Physiology of Muscle Tissue

By

Dr. Hassan Y. Hassan

Department of physiology

2nd year

Lecture 1

Learning Objectives

- Describe types and characteristics of muscular tissue
- Explain microscopic anatomy of skeletal muscle
- Clarify nerve-muscle relationship

Aim of Lecture

- By the end of this lecture, students should be able to identify types and characteristics of muscular tissue, especially skeletal muscle.

Introduction to Muscle

- movement is a fundamental characteristic of all living things
- muscle cells are capable of converting the chemical energy of ATP into mechanical energy
- types of muscle
  - skeletal, cardiac and smooth
- physiology of skeletal muscle
  - basis of warm-up, quickness, strength, endurance and fatigue

Characteristics of Muscle

- responsiveness (excitability)
  - to chemical signals, stretch and electrical changes across the plasma membrane
- conductivity
  - local electrical change triggers a wave of excitation that travels along the muscle fiber
- contractility
  - shortens when stimulated
- extensibility
  - capable of being stretched between contractions
- elasticity
  - returns to its original resting length after being stretched

Skeletal Muscle

- skeletal muscle - voluntary, striated muscle attached to one or more bones
- striations - alternating ligh and dark transverse banc
  - results from an overlapping internal contractile proteins
- voluntary – usually subject to conscious control
- muscle cell, muscle fiber, (myofiber) as long as 30 cm

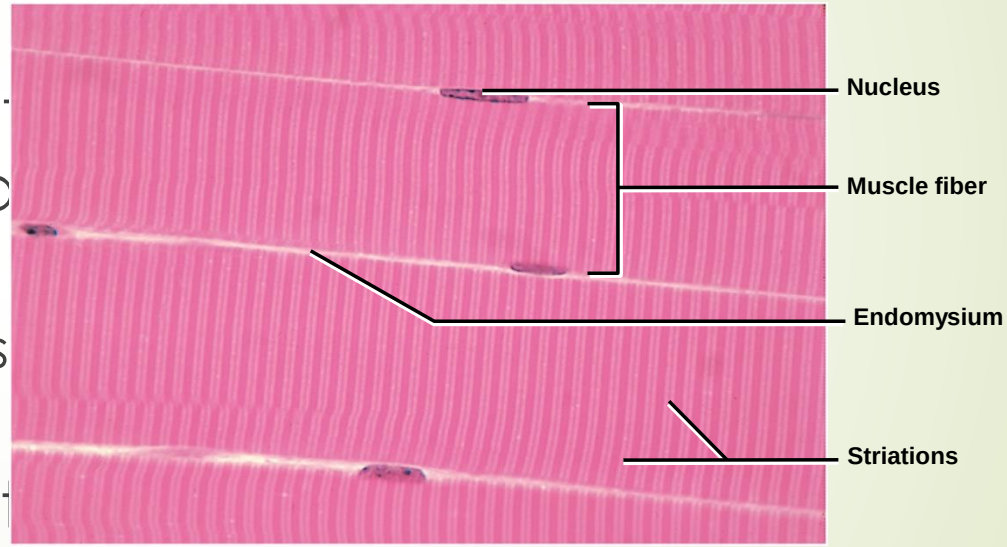


Figure 11.1

Connective Tissue Elements

- tendons are attachments between muscle and bone matrix
  - endomysium – connective tissue around muscle cells
  - perimysium – connective tissue around muscle fascicles
  - epimysium – connective tissue surrounding entire muscle
  - continuous with collagen fibers of tendons
  - in turn, with connective tissue of bone matrix
- collagen is somewhat extensible and elastic
  - stretches slightly under tension and recoils when released
    - resists excessive stretching and protects muscle from injury
    - returns muscle to its resting length
    - contribute to power output and muscle efficiency

Structure of a Skeletal Muscle Fiber

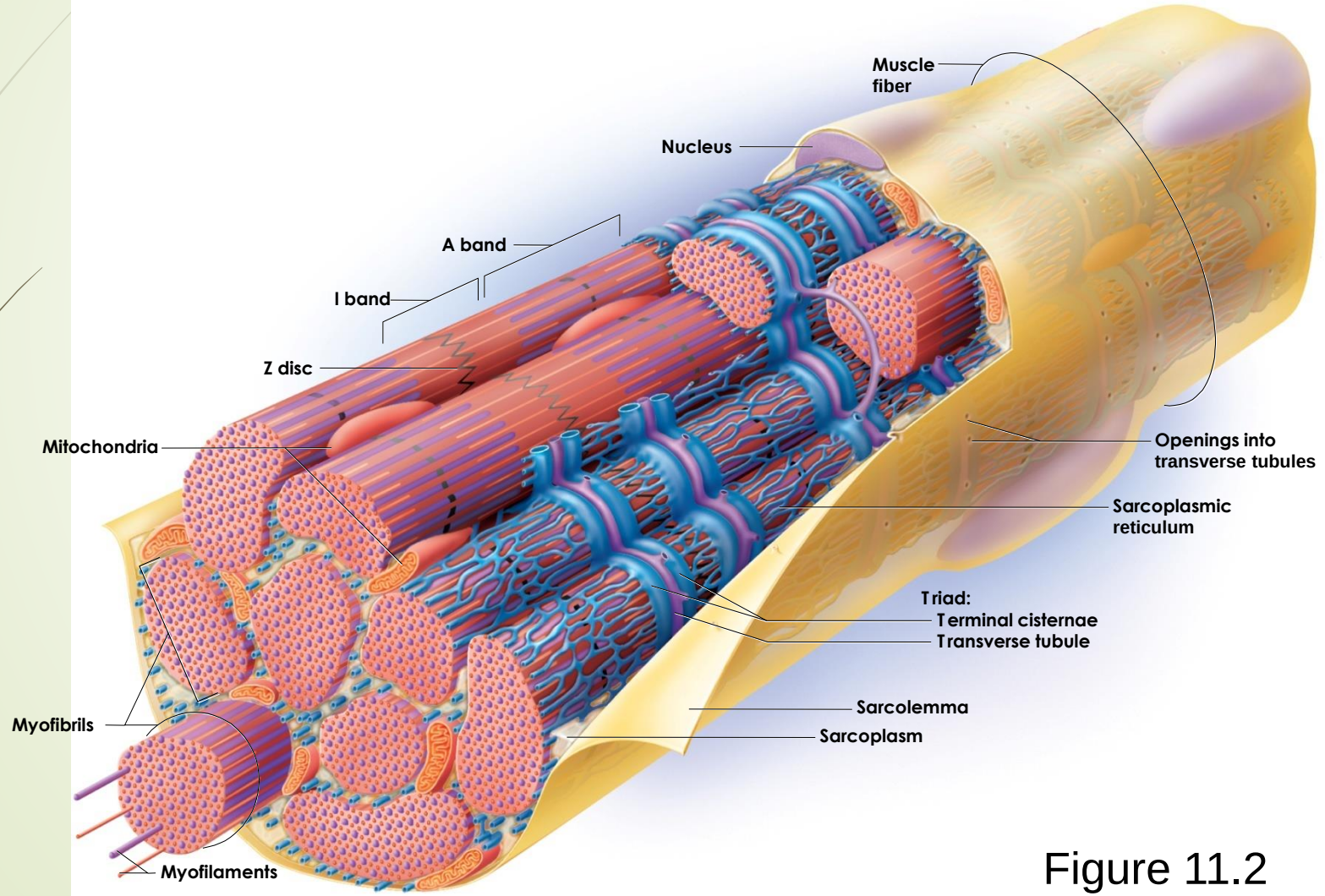


Figure 11.2

The Muscle Fiber

- sarcolemma – plasma membrane of a muscle fiber
- sarcoplasm – cytoplasm of a muscle fiber
- myofibrils – long protein bundles that occupies the main portion of the sarcoplasm
  - glycogen – stored in abundance to provide energy with heightened exercise
  - myoglobin – red pigment – stores oxygen needed for muscle activity
- multiple nuclei – flattened nuclei pressed against the inside of the sarcolemma
  - myoblasts – stem cells that fuse to form each muscle fiber
  - satellite cells – unspecialized myoblasts remaining between the muscle fiber and endomysium
    - may multiply and produce new muscle fibers to some degree
- repair by fibrosis rather than regeneration of functional muscle
- mitochondria – packed in spaces between myofibrils
- sarcoplasmic reticulum (SR) - smooth ER that forms a network around each myofibril – calcium reservoir
  - calcium activates the muscle contraction process
- terminal cisternae – dilated end-sacs of SR which cross muscle fiber from one side to the other
- T tubules – tubular infoldings of the sarcolemma which penetrate through the cell and emerge on the other side
- triad – a T tubule and two terminal cisterns

Thick Myofilaments

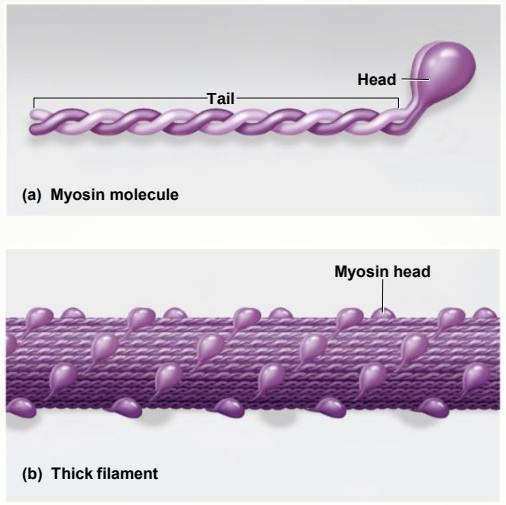


Figure 11.3 a-b

- made of several hundred myosin molecules
  - shaped like a golf club
    - two chains intertwined to form a shaft-like tail
    - double globular head
  - heads directed outward in a helical array around the bundle
    - heads on one half of the thick filament angle to the left
    - heads on the other half angle to the right
    - bare zone with no heads in the middle

Thin Myofilaments

- fibrous (F) actin - two intertwined strands
  - string of globular (G) actin subunits each with an active site that can bind to head of myosin molecule
- tropomyosin molecules
  - each blocking 6 or 7 active sites on G actin subunits
- troponin molecule - small, calcium-binding protein on each tropomyosin molecule

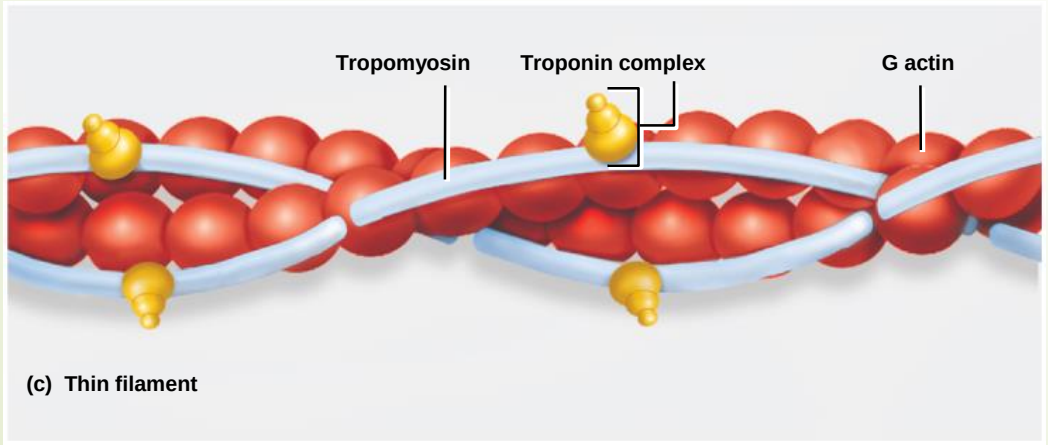


Figure 11.3c

Elastic Myofilaments

- titin (connectin) – huge springy protein
  - flank each thick filament and anchor it to the Z disc
  - helps stabilize the thick filament
  - center it between the thin filaments
  - prevents over stretching

Regulatory and Contractile Proteins

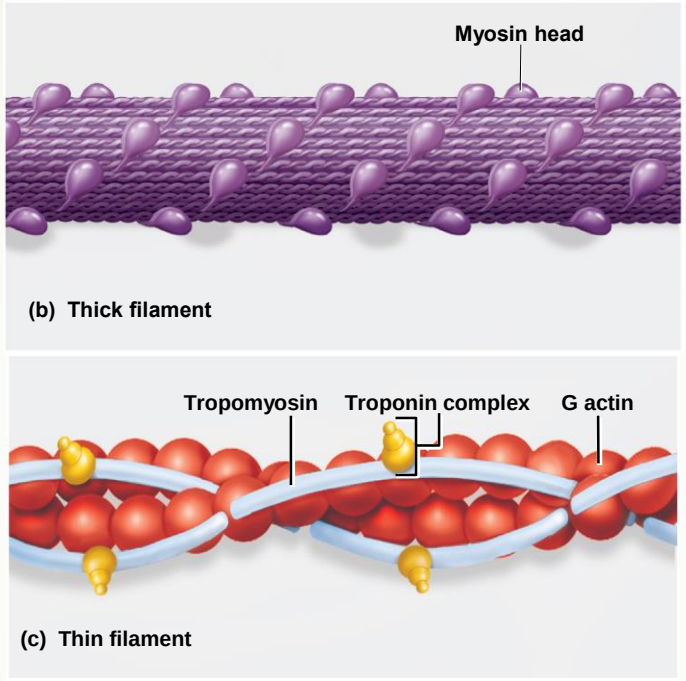


Figure 11.3 b-c

- contractile proteins - myosin and actin
  - do the work
- regulatory proteins - tropomyosin and troponin
  - like a switch that determine when the fiber can contract and when it cannot
  - contraction activated by release of calcium into sarcoplasm and its binding to troponin,
  - troponin changes shape and moves tropomyosin off the active sites on actin

Overlap of Thick and Thin Filaments

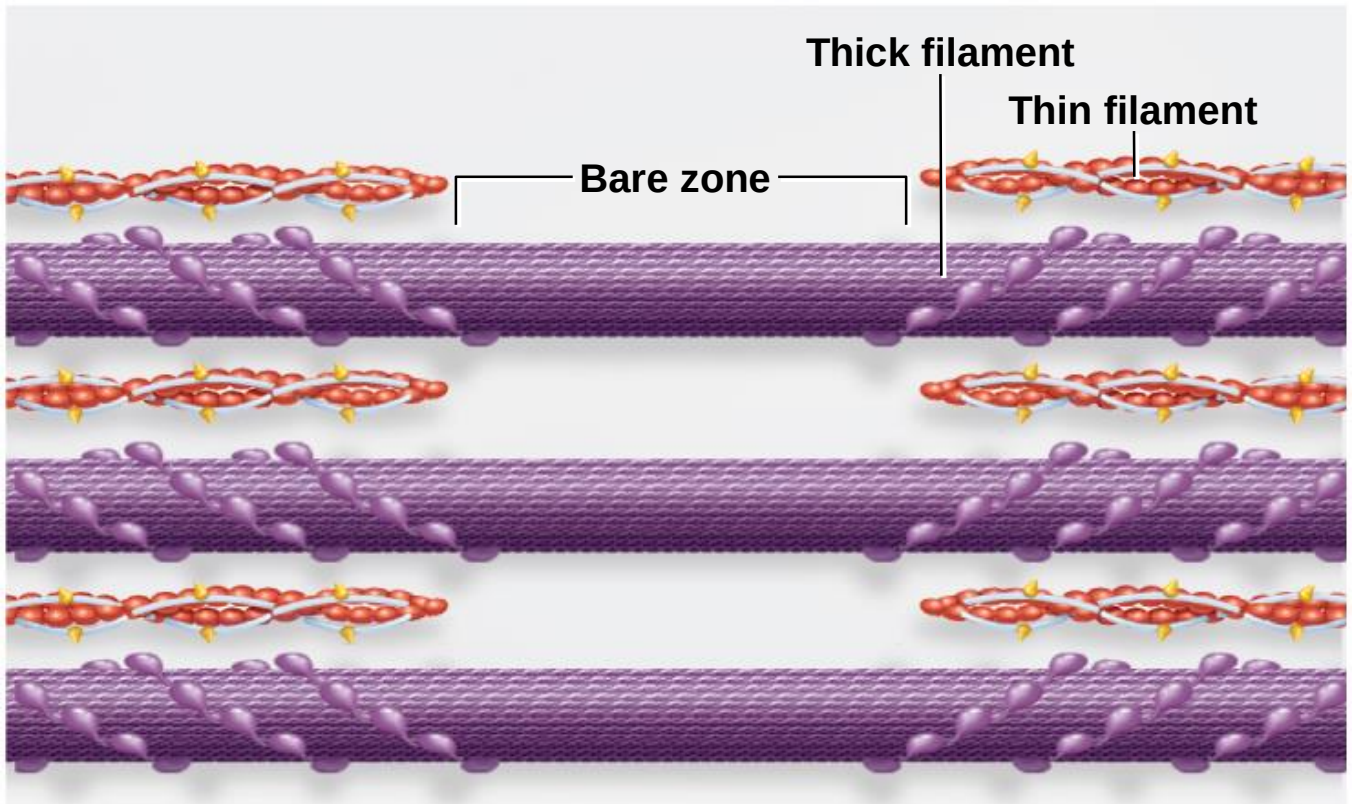


Figure 11.3d

Accessory Proteins

- at least seven other accessory proteins in or associated with thick or thin filaments
  - anchor the myofilaments, regulate length of myofilaments, alignment of myofilaments for maximum effectiveness
- dystrophin – most clinically important
  - links actin in outermost myofilaments to transmembrane proteins and eventually to fibrous endomysium surrounding the entire muscle cell
  - transfers forces of muscle contraction to connective tissue around muscle cell

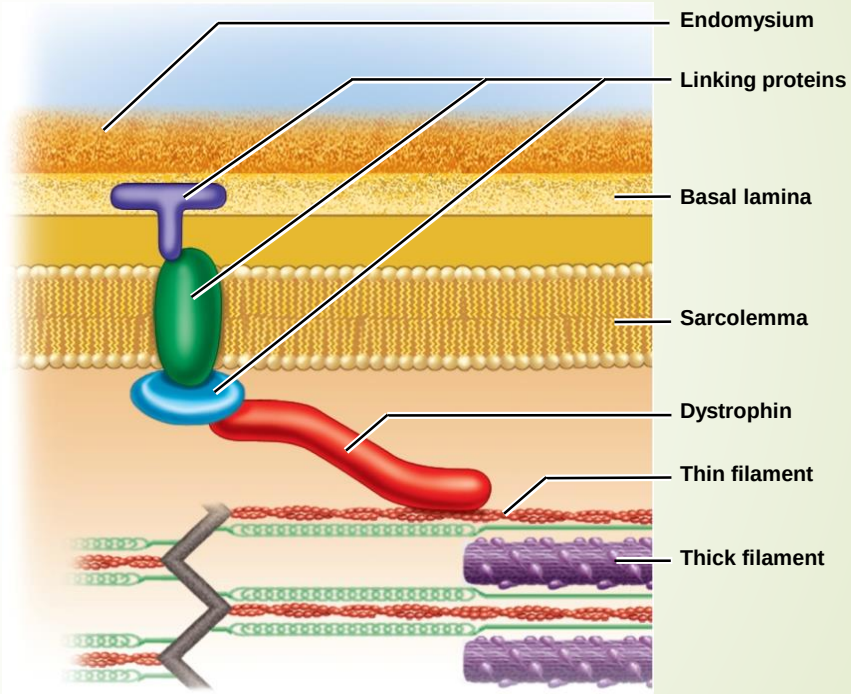


Figure 11.4

Striations

- myosin and actin are proteins that occur in all cells
  - function in cellular motility, mitosis, transport of intracellular material
- organized in a precise way in skeletal and cardiac muscle
  - A band – dark – A stands for anisotropic
    - part of A band where thick and thin filaments overlap is especially dark
    - H band in the middle of A band – just thick filaments
    - M line is in the middle of the H band
  - I band – alternating lighter band – I stands for isotropic
    - the way the bands reflect polarized light
  - z disc – provides anchorage for thin filaments and elastic filaments
    - bisects I band
  - sarcomere – the segment of the myofibril from one z disc to the next

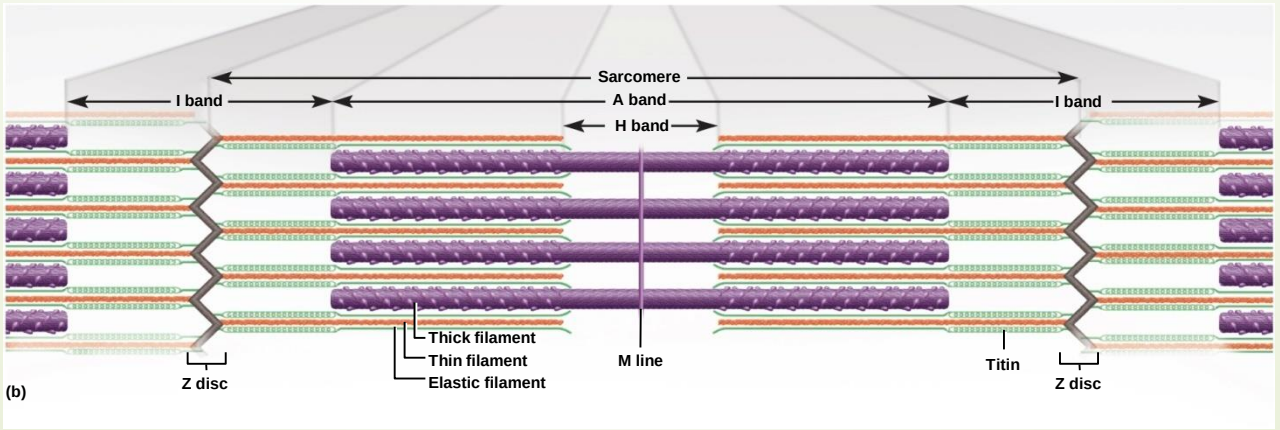
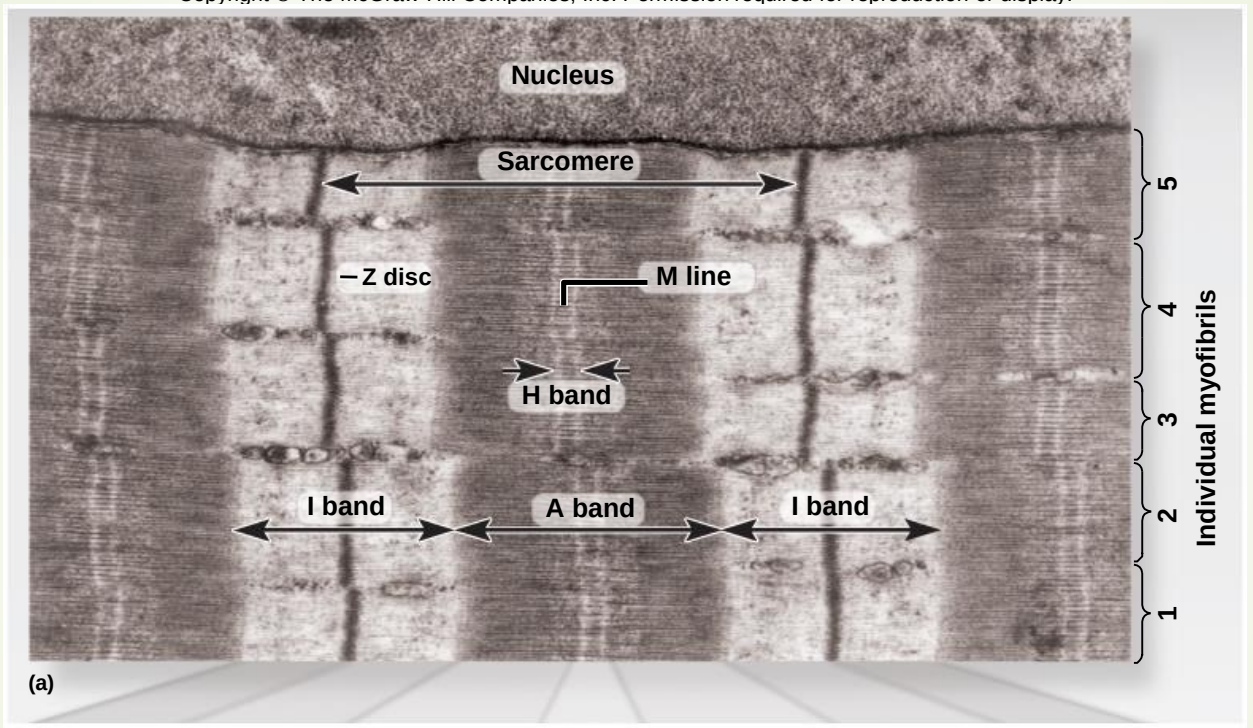


Figure 11.5b

Striations and Sarcomeres



Visuals Unlimited

Figure 11.5a

- sarcomere – *functional contractile unit of the muscle fiber*
  - muscle shortens because individual sarcomeres shorten
  - pulls z discs closer to each other

Sarcomeres

- sarcomere - segment from Z disc to Z disc
  - functional contractile unit of muscle fiber
- muscle cells shorten because their individual sarcomeres shorten
  - Z disc (Z lines) are pulled closer together as thick and thin filaments slide past each other
- neither thick nor thin filaments change length during shortening
  - only the amount of overlap changes
- during shortening dystrophin & linking proteins also pull on extracellular proteins
  - transfers pull to extracellular tissue

The Nerve-Muscle Relationship

- skeletal muscle never contracts unless stimulated by a nerve
- if nerve connections are severed or poisoned, a muscle is paralyzed
- denervation atrophy – shrinkage of paralyzed muscle when connection not restored
- somatic motor neurons – nerve cells whose cell bodies are in the brainstem and spinal cord that serve skeletal muscles
- somatic motor fibers –their axons that lead to the skeletal muscle
  - each nerve fiber branches out to a number of muscle fibers
  - each muscle fiber is supplied by only one motor neuron

Motor Units

- motor unit – one nerve fiber and all the muscle fibers innervated by it
- muscle fibers of one motor unit
  - dispersed throughout the muscle
  - contract in unison
  - produce weak contraction over wide area
  - provides ability to sustain long-term contraction as motor units take turns contracting (postural control)
  - effective contraction usually requires the contraction of several motor units at once
- average motor unit – 200 muscle fibers for each motor unit
- small motor units - fine degree of control
  - 3-6 muscle fibers per neuron
  - eye and hand muscles
- large motor units – more strength than control
  - powerful contractions supplied by large motor units – gastrocnemius – 1000 muscle fibers per neuron
  - many muscle fibers per motor unit

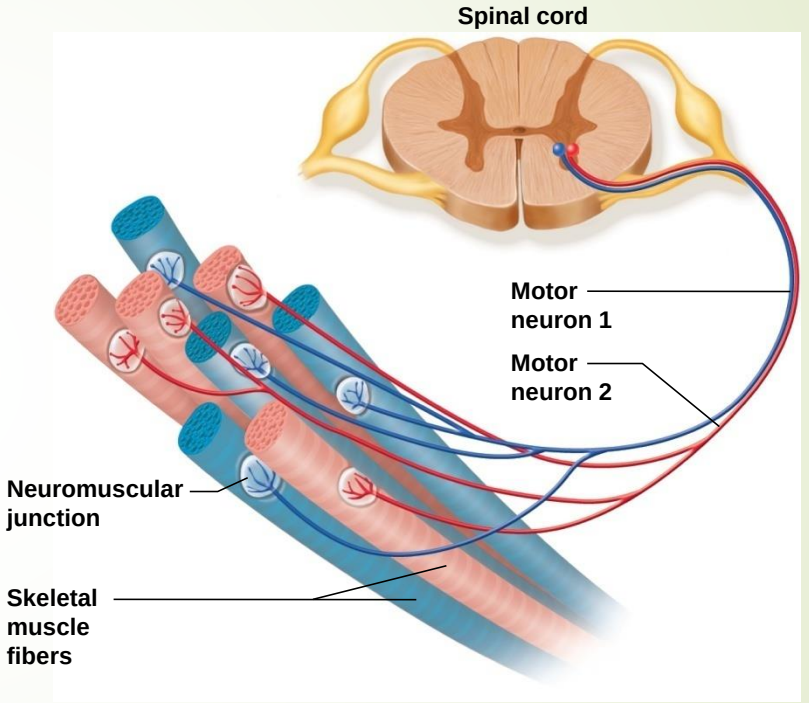


Figure 11.6

The Neuromuscular Junction

- synapse – point where a nerve fiber meets its target cell
- neuromuscular junction (NMJ) - when target cell is a muscle fiber
- each terminal branch of the nerve fiber within the NMJ forms separate synapse with the muscle fiber
- one nerve fiber stimulates the muscle fiber at several points within the NMJ

Components of Neuromuscular Junction

- synaptic knob - swollen end of nerve fiber
  - contains synaptic vesicles filled with acetylcholine (ACh)
- synaptic cleft - tiny gap between synaptic knob and muscle sarcolemma
- Schwann cell envelops & isolates all of the NMJ from surrounding tissue fluid
- synaptic vesicles undergo exocytosis releasing ACh into synaptic cleft
- 50 million ACh receptors – proteins incorporated into muscle cell plasma membrane
  - junctional folds of sarcolemma beneath synaptic knob
    - increases surface area holding ACh receptors
      - lack of receptors leads to paralysis in disease myasthenia gravis
- basal lamina - thin layer of collagen and glycoprotein separates Schwann cell and entire muscle cell from surrounding tissues
  - contains acetylcholinesterase (AChE) that breaks down ACh after contraction causing relaxation

Neuromuscular Junction

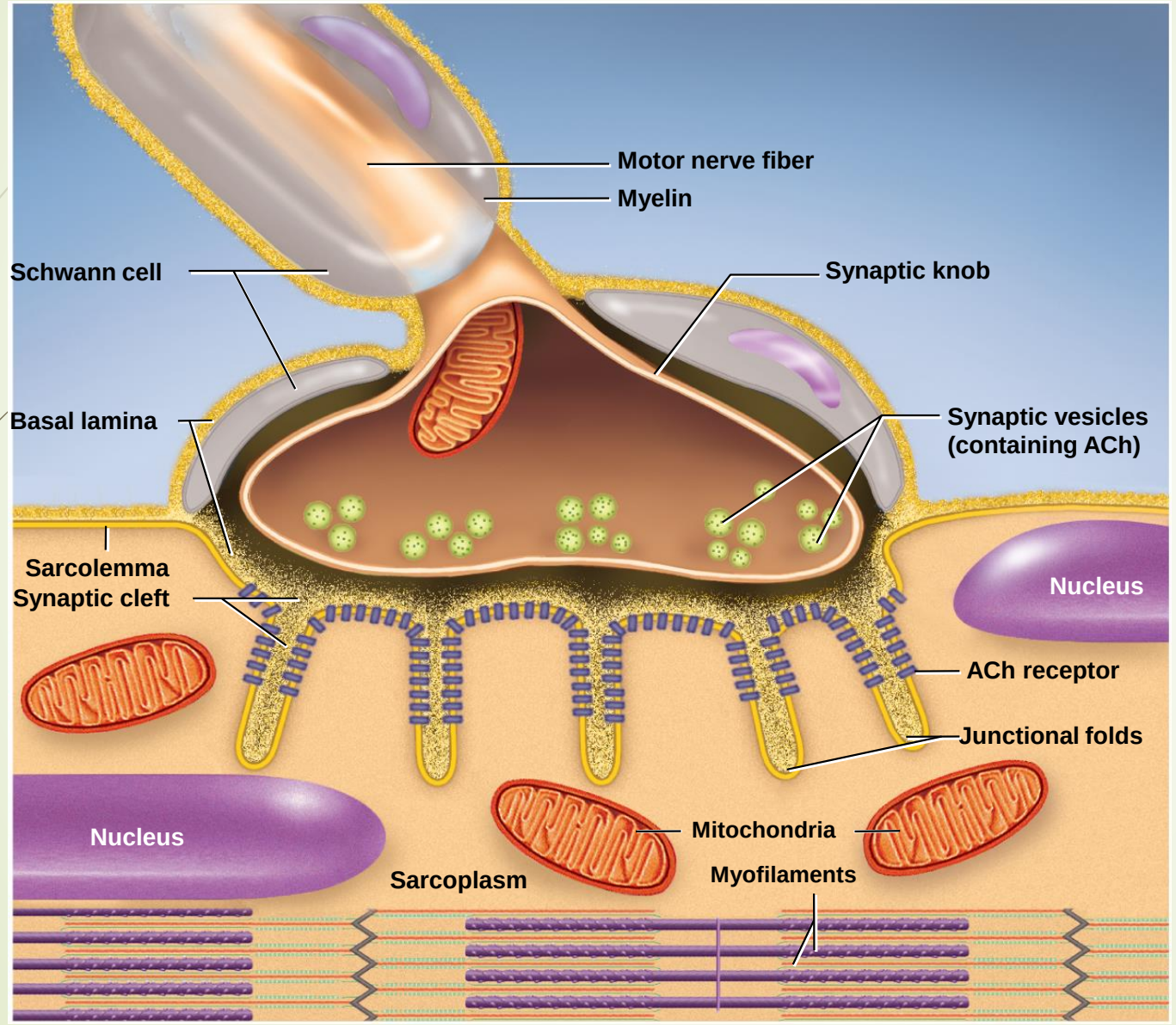


Figure 11.7b

Neuromuscular Junction - LM

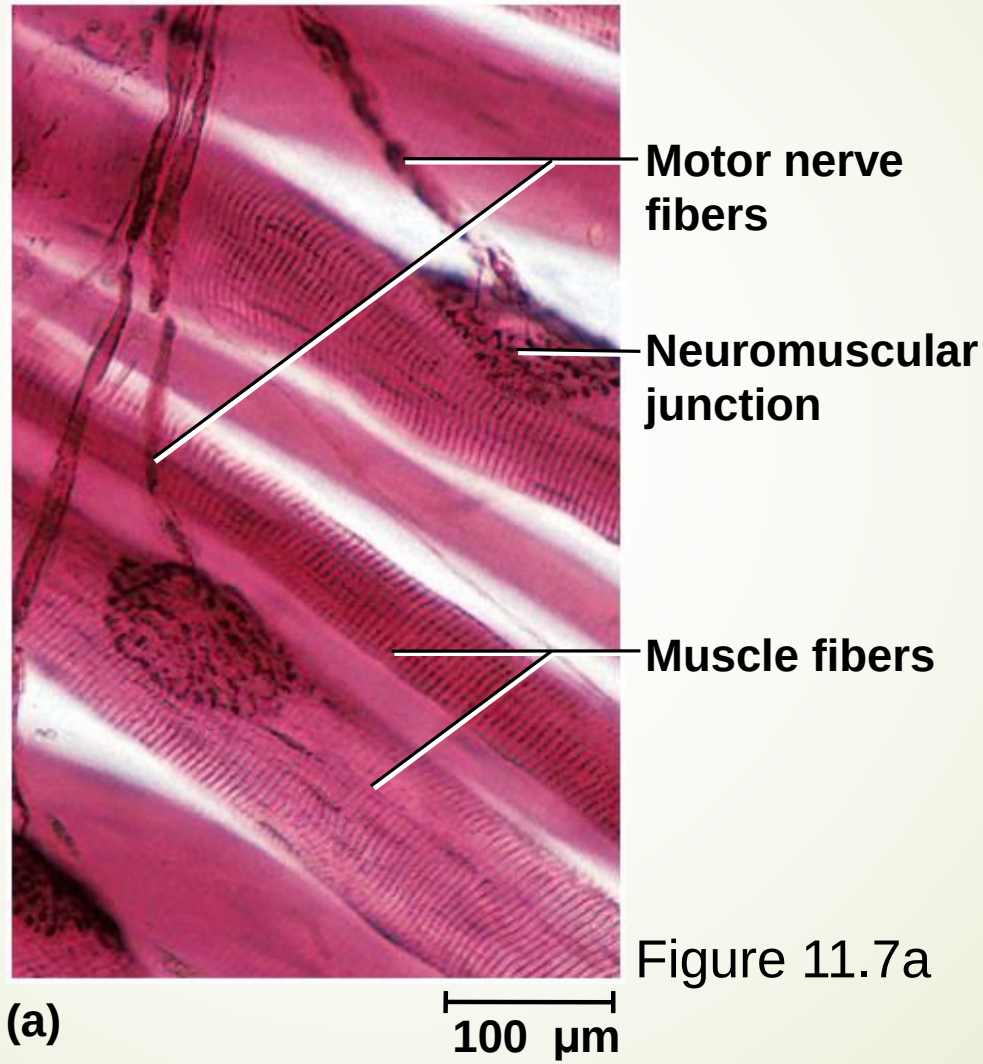


Figure 11.7a

Victor B. Eichler

Neuromuscular Toxins

- toxins that interfere with synaptic function can paralyze the muscles
- some pesticides contain cholinesterase inhibitors
  - bind to acetylcholinesterase and prevent it from degrading ACh
  - spastic paralysis - a state of continual contraction of the muscles
  - possible suffocation
- tetanus (lockjaw) is a form of spastic paralysis caused by toxin of *Clostridium tetani*
  - glycine in the spinal cord normally stops motor neurons from producing unwanted muscle contractions
  - tetanus toxin blocks glycine release in the spinal cord and causes overstimulation and spastic paralysis of the muscles
- flaccid paralysis – a state in which the muscles are limp and cannot contract
  - curare – compete with ACh for receptor sites, but do not stimulate the muscles
  - plant poison used by South American natives to poison blowgun darts
- botulism – type of food poisoning caused by a neuromuscular toxin secreted by the bacterium *Clostridium botulinum*
  - blocks release of ACh causing flaccid paralysis
  - Botox Cosmetic injections for wrinkle removal

Electrically Excitable Cells

- muscle fibers and neurons are electrically excitable cells
  - their plasma membrane exhibits voltage changes in response to stimulation
- electrophysiology - the study of the electrical activity of cells
- in an unstimulated (resting) cell
  - there are more anions (negative ions) on the inside of the plasma membrane than on the outside
  - the plasma membrane is electrically polarized (charged)
  - there are excess sodium ions (Na^+) in the extracellular fluid (ECF)
  - there are excess potassium ions (K^+) in the intracellular fluid (ICF)
  - also in the ICF, there are anions such as proteins, nucleic acids, and phosphates that cannot penetrate the plasma membrane
  - these anions make the inside of the plasma membrane negatively charged by comparison to its outer surface
- voltage (electrical potential) – a difference in electrical charge from one point to another
- resting membrane potential – about -90mV
  - maintained by sodium-potassium pump

Electrically Excitable Cells

- stimulated (active) muscle fiber or nerve cell
  - ion gates open in the plasma membrane
  - Na^+ instantly diffuses down its concentration gradient into the cell
  - these cations override the negative charges in the ICF
  - depolarization - inside of the plasma membrane becomes briefly positive
  - immediately, Na^+ gates close and K^+ gates open
  - K^+ rushes out of cell
  - repelled by the positive sodium charge and partly because of its concentration gradient
  - loss of positive potassium ions turns the membrane negative again (repolarization)
  - action potential – quick up-and-down voltage shift from the negative RMP to a positive value, and back to the negative value again.
  - RMP is a stable voltage seen in a waiting muscle or nerve cell
  - action potential is a quickly fluctuating voltage seen in an active stimulated cell
  - an action potential at one point on a plasma membrane causes another one to happen immediately in front of it, which triggers another one a little farther along and so forth

Muscle Contraction & Relaxation

- four major phases of contraction and relaxation
  - excitation
    - the process in which nerve action potentials lead to muscle action potentials
  - excitation-contraction coupling
    - events that link the action potentials on the sarcolemma to activation of the myofilaments, thereby preparing them to contract
  - contraction
    - step in which the muscle fiber develops tension and may shorten
  - relaxation
    - when its work is done, a muscle fiber relaxes and returns to its resting length

Excitation of a Muscle Fiber

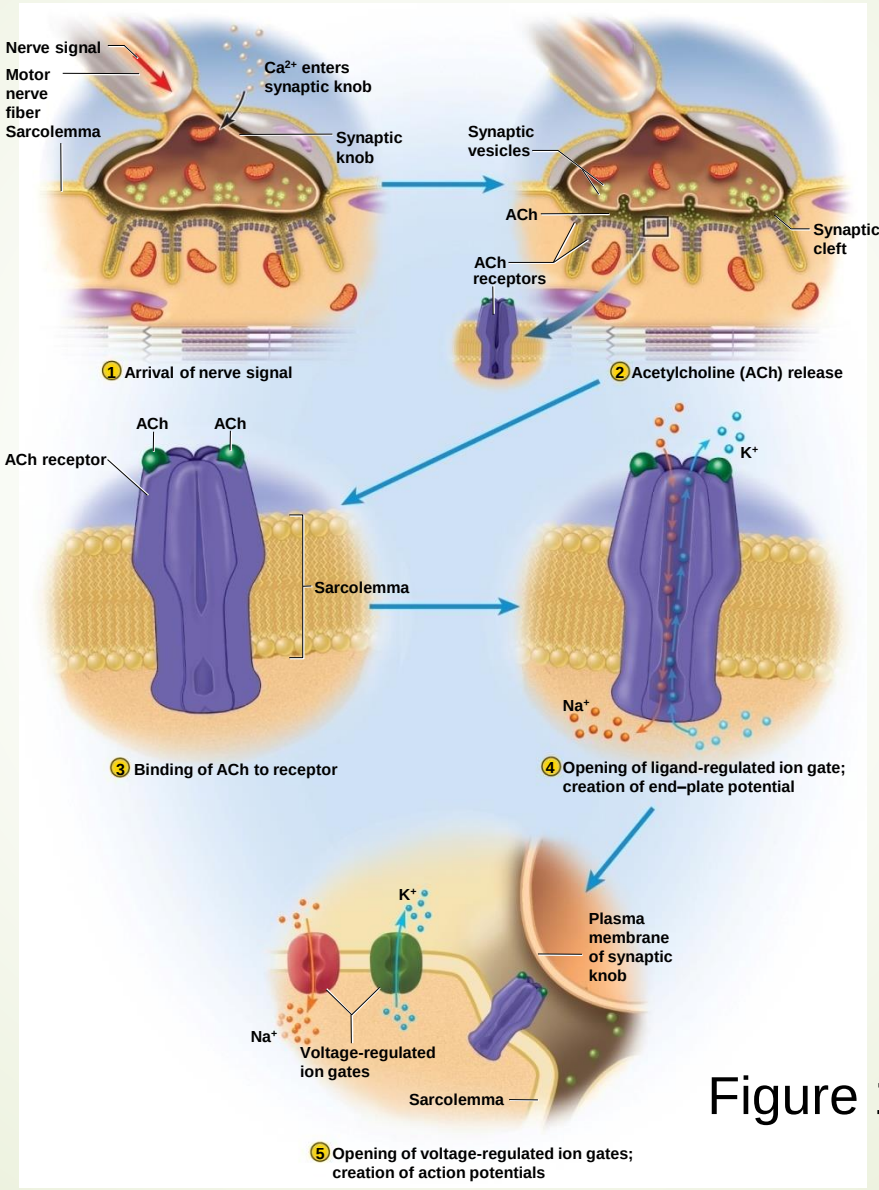


Figure 11.8

Excitation (steps 1 and 2)

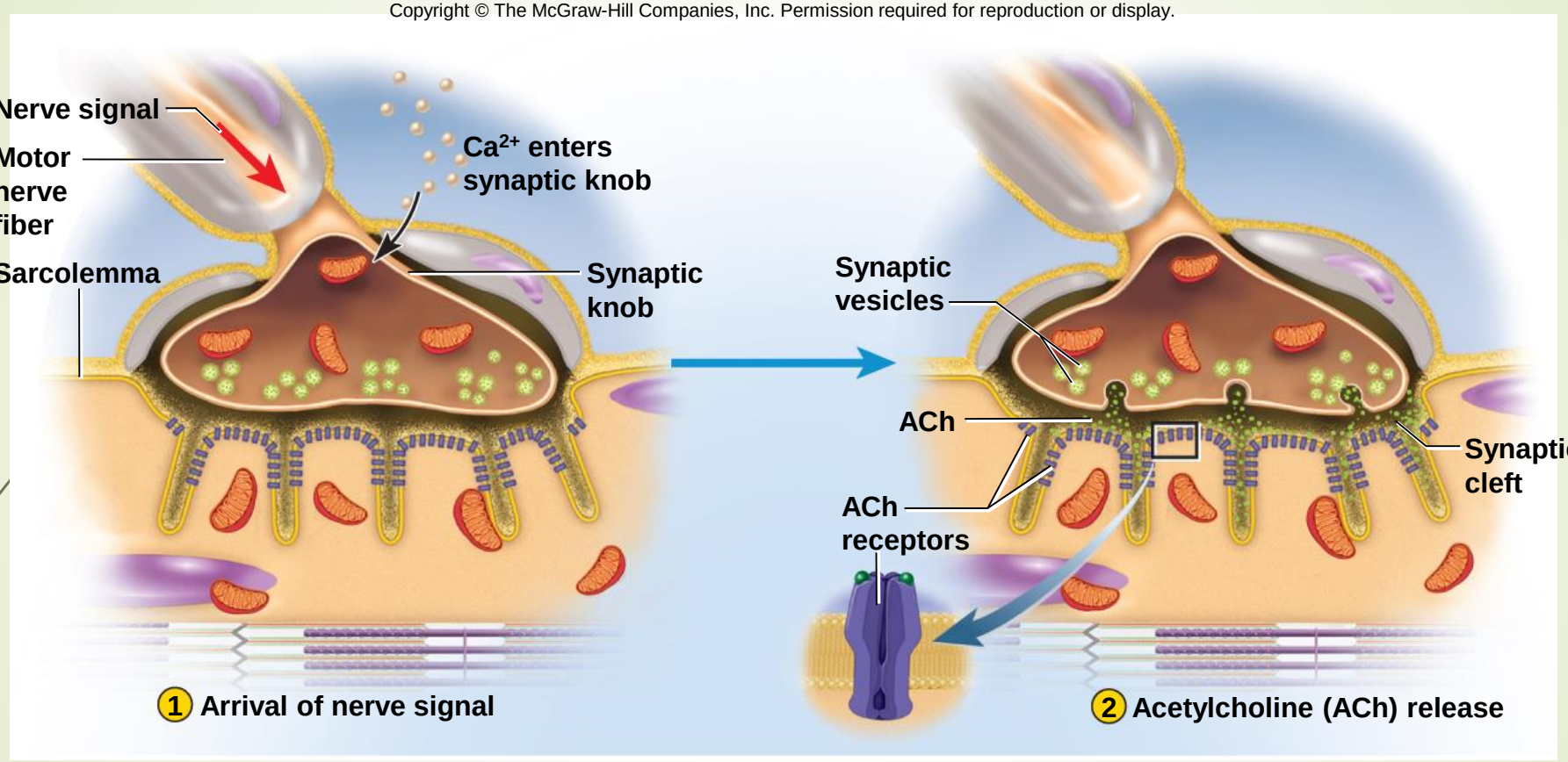
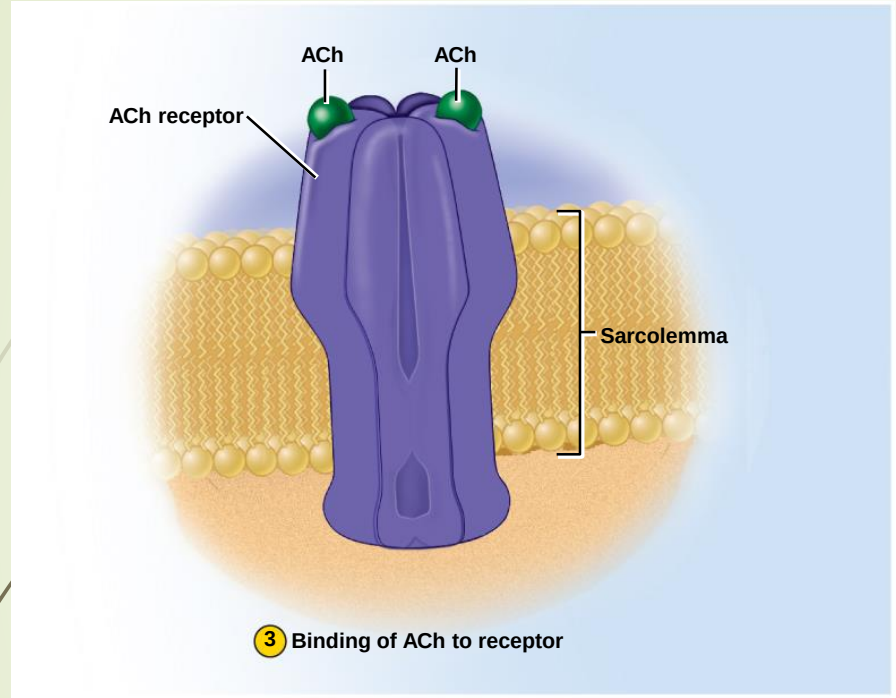


Figure 11.8 (1-2)

- nerve signal opens voltage-gated calcium channels in synaptic knob
- calcium stimulates exocytosis of ACh from synaptic vesicles
- ACh released into synaptic cleft

Excitation (steps 3 and 4)



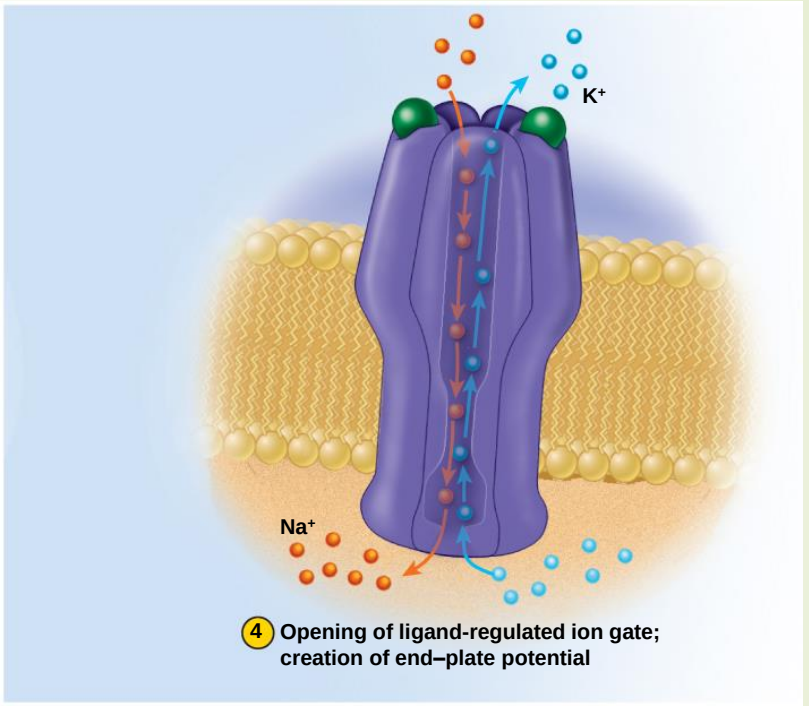


Figure 11.8 (3-4)

- two ACh molecules bind to each receptor protein, opening Na^+ and K^+ channels.
- Na^+ enters shifting RMP goes from -90mV to +75mV, then K^+ exits and RMP returns to -90mV - quick voltage shift is called an end-plate potential (EPP).

Excitation (step 5)

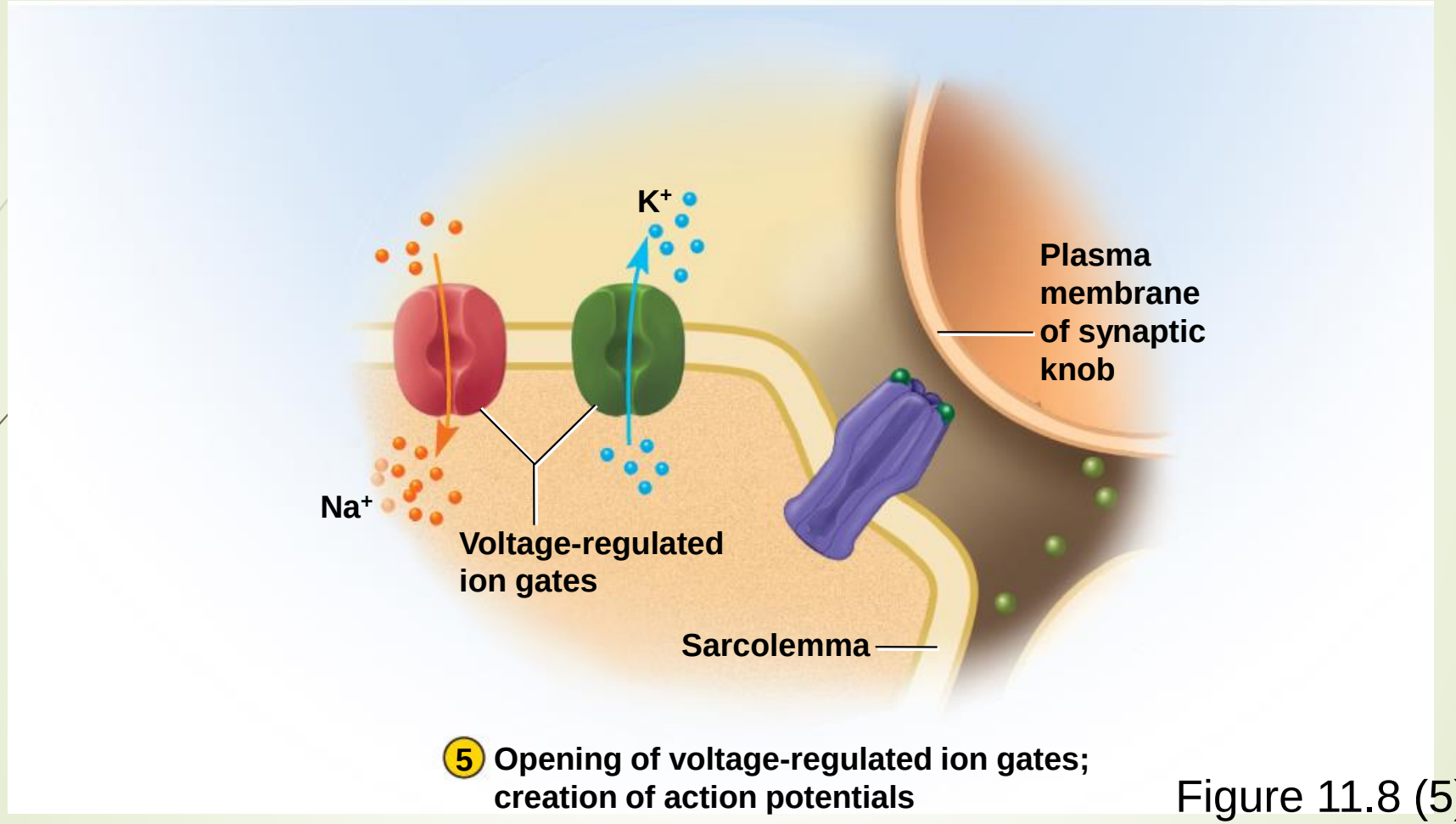


Figure 11.8 (5)

- voltage change (EPP) in end-plate region opens nearby voltage-gated channels producing an action potential that spreads over muscle surface.

Excitation-Contraction Coupling in Skeletal Muscle

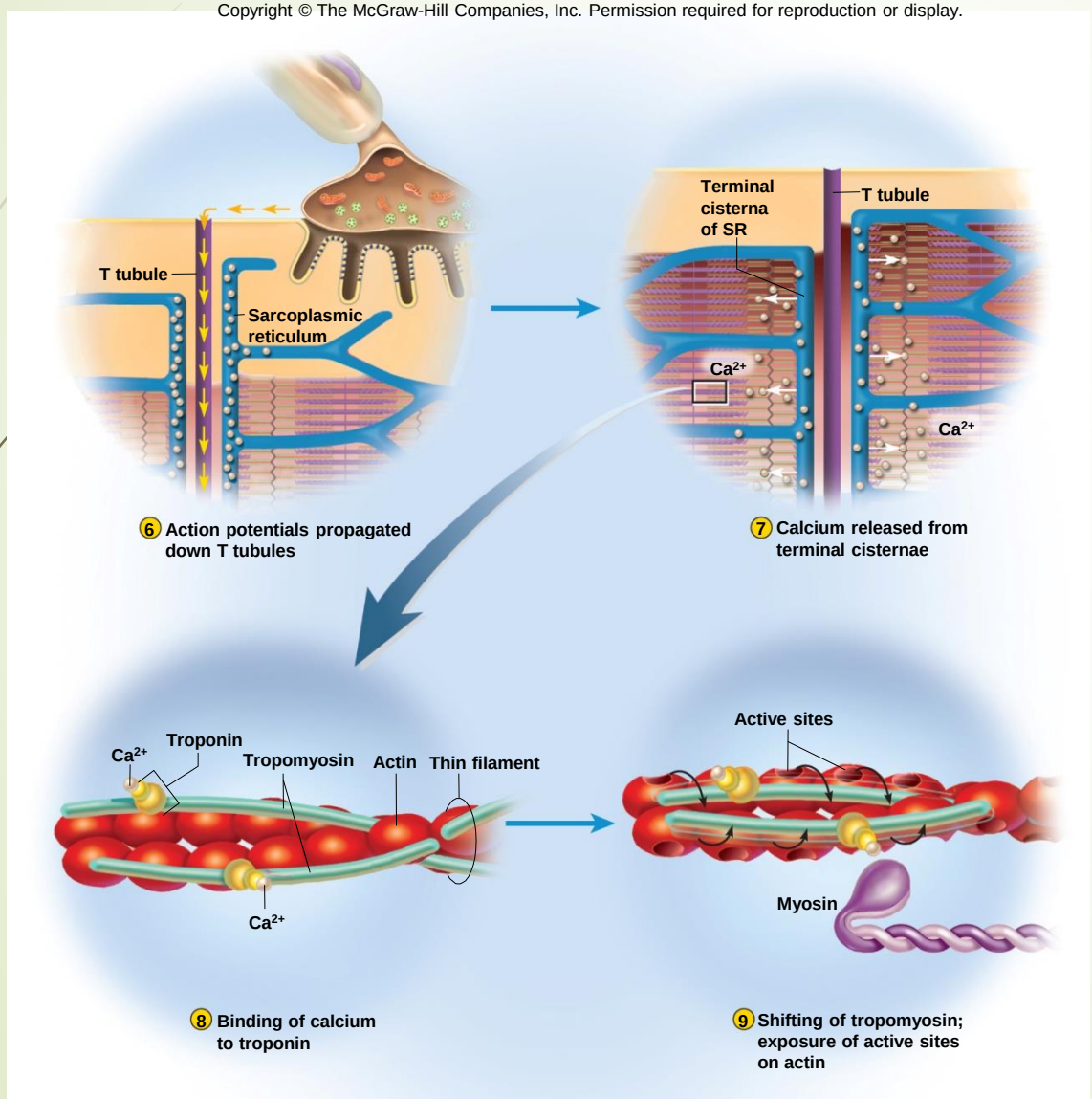


Figure 11.9 (6-9)

Excitation-Contraction Coupling (steps 6 and 7)

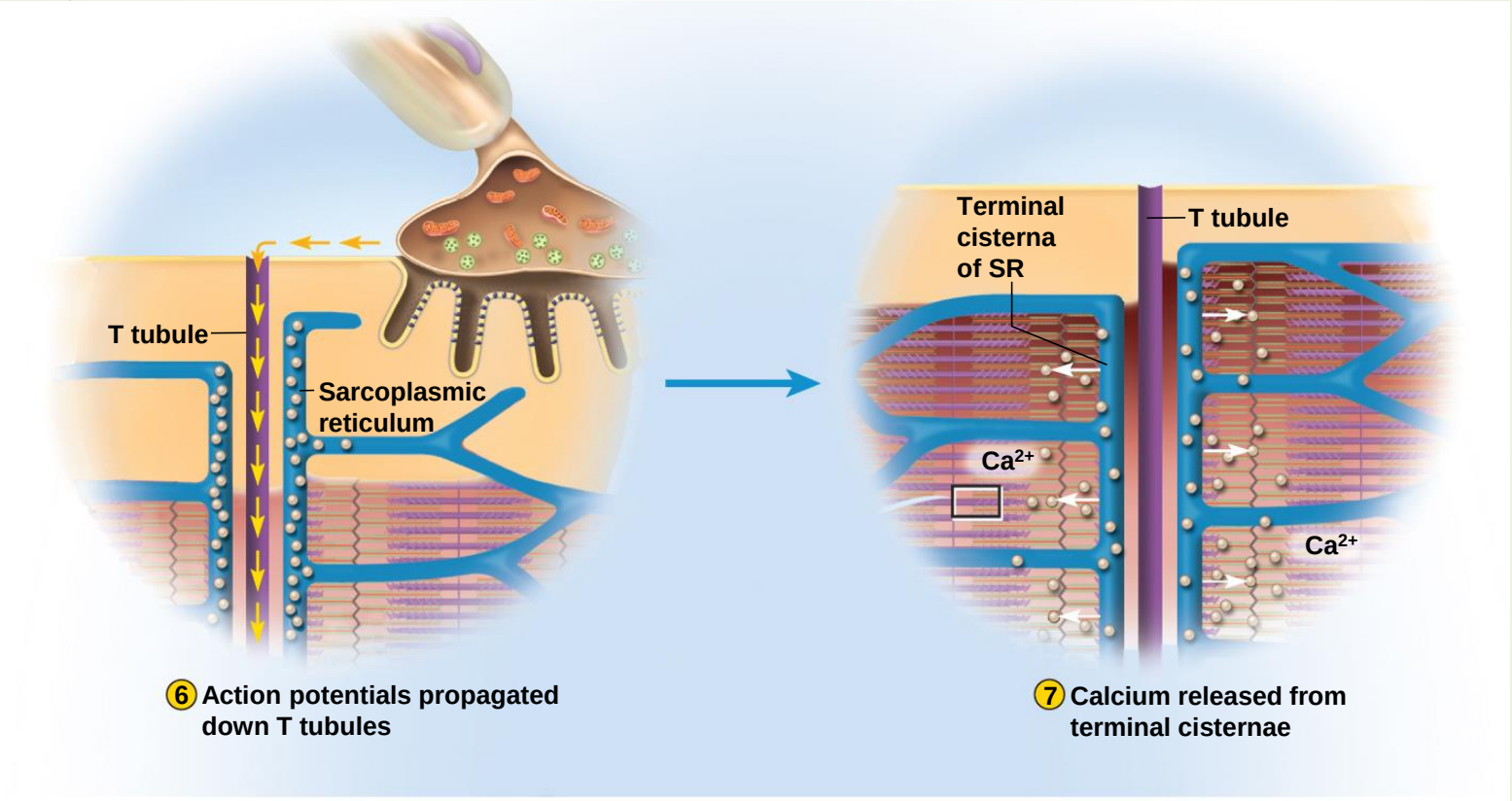


Figure 11.9 (6-7)

- action potential spreads down into T tubules
- opens voltage-gated ion channels in T tubules and Ca^{+2} channels in SR
- Ca^{+2} enters the cytosol

Excitation-Contraction Coupling (steps 8 and 9)

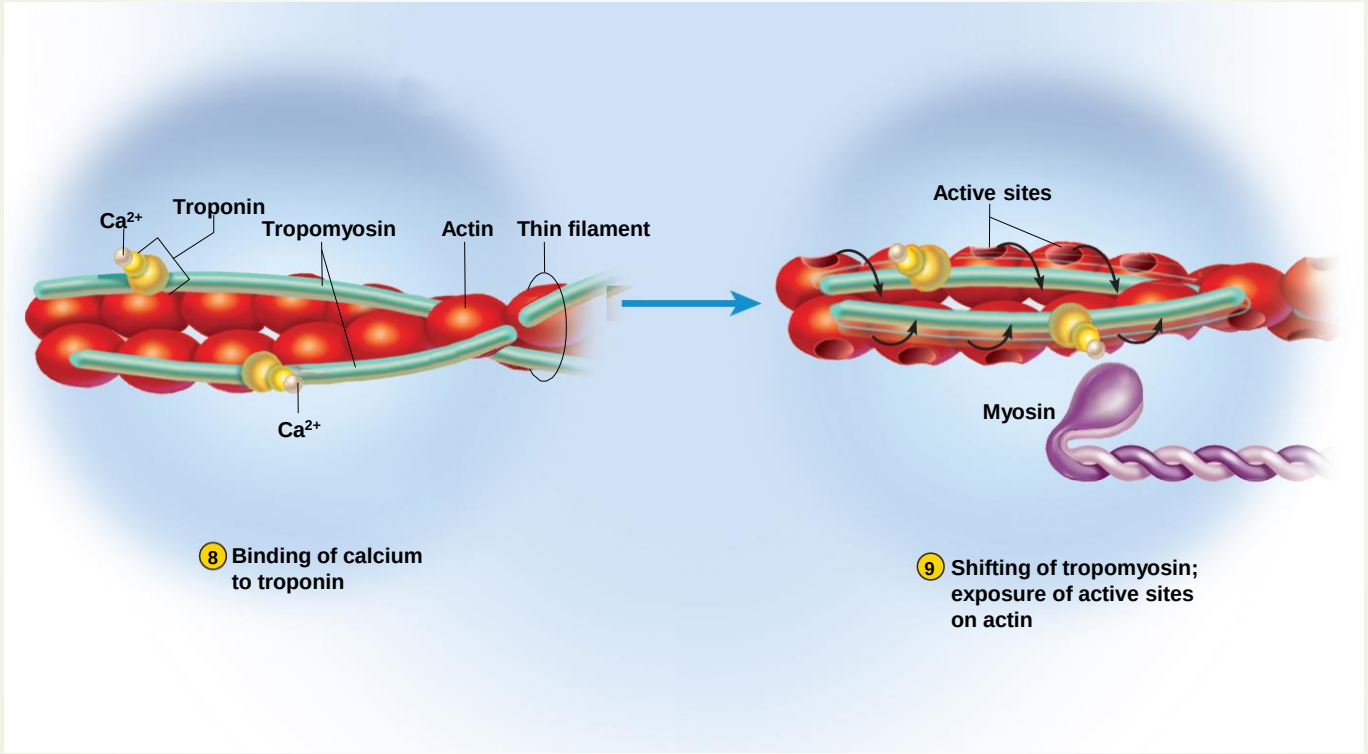


Figure 11.9 (8-9)

- calcium binds to troponin in thin filaments
- troponin-tropomyosin complex changes shape and exposes active sites on actin

Contraction (steps 10 and 11)

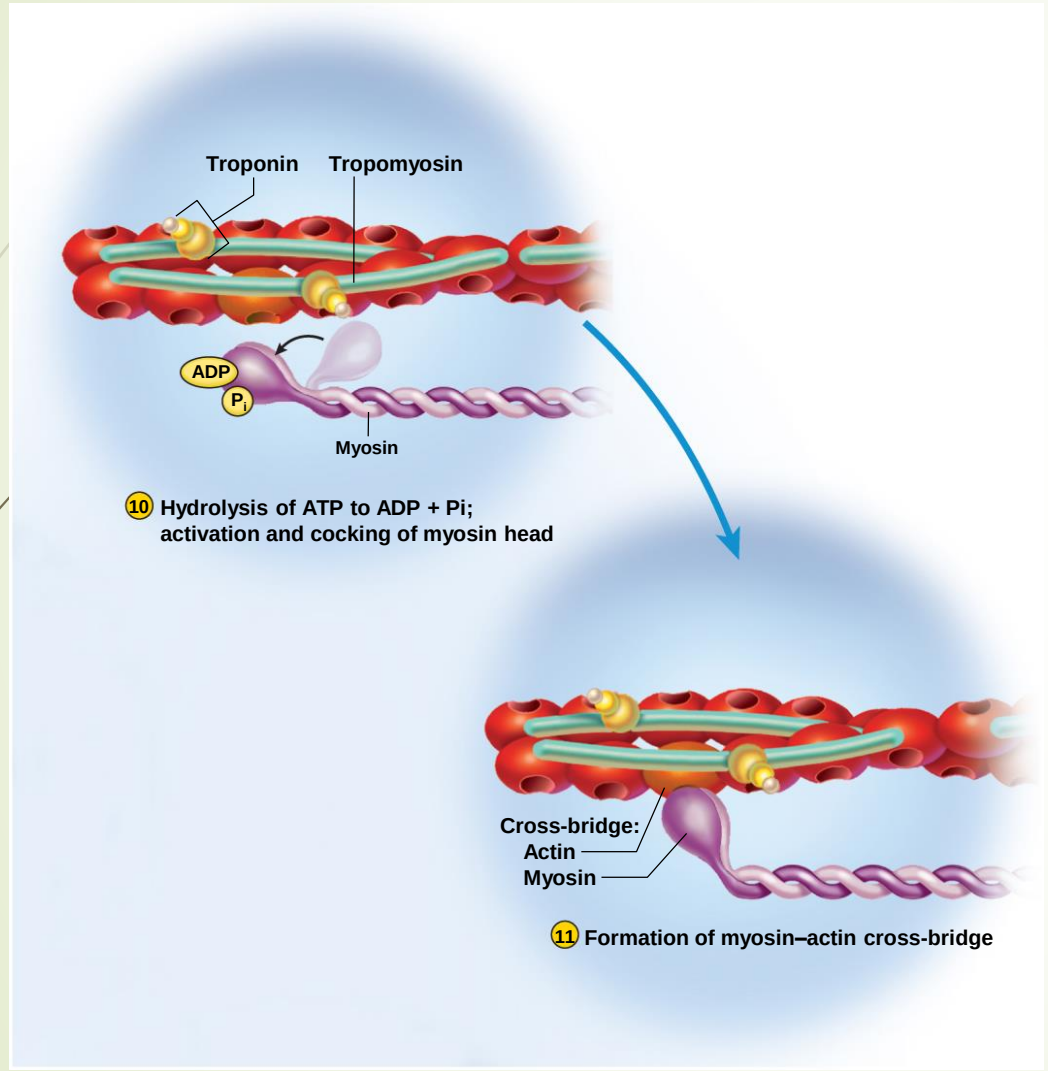


Figure 11.10 (10-11)

- myosin ATPase enzyme in myosin head hydrolyzes an ATP molecule
- activates the head "cocking" it in an extended position
  - ADP + P_i remain attached
- head binds to actin active site forming a myosin - actin cross-bridge

Contraction (steps 12 and 13)

- myosin head releases ADP and P_i, flexes pulling thin filament past thick - power stroke
- upon binding more ATP, myosin releases actin and process is repeated
  - each head performs 5 power strokes per second
  - each stroke utilizes one molecule of ATP

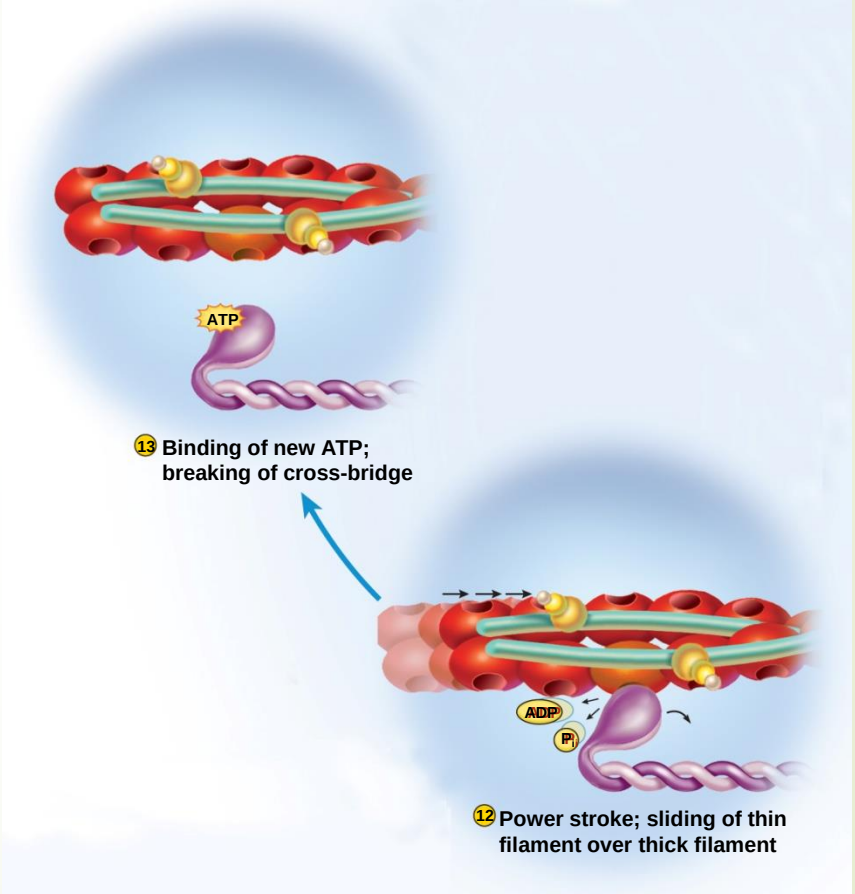


Figure 11.10 (12-13)

Relaxation (steps 14 and 15)

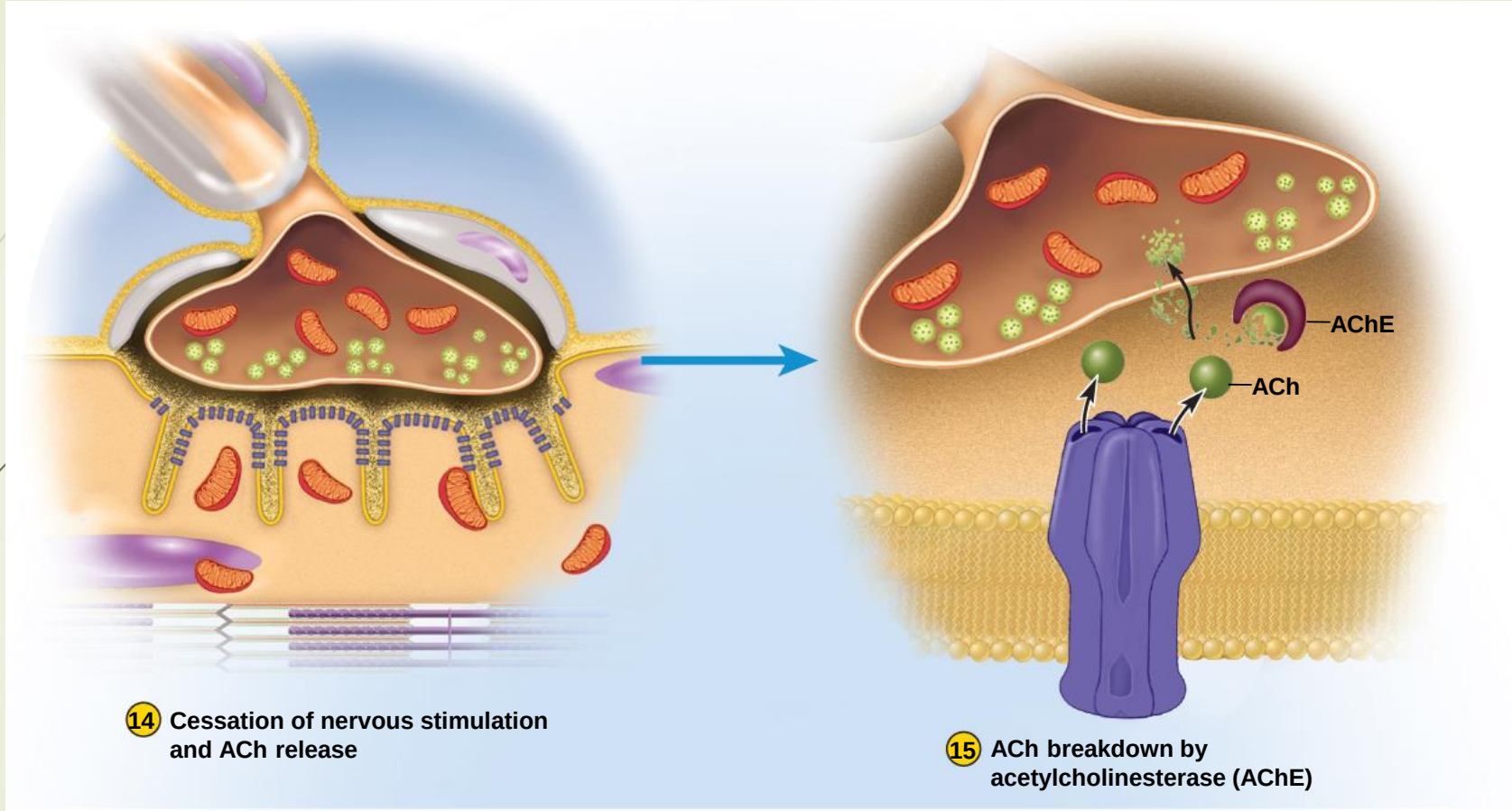


Figure 11.11 (14-15)

- nerve stimulation & ACh release stop
- AChE breaks down ACh & fragments reabsorbed into synaptic knob
- stimulation by ACh stops

Relaxation (step 16)

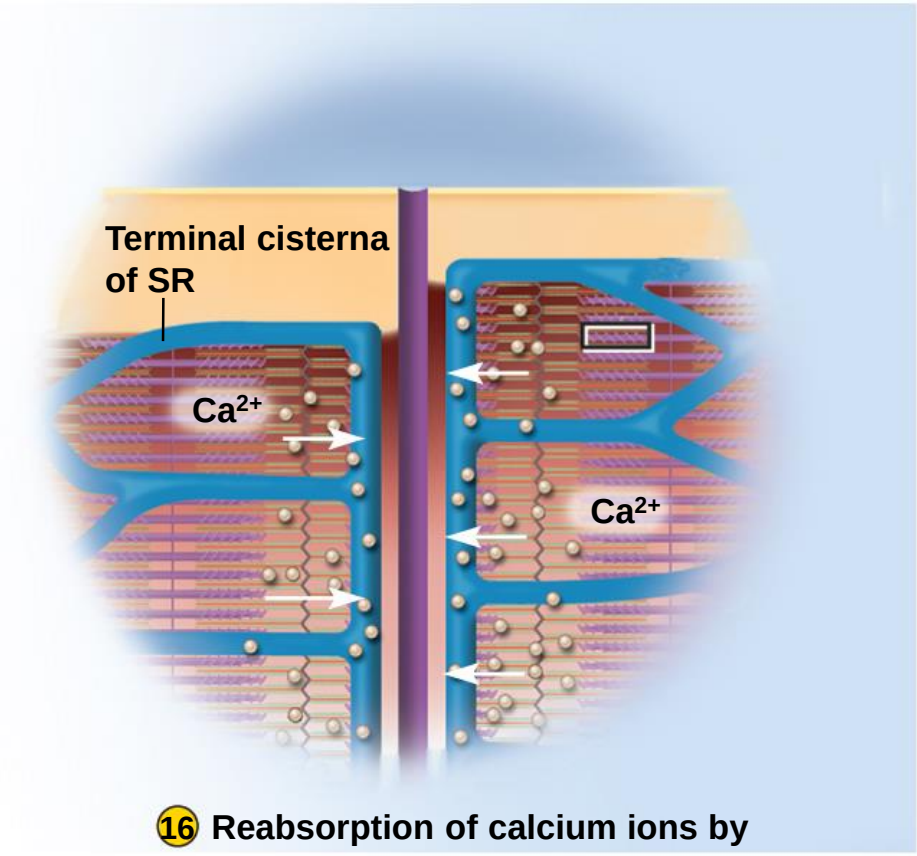


Figure 11.11 (16)

- Ca^{+2} pumped back into SR by active transport. Ca^{+2} binds to calsequestrin while in storage in SR
- ATP is needed for muscle relaxation as well as muscle contraction.

Relaxation (steps 17 and 18)

- Ca^{+2} removed from troponin is pumped back into SR
- tropomyosin reblocks the active sites
- muscle fiber ceases to produce or maintain tension
- muscle fiber returns to its resting length
  - due to recoil of elastic components & contraction of antagonistic muscles

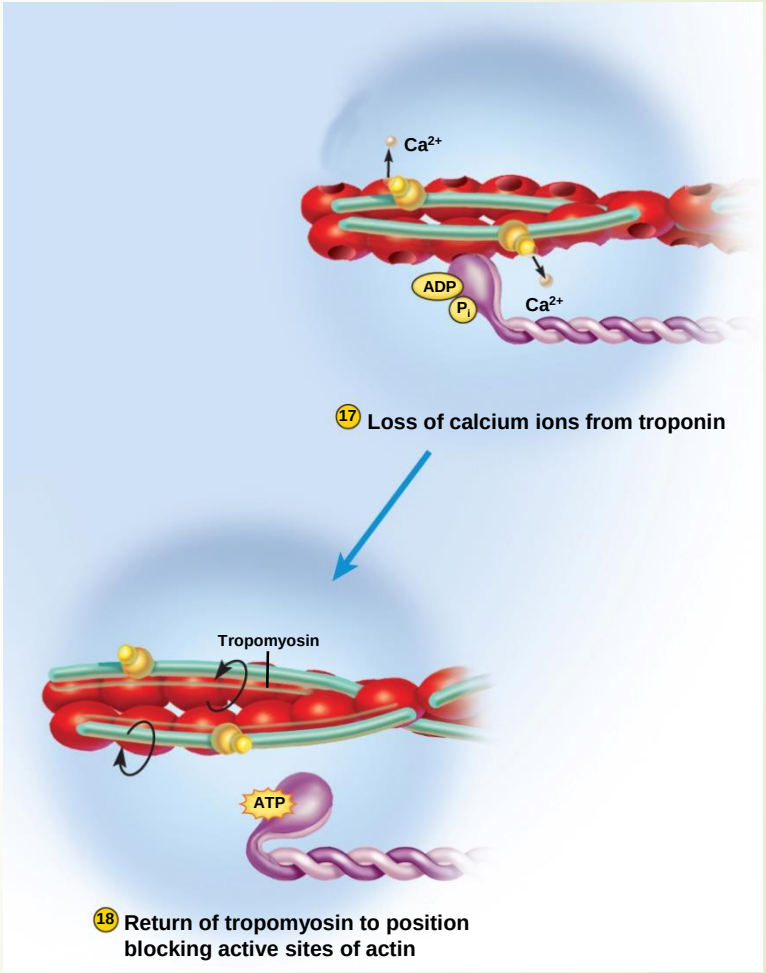


Figure 11.11 (17-18)

Rigor Mortis

- rigor mortis - hardening of muscles and stiffening of body beginning 3 to 4 hours after death
  - deteriorating sarcoplasmic reticulum releases Ca^{+2}
  - deteriorating sarcolemma allows Ca^{+2} to enter cytosol
  - Ca^{+2} activates myosin-actin cross-bridging
  - muscle contracts, but can not relax.
- muscle relaxation requires ATP, and ATP production is no longer produced after death
  - fibers remain contracted until myofilaments begins to decay
- rigor mortis peaks about 12 hours after death, then diminishes over the next 48 to 60 hours