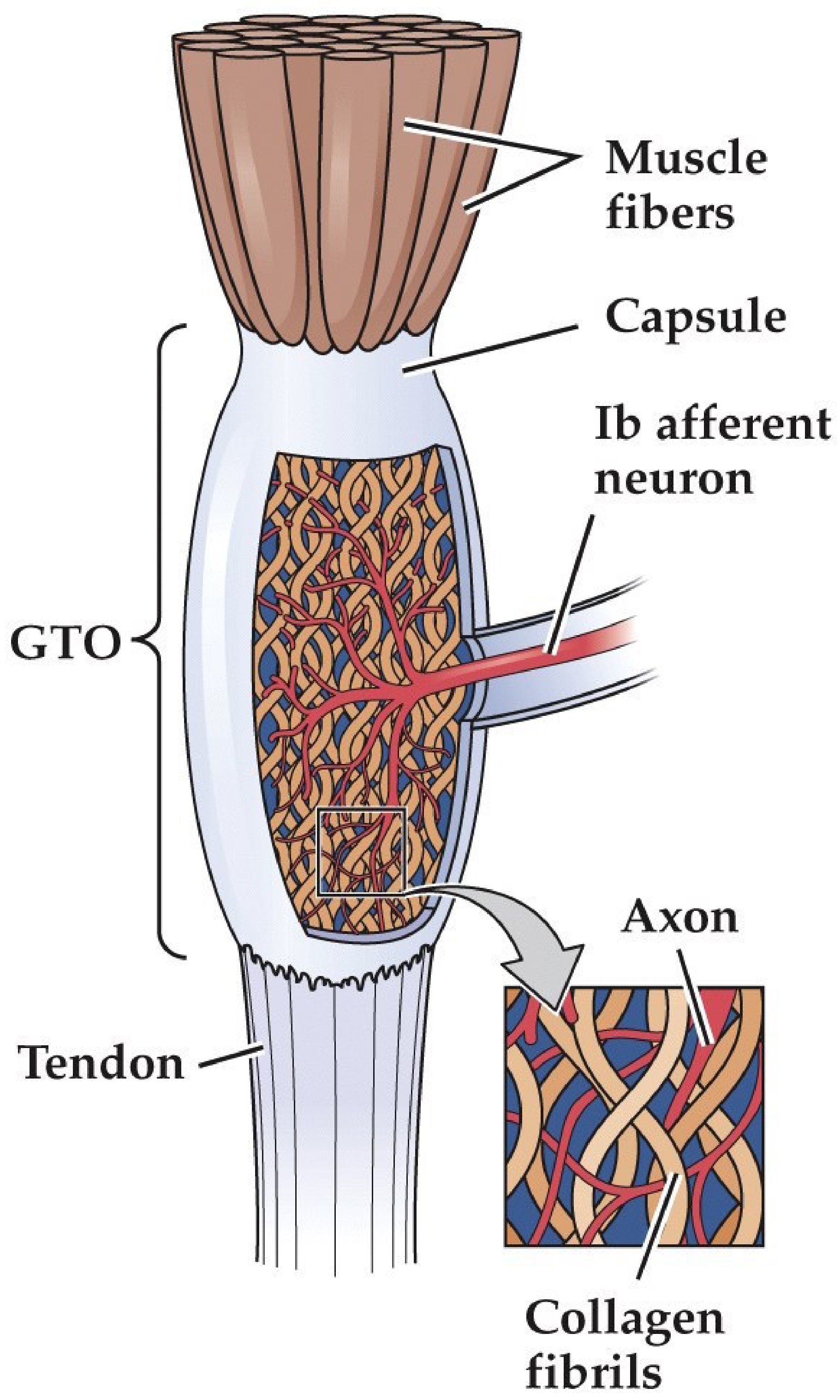
Neuroscience 5e Animation 16.1

Speaker notes

No notes on this slide.

Golgi tendon organs

- Encapsulated afferent nerve endings located at the junction of the muscle and tendon
- Each tendon is innervated by a single sensory group Ib sensory axon
- Unlike spindle fibers, golgi tendon organs fire when muscle contracts
- Ib axons from Golgi tendon organs contact inhibitory local circuit neurons in the spinal cord (Ib inhibitory neurons) that synapse with the α motor neurons that innervate the same muscle
- Helps prevent fatigue



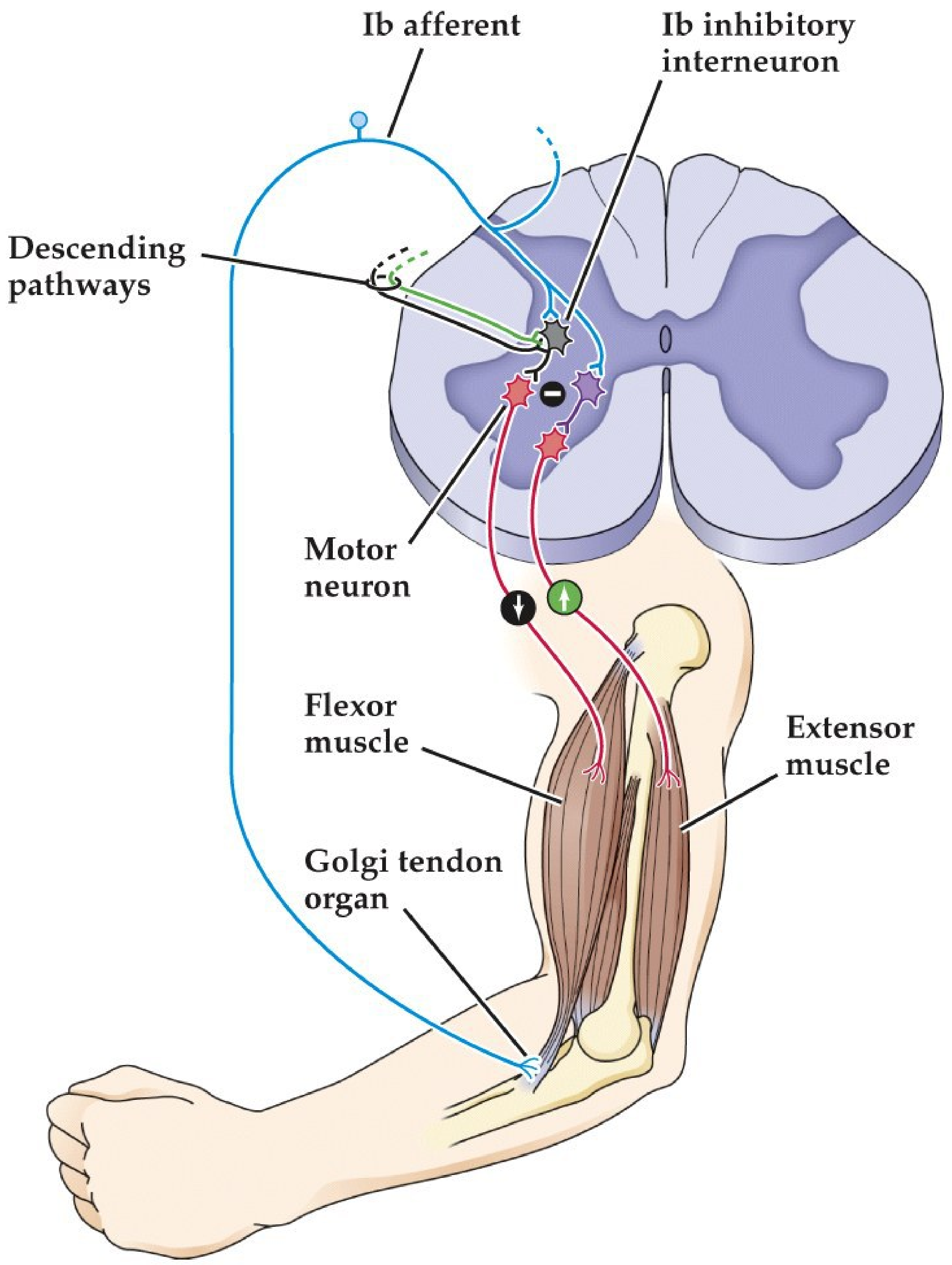
Neuroscience 5e Fig. 16.12

Speaker notes

- spindle system is feedback system to monitor and maintain muscle stretch
- Golgi tendon organ is feedback system to maintain muscle force

Negative feedback regulation of muscle tension by Golgi tendon organs

- Negative feedback provided by by Golgi tendon organs
- When muscle contracts there is a feedback mechanism to prevent more contractions. Prevents damage and fatigue



Neuroscience 5e Fig. 16.13

Speaker notes

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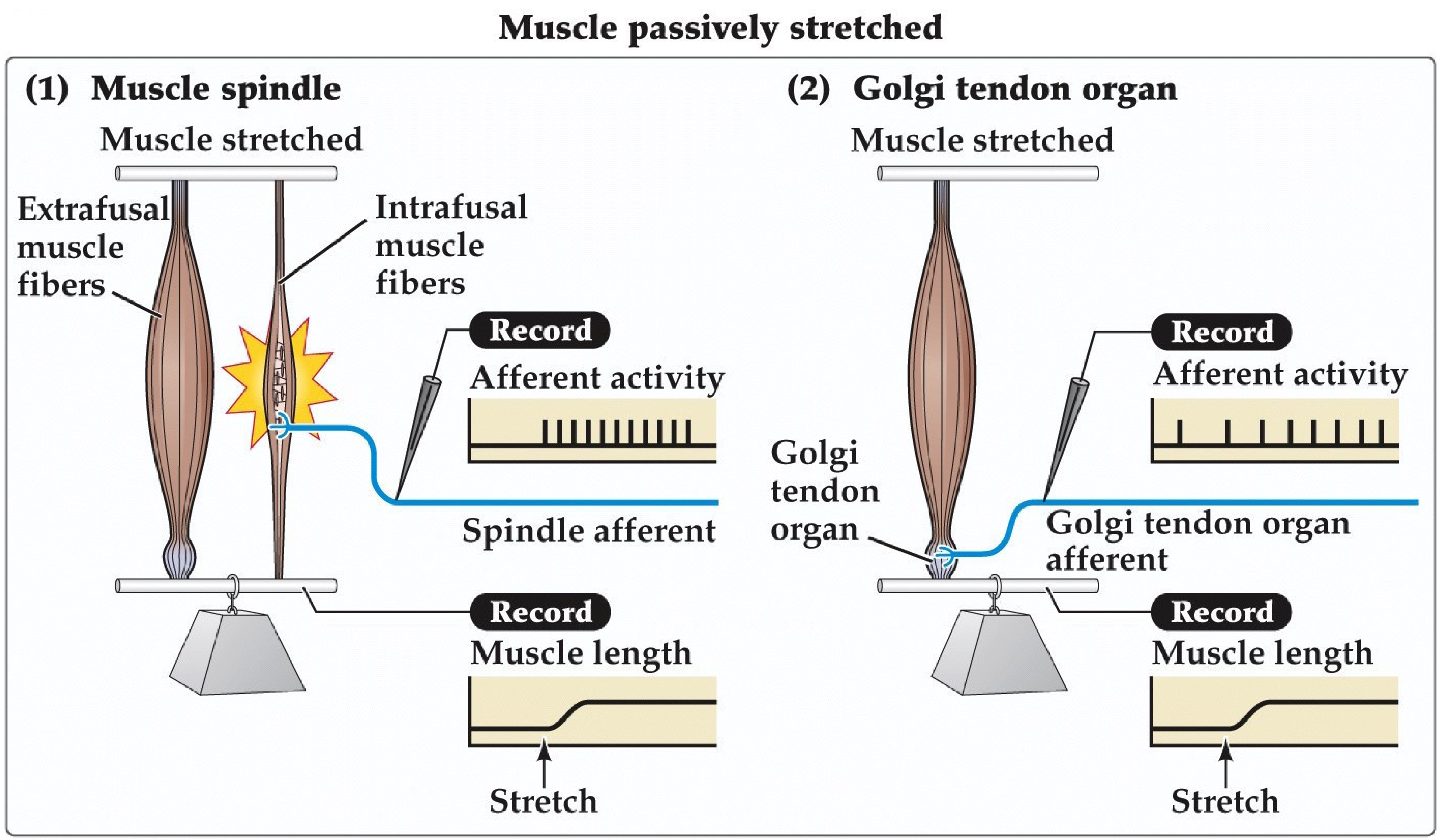
Comparison of the function of muscle spindles and Golgi tendon organs



Neuroscience 5e Fig. 16.12

Speaker notes

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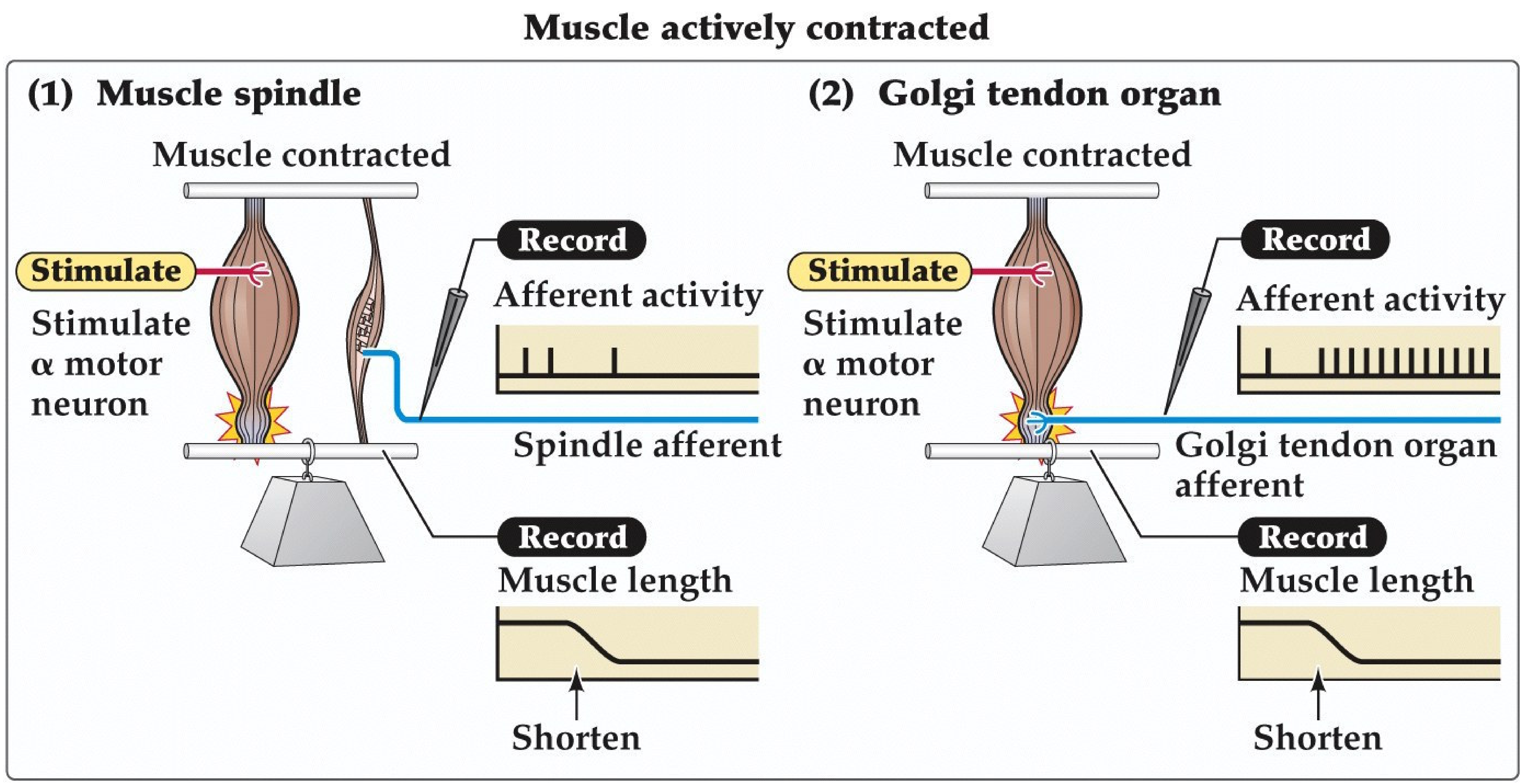
Comparison of the function of muscle spindles and Golgi tendon organs



Neuroscience 5e Fig. 16.12

Speaker notes

Flexion reflex pathways

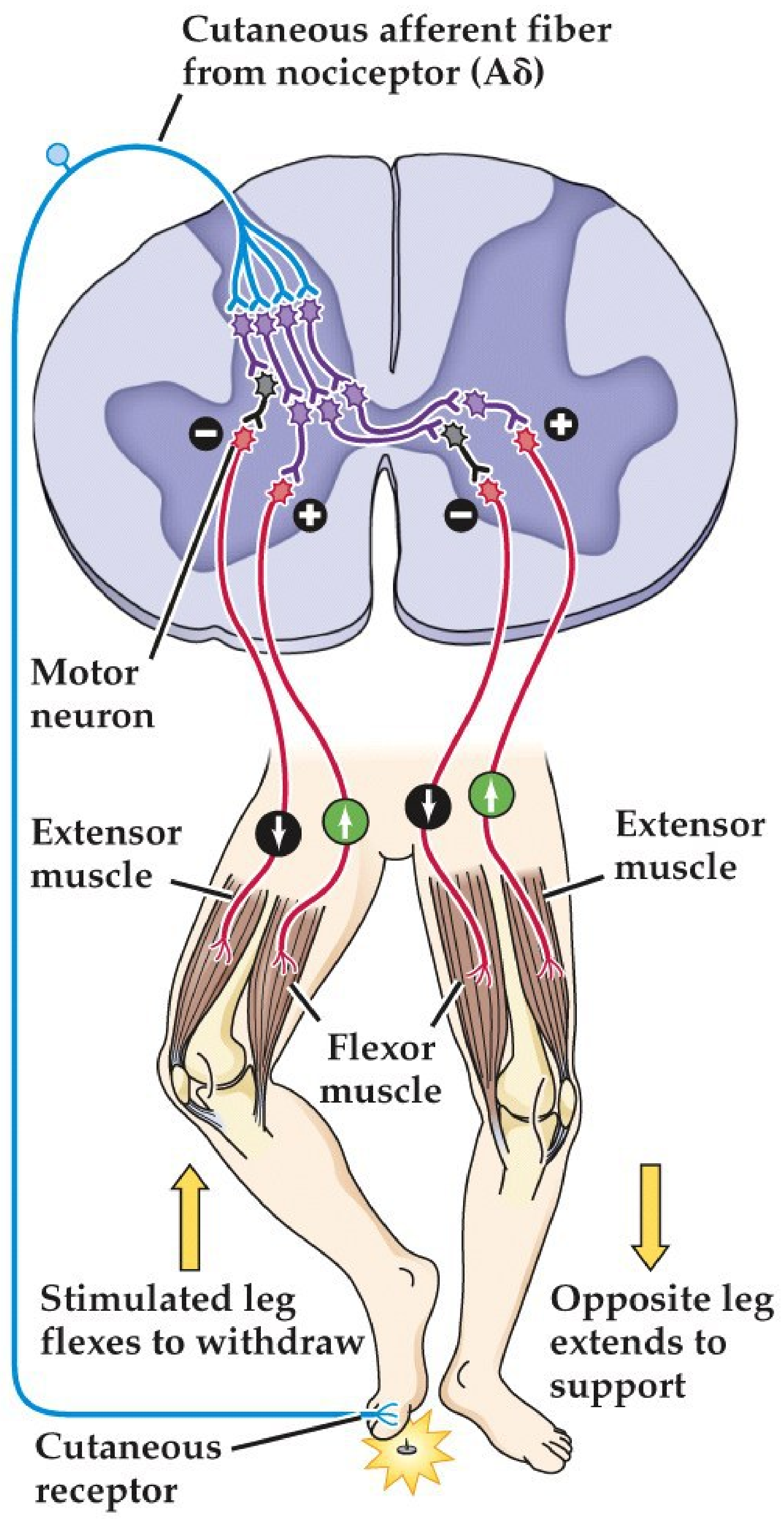
- Reflexes that compensate posture when we withdraw from pain
- Involves several synaptic links
- Excitation of nociceptor leads to ipsilateral and contralateral responses
- Flexion reflex– stimulation of cutaneous receptors in the foot leads to activation of spinal cord local circuits that both withdrawal stimulated side and extend other side to provide compensatory support

Speaker notes

CPG interneurons Type Axon projection in embryonic cord V0 Commissural Rostrally V1 Inhibitory (Renshaw cells and Ia interneurons) Rostrally and ipsilaterally V2 Glutamatergic V2a and Inhibitory V2b Ipsilaterally and caudally V3 Excitatory Commissural Caudally

Goulding M (July 2009). "Circuits controlling vertebrate locomotion: moving in a new direction". Nature Reviews Neuroscience. 10 (7): 507–18. doi:10.1038/nrn2608. PMC 2847453 PMID 19543221.

Spinal cord circuitry responsible for the flexion reflex



Neuroscience 5e Fig. 16.14

Speaker notes

No notes on this slide.

Flexion reflex video summary

Neuroscience 5e Animation 16.2

Speaker notes

No notes on this slide.

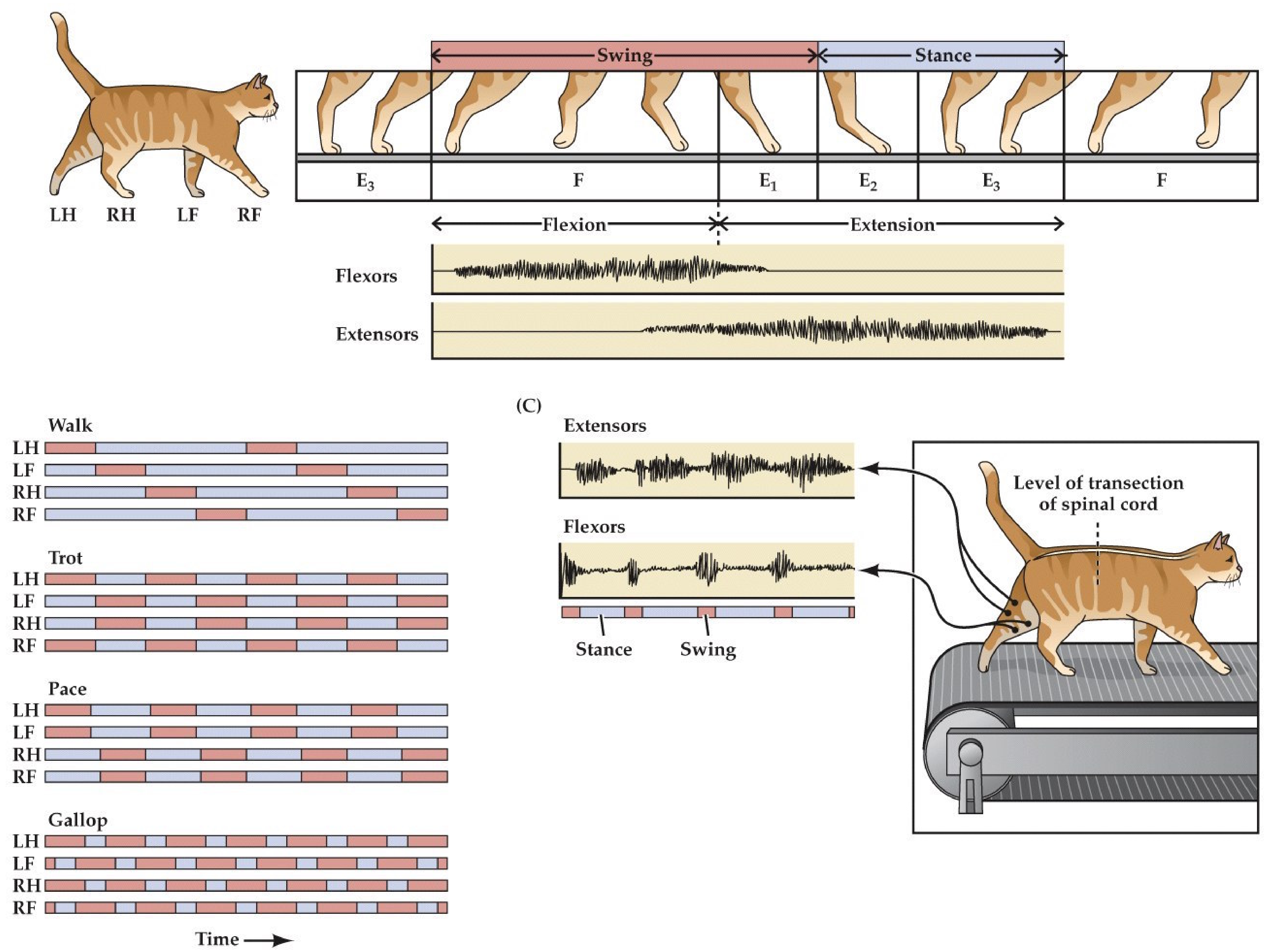
Locomotion– an essential feature of animal life

- Locomotion is a stereotyped action involving repetitions of the same movement
- Locomotion– a single limb can be thought of having two phases, a stance phase (limb is extended and in contact with the ground) and a swing phase (limb is flexed to leave the ground and then brought forward to begin next stance phase)
- Increases of speed reduce the amount of time it takes to complete the cycle. Stance phase gets quicker, swing phase stays relatively constant
- For quadrupeds, changes in speed are also accompanied by changes in the order of steps taken. At low speeds, back to front occurs first on one side then on the other. At a trot, right forelimb and left hindlimb are synchronized. At high speeds, two front limbs are synchronized as are the two hind limbs
- Pattern generators– once initiated by upper motor pathways or sensory input, pattern generators can keep locomotion going quite well until there is a signal to get out

Speaker notes

- Flexion describes a bending movement that decreases the angle between a segment and its proximal segment
- Extension describing a straightening movement that increases the angle between body parts
- Abduction refers to a motion that pulls a structure or part away from the midline of the body
- Adduction refers to a motion that pulls a structure or part toward the midline of the body

Central pattern generators organize the cycle of activity for locomotion



Neuroscience 5e Fig. 16.15

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Speaker notes

- Defects in spinal cord connectivity interrupt pattern generation
  - cell article
- Activating the mesencephalic locomotor region can trigger locomtion and change speed of movement by amount of input to spinal cord.
- Transection at thoracic level will still allow for coordinated locomotor movements. It is not only a stretch reflex, because there are CPGs present for each limb. The CPGs are all connected together in circuits spanning spinal cord segments.
- However human locomotion requires more descending input from the brain-- Transection would not allow for good walking in humans-- perhaps bipedalism requires more upper motor neuron control due to the greater postural control requirements

Central pattern generators organize the cycle of activity for locomotion

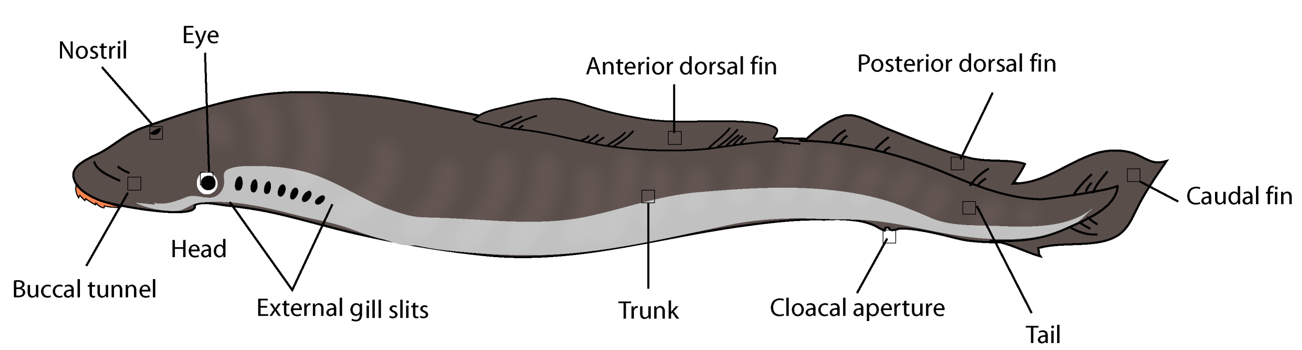
Locomotion in decerebrate cat

Speaker notes

S Grillner, P Zangger. On the central generation of locomotion in the low spinal cat. Experimental Brain Research, 1979

Central pattern generator circuit model for swimming

Lamprey



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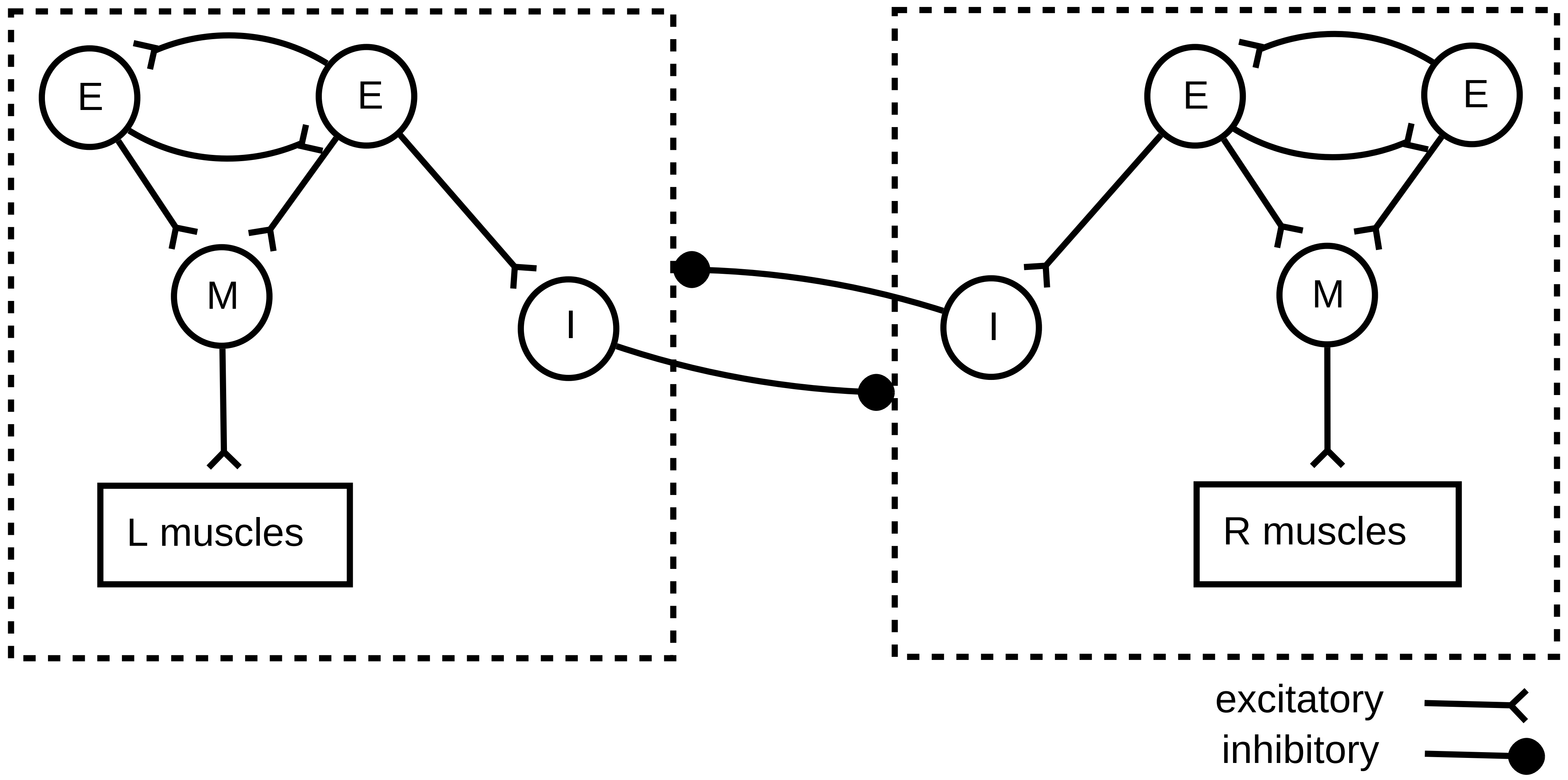
Simplified lamprey CPG model. E, excitatory; I, inhibitory; M, motor neuron



J. Ackman, CC0. Based on Grillner et al., *Brain Res Rev* 2008

Speaker notes

lamprey : ancient vertebrate
: jawless fish
: good model for cpg spinal cord circuits, well worked out

simple network of neurons that could result in alternating flexor and extensor muscle movements for locomotion and be basis of a central pattern generator circuit.

spinal locomotor and brainstem respiratory CPGs (Yuste et al, Nat Rev Neurosci 2005)
: have an 'excitatory core' of mutually excitatory interneurons
: ea. hemisegment of the spinal cord has this a core : reciprocal inhibition between contralateral hemisegments results in alternating left–right motor output

todo: add midline, interneuron labels to svg file. todo: add neurons for more complete model representation todo: make model with flexor/extensors for vertebrate locomotion