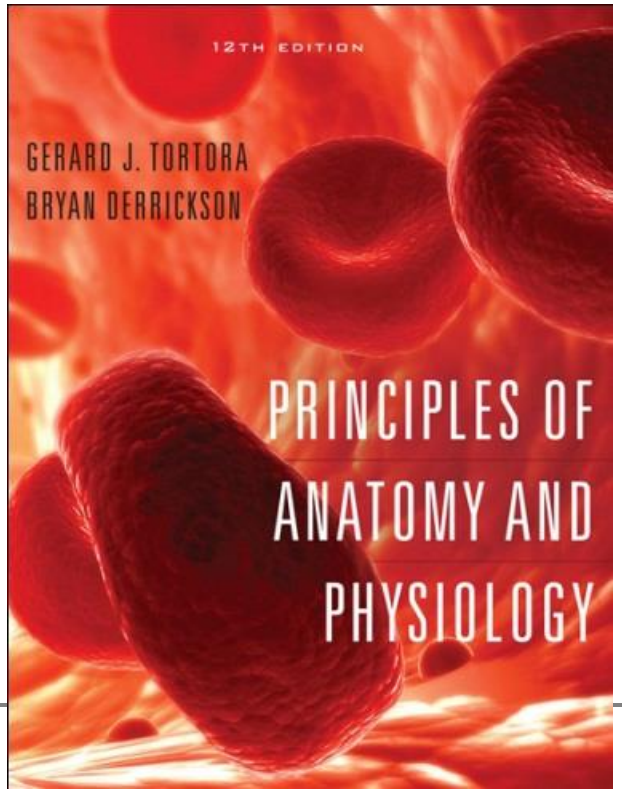
Excitation contraction coupling Muscular Tissue



Muscular Tissue

- Overview of Muscular Tissue
- Skeletal Muscle Tissue
- Contraction and Relaxation of Skeletal Muscle Fibers
- Muscle Metabolism
- Control of Muscle Tension
- Action potential in muscle fiber
- Types of Skeletal Muscle Fibers
- EC coupling
- Applied physiology
- Pharmacophysiology

Overview of Muscular Tissue

- **Types of Muscular Tissue**
  - The three types of muscular tissue
    - Skeletal
    - Cardiac
    - Smooth
- **Skeletal Muscle Tissue**
  - So named because most skeletal muscles move bones
  - Skeletal muscle tissue is striated:
    - Alternating light and dark bands (striations) as seen when examined with a microscope
  - Skeletal muscle tissue works mainly in a voluntary manner
    - Its activity can be consciously controlled
  - Most skeletal muscles also are controlled subconsciously to some extent
    - Ex: the diaphragm alternately contracts and relaxes without conscious control

Overview of Muscular Tissue

- **Cardiac Muscle Tissue**
  - Found only in the walls of the heart
  - Striated like skeletal muscle
  - Action is involuntary
    - Contraction and relaxation of the heart is not consciously controlled
    - Contraction of the heart is initiated by a node of tissue called the “pacemaker”
- **Smooth Muscle Tissue**
  - Located in the walls of hollow internal structures
    - Blood vessels, airways, and many organs
  - Lacks the striations of skeletal and cardiac muscle tissue
  - Usually involuntary

Overview of Muscular Tissue

- **Functions of Muscular Tissue**
  - **Producing Body Movements**
    - Walking and running
  - **Stabilizing Body Positions**
    - Posture
  - **Moving Substances Within the Body**
    - Heart muscle pumping blood
    - Moving substances in the digestive tract
  - **Generating heat**
    - Contracting muscle produces heat
    - Shivering increases heat production

Overview of Muscular Tissue

- **Properties of Muscular Tissue**
  - Properties that enable muscle to function and contribute to homeostasis
    - **Excitability**
      - Ability to respond to stimuli
    - **Contractility**
      - Ability to contract forcefully when stimulated
    - **Extensibility**
      - Ability to stretch without being damaged
    - **Elasticity**
      - Ability to return to an original length

Skeletal Muscle Tissue

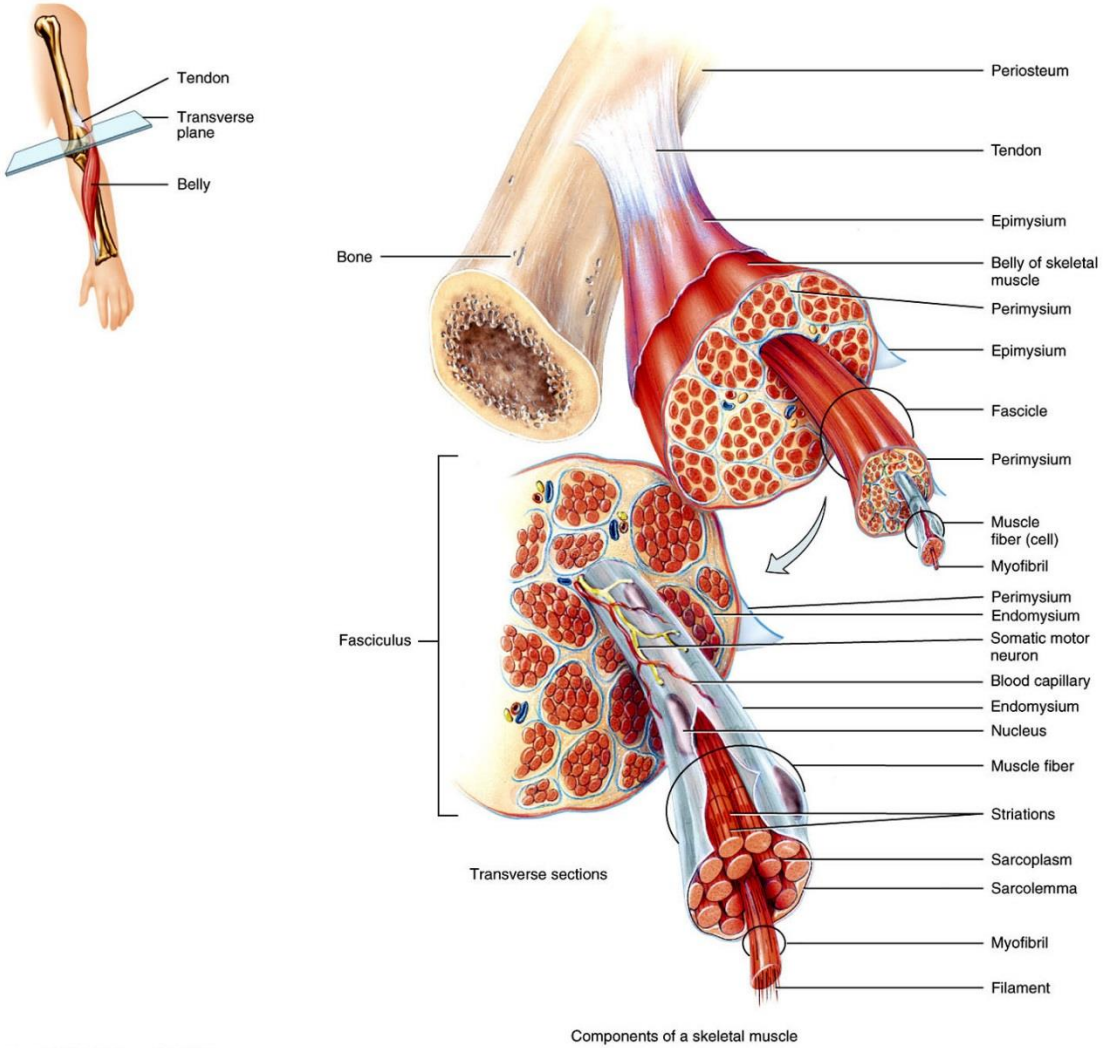


Figure 10.01 Tortora - PAP 12/e

Skeletal Muscle Tissue

- **Nerve and Blood Supply**
  - Neurons that stimulate skeletal muscle to contract are somatic motor neurons
  - The axon of a somatic motor neuron typically branches many times
    - Each branch extending to a different skeletal muscle fiber
  - Each muscle fiber is in close contact with one or more capillaries

Skeletal Muscle Tissue

- **Microscopic Anatomy**
  - The number of skeletal muscle fibers is set before you are born
    - Most of these cells last a lifetime
  - Muscle growth occurs by hypertrophy
    - An enlargement of existing muscle fibers
  - Testosterone and human growth hormone stimulate hypertrophy
  - Satellite cells retain the capacity to regenerate damaged muscle fibers

Skeletal Muscle Tissue

- **Sarcolemma**
  - The plasma membrane of a muscle cell
- **Transverse (T tubules)**
  - Tunnel in from the plasma membrane
  - Muscle action potentials travel through the T tubules
- **Sarcoplasm,** the cytoplasm of a muscle fiber
  - Sarcoplasm includes glycogen used for synthesis of ATP and a red-colored protein called myoglobin which binds oxygen molecules
  - Myoglobin releases oxygen when it is needed for ATP production

Skeletal Muscle Tissue

- **Myofibrils**
  - Thread like structures which have a contractile function
- **Sarcoplasmic reticulum (SR)**
  - Membranous sacs which encircles each myofibril
  - Stores calcium ions (Ca^{++})
  - Release of Ca^{++} triggers muscle contraction
- **Filaments**
  - Function in the contractile process
  - Two types of filaments (Thick and Thin)
  - There are two thin filaments for every thick filament
- **Sarcomeres**
  - Compartments of arranged filaments
  - Basic functional unit of a myofibril

Skeletal Muscle Tissue

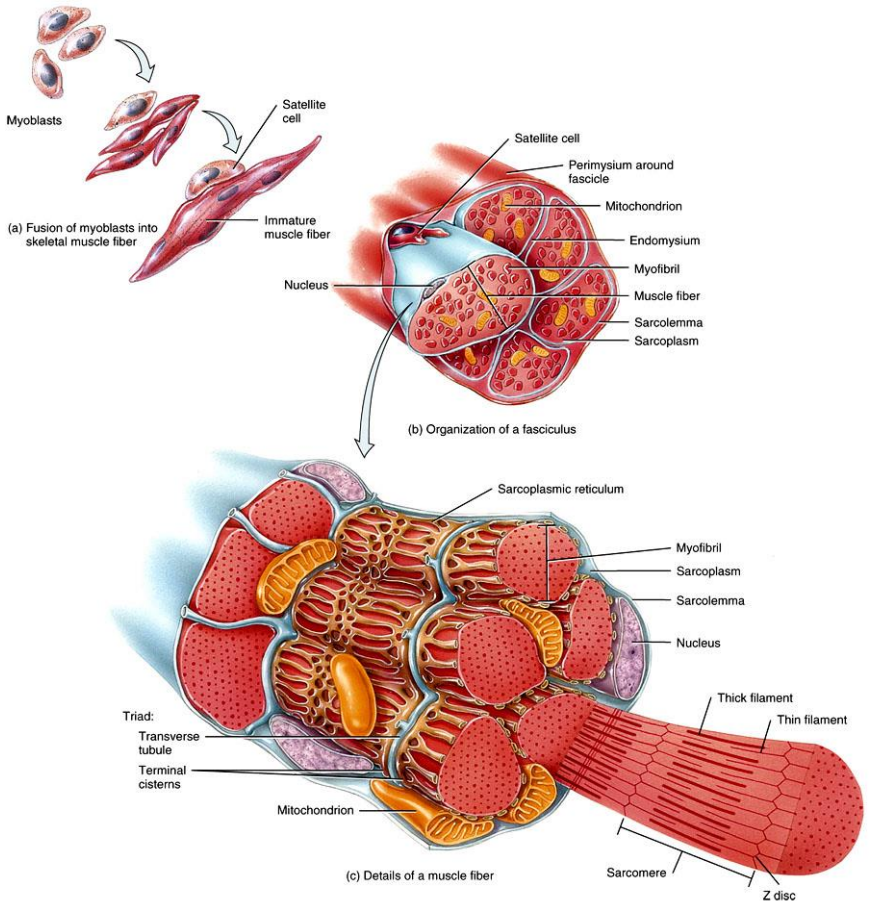


Figure 10.02abc Tortora - PAP 12/e

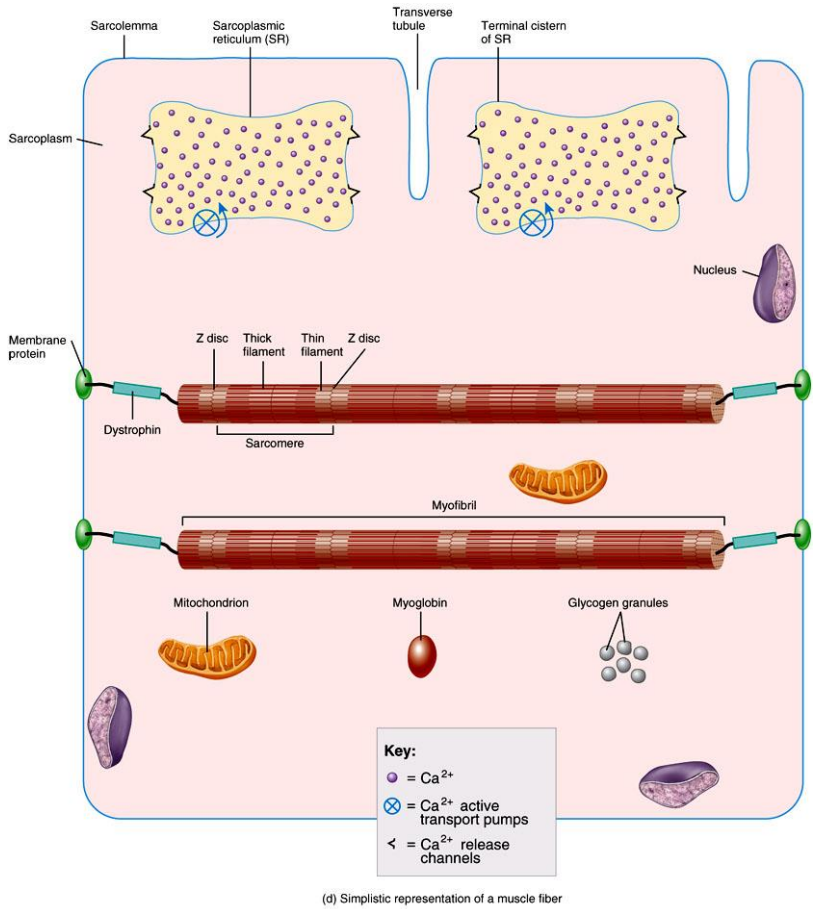


Figure 10.02d Tortora - PAP 12/e

Contraction and Relaxation of Skeletal Muscle

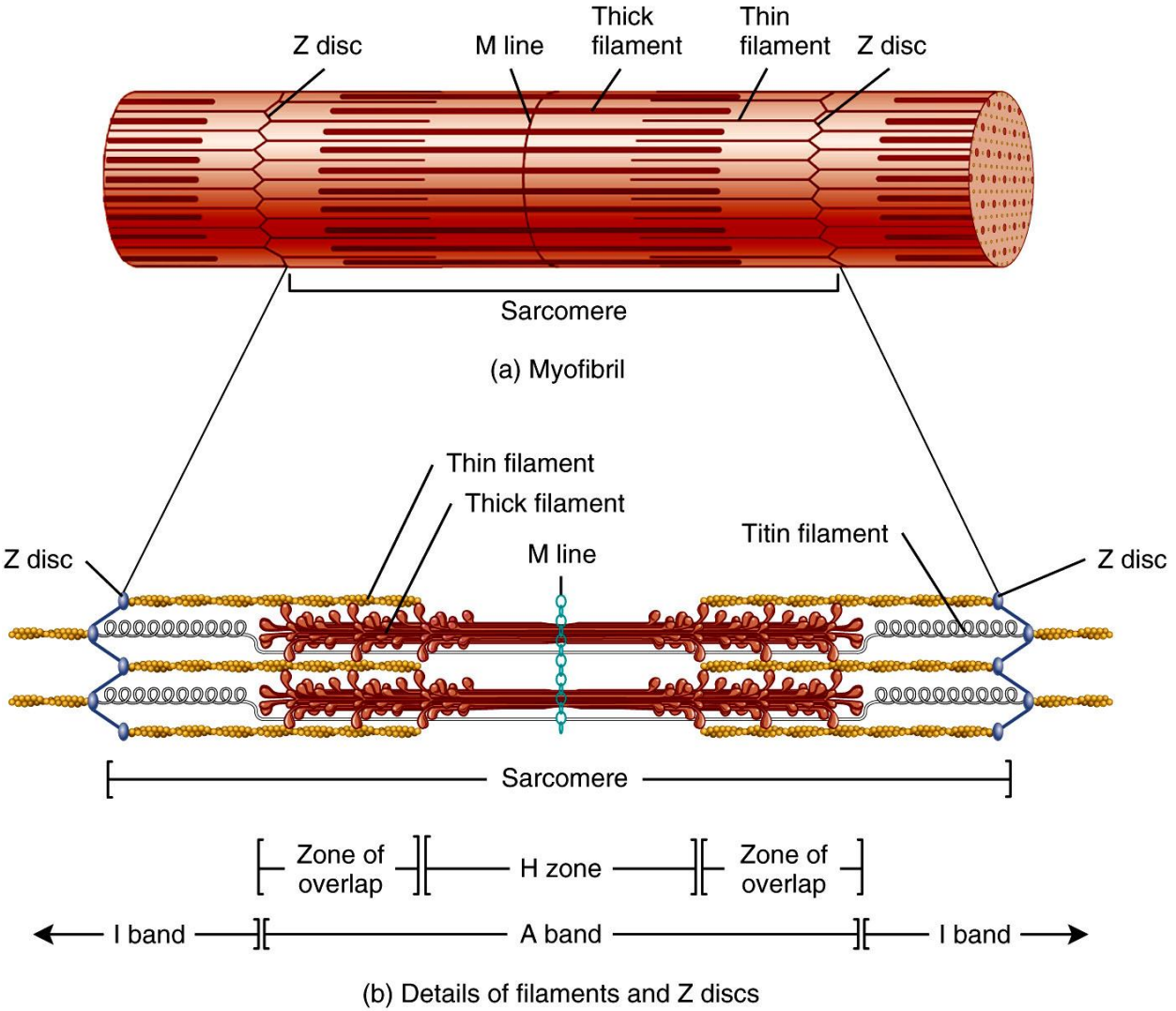


Figure 10.03 Tortora - PAP 12/e

Skeletal Muscle Tissue

- **Muscle Proteins**
  - Myofibrils are built from three kinds of proteins
    - 1) Contractile proteins
      - Generate force during contraction
    - 2) Regulatory proteins
      - Switch the contraction process on and off
    - 3) Structural proteins
      - Align the thick and thin filaments properly
      - Provide elasticity and extensibility
      - Link the myofibrils to the sarcolemma

Skeletal Muscle Tissue

- Contractile Proteins
  - **Myosin**
    - Thick filaments
    - Functions as a motor protein which can achieve motion
    - Convert ATP to energy of motion
    - Projections of each myosin molecule protrude outward (myosin head)
  - **Actin**
    - Thin filaments
    - Actin molecules provide a site where a myosin head can attach
    - Tropomyosin and troponin are also part of the thin filament
    - In relaxed muscle= Myosin is blocked from binding to actin
    - Strands of tropomyosin cover the myosin-binding sites
    - Calcium ion binding to troponin moves tropomyosin away from myosin-binding sites
    - Allows muscle contraction to begin as myosin binds to actin

Skeletal Muscle Tissue

- Structural Proteins
  - **Titin**
    - Stabilize the position of myosin
    - accounts for much of the elasticity and extensibility of myofibrils
  - **Dystrophin**
    - Links thin filaments to the sarcolemma

Contraction and Relaxation of Skeletal Muscle

- **The Sliding Filament Mechanism**
  - Myosin heads attach to and "walk" along the thin filaments at both ends of a sarcomere
  - Progressively pulling the thin filaments toward the center of the sarcomere
  - Z discs come closer together and the sarcomere shortens
  - Leading to shortening of the entire muscle

Contraction and Relaxation of Skeletal Muscle

TABLE 10.1

Components of the Sarcomere

COMPONENT	DESCRIPTION
Z discs	Narrow, plate-shaped regions of dense material that separate one sarcomere from the next.
A band	The dark, middle part of the sarcomere that extends the entire length of the thick filaments and also includes those parts of the thin filaments that overlap with the thick filaments.
I band	The lighter, less dense area of the sarcomere that contains the rest of the thin filaments but no thick filaments. A Z disc passes through the center of each I band.
H zone	A narrow region in the center of each A band that contains thick filaments but no thin filaments.
M line	A region in the center of the H zone that contains proteins that hold the thick filaments together at the center of the sarcomere.

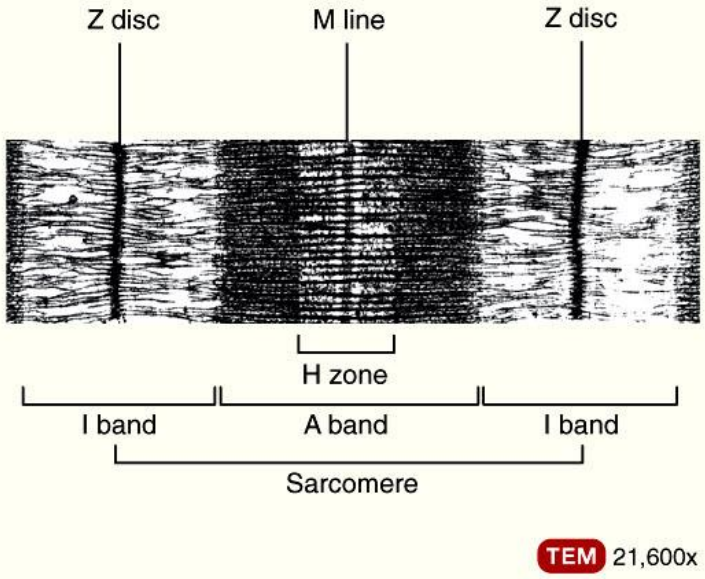
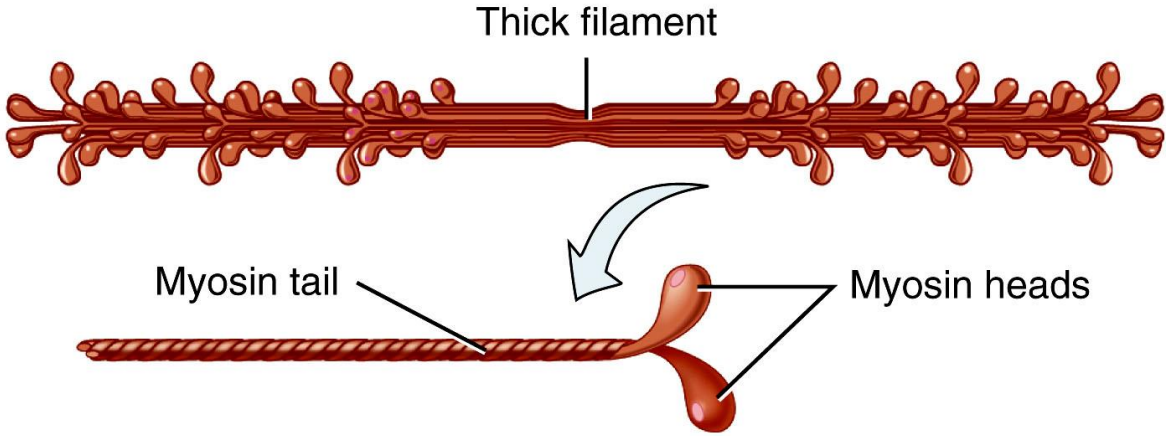
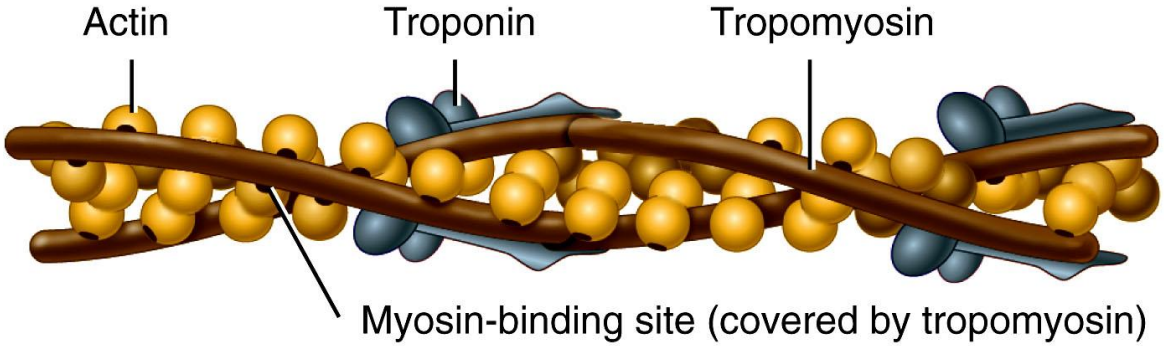


Table 10.01 Tortora - PAP 12/e

Contraction and Relaxation of Skeletal Muscle



(a) One thick filament and a myosin molecule



(b) Portion of a thin filament

Figure 10.05 Tortora - PAP 12/e

Contraction and Relaxation of Skeletal Muscle

- **The Contraction Cycle**
  - The onset of contraction begins with the SR releasing calcium ions into the muscle cell
  - Where they bind to actin opening the myosin binding sites

Contraction and Relaxation of Skeletal Muscle

- The contraction cycle consists of 4 steps
  - **1) ATP hydrolysis = ADP**
    - Hydrolysis of ATP reorients and energizes the myosin head
  - **2) Formation of cross-bridges**
    - Myosin head attaches to the myosin-binding site on actin
  - **3) Power stroke**
    - During the power stroke the crossbridge rotates, sliding the filaments
  - **4) Detachment of myosin from actin**
    - As the next ATP binds to the myosin head, the myosin head detaches from actin
    - The contraction cycle repeats as long as ATP is available and the Ca^{++} level is sufficiently high
    - Continuing cycles applies the force that shortens the sarcomere

Contraction and Relaxation of Skeletal Muscle

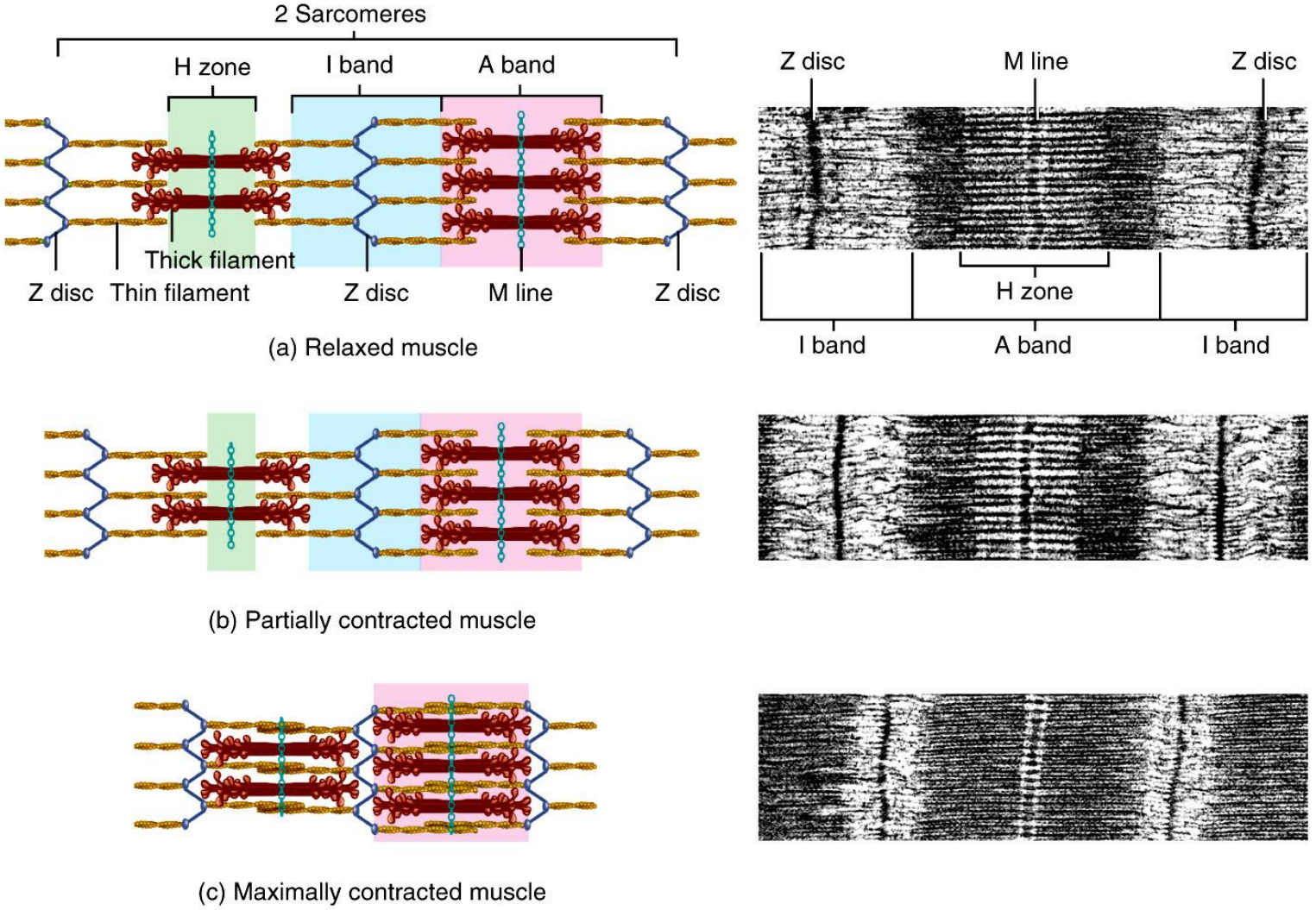
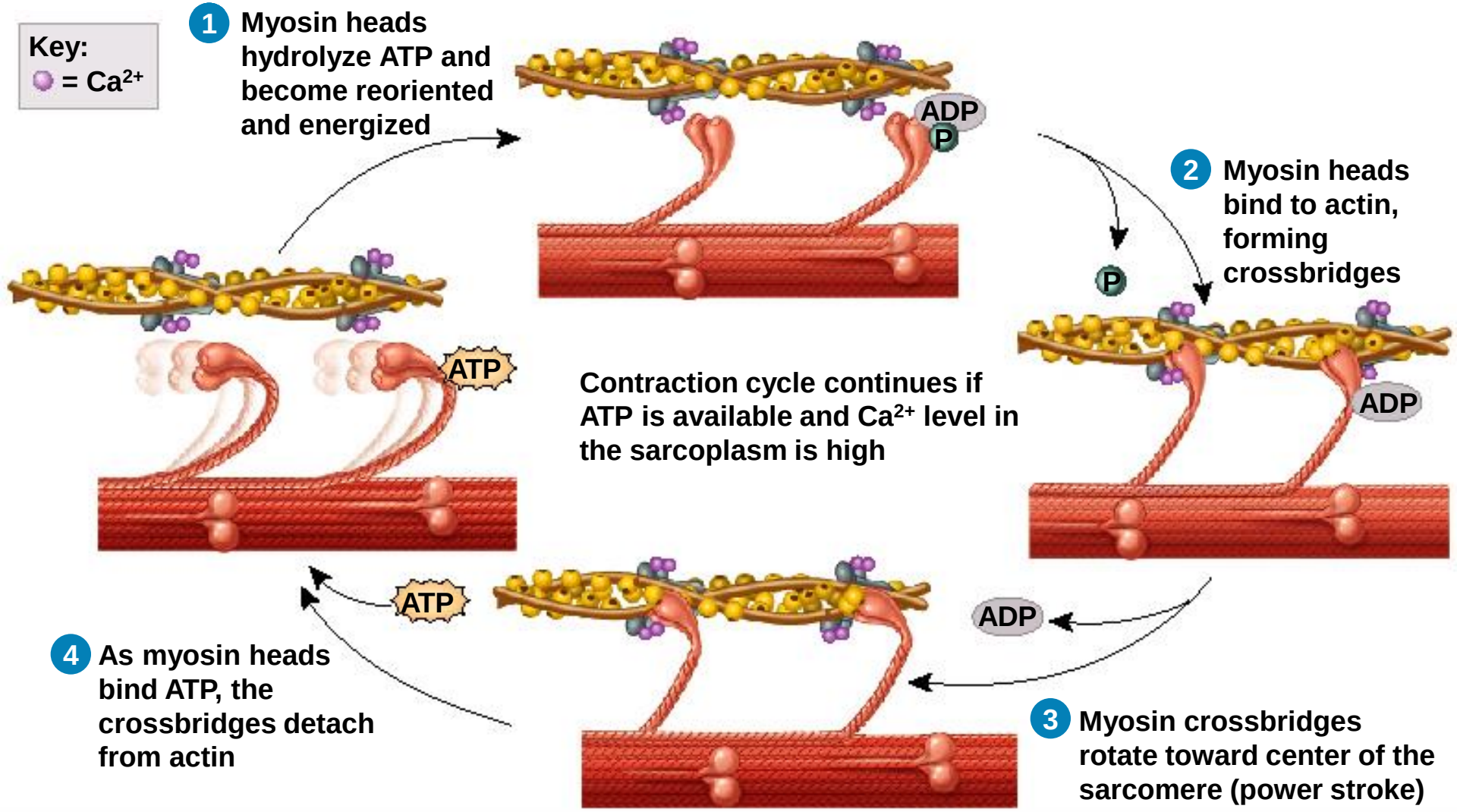


Figure 10.06 Tortora - PAP 12/e


Key:
= Ca^{2+}
1 Myosin heads hydrolyze ATP and become reoriented and energized
ADP
P
2 Myosin heads bind to actin, forming crossbridges
P
ADP
ATP
Contraction cycle continues if ATP is available and Ca^{2+} level in the sarcoplasm is high
ATP
ADP
4 As myosin heads bind ATP, the crossbridges detach from actin
3 Myosin crossbridges rotate toward center of the sarcomere (power stroke)

Contraction and Relaxation of Skeletal Muscle

- **Excitation–Contraction Coupling= [AP + Ca + Head + ATP] (for molecular level)**

  - An increase in Ca^{++} concentration in the muscle starts contraction
  - A decrease in Ca^{++} stops it
  - Action potentials causes Ca^{++} to be released from the SR into the muscle cell
  - Ca^{++} moves tropomyosin away from the myosin-binding sites on actin allowing cross-bridges to form
  - The muscle cell membrane contains Ca^{++} pumps to return Ca^{++} back to the SR quickly
    - Decreasing calcium ion levels
  - As the Ca^{++} level in the cell drops, myosin-binding sites are covered and the muscle relaxes

Contraction and Relaxation of Skeletal Muscle

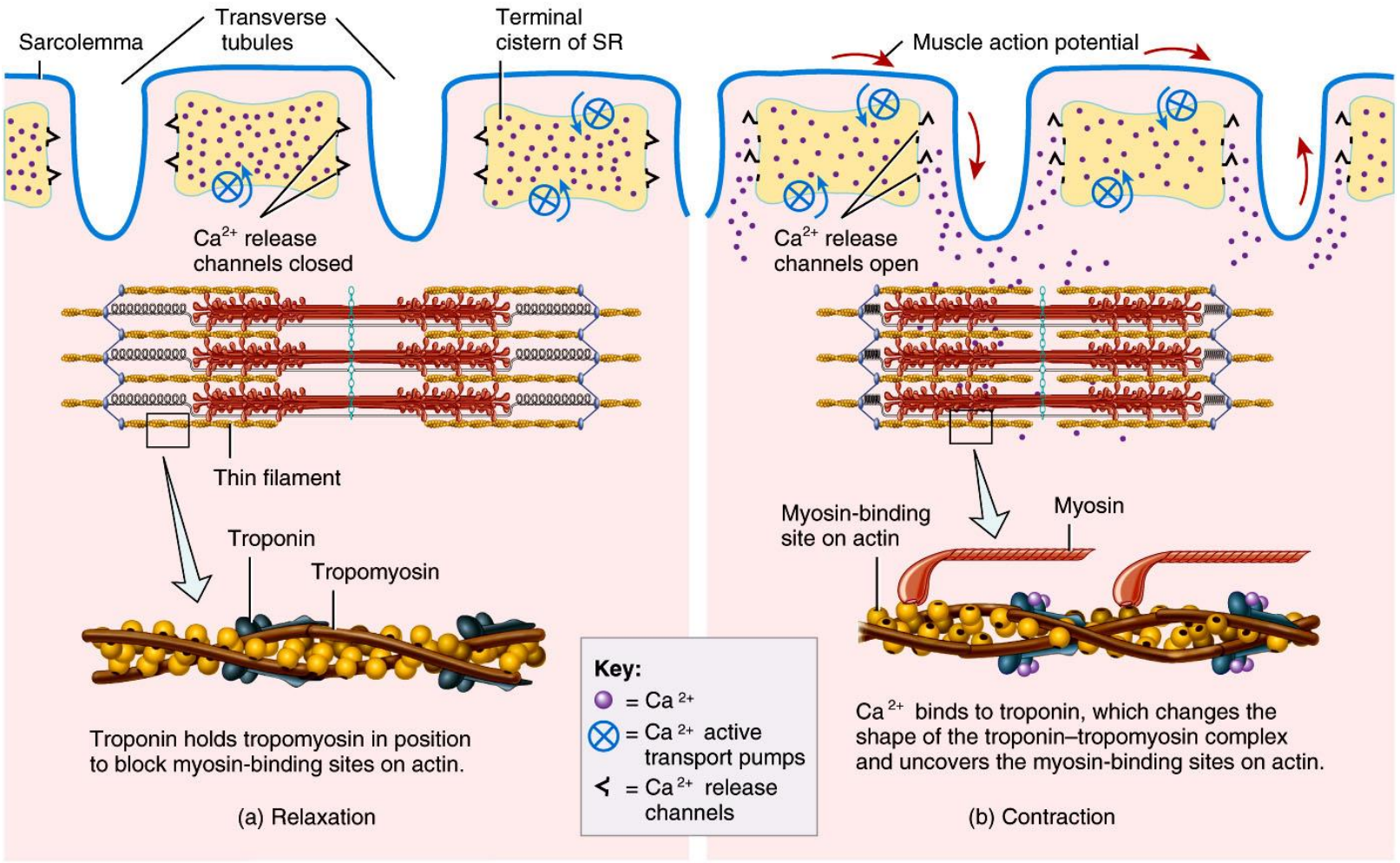


Figure 10.08 Tortora - PAP 12/e

Length–Tension Relationship

- The forcefulness of muscle contraction depends on the length of the sarcomeres
- When a muscle fiber is stretched there is less overlap between the thick and thin filaments and tension (forcefulness) is diminished
- When a muscle fiber is shortened the filaments are compressed and fewer myosin heads make less contact with thin filaments and tension is diminished
- Optimal length = maximal tension

Contraction and Relaxation of Skeletal Muscle

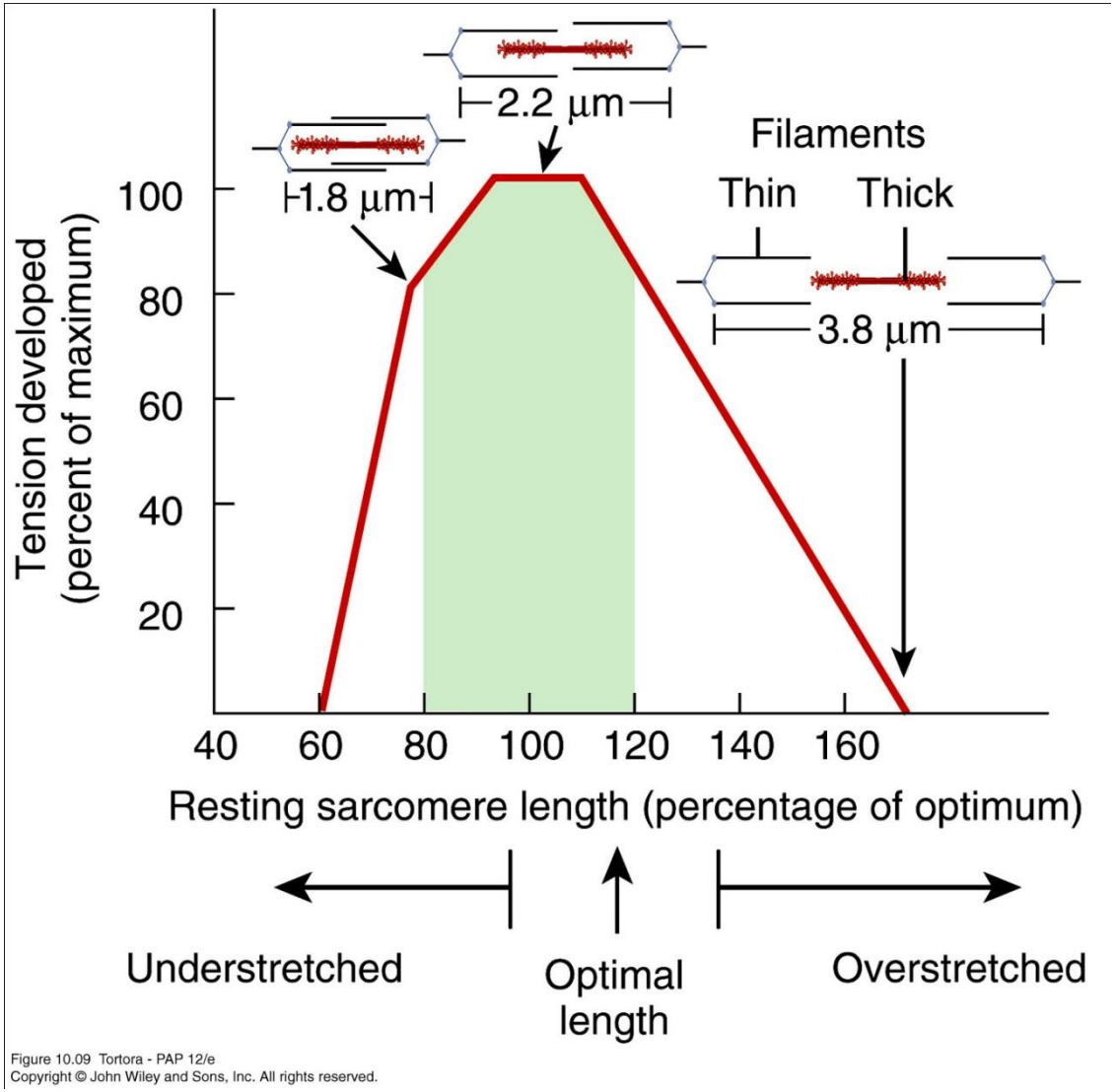


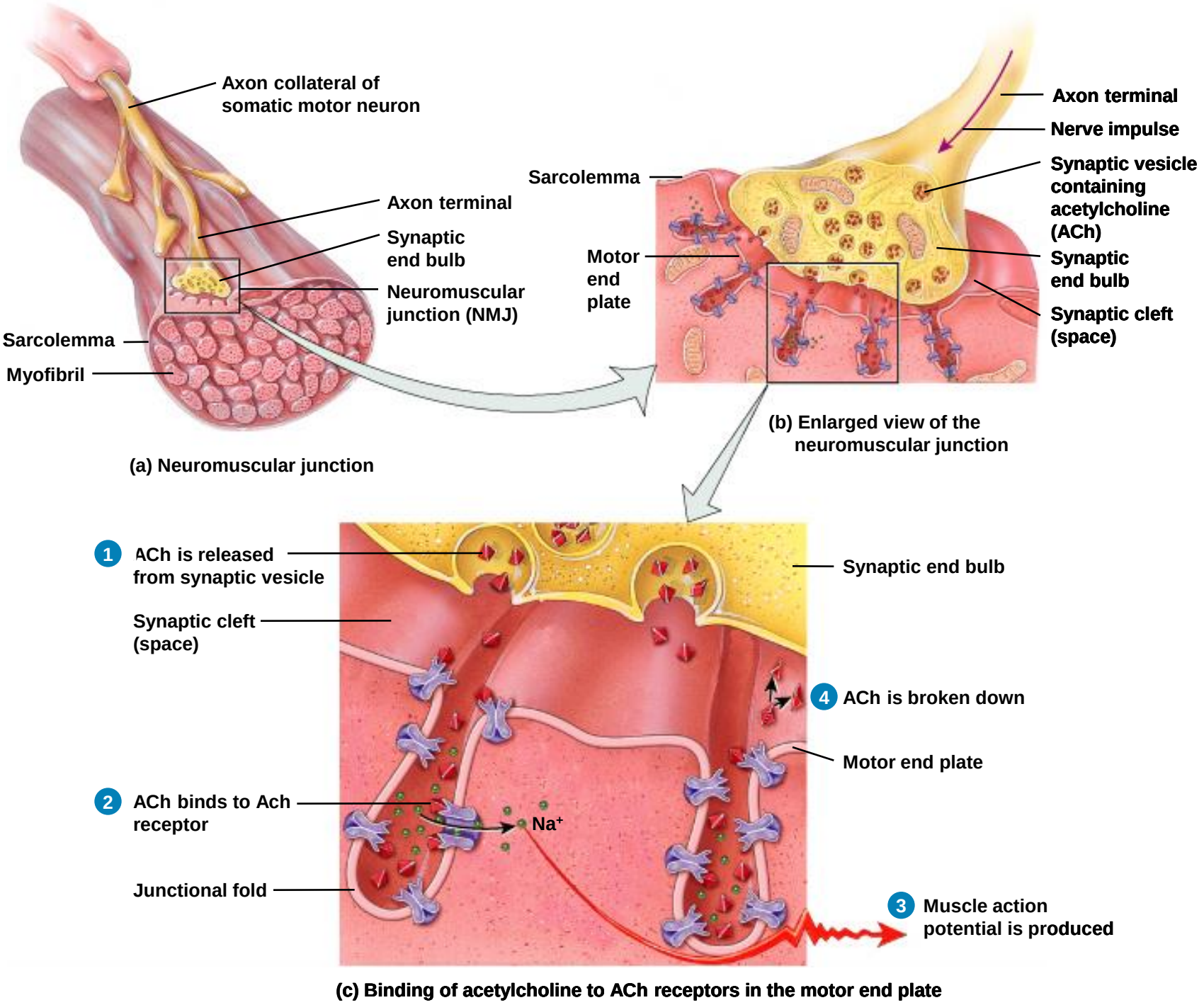
Figure 10.09 Tortora - PAP 12/e

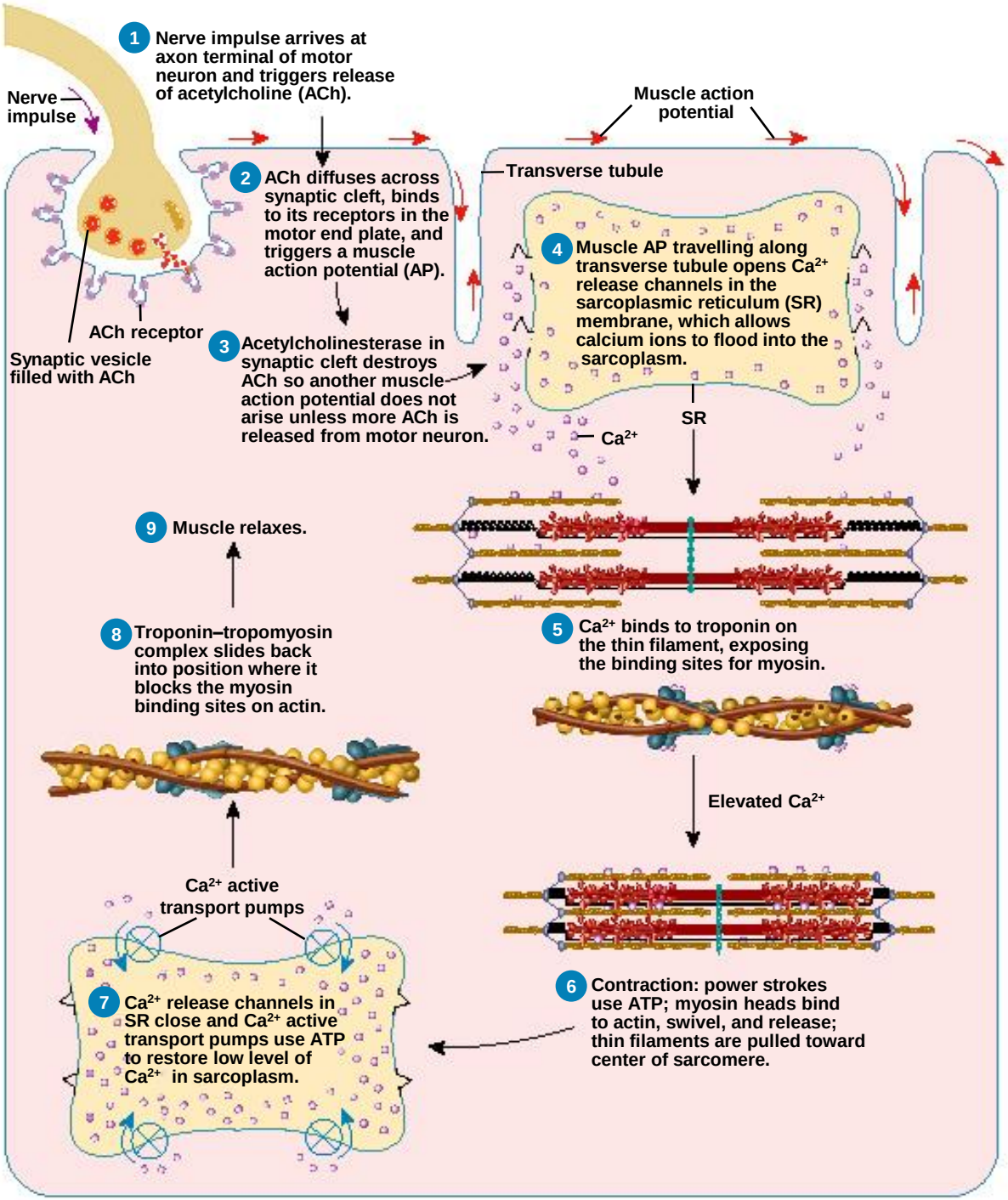
Contraction and Relaxation of Skeletal Muscle

- **The Neuromuscular Junction**
  - Motor neurons have a threadlike axon that extends from the brain or spinal cord to a group of muscle fibers
- **Neuromuscular junction (NMJ)**
  - Action potentials arise at the interface of the motor neuron and muscle fiber
- **Synapse**
  - Where communication occurs between a somatic motor neuron and a muscle fiber
- **Synaptic cleft**
  - Gap that separates the two cells
- **Neurotransmitter**
  - Chemical released by the initial cell communicating with the second cell
- **Synaptic vesicles**
  - Sacs suspended within the synaptic end bulb containing molecules of the neurotransmitter acetylcholine (Ach)
- **Motor end plate**
  - The region of the muscle cell membrane opposite the synaptic end bulbs
  - Contain acetylcholine receptors

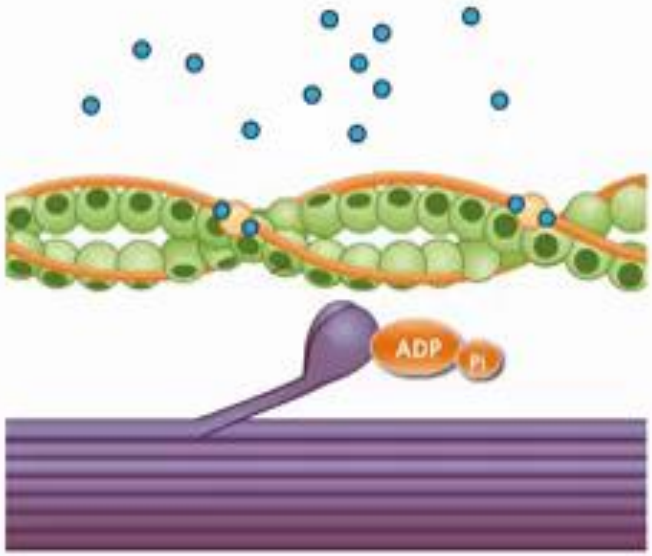
Contraction and Relaxation of Skeletal Muscle

- Nerve impulses elicit a muscle action potential in the following way
  - **1) Release of acetylcholine**
    - Nerve impulse arriving at the synaptic end bulbs causes many synaptic vesicles to release ACh into the synaptic cleft
  - **2) Activation of ACh receptors**
    - Binding of ACh to the receptor on the motor end plate opens an ion channel
    - Allows flow of Na^+ to the inside of the muscle cell
  - **3) Production of muscle action potential**
    - The inflow of Na^+ makes the inside of the muscle fiber more positively charged triggering a muscle action potential
    - The muscle action potential then propagates to the SR to release its stored Ca^{++}
    - **4) Termination of ACh activity**
    - Ach effects last only briefly because it is rapidly broken down by acetylcholinesterase (AChE)


Axon collateral of somatic motor neuron
Axon terminal
Synaptic end bulb
Neuromuscular junction (NMJ)
Sarcolemma
Myofibril
(a) Neuromuscular junction
Sarcolemma
Motor end plate
Axon terminal
Nerve impulse
Synaptic vesicle containing acetylcholine (ACh)
Synaptic end bulb
Synaptic cleft (space)
(b) Enlarged view of the neuromuscular junction
1 ACh is released from synaptic vesicle
Synaptic cleft (space)
Synaptic end bulb
4 ACh is broken down
Motor end plate
2 ACh binds to Ach receptor
Na+
Junctional fold
3 Muscle action potential is produced
(c) Binding of acetylcholine to ACh receptors in the motor end plate


1 Nerve impulse arrives at axon terminal of motor neuron and triggers release of acetylcholine (ACh).
Nerve impulse
2 ACh diffuses across synaptic cleft, binds to its receptors in the motor end plate, and triggers a muscle action potential (AP).
ACh receptor
Synaptic vesicle filled with ACh
3 Acetylcholinesterase in synaptic cleft destroys ACh so another muscle action potential does not arise unless more ACh is released from motor neuron.
Muscle action potential
Transverse tubule
4 Muscle AP travelling along transverse tubule opens Ca2+ release channels in the sarcoplasmic reticulum (SR) membrane, which allows calcium ions to flood into the sarcoplasm.
SR
Ca2+
5 Ca2+ binds to troponin on the thin filament, exposing the binding sites for myosin.
Elevated Ca2+
6 Contraction: power strokes use ATP; myosin heads bind to actin, swivel, and release; thin filaments are pulled toward center of sarcomere.
7 Ca2+ release channels in SR close and Ca2+ active transport pumps use ATP to restore low level of Ca2+ in sarcoplasm.
Ca2+ active transport pumps
8 Troponin–tropomyosin complex slides back into position where it blocks the myosin binding sites on actin.
9 Muscle relaxes.

Contraction at myosin



1. Calcium binds

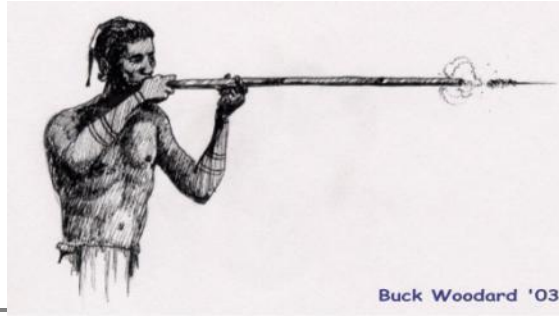
2. Cross bridge

Applied physiology

- **Botulinum toxin**
  - Blocks release of ACh from synaptic vesicles
  - May be found in improperly canned foods
    - A tiny amount can cause death by paralyzing respiratory muscles
  - Used as a medicine (Botox®)
    - Strabismus (crossed eyes)
    - Blepharospasm (uncontrollable blinking)
    - Spasms of the vocal cords that interfere with speech
    - Cosmetic treatment to relax muscles that cause facial wrinkles
    - Alleviate chronic back pain due to muscle spasms in the lumbar region

Contraction and Relaxation of Skeletal Muscle

- **Curare**
  - A plant poison used by South American Indians on arrows and blowgun darts
  - Causes muscle paralysis by blocking ACh receptors inhibiting Na^+ ion channels
  - Derivatives of curare are used during surgery to relax skeletal muscles
- **Anticholinesterase**
  - Slows actions of acetylcholinesterase and slows removal of ACh
  - Can strengthen weak muscle contractions
    - Ex: Neostigmine
      - Treatment for myasthenia gravis
      - Antidote for curare poisoning
      - Terminate the effects of curare after surgery



Muscle Metabolism

- **Production of ATP in Muscle Fibers**
  - 1) From creatine phosphate
  - 2) By anaerobic cellular respiration
  - 3) By aerobic cellular respiration

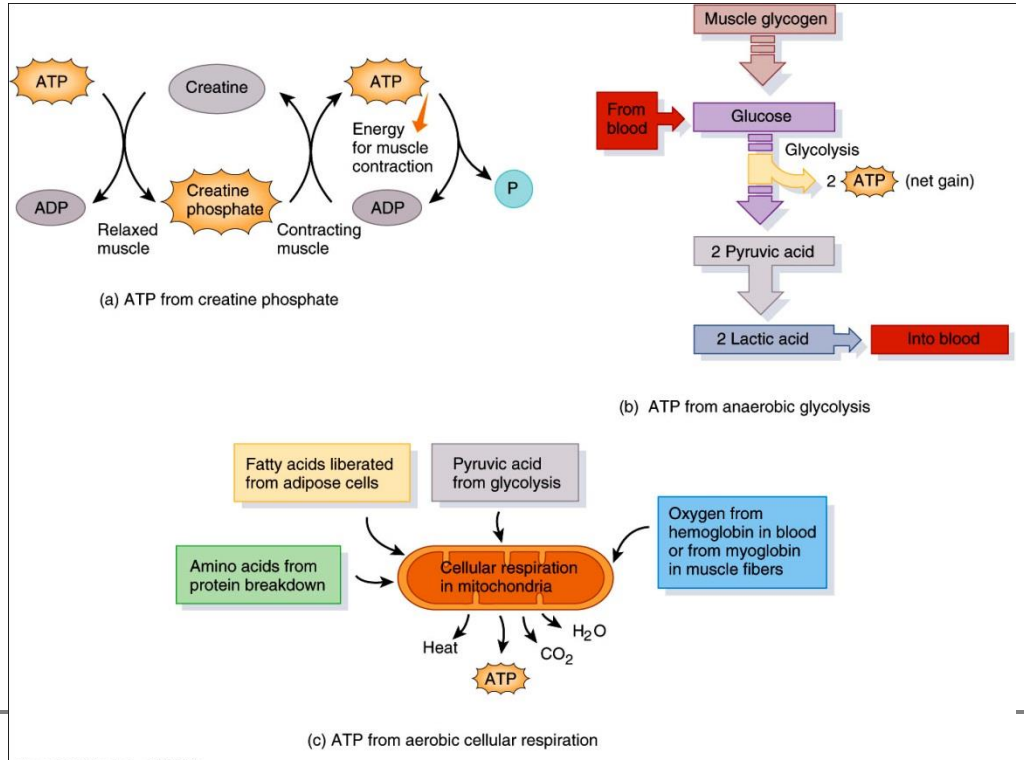


Figure 10.12 Tortora - PAP 12/e

Muscle Metabolism

- **Creatine Phosphate**
  - Excess ATP is used to synthesize creatine phosphate
    - Energy-rich molecule
  - Creatine phosphate transfers its high energy phosphate group to ADP regenerating new ATP
  - Creatine phosphate and ATP provide enough energy for contraction for about 15 seconds

Control of Muscle Tension

- The tension or force of muscle cell contraction varies

- Maximum Tension (force) is dependent on
  - The rate at which nerve impulses arrive
  - The amount of stretch before contraction
  - The nutrient and oxygen availability
  - The size of the motor unit

Control of Muscle Tension

- **Motor Units**
  - Consists of a motor neuron and the muscle fibers it stimulates
  - The axon of a motor neuron branches out forming neuromuscular junctions with different muscle fibers
  - A motor neuron makes contact with about 150 muscle fibers
  - Control of precise movements consist of many small motor units
    - Muscles that control voice production have 2 - 3 muscle fibers per motor unit
    - Muscles controlling eye movements have 10 - 20 muscle fibers per motor unit
    - Muscles in the arm and the leg have 2000 - 3000 muscle fibers per motor unit
  - The total strength of a contraction depends on the size of the motor units and the number that are activated

Motor unit

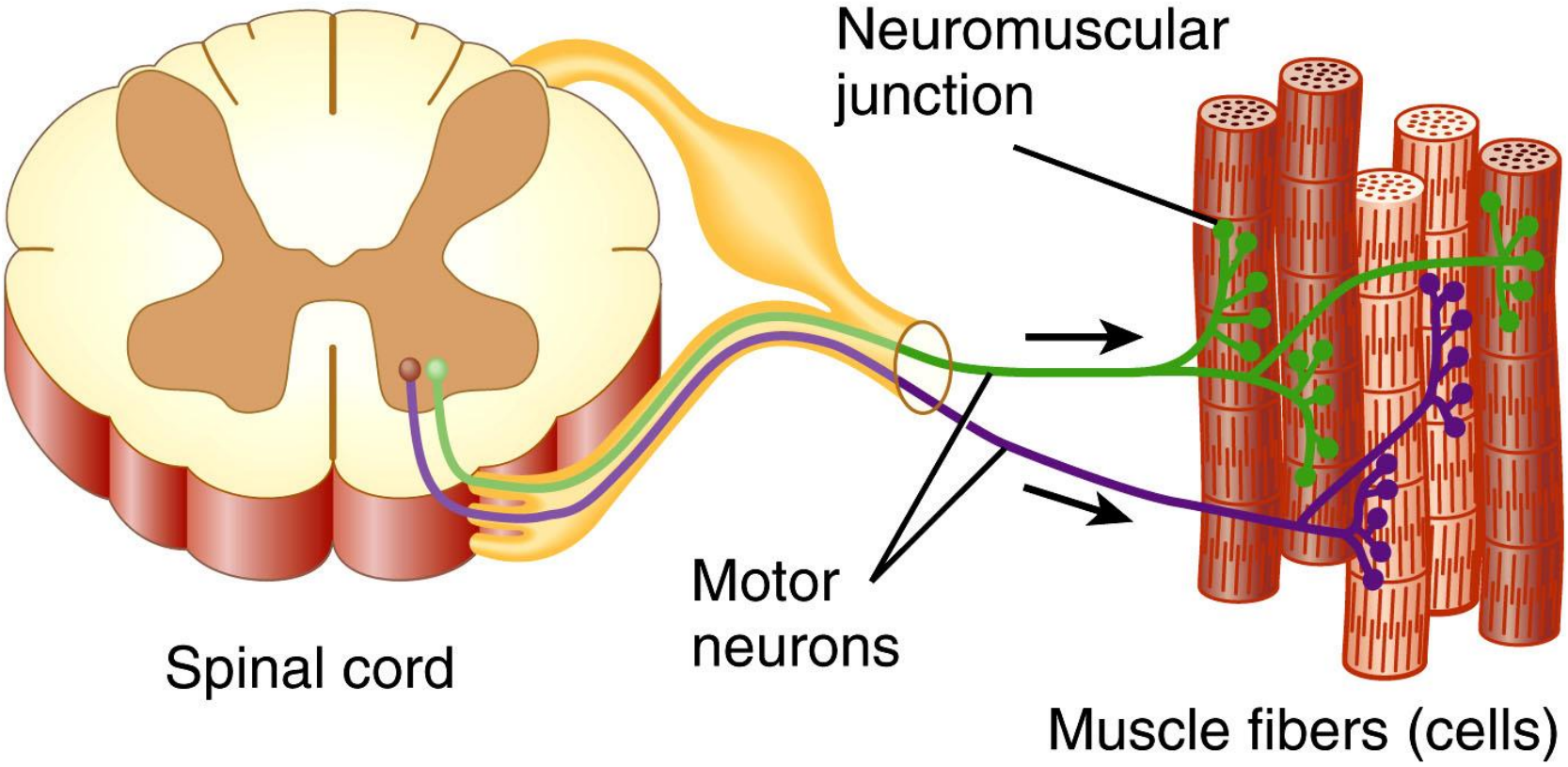


Figure 10.13 Tortora - PAP 12/e

- **Twitch Contraction (for whole muscle)**
  - The brief contraction of the muscle fibers in a motor unit in response to an action potential
  - Twitches last from 20 to 200 msec L
  - **Latent period** (2 msec)
    - A brief delay between the stimulus and muscular contraction
    - The action potential sweeps over the sarcolemma and Ca^{++} is released from the SR
  - **Contraction period (**10–100 msec)
    - Ca^{++} binds to troponin
    - Myosin-binding sites on actin are exposed
    - Cross-bridges form

Control of Muscle Tension

- **Relaxation period (**10–100 msec)
  - Ca^{++} is transported into the SR
  - Myosin-binding sites are covered by tropomyosin
  - Myosin heads detach from actin
    - Muscle fibers that move the eyes have contraction periods lasting 10 msec
    - Muscle fibers that move the legs have contraction periods lasting 100 msec
- **Refractory period**
  - When a muscle fiber contracts, it temporarily cannot respond to another action potential
    - Skeletal muscle has a refractory period of 5 milliseconds
    - Cardiac muscle has a refractory period of 300 milliseconds- so no tetanus.

Control of Muscle Tension

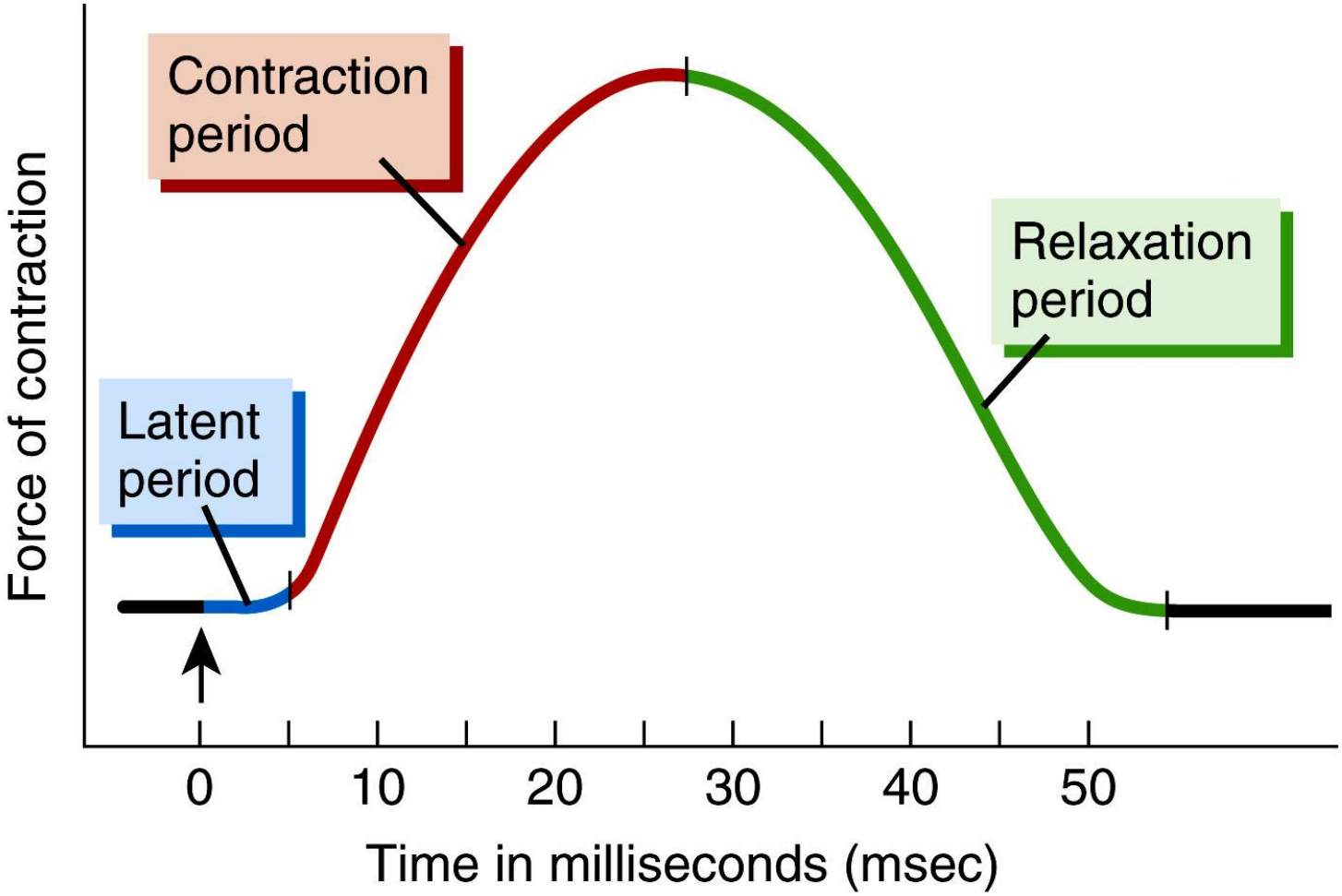


Figure 10.14 Tortora - PAP 12/e

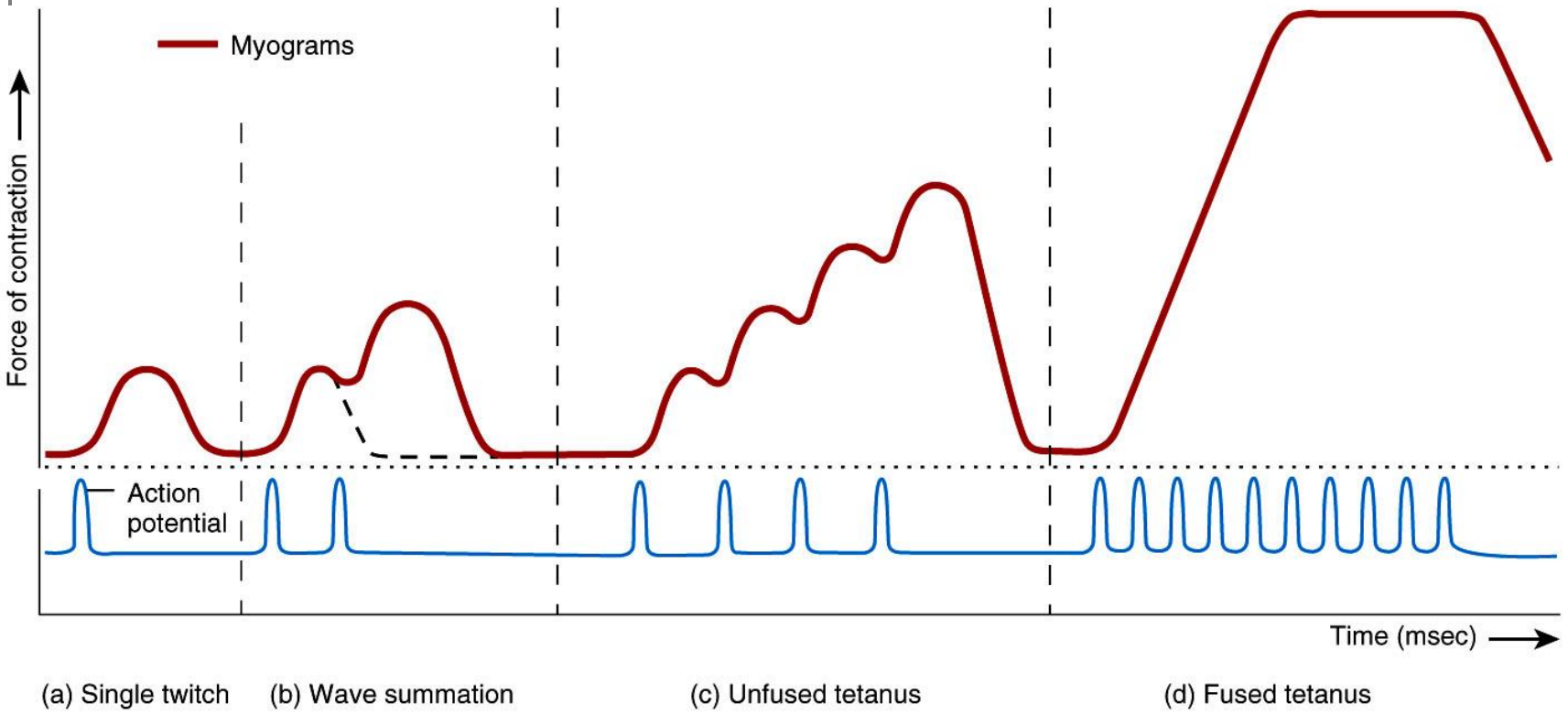


Figure 10.15 Tortora - PAP 12/e

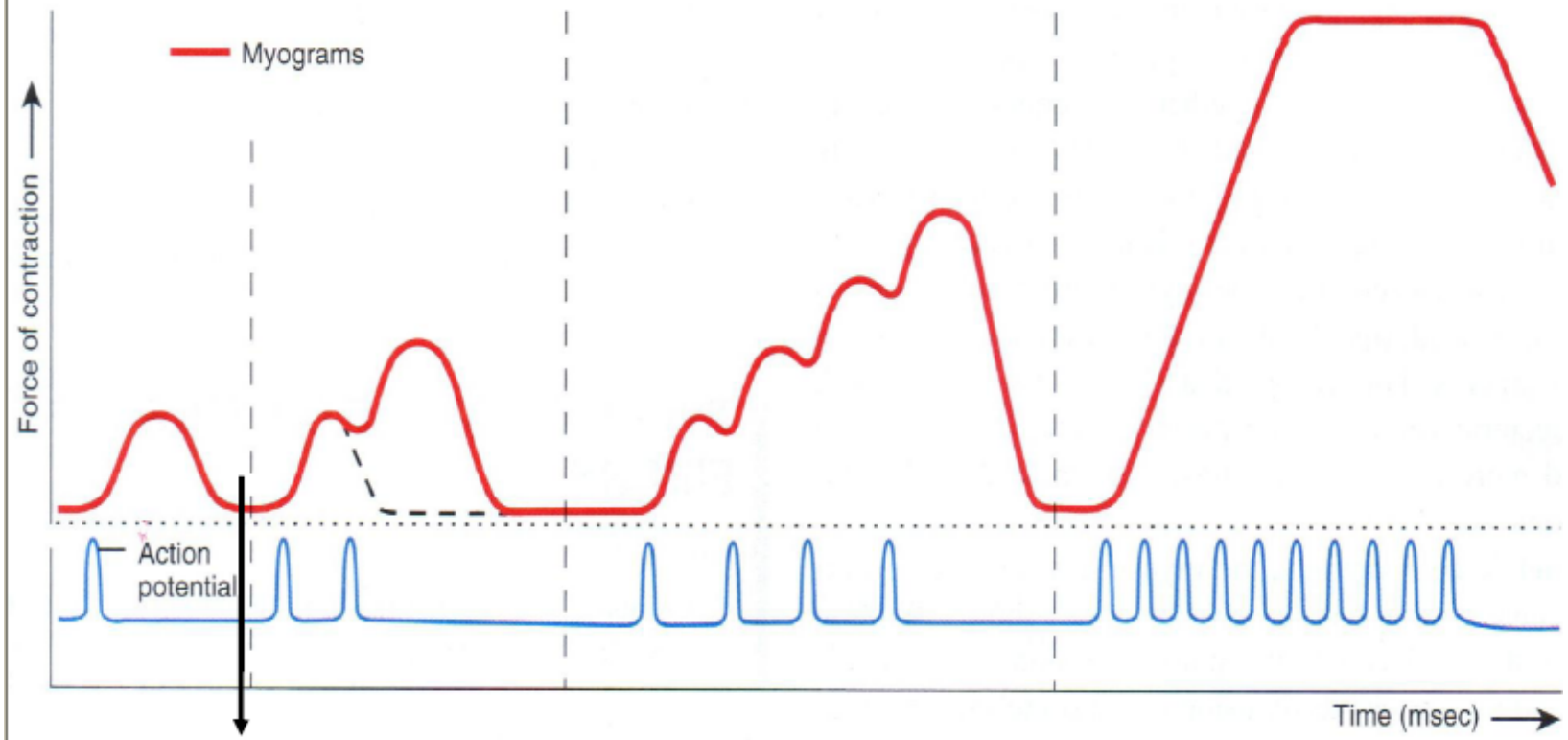
Application - evaluation of muscle fatigue degree spinal nerve compression, carpal tunnel syndrome myasthenia gravis, and muscular dystrophy

Summation

- ►Adding together of individual twitch contractions to increase the intensity of overall muscle contraction
- 1) Multiple fiber summation
- 2) Frequency summation

- Multiple fiber summation
- ►More the fibers (motor units) taking part in contraction more will be the force of contraction
- ►For weak contraction, smaller and fewer motor units are stimulated
- ►For stronger contractions more & more motor units are stimulated (recruitment)
- Frequency summation, tetanus or tetanization
- ►Sustained contraction due to repeated stimuli of high frequency

Frequency summation



Stimulus here will lead to 'treppe' or staircase effect (individual twitch contractions but every subsequent contraction will have higher amplitude)

Muscle fiber types

Slow fibers (Type I) (oxidative)	Fast fibers (Type II)	
	Fast oxidative (IIa)	Fast glycolytic (IIb)
Source of ATP: Oxidative	Source of ATP: Oxidative	Source of ATP: Glycolysis
Contraction velocity: Slow	Contraction velocity: Fast	Contraction velocity: Fast
Mitochondria: Many	Mitochondria: Many	Mitochondria: Few
Capillaries: Many	Capillaries: Many	Capillaries: Few
Myoglobin content: High (red muscle)	Myoglobin content: High (red muscle)	Myoglobin content: Low (white muscle)
Glycolytic enzymes: Low	Glycolytic enzymes: Intermediate	Glycolytic enzymes: High

Slow fibers (Type I) (oxidative)	Fast fibers (Type II)	
	Fast oxidative (IIa)	Fast glycolytic (IIb)
Glycogen content: low	Glycogen content: Intermediate	Glycogen content: High
Rate of fatigue: Slow	Rate of fatigue: intermediate	Rate of fatigue: Fast
ATPase activity: Low	ATPase activity: High	ATPase activity: High
Fiber diameter: Small	Fiber diameter: intermediate	Fiber diameter: Large
Motor unit size: Small	Motor unit size: intermediate	Motor unit size: Large
Innervating by: Small neurons	Innervating by: Intermediate sized neurons	Innervating by: Large neurons

- Muscle tone

Tautness in muscle when at rest

Due to continuous firing of some motor neurons

Contraction of some motor units

Alternating pattern of motor units contraction

Remodeling of muscle

- Muscle remodels to match its function
- Hypertrophy
- Increase in total mass of muscle
- Occurs in strength exercise (anaerobic exercise) -weight lifting
- Increase in fiber size
- Increase number of actin and myosin
- Change in metabolic machinery

- Atrophy
- Decrease in total mass of muscle
- Denervation atrophy
- Abolishment of trophic signals
- Disuse atrophy
- When muscle is not used for long time

Clinical physiology

- **Hypocalcemic tetany**
- ↓ ECF Ca++→ ↑ Na+permeability
- Spontaneous contractions
- Muscle cramps
- Involuntary tetanic contractions due to abnormally high rates of action potentials
- due to over-exercise
- Dehydration
- Electrolyte imbalance

- **Rigor mortis**

Contracture of muscles after death

Cause

Non availability of ATP

Cytosolic Ca++rises (failure of Ca++pump)

Myosin heads can not detach from actin

Subsides after several hours/days

Due to destruction of contractile proteins

Isometric contraction

Tension during contraction increases but length of muscle remains the same

Load > tension

Trying to lift heavy loads (but not actually lifting up)

- **Isotonic contraction**
- Tension during contraction remains the same but muscle length changes
- **1) Concentric isotonic contraction**
- Load < tension
- Muscle shortens during contraction
- Lifting a weight up running, walking etc
- **2) Eccentric isotonic contraction**
- Load > tension
- Already contracted muscle lengthens
- Lowering a weight to ground

Thank you ……