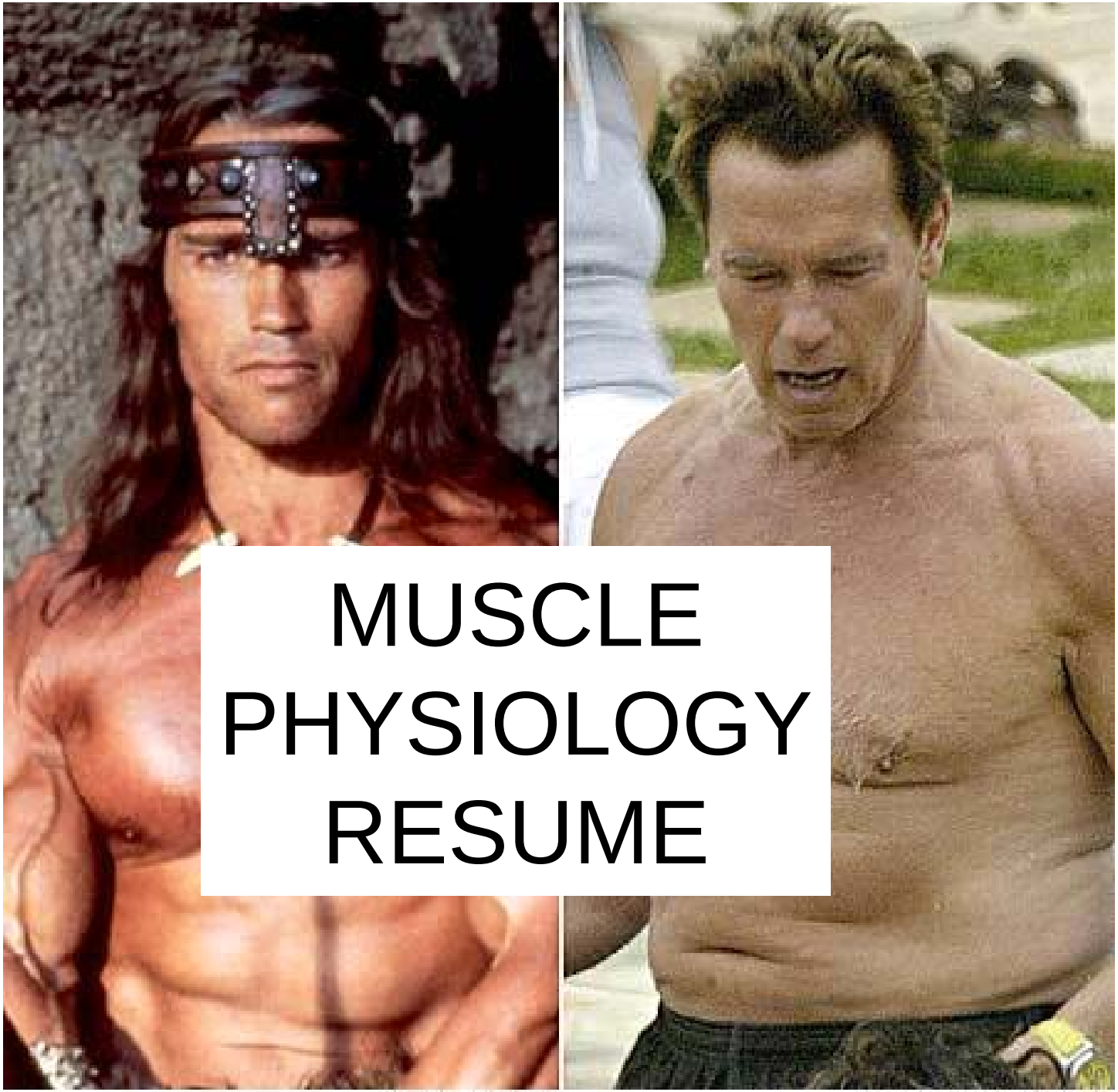
MUSCLE PHYSIOLOGY RESUME

D.HAMMOUDI.
MD



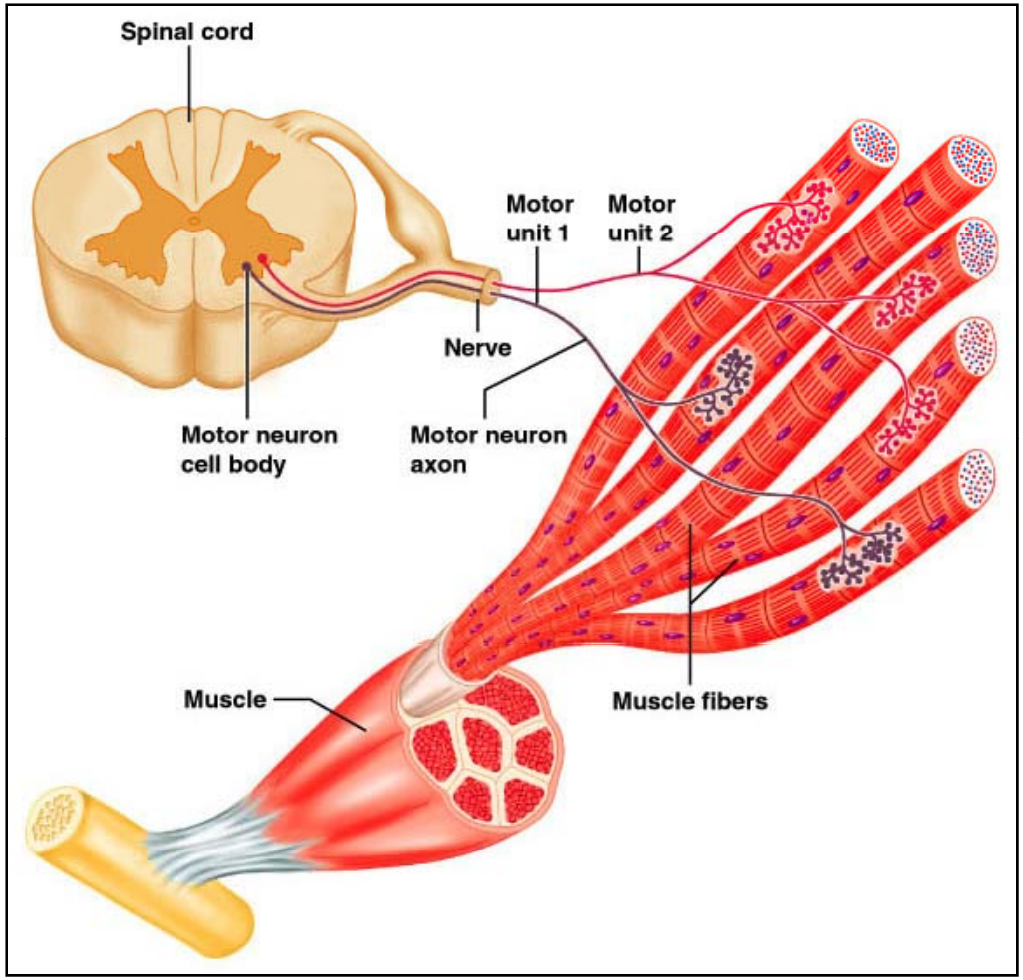
We can actually divide the whole process of muscle contraction into 4 steps:

- **Excitation**
- **Excitation-contraction coupling**
- **Contraction**
- **Relaxation**

Motor Unit: The Nerve-Muscle Functional Unit

Each muscle has at least one motor nerve that may contain hundreds of motor neuron axons.

Axons branch into terminals, each forming a neuromuscular junction with a single muscle fiber



A motor neuron and all the muscle fibers it supplies is called a Motor Unit

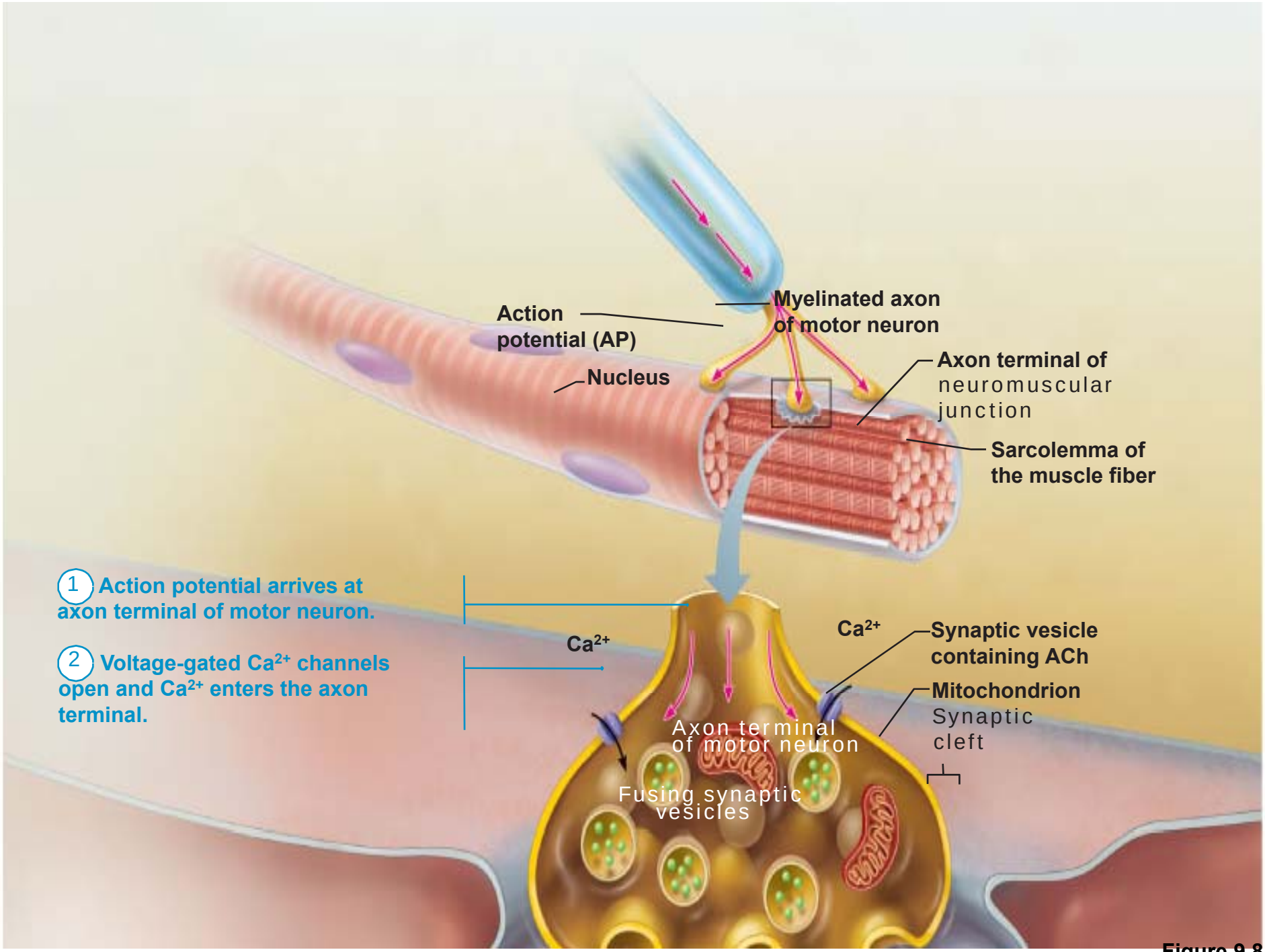

Action potential (AP)
Myelinated axon of motor neuron
Nucleus
Axon terminal of neuromuscular junction
Sarcolemma of the muscle fiber
1 Action potential arrives at axon terminal of motor neuron.
2 Voltage-gated Ca^{2+} channels open and Ca^{2+} enters the axon terminal.
Ca^{2+}
Ca^{2+}
Synaptic vesicle containing ACh
Mitochondrion
Synaptic cleft
Axon terminal of motor neuron
Fusing synaptic vesicles

Figure 9.8

Sarcomere Structure -

A) **Thick filaments**

1) mostly myosin protein

a) ~200 twisted myosin proteins form thick filament ("golf clubs")

b) held in place by elastic filament (titin protein)

c) can bind ATP

d) splits ATP to ADP

e) can bind actin proteins

B) **Thin filaments**

1) Actin protein

a) "bean-shaped" protein in strands

b) has myosin-binding site

2) **Tropomyosin**

a) covers myosin-binding site

3) **Troponin**

a) **can bind calcium**

b) regulates action of tropomyosin

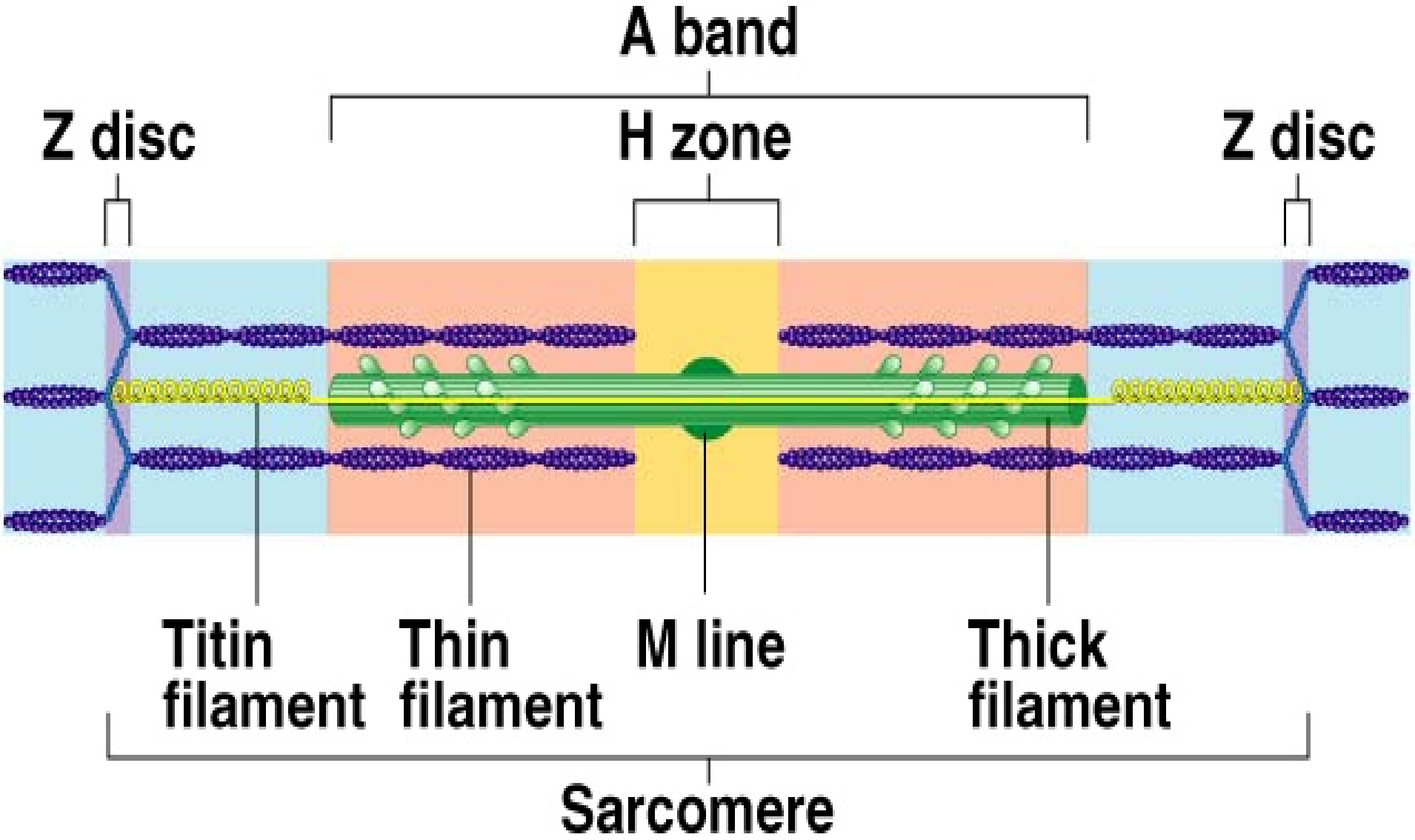
C) Contractile proteins

actin & myosin

D) **Regulatory proteins**

troponin & tropomyosin

SARCOMERE


A band
Z disc
H zone
Z disc
Titin filament
Thin filament
M line
Thick filament
Sarcomere

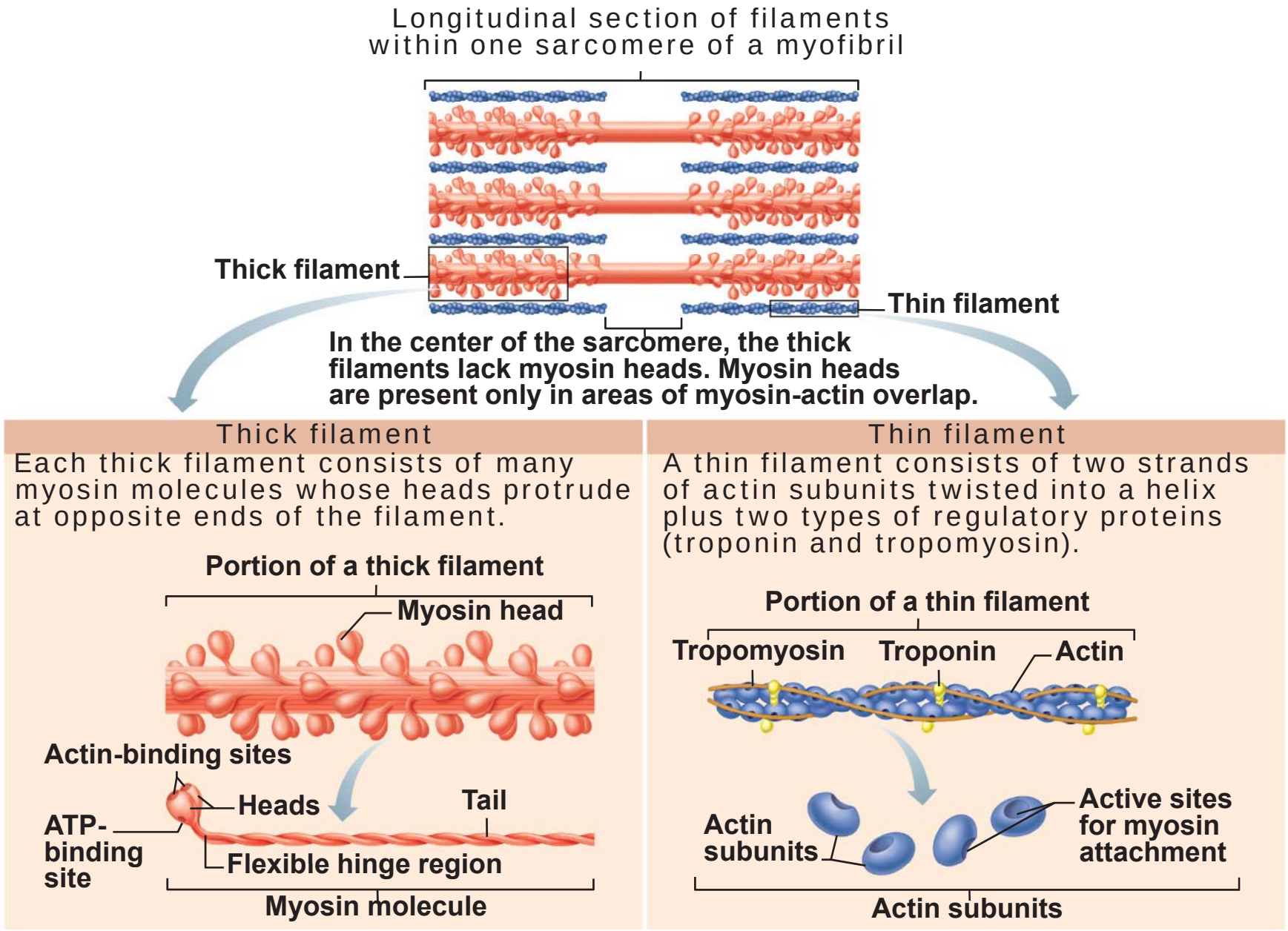
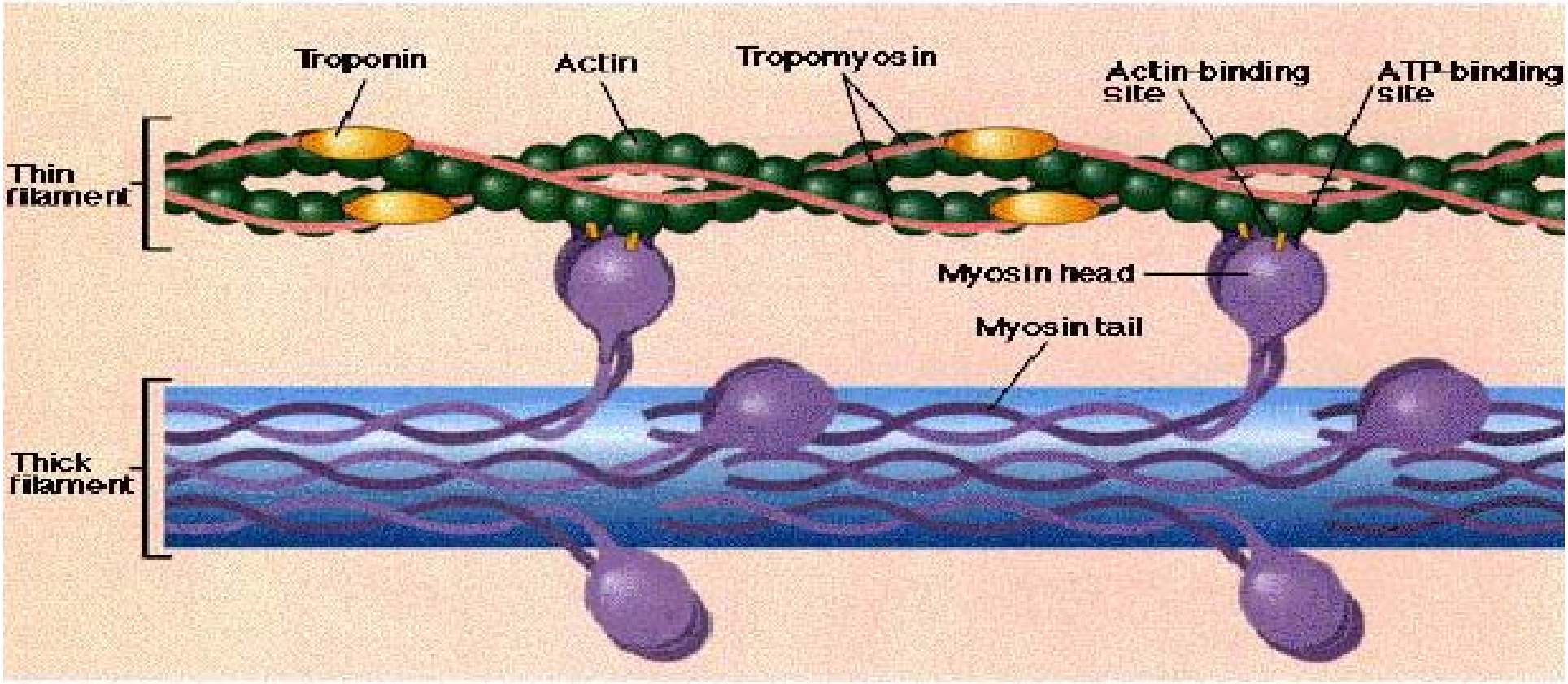
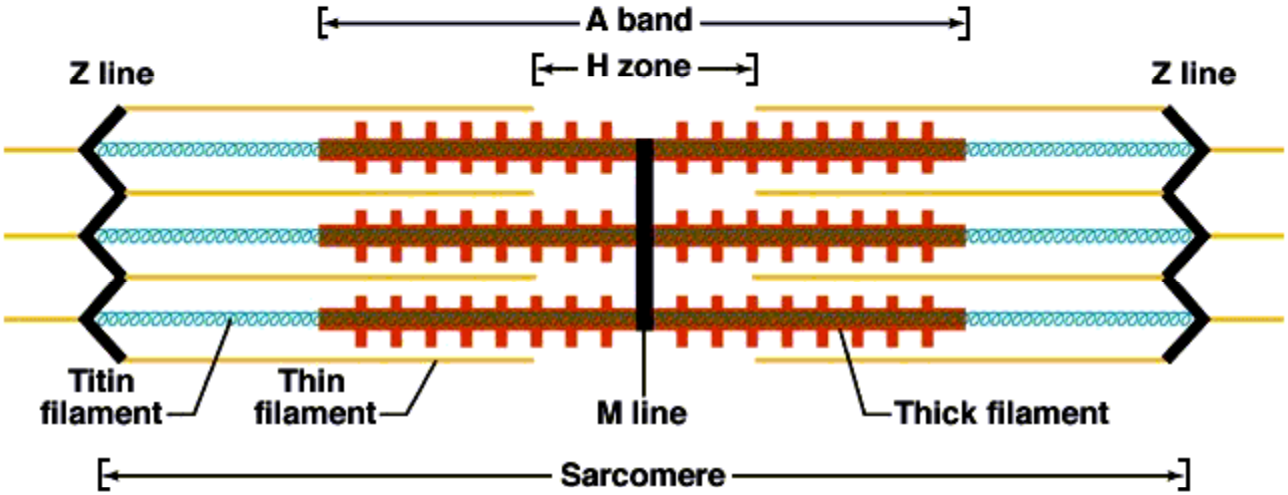

Longitudinal section of filaments within one sarcomere of a myofibril
Thick filament
Thin filament
In the center of the sarcomere, the thick filaments lack myosin heads. Myosin heads are present only in areas of myosin-actin overlap.
Thick filament
Each thick filament consists of many myosin molecules whose heads protrude at opposite ends of the filament.
Portion of a thick filament
Myosin head
Actin-binding sites
Heads
Tail
ATP-binding site
Flexible hinge region
Myosin molecule
Thin filament
A thin filament consists of two strands of actin subunits twisted into a helix plus two types of regulatory proteins (troponin and tropomyosin).
Portion of a thin filament
Tropomyosin
Troponin
Actin
Actin subunits
Active sites for myosin attachment
Actin subunits

Figure 9.3

Myosin & the Thick Filament



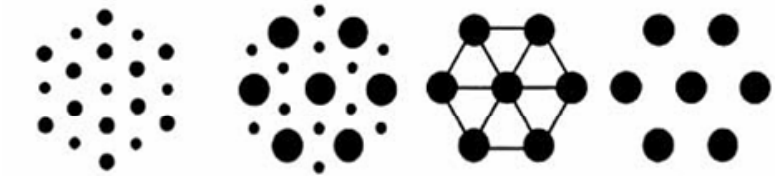
Sarcomere: functional unit of striated muscle



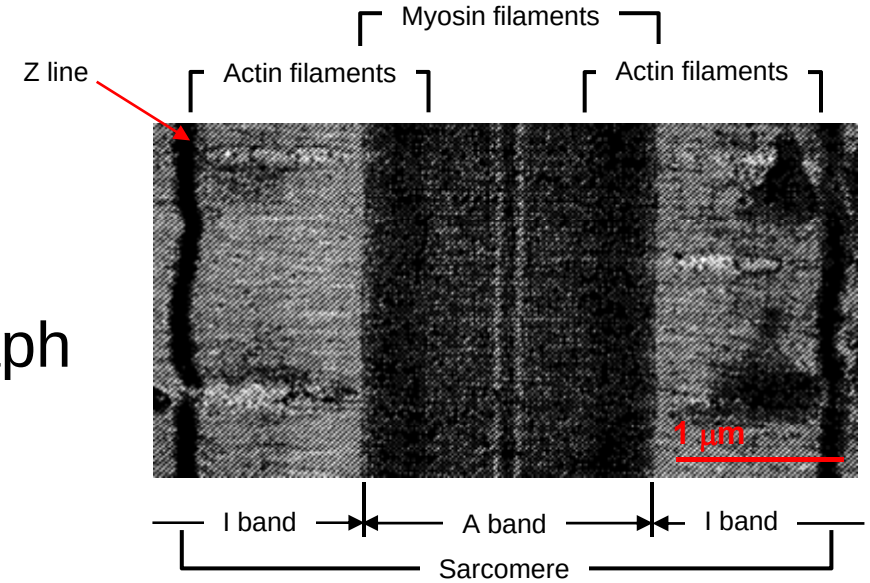
©The McGraw-Hill Companies, Inc.

Modified from Vander, Sherman, Luciano *Human Physiology,* McGraw-Hill.

Cross-sectional views of:

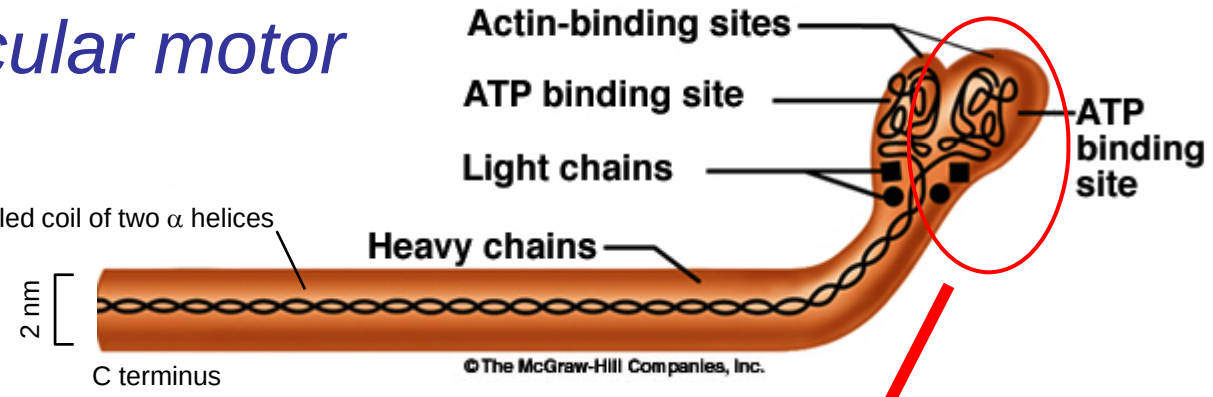


Electron micrograph

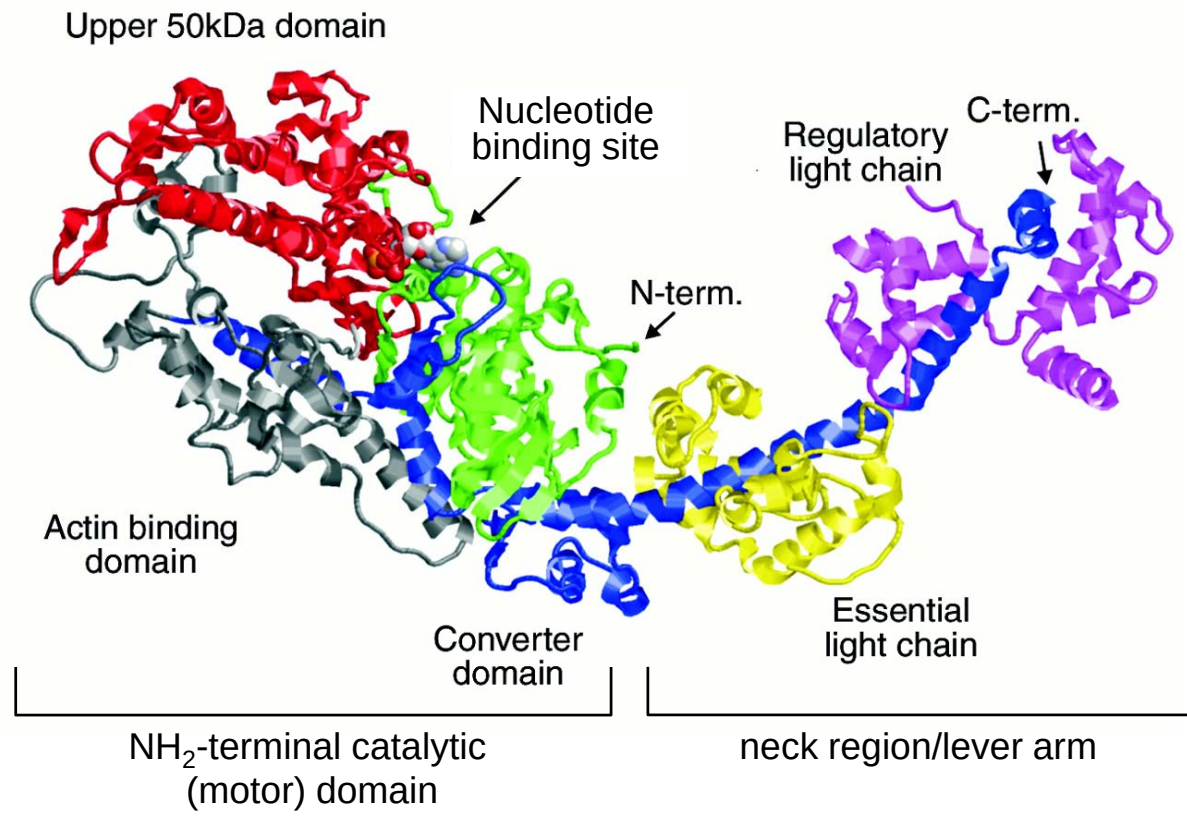


Myosin is a molecular motor

Modified from Vander, Sherman, Luciano
Human Physiology, McGraw-Hill.



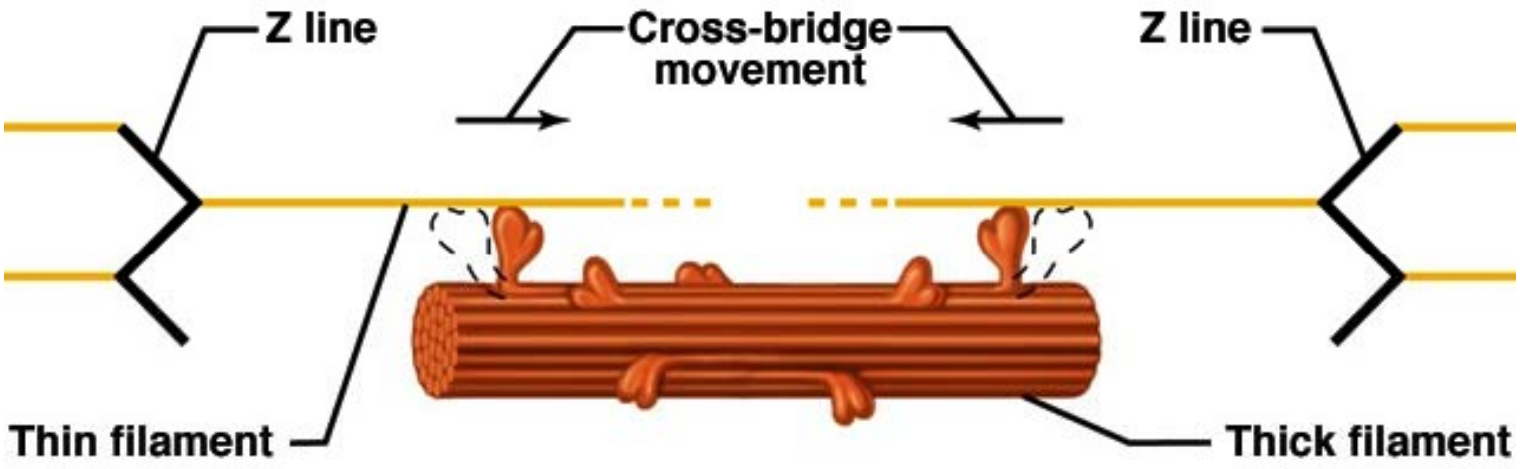
Myosin head: retains all of the motor functions of myosin, i.e. the ability to produce movement and force.



Myosin S1 fragment crystal structure

Ruegg et al., (2002)
News Physiol Sci 17:213-218.

How striated muscle works: The Sliding Filament Model



© The McGraw-Hill Companies, Inc.

From Vander, Sherman, Luciano
Human Physiology, McGraw-Hill.

The lever movement drives displacement of the actin filament relative to the myosin head (~5 nm), and by deforming internal elastic structures, produces force (~5 pN).

Thick and thin filaments interdigitate and “slide” relative to each other.

Events of Muscle Contraction

1) arrival of neuronal action potential at neuromuscular junction

2) release and diffusion of acetylcholine into synaptic cleft

3) binding of acetylcholine to receptor at motor end plate

4) activation of action potential on muscle surface (sarcolemma)

5) release of calcium from sarcoplasmic reticulum inside muscle fiber

6) binding of calcium to troponin/tropomyosin complex

7) exposure of myosin-binding site on actin

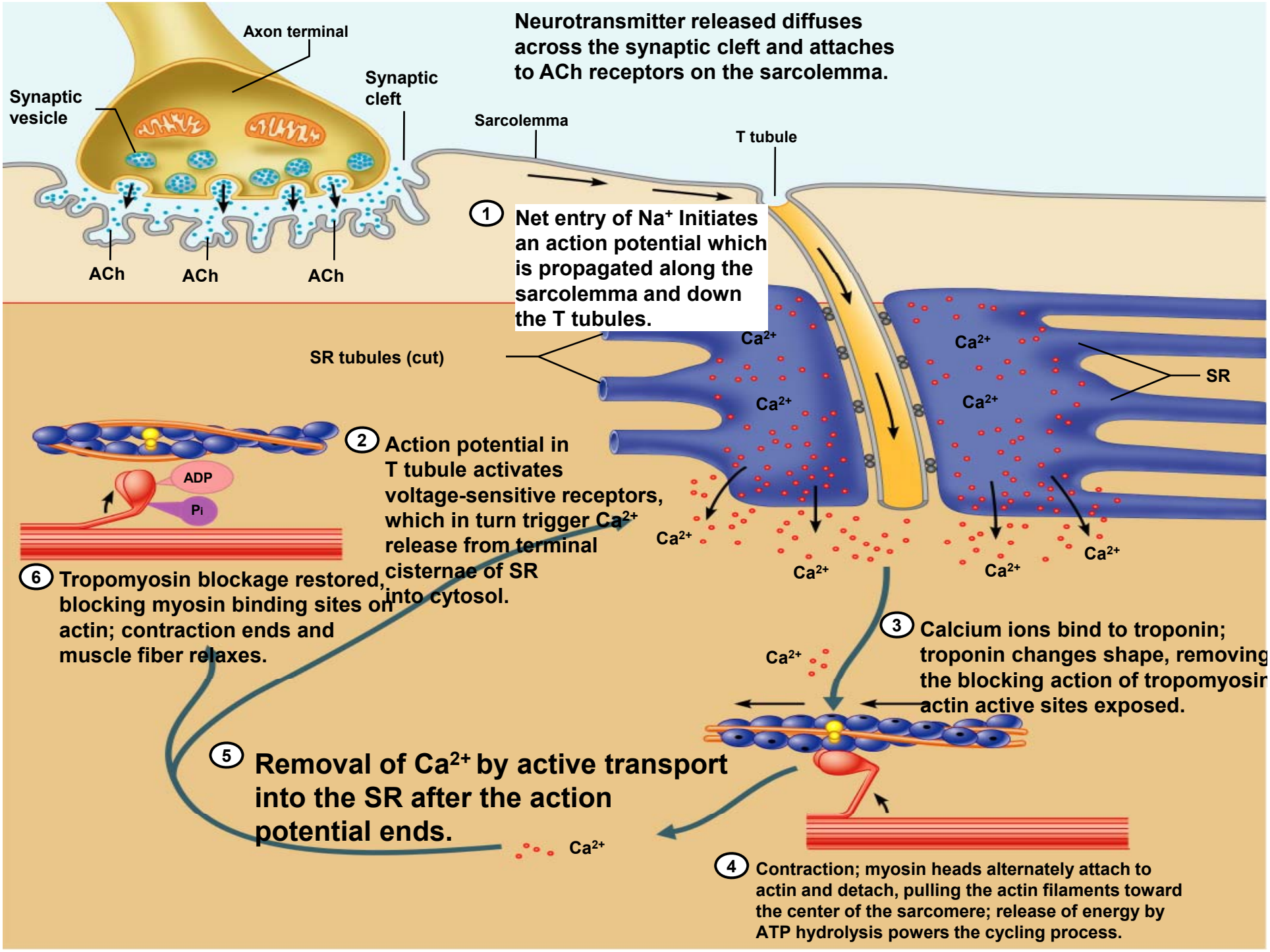
8) binding of actin and myosin and "Power stroke" single ratchet of myosin to pull actin and release ADP

9) myosin releases actin, swivels back, binds and splits ATP ("reset")

10) repeat binding myosin to actin (Repeat step 8-10)

Exitation-contraction Coupling Role of Ca^{++}

- Ca^{++} combines with Troponin-C
- Complex inhibits Troponin-I (has strong affinity for Actin)
- Inhibition of Tn-1 reveals active sites on Actin
- M heads combine, detach and recombine
- Binding causes conformational change in the head
- Binding of actin and myosin activates ATPase
- ATPase splits ATP
- MH + ATP $\rightarrow$ ADP + Pi + energy released
- Head tilts backwards toward the arm
- The process repeated using more ATP and Ca^{++}
- In fast twitch muscle fibers, the ATPase activity is high


Axon terminal
Synaptic vesicle
Synaptic cleft
Neurotransmitter released diffuses across the synaptic cleft and attaches to ACh receptors on the sarcolemma.
Sarcolemma
T tubule
ACh
ACh
ACh
1
Net entry of Na+ Initiates an action potential which is propagated along the sarcolemma and down the T tubules.
SR tubules (cut)
Ca2+
Ca2+
Ca2+
Ca2+
SR
ADP
Pi
2
Action potential in T tubule activates voltage-sensitive receptors, which in turn trigger Ca2+ release from terminal cisternae of SR into cytosol.
Ca2+
Ca2+
Ca2+
Ca2+
6
Tropomyosin blockage restored, blocking myosin binding sites on actin; contraction ends and muscle fiber relaxes.
3
Calcium ions bind to troponin; troponin changes shape, removing the blocking action of tropomyosin actin active sites exposed.
Ca2+
5
Removal of Ca2+ by active transport into the SR after the action potential ends.
Ca2+
4
Contraction; myosin heads alternately attach to actin and detach, pulling the actin filaments toward the center of the sarcomere; release of energy by ATP hydrolysis powers the cycling process.

Neuromuscular Junction

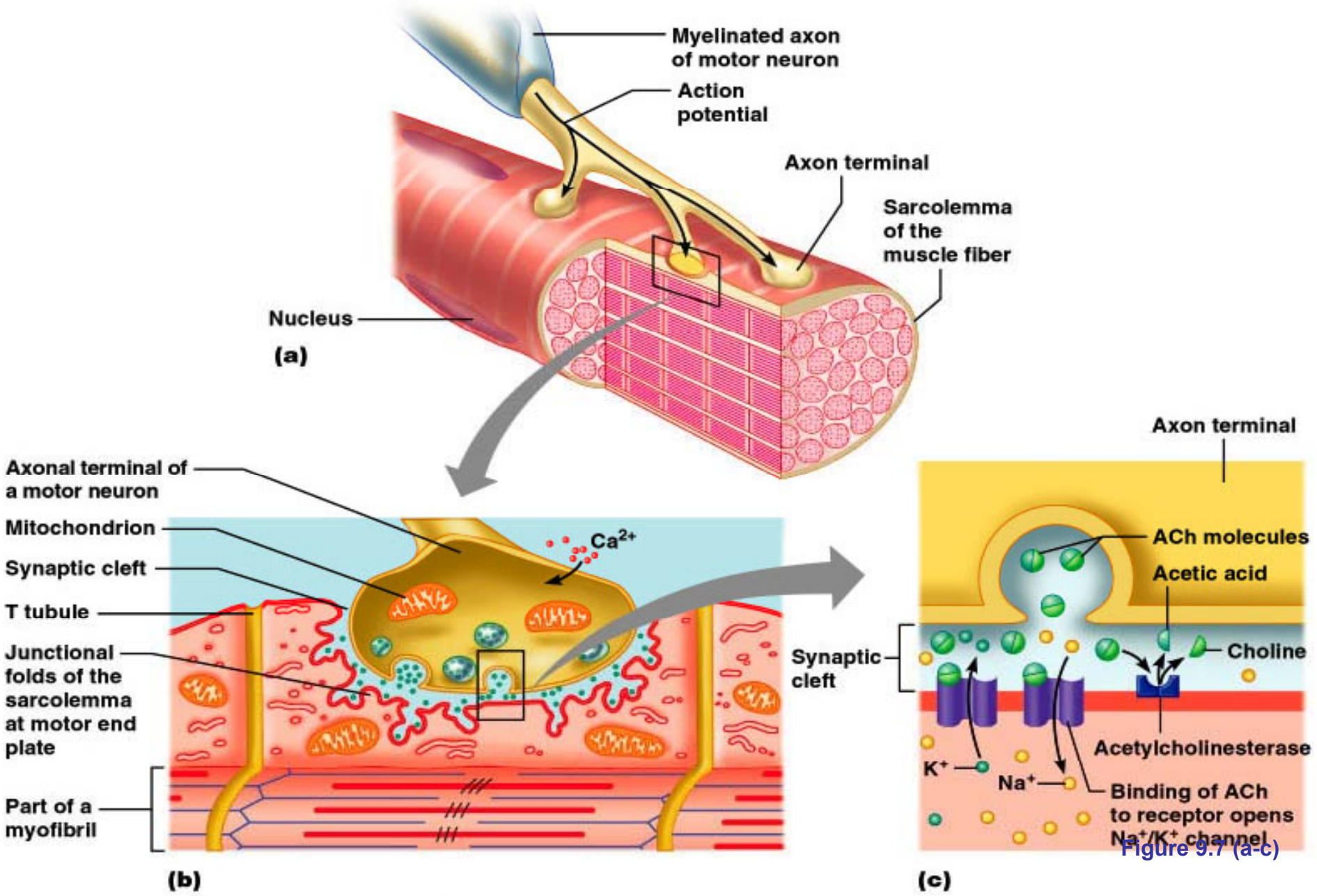


Figure 9.7 (a-c)

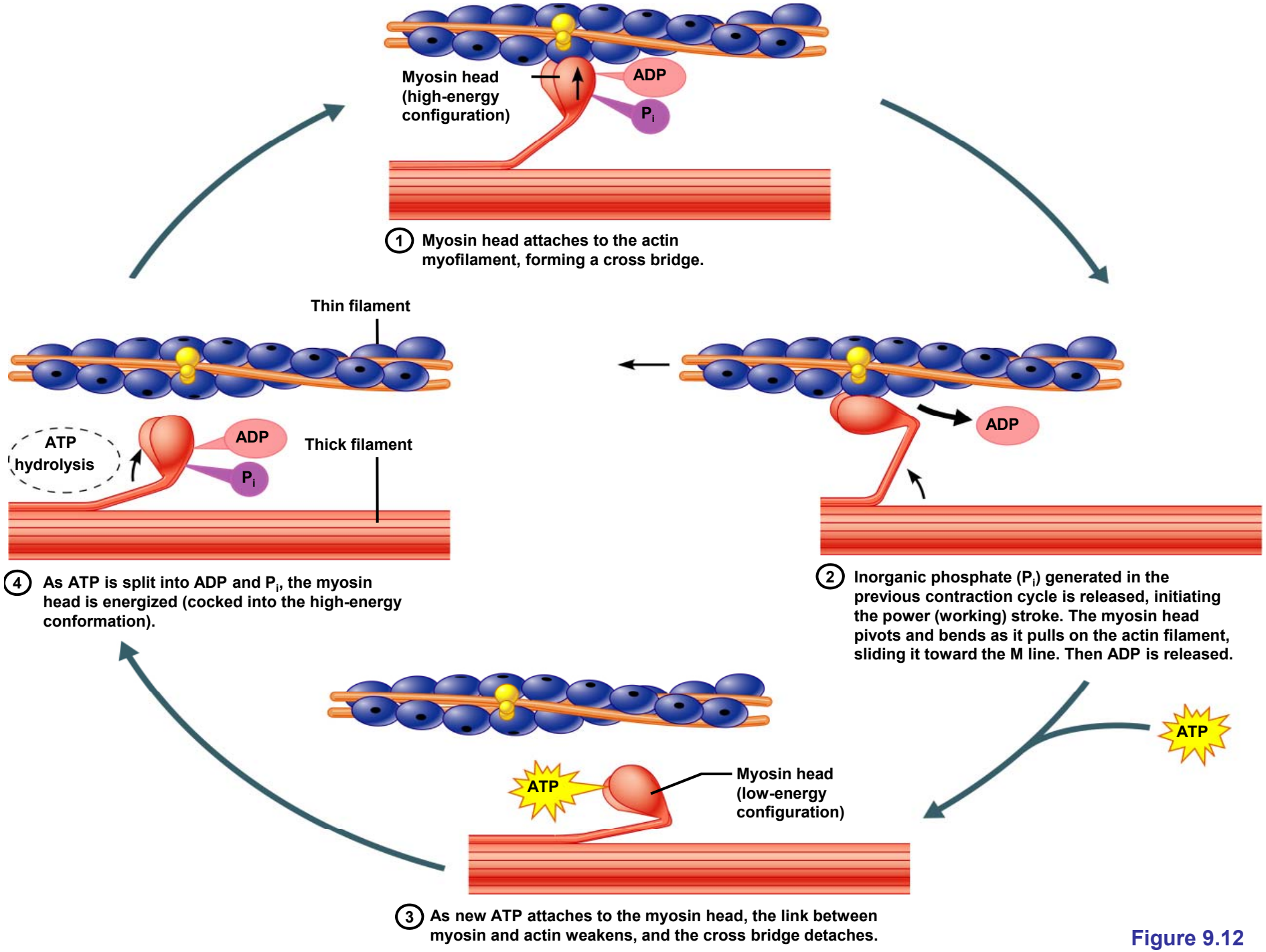
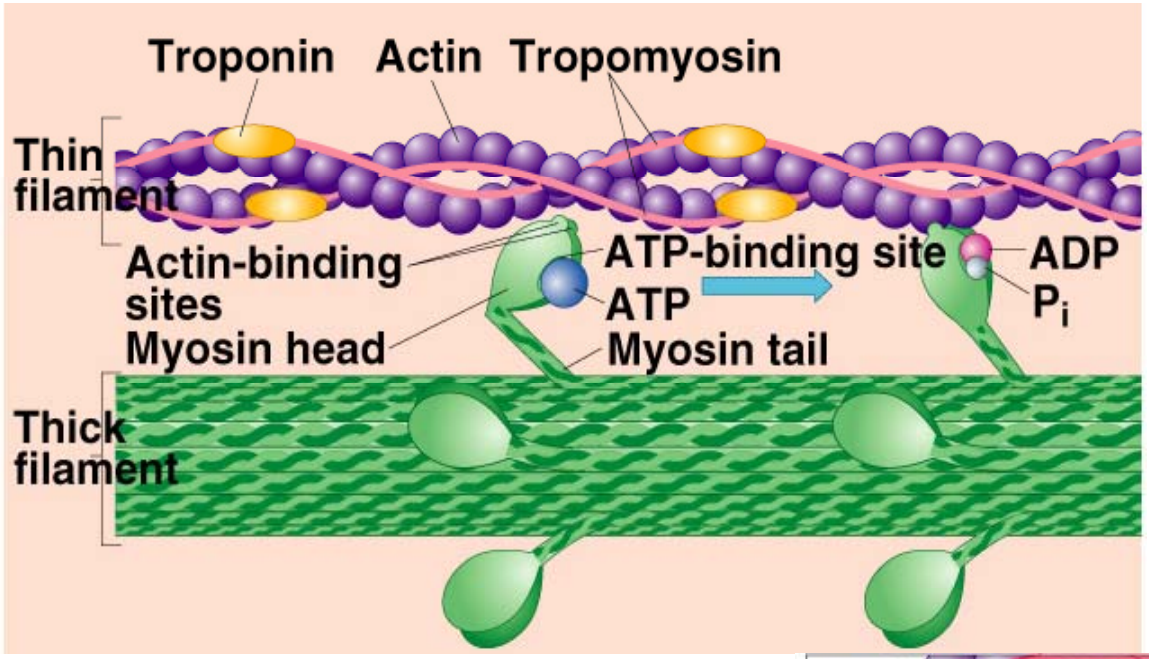
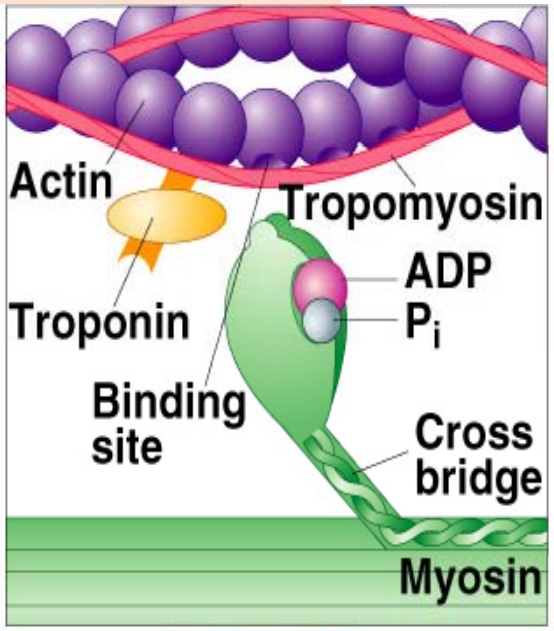

Myosin head
(high-energy
configuration)
ADP
P_i
1 Myosin head attaches to the actin myofilament, forming a cross bridge.
2 Inorganic phosphate (P_i) generated in the previous contraction cycle is released, initiating the power (working) stroke. The myosin head pivots and bends as it pulls on the actin filament, sliding it toward the M line. Then ADP is released.
ADP
3 As new ATP attaches to the myosin head, the link between myosin and actin weakens, and the cross bridge detaches.
ATP
Myosin head
(low-energy
configuration)
ATP
4 As ATP is split into ADP and P_i, the myosin head is energized (cocked into the high-energy conformation).
ATP
hydrolysis
ADP
P_i
Thin filament
Thick filament

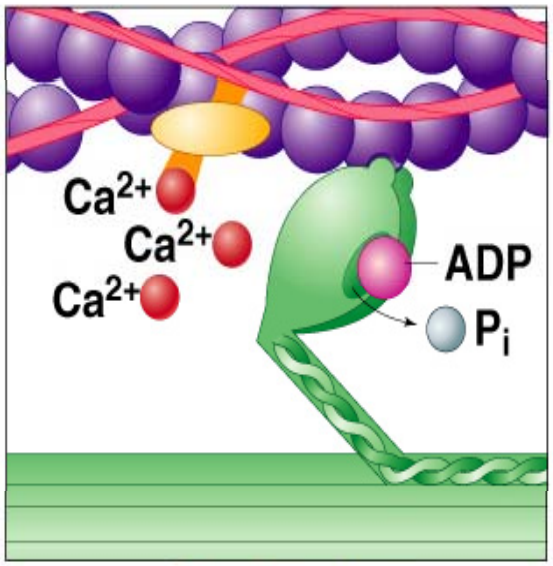
Figure 9.12

Regulation





Relaxed muscle



Contracting muscle

Role of Calcium (Ca^{2+}) in Contraction

- At low intracellular Ca^{2+} concentration:
  - Tropomyosin blocks the active sites on actin
  - Myosin heads cannot attach to actin
  - Muscle fiber relaxes

Role of Calcium (Ca^{2+}) in Contraction

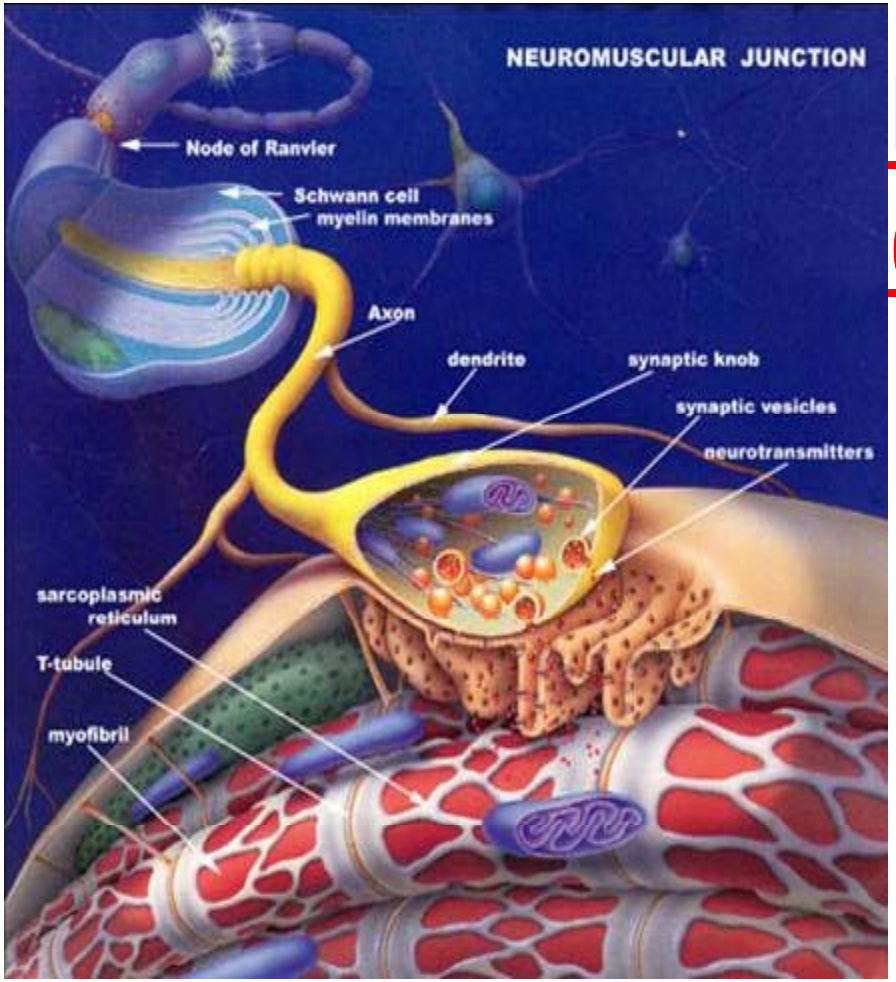
- At higher intracellular Ca^{2+} concentrations:
  - Ca^{2+} binds to troponin
  - Troponin changes shape and moves tropomyosin away from active sites
  - Events of the cross bridge cycle occur
  - When nervous stimulation ceases, Ca^{2+} is pumped back into the SR and contraction ends

Cross Bridge Cycle

- Continues as long as the Ca2+ signal and adequate ATP are present
- Cross bridge formation—high-energy myosin head attaches to thin filament
- Working (power) stroke—myosin head pivots and pulls thin filament toward M line

Cross Bridge Cycle

- Cross bridge detachment—ATP attaches to myosin head and the cross bridge detaches
- “Cocking” of the myosin head—energy from hydrolysis of ATP cocks the myosin head into the high-energy state



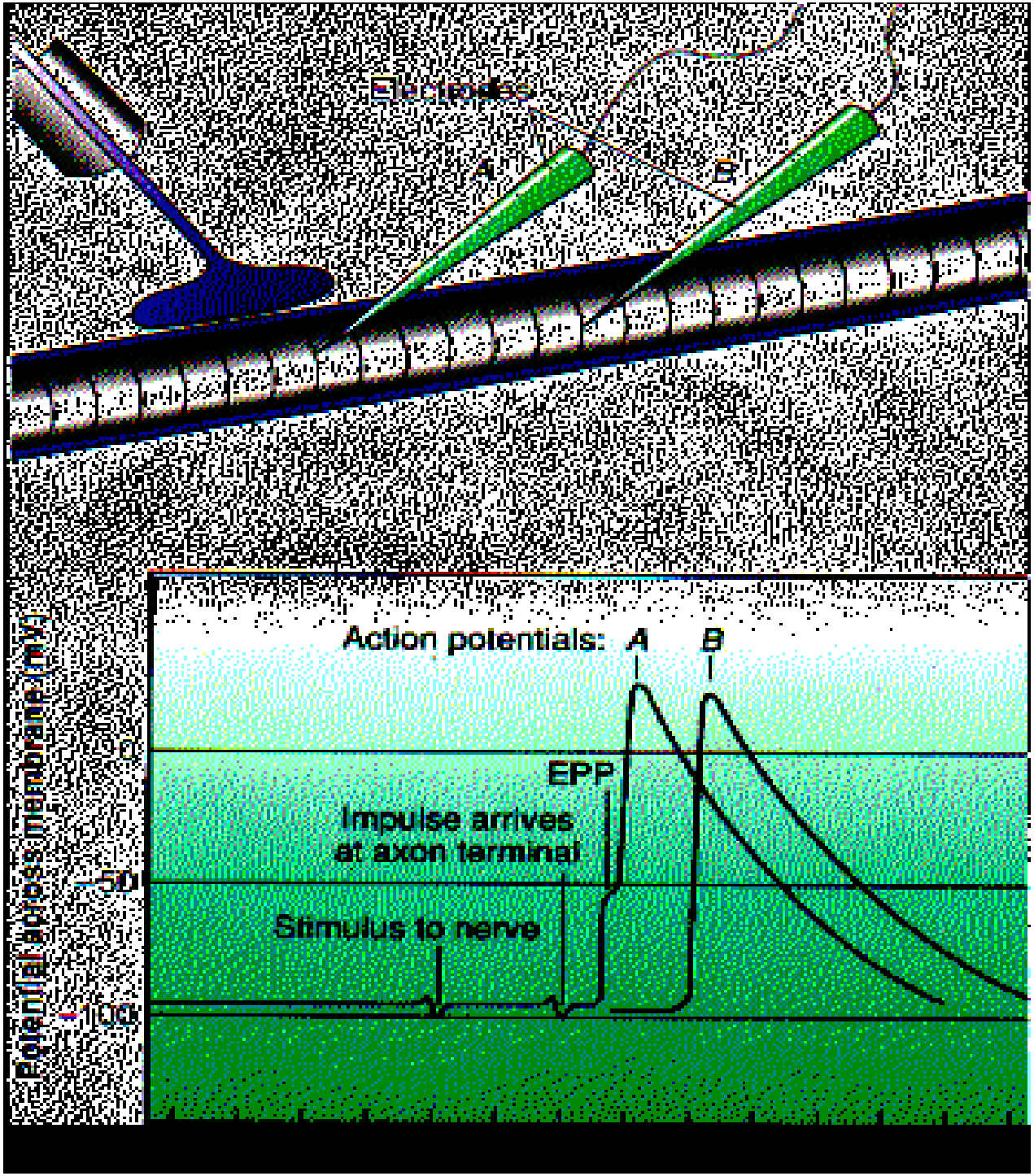
End plate potential (EPP)

Are the **depolarizations** of skeletal muscle fibers caused by neurotransmitters binding to the postsynaptic membrane in the neuromuscular junction.

They are called "end plates" because the postsynaptic terminals of muscle fibers have a large, saucer-like appearance.

Miniature End Plate Potentials (MEPPs)

Miniature end plate potentials are the small (~0.5mV) depolarisations of the postsynaptic terminal caused by the release of a single vesicle into the synaptic cleft.

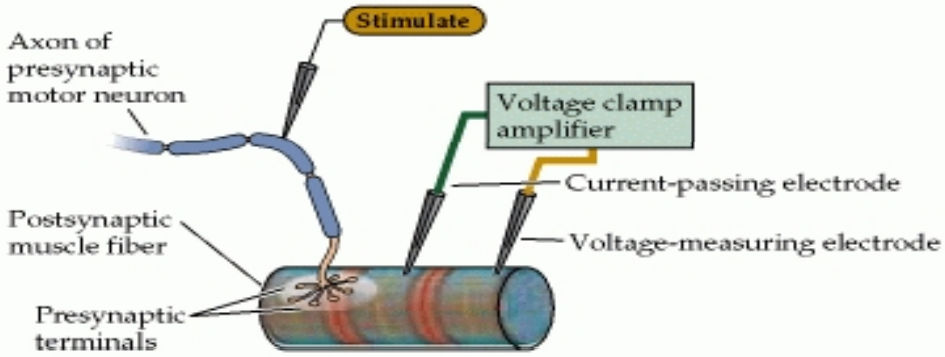


Arrival of a nerve impulse at the axon terminal of the motor neuron

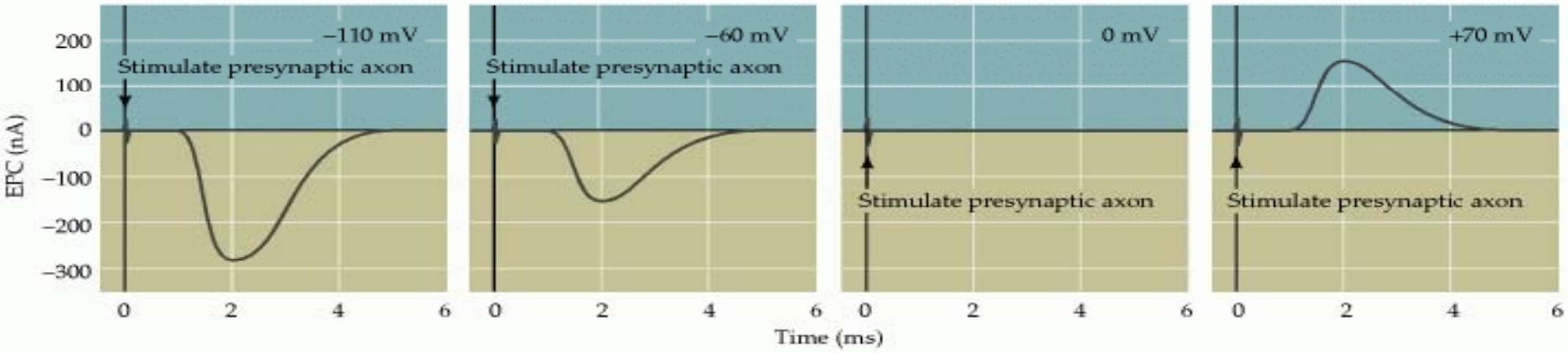
causes acetylcholine to be released into the neuromuscular junction which creates an **end plate potential** (**EPP**) in the membrane beneath it (**A**) but not farther away (**B**).

When the EPP reaches the threshold of the fiber (about -50 mv), an **action potential** is generated that sweeps along the fiber (**B**)

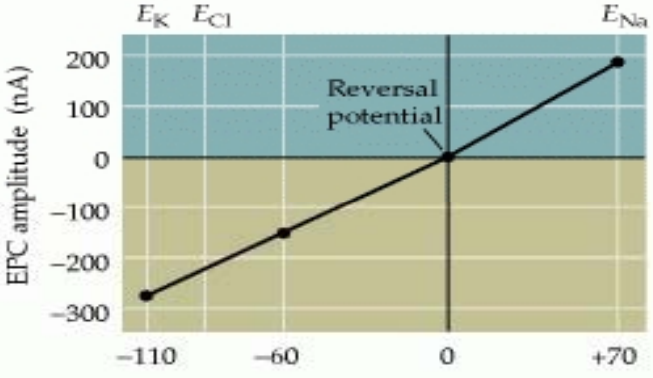
(A) Scheme for voltage clamping postsynaptic muscle fiber



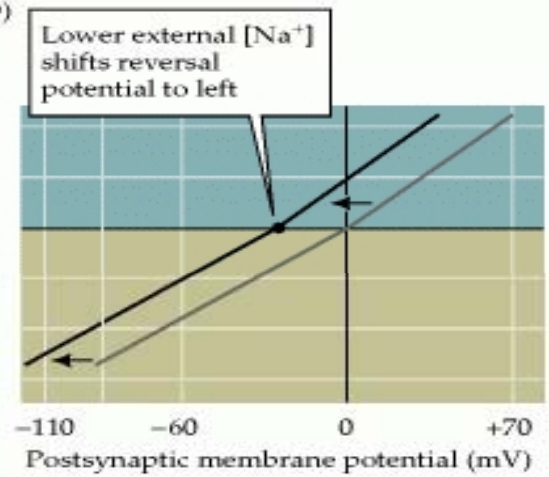
(B) Effect of membrane voltage on postsynaptic end plate currents



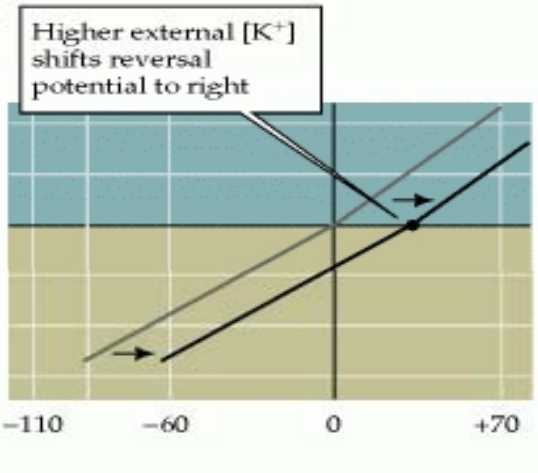
(C)



(D)



(E)



Action Potential Scan

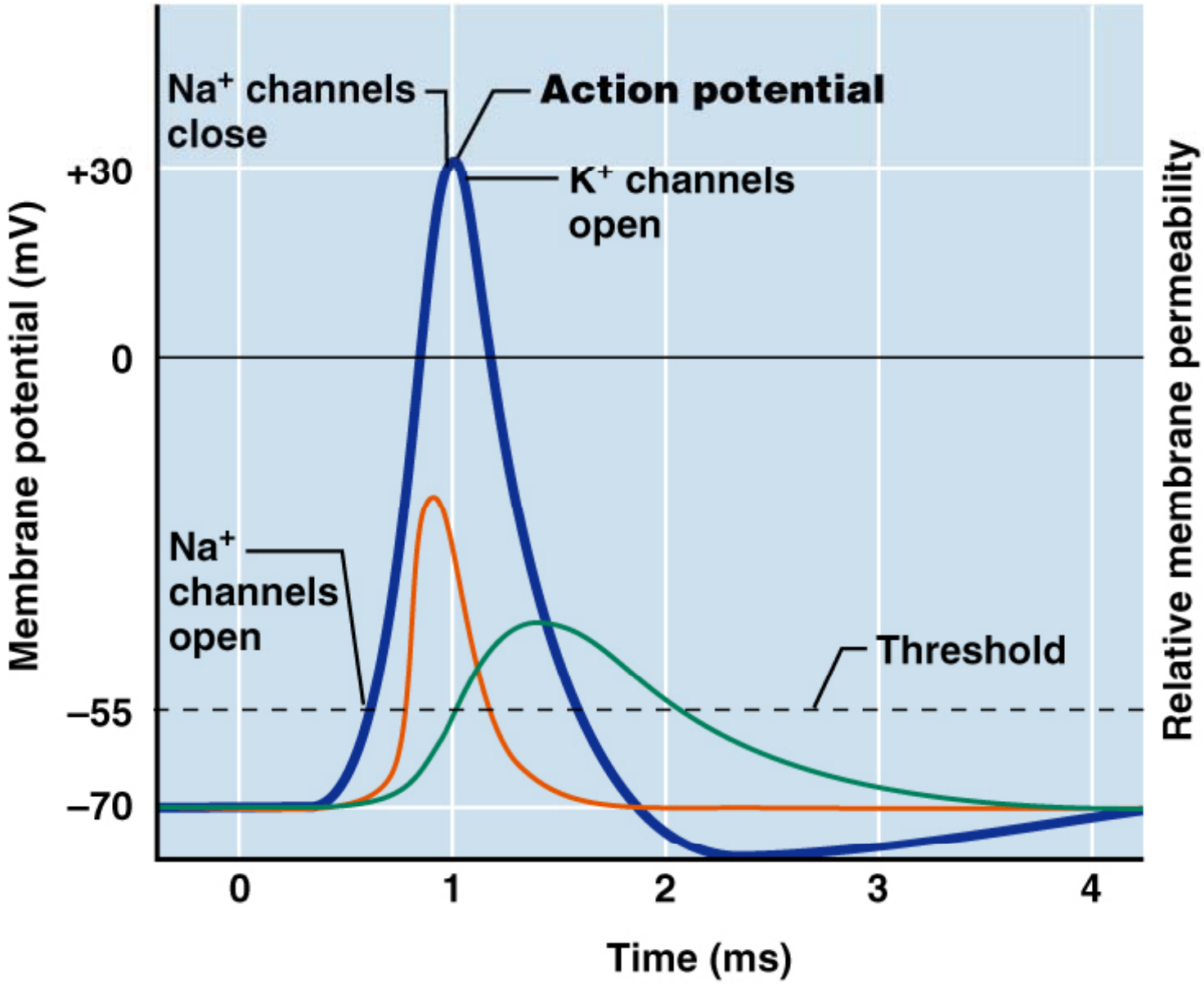


Figure 9.9

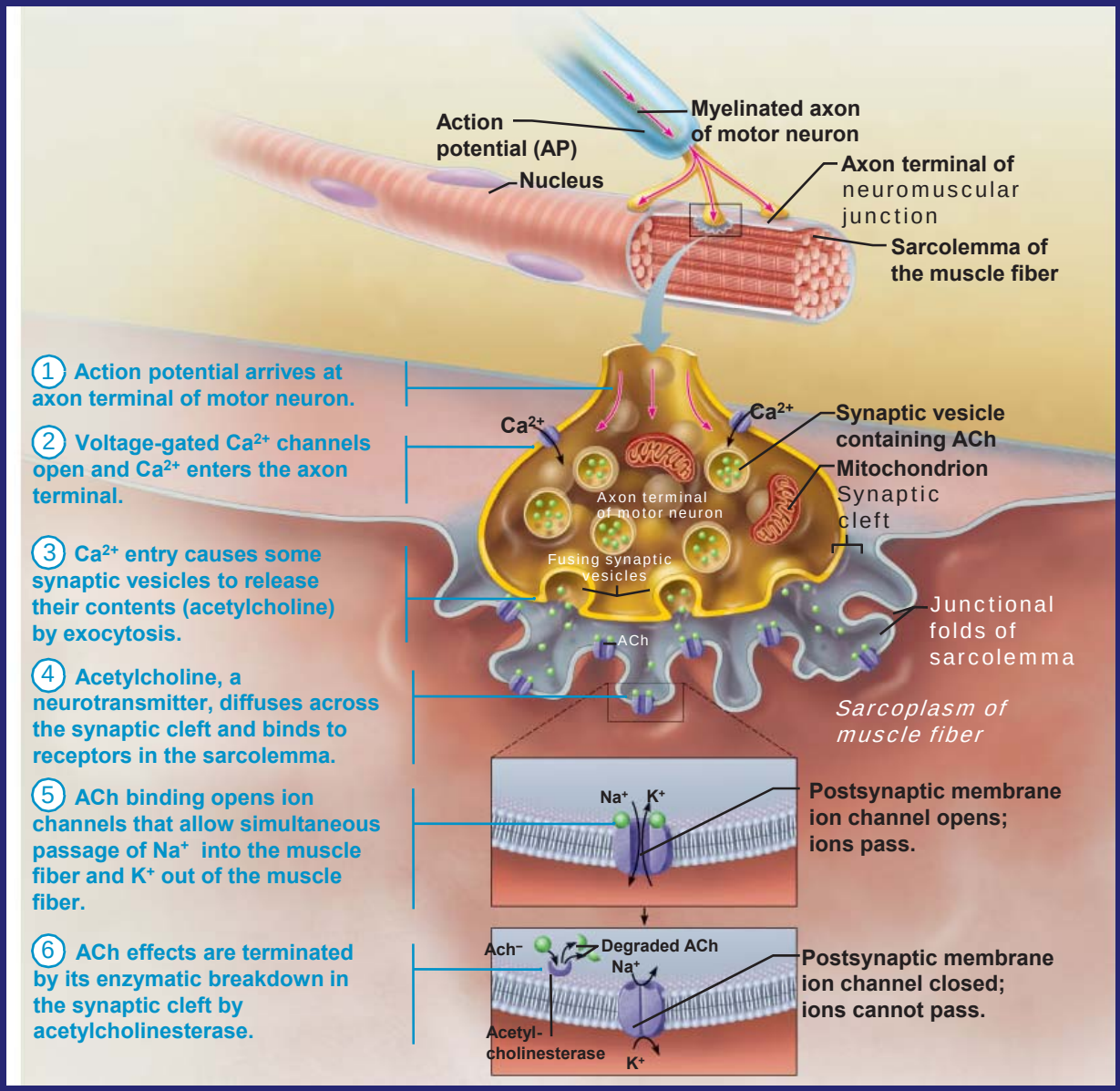

Action potential (AP)
Myelinated axon of motor neuron
Nucleus
Axon terminal of neuromuscular junction
Sarcolemma of the muscle fiber
1 Action potential arrives at axon terminal of motor neuron.
2 Voltage-gated Ca2+ channels open and Ca2+ enters the axon terminal.
3 Ca2+ entry causes some synaptic vesicles to release their contents (acetylcholine) by exocytosis.
4 Acetylcholine, a neurotransmitter, diffuses across the synaptic cleft and binds to receptors in the sarcolemma.
5 ACh binding opens ion channels that allow simultaneous passage of Na+ into the muscle fiber and K+ out of the muscle fiber.
6 ACh effects are terminated by its enzymatic breakdown in the synaptic cleft by acetylcholinesterase.
Ca2+
Ca2+
Synaptic vesicle containing ACh
Mitochondrion
Synaptic cleft
Axon terminal of motor neuron
Fusing synaptic vesicles
ACh
Junctional folds of sarcolemma
Sarcoplasm of muscle fiber
Na+ K+
Postsynaptic membrane ion channel opens; ions pass.
Ach−
Degraded ACh
Na+
Acetyl-cholinesterase
K+
Postsynaptic membrane ion channel closed; ions cannot pass.

Figure 9.8

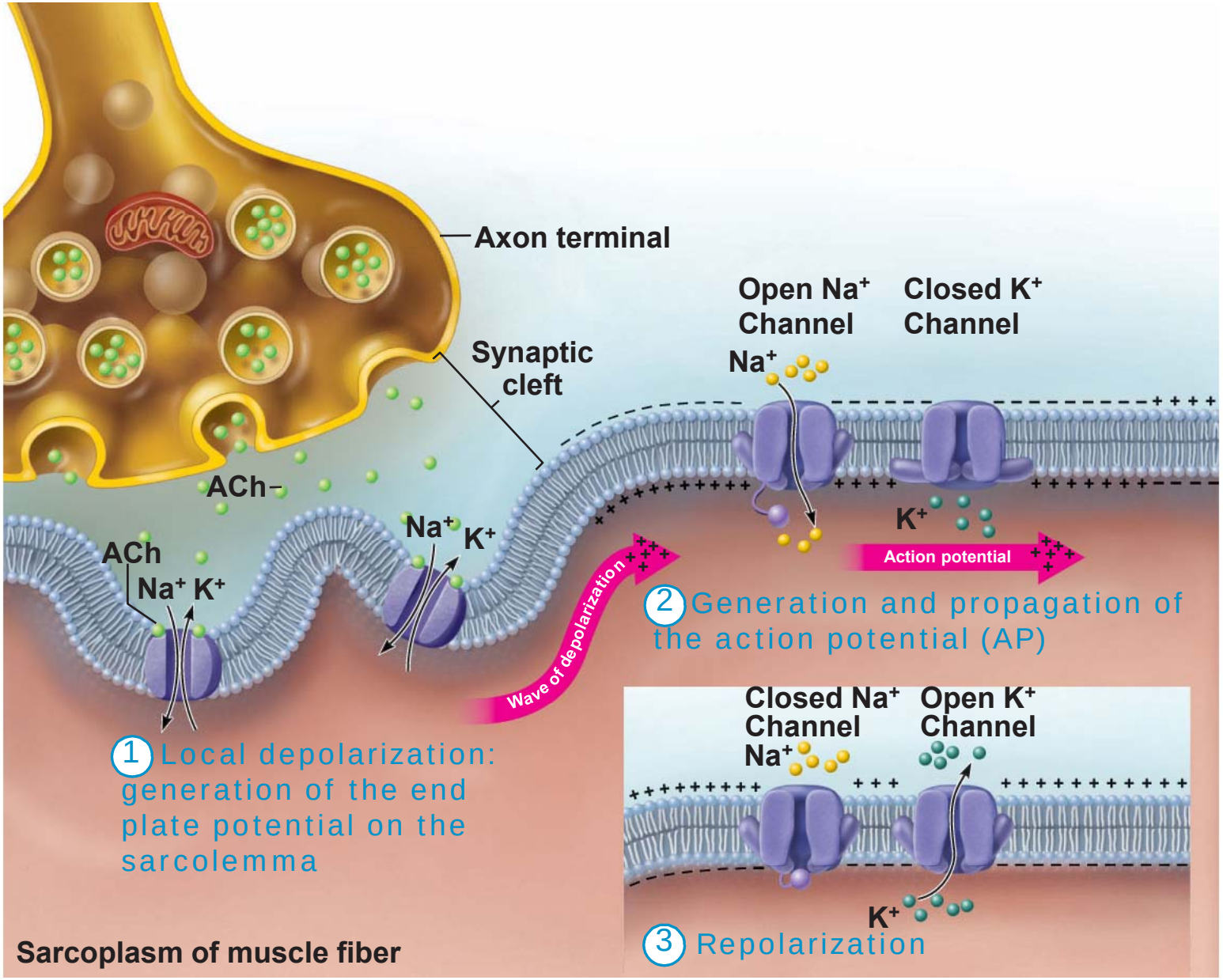

Axon terminal
Synaptic cleft
ACh
ACh
Na+ K+
Na+
K+
Open Na+ Channel
Closed K+ Channel
Na+
K+
Action potential
Wave of depolarization
2 Generation and propagation of the action potential (AP)
1 Local depolarization: generation of the end plate potential on the sarcolemma
Closed Na+ Channel
Open K+ Channel
Na+
K+
3 Repolarization
Sarcoplasm of muscle fiber

Figure 9.9

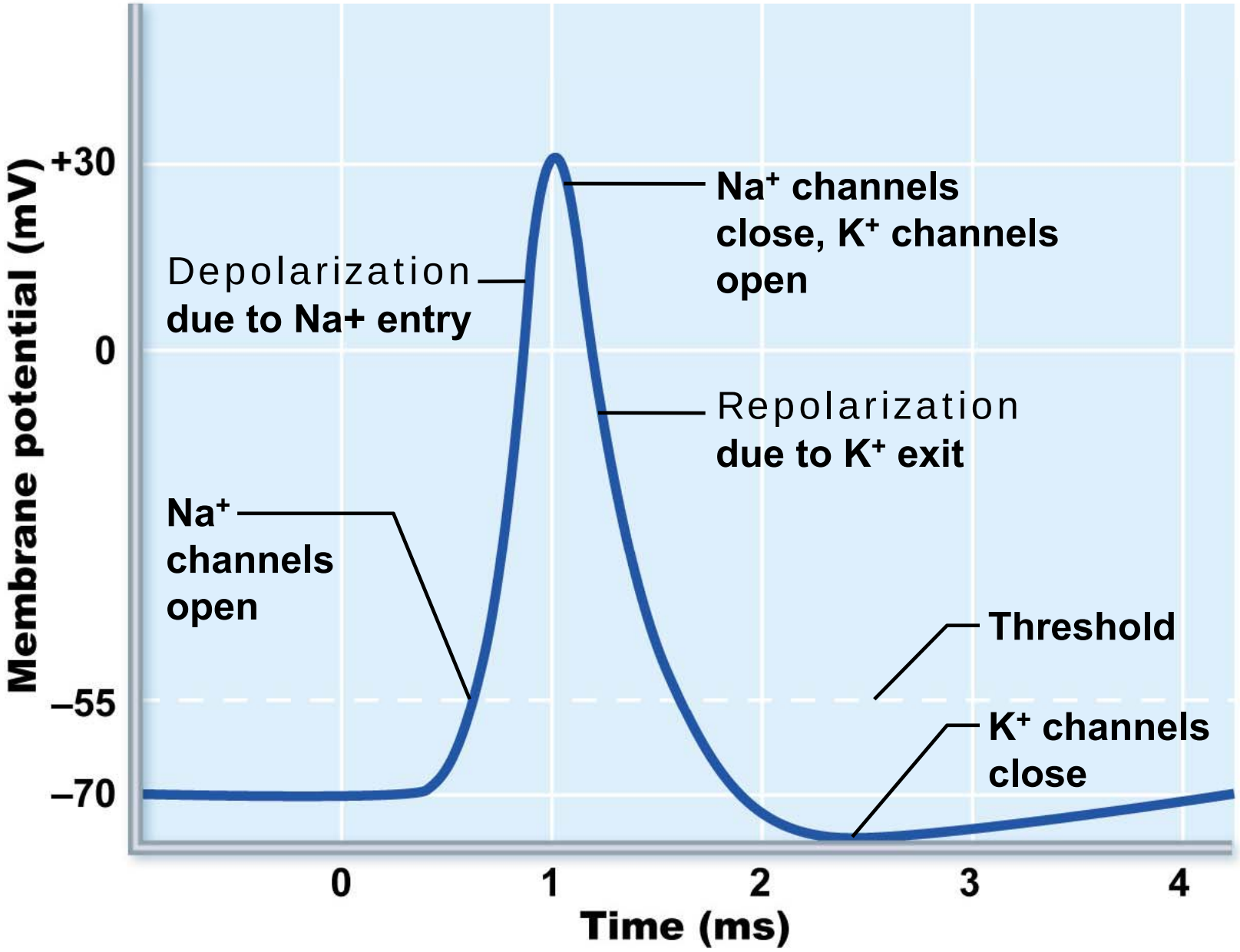
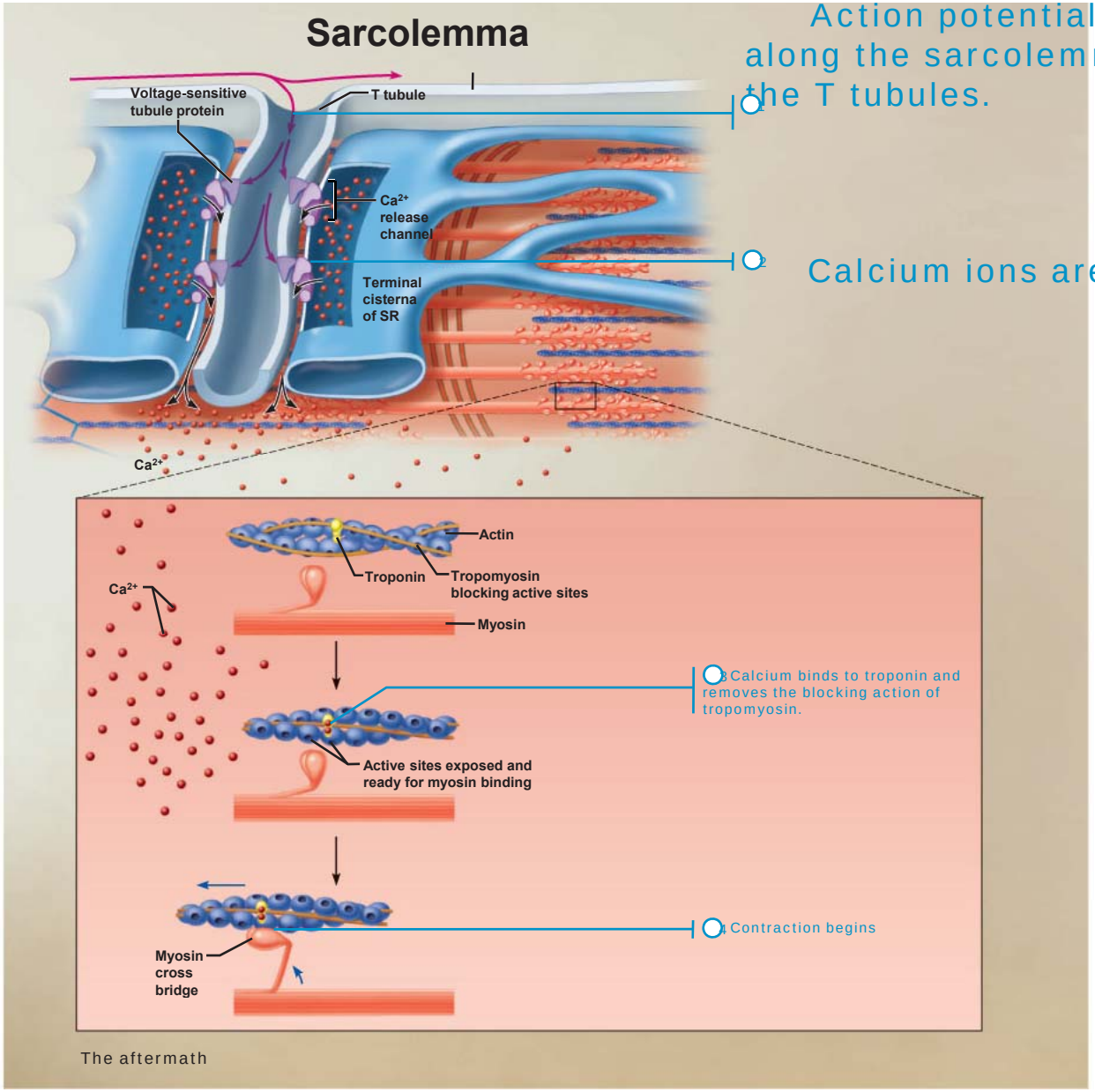

Membrane potential (mV)
+30
0
–55
–70
0
1
2
3
4
Time (ms)
Depolarization
due to Na+ entry
Na+ channels
close, K+ channels
open
Repolarization
due to K+ exit
Na+
channels
open
Threshold
K+ channels
close

Figure 9.10

Excitation-Contraction (E-C) Coupling

- Sequence of events by which transmission of an AP along the sarcolemma leads to sliding of the myofilaments
- Latent period:
  - Time when E-C coupling events occur
  - Time between AP initiation and the beginning of contraction

Steps in E-C Coupling:



1 Action potential is propagated along the sarcolemma and down the T tubules.

2 Calcium ions are released.

3 Calcium binds to troponin and removes the blocking action of tropomyosin.

4 Contraction begins

Figure 9.11, step 2

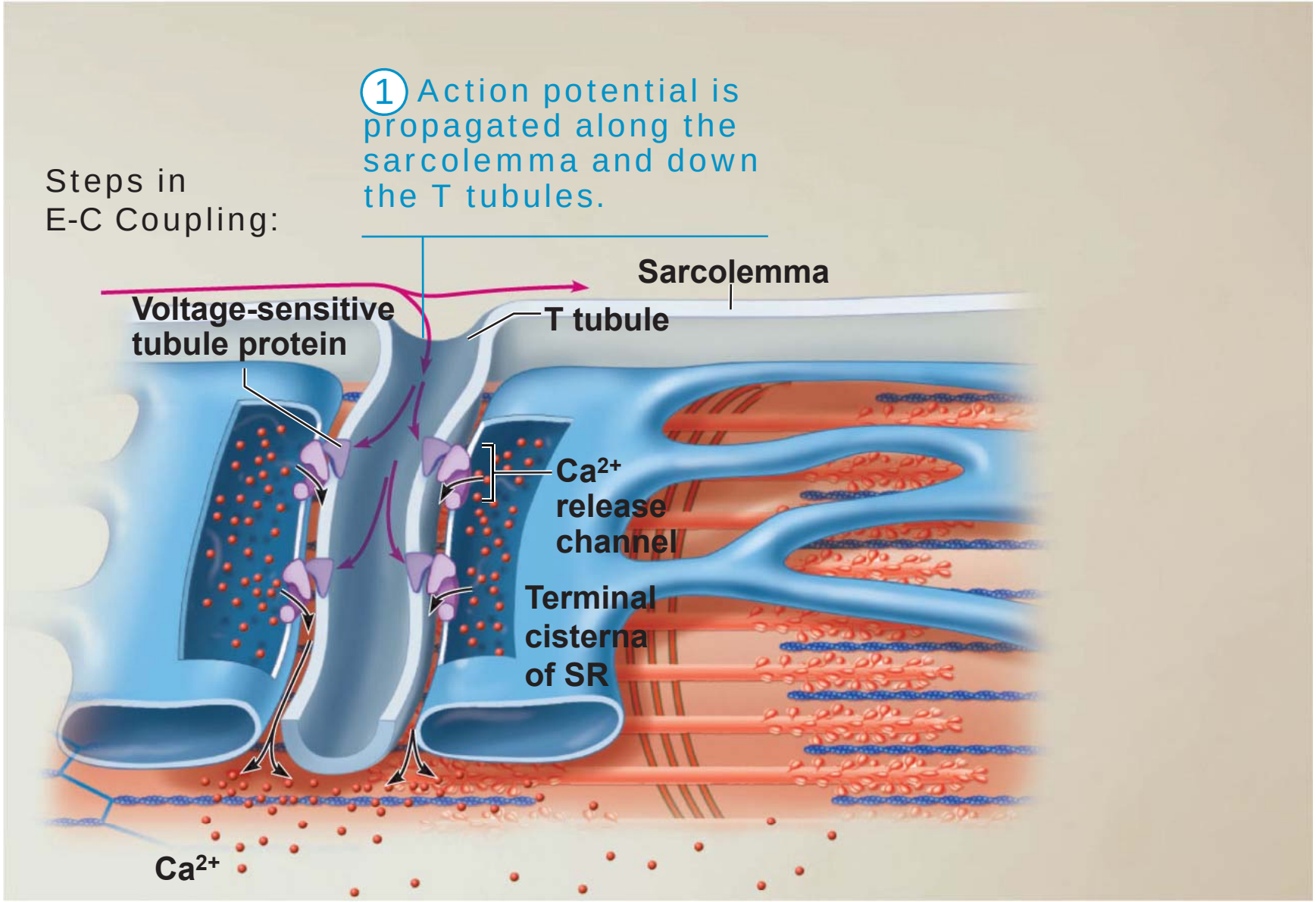


Figure 9.11, step 3

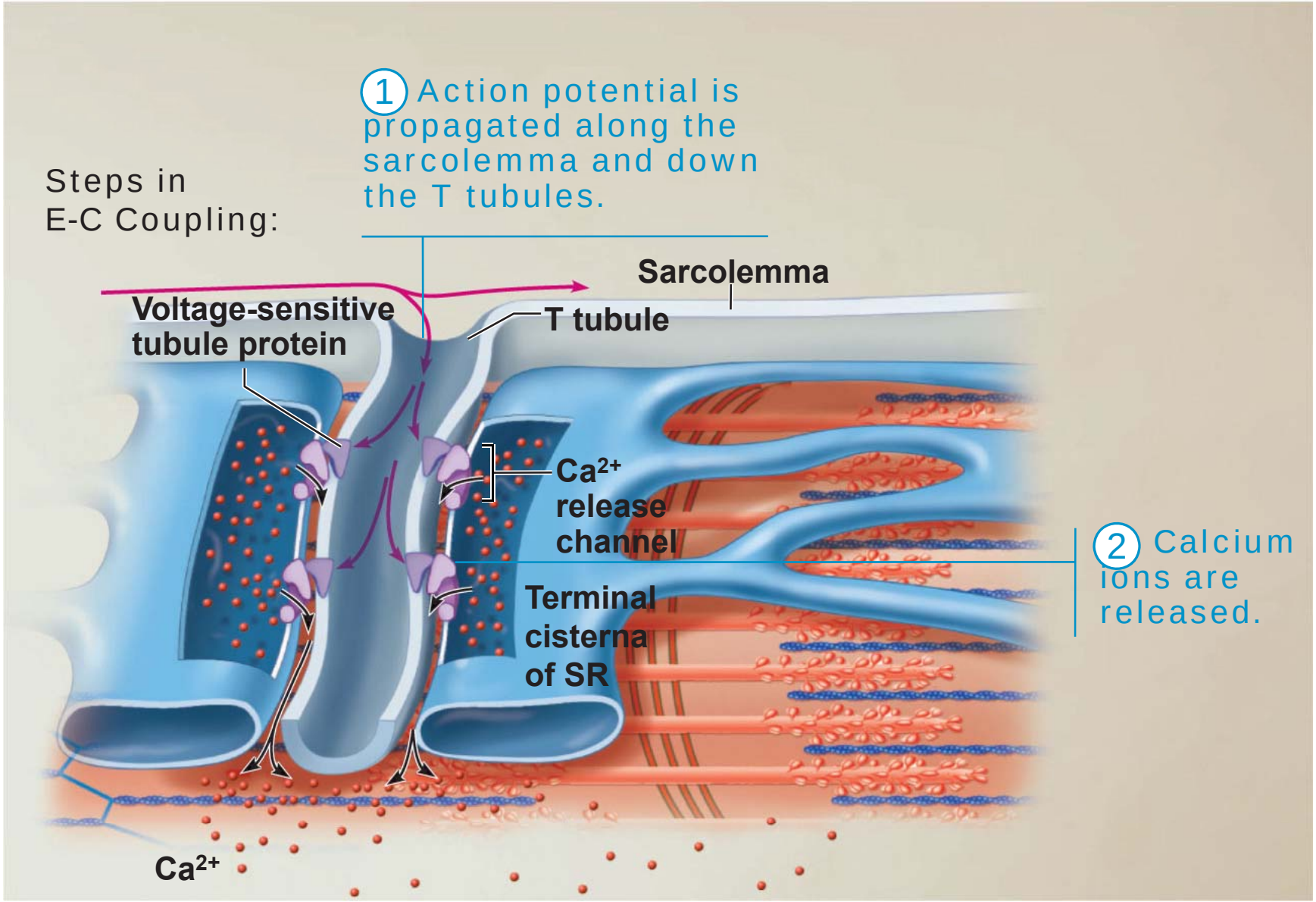


Figure 9.11, step 4

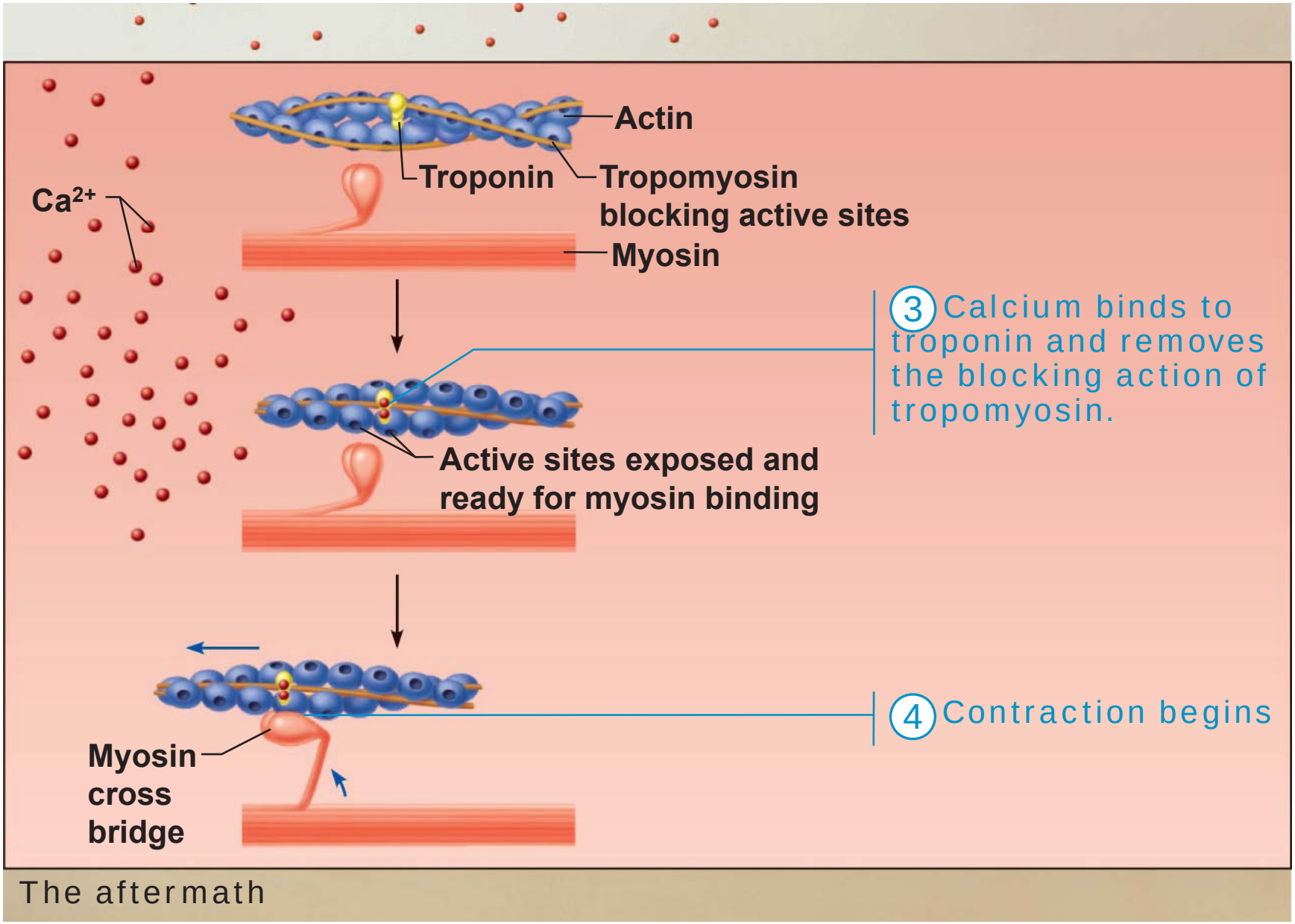


Figure 9.11, step 7

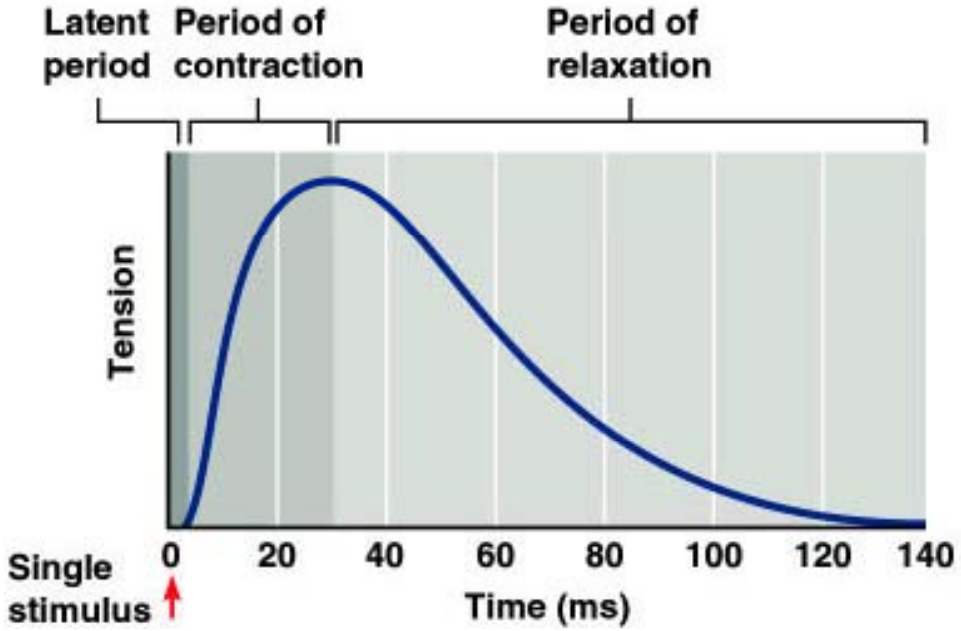
Muscle Twitch

A muscle twitch is the response of a muscle to a single action potential of its motor neuron.

The fibers contract quickly and then relax.

Three phases:

- Latent Period
- Period of Contraction
- Period of Relaxation



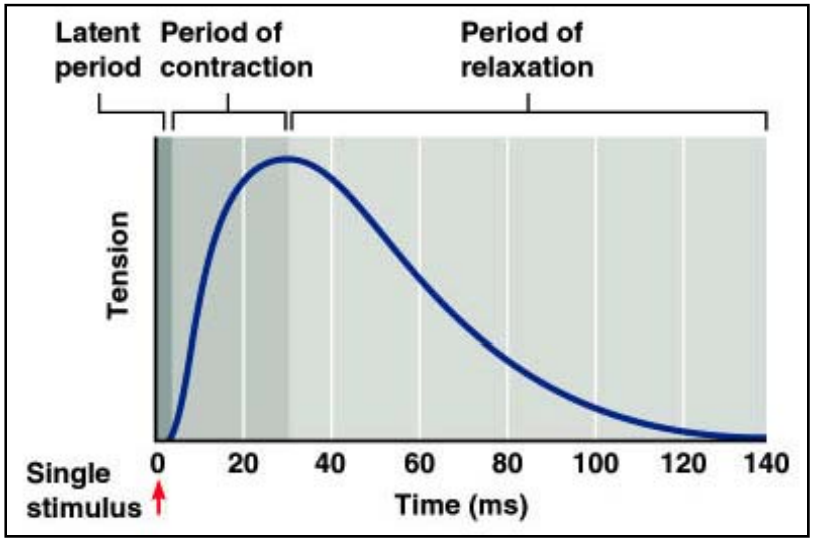
Myogram – graphic recording of contractile activity

Muscle Twitch

Latent Period – the first few ms after stimulation when excitation-contraction is occurring

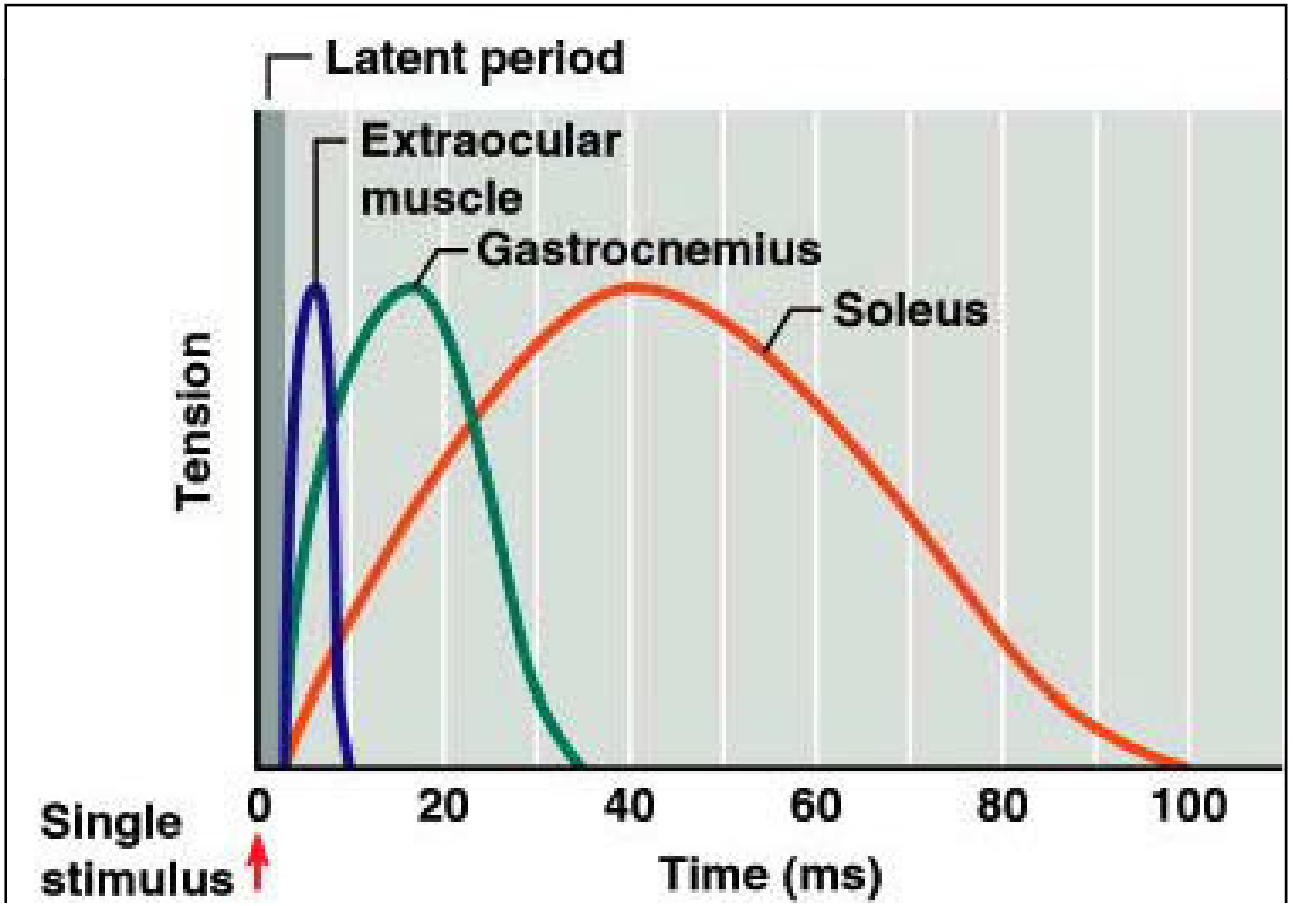
Period of Contraction – cross bridges are active and the muscle shortens if the tension is great enough to overcome the load

Period of Relaxation – Ca^{2+} is pumped back into SR and muscle tension decreases to baseline level



Muscle Twitch

Twitch contraction of some muscles (extraocular) are rapid and brief, others (gastrocnemius, soleus) are slower and longer



The three primary fiber types in human skeletal muscle

- Slow twitch oxidative (SO)
- Fast twitch oxidative glycolytic (FOG)
- Fast twitch glycolytic (FG)

Muscle at rest

ATP from metabolism + creatine → ADP + phosphocreatine

Working muscle

Phosphocreatine + ADP —(creatine kinase)→ Creatine + ATP

Creatine + ATP → needed for →

- Myosin ATPase (contraction)
- Ca^{2+}-ATPase (relaxation)
- Na^{+}-K^{+}-ATPase (restores ions that cross cell membrane during action potential to their original compartments)

Graded Muscle Responses

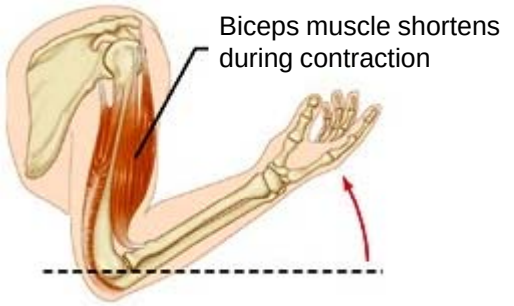
Graded muscle responses are:

- Variations in the degree or strength of muscle contraction in response to demand
- Required for proper control of skeletal movement

- Muscle contraction can be graded (varied) in two ways:
  - By changing the Frequency of the stimulus
  - By changing the Strength of the stimulus

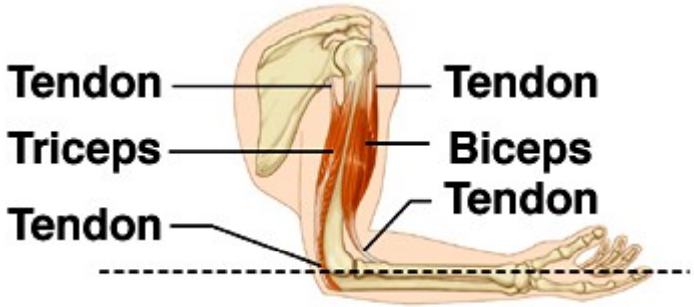
Three potential actions during muscle contraction:

- shortening

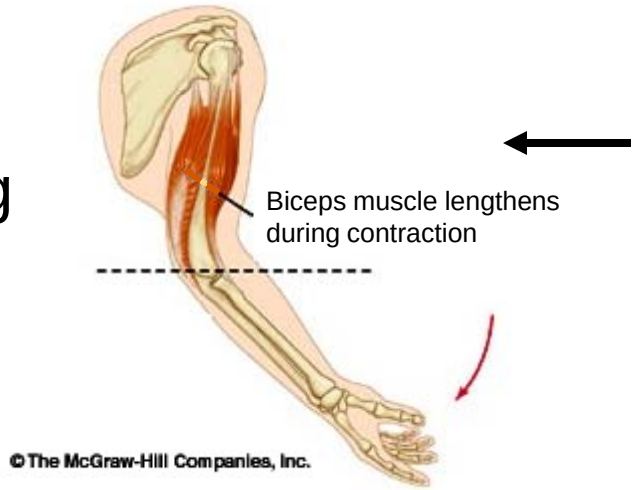


(Isotonic: shortening against fixed load, speed dependent on M·ATPase activity and load)

- isometric



- lengthening

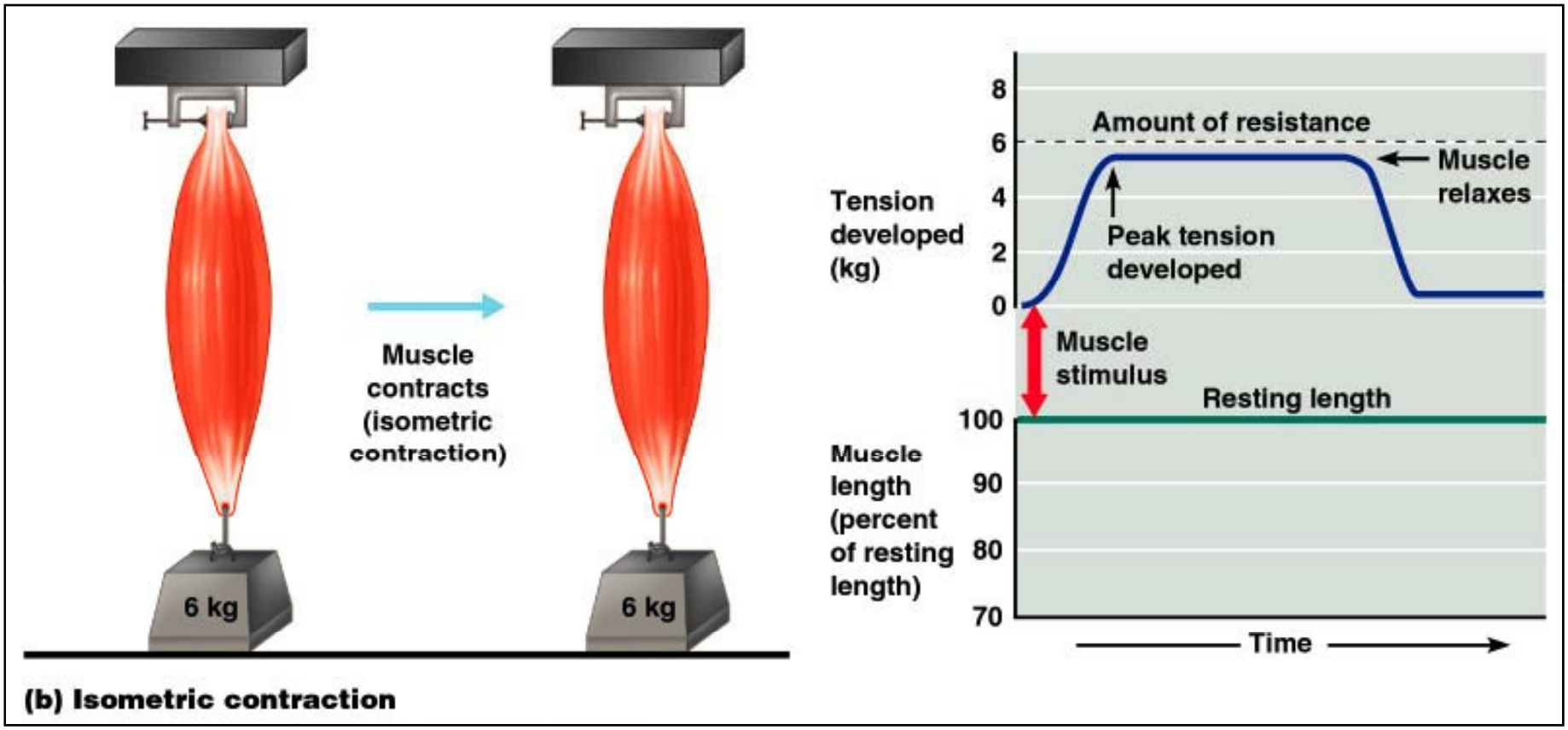


Most likely to cause muscle injury

Modified from Vander, Sherman, Luciano *Human Physiology,* McGraw-Hill.

Isometric Contractions

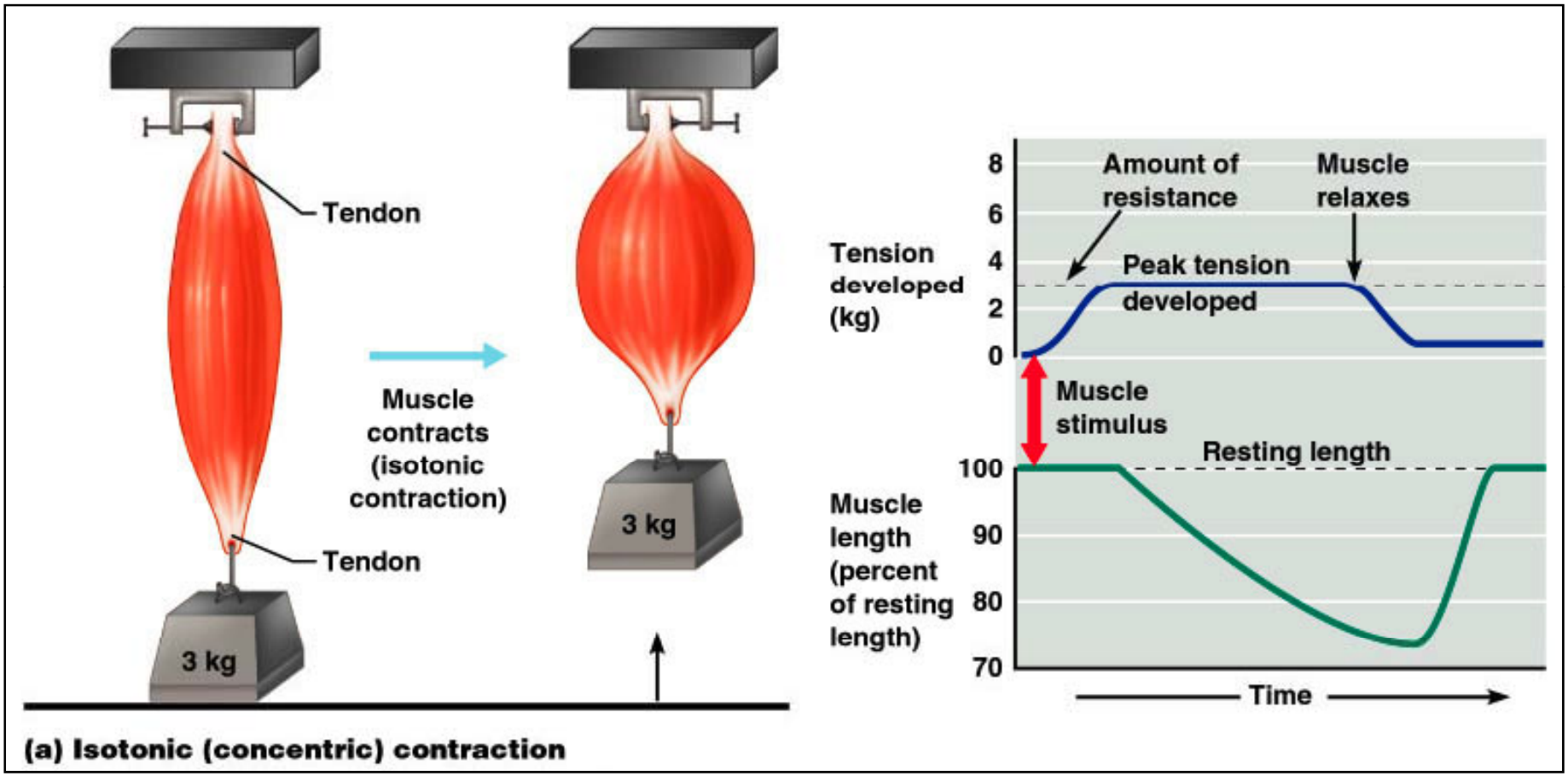
No change in overall muscle length



In isometric contractions, increasing muscle tension (force) is measured

Isotonic Contraction

This illustrates a concentric isotonic contraction



In isotonic contractions, the amount of shortening (distance in mm) is measured

Muscle Response to Stronger Stimuli

- Threshold stimulus – the stimulus strength at which the first observable muscle contraction occurs
- Beyond threshold, muscle contracts more vigorously as stimulus strength is increased
- Force of contraction is precisely controlled by multiple motor unit summation
- This phenomenon, called recruitment, brings more and more muscle fibers into play

Energy Metabolism in Skeletal Muscle -

A) **Creatine-phosphagen system**
- 1) uses creatine phosphokinase (CPK or CK)
  - a) CPK-MM in skeletal muscle
  - b) CPK-MB in cardiac muscle
- 2) delivers ~ 30 sec max. activity

B) **Lactic acid pathway (glycolytic pathway)**
- 1) anaerobic use of glucose (glycolysis mainly)
- 2) 2ATP/glucose
- 3) lactic acid waste product
- 4) can be "recycled" by liver

C) **Aerobic respiration (oxidative) pathway**
- 1) most efficient use of glucose
- 2) 36ATP/glucose
- 3) requires oxygen
- 4) occurs in mitochondria

D) **Sources of glucose**
- 1) blood glucose
- 2) stored glycogen

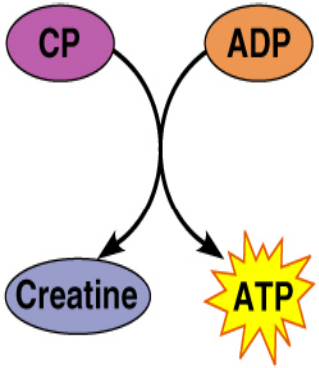
E) **Sources/carriers of oxygen**
- 1) hemoglobin
- 2) myoglobin

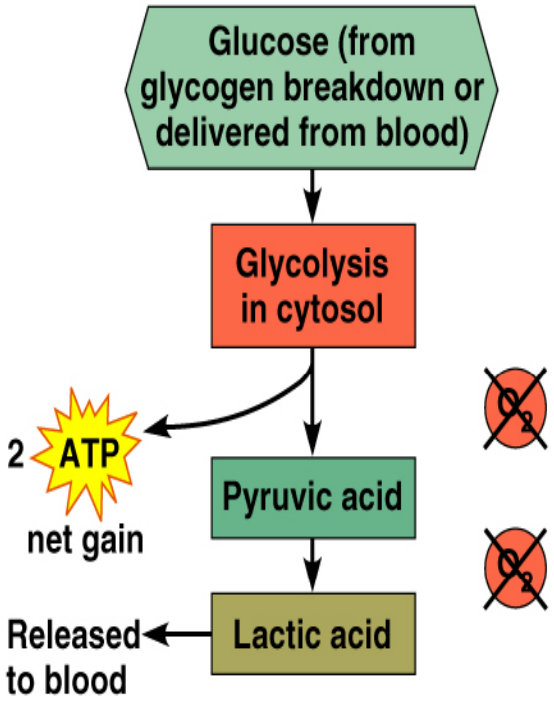
F) **Recovery oxygen consumption**

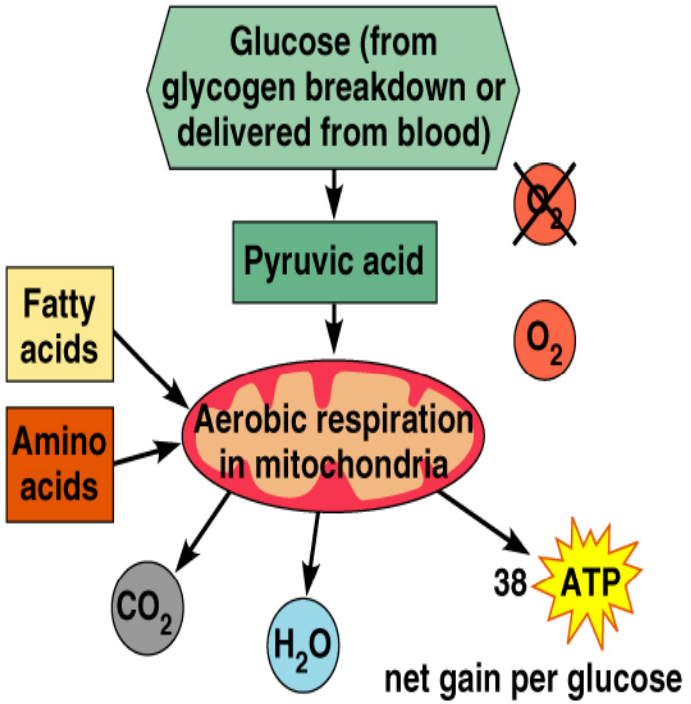
1) due to increased metabolic rate and continued use

2) 2) lactic acid can be recycled in liver

a) 4 lactic acid converted to glucose, 1 converted to carbon dioxide







(a) Direct phosphorylation [coupled reaction of creatine phosphate (CP) and ADP]	(b) Anaerobic mechanism (glycolysis and lactic acid formation)	(c) Aerobic mechanism (aerobic cellular respiration)
Energy source: CP	Energy source: glucose	Energy source: glucose; pyruvic acid; free fatty acids from adipose tissue; amino acids from protein catabolism
Oxygen use: None Products: 1 ATP per CP, creatine Duration of energy provision: 15 s.	Oxygen use: None Products: 2 ATP per glucose, lactic acid Duration of energy provision: 30–60 s.	Oxygen use: Required Products: 38 ATP per glucose, CO_2, H_2O Duration of energy provision: Hours

Muscle Metabolism: Energy

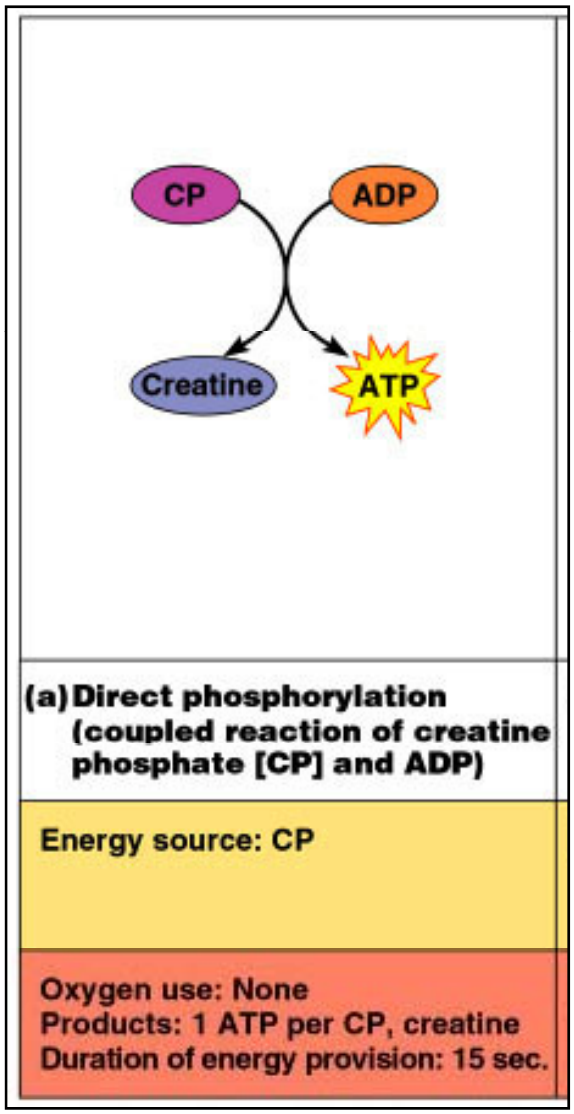
ATP is the only energy source that is used directly for contractile activity

As soon as available ATP is hydrolyzed (4-6 seconds), it is regenerated by three pathways:

- Interaction of ADP with Creatine Phosphate (CP)
- From stored glycogen via Anaerobic Glycolysis
- From Aerobic Respiration

CP-ADP Reaction

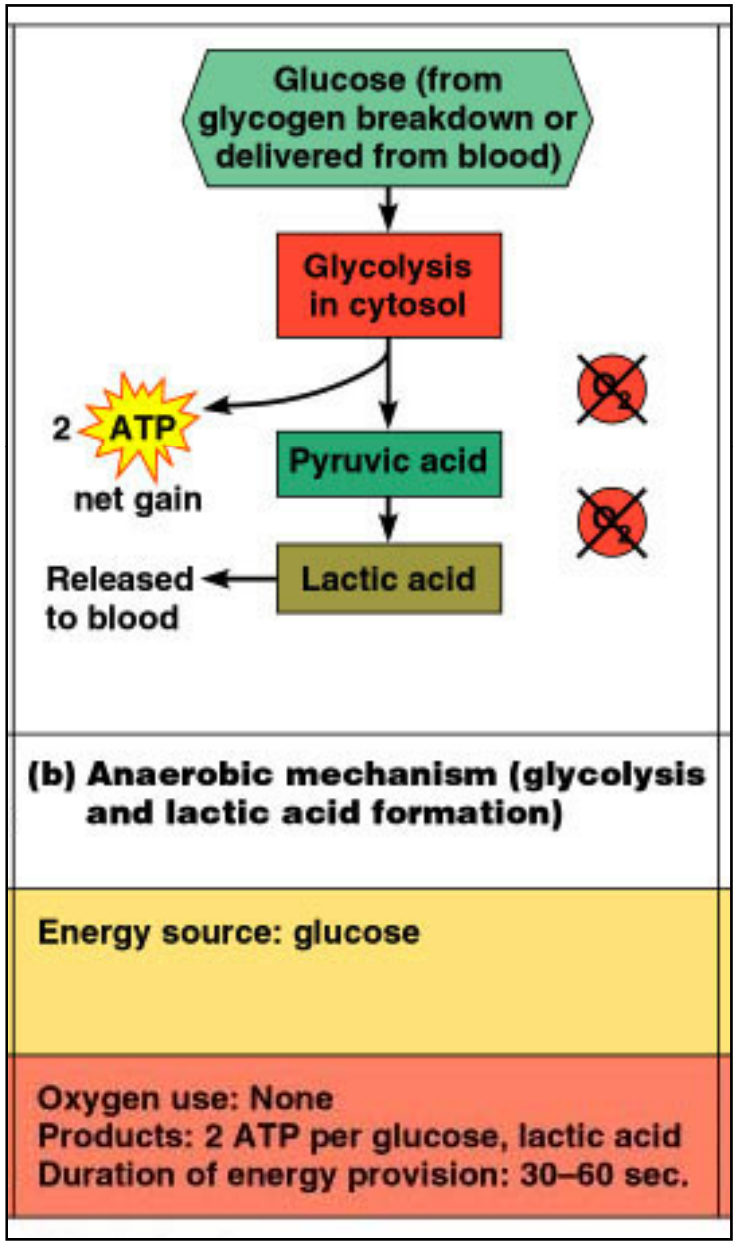
Creatine phosphate + ADP → creatine + ATP



Transfer of energy as a phosphate group is moved from CP to ADP – the reaction is catalyzed by the enzyme creatine kinase

Stored ATP and CP provide energy for maximum muscle power for 10-15 seconds

Anaerobic Glycolysis

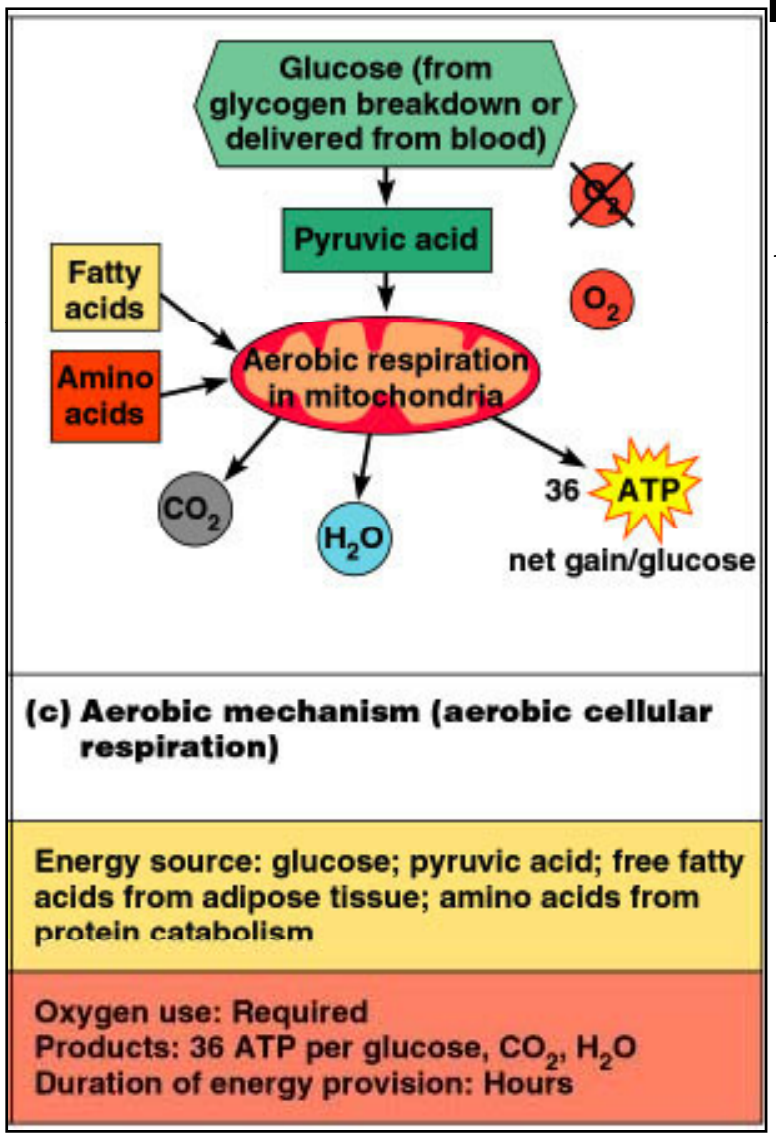


When muscle contractile activity reaches 70% of maximum:

- Muscles compress blood vessels and O_2 delivery is impaired (anaerobic conditions)
- Pyruvic acid is converted into lactic acid
- Lactic acid diffuses into the bloodstream – can be used as energy source by the liver, kidneys, and heart

Can be converted back into pyruvic acid, glucose, or glycogen by the liver

Glycolysis and Aerobic Respiration

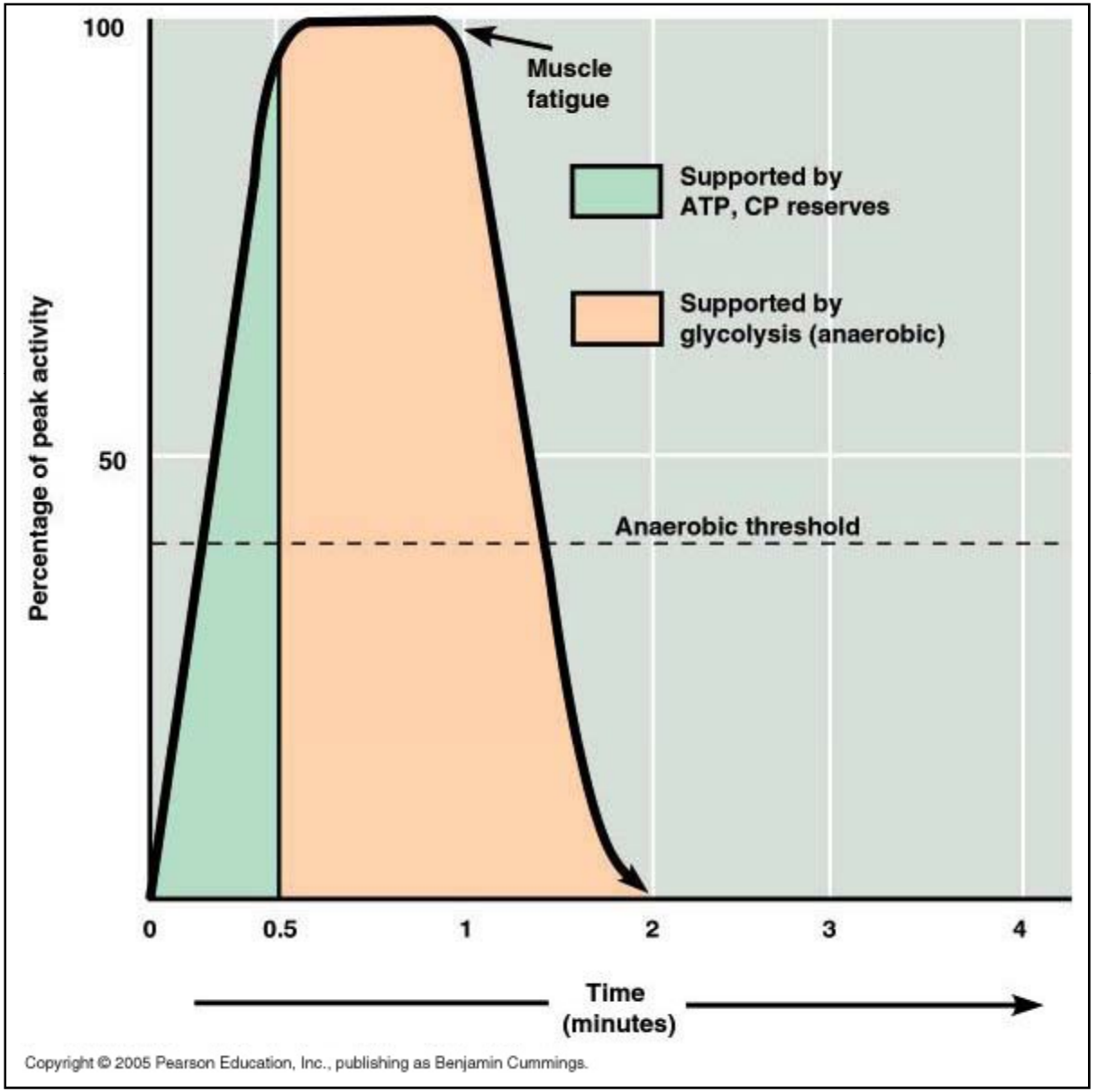


$$\text{Glucose} + O_2 \rightarrow CO_2 + H_2O + \text{ATP}$$

Aerobic respiration occurs in mitochondria - requires O_2

A series of reactions where glucose is fully broken down with a high yield of ATP

Energy System or Source



Muscle Fatigue

Muscle fatigue – the muscle is physiologically not able to contract

Occurs when oxygen is limited and ATP production fails to keep pace with ATP use

- Lactic acid accumulation and ionic imbalances may also contribute to muscle fatigue

When no ATP is available, contractures (continuous contraction) may result because cross bridges are unable to detach

Muscle Fatigue

Intense exercise produces rapid muscle fatigue (with rapid recovery)

Na^+-K^+ pumps cannot restore ionic balances quickly enough

Low-intensity exercise produces slow-developing fatigue (with longer recovery period)

SR may be damaged, interfering with Ca^{2+} regulation

Oxygen Debt

Vigorous exercise can cause dramatic changes in muscle chemistry

For a muscle to return to its pre-exercise state:

- Oxygen reserves must be replenished
- (Lactic acid must be converted to pyruvic acid?)
- Glycogen stores must be replaced
- ATP and CP reserves must be resynthesized

Oxygen debt – the extra amount of O_2 needed for the above restorative processes

Heat Production During Muscle Activity

Only 40% of the energy released in muscle activity is useful as work

The remaining 60% is given off as heat

Heat is dissipated by radiation of heat from the skin and sweating

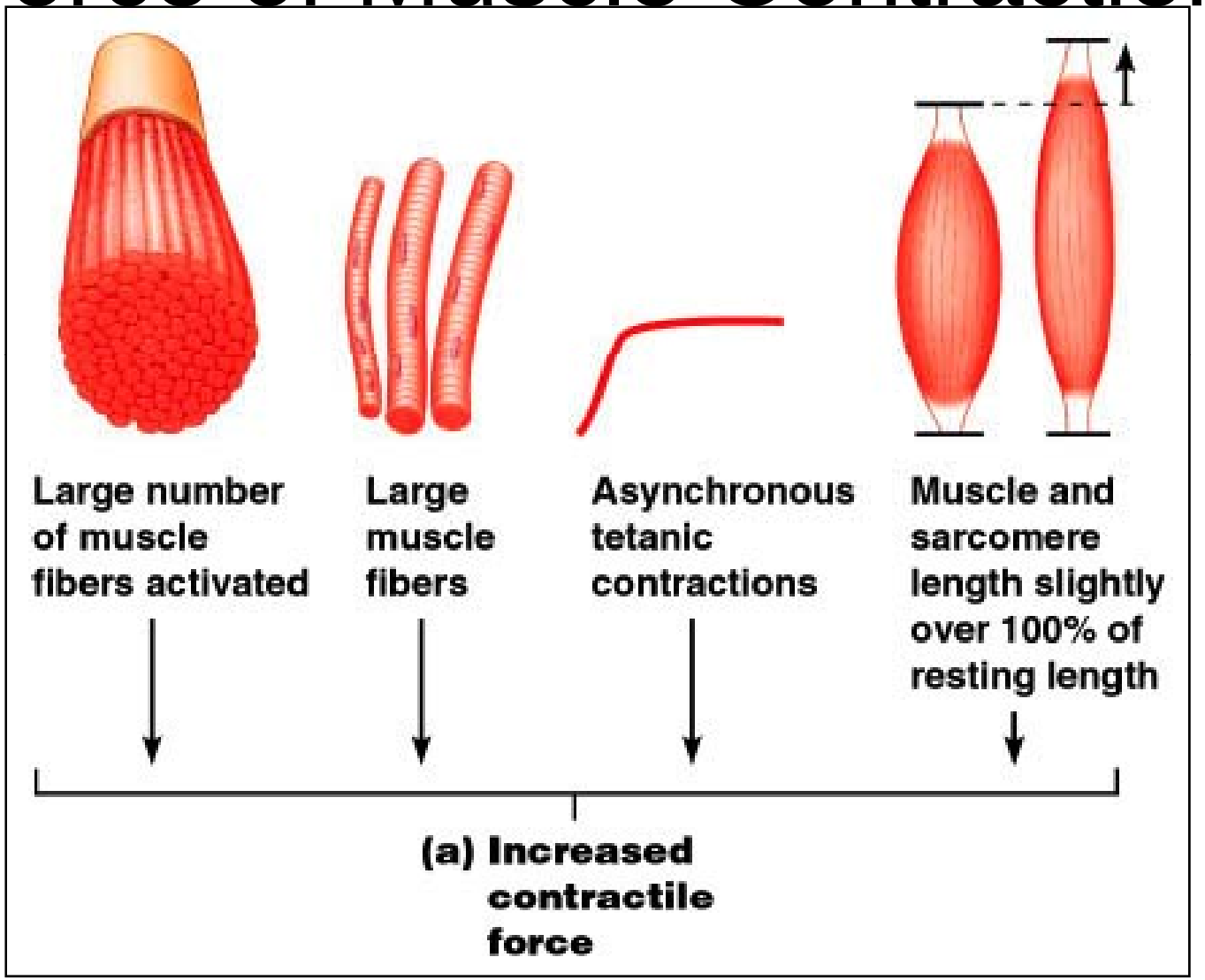
Heat Production During Muscle Activity

Only 40% of the energy released in muscle activity is useful as work

The remaining 60% is given off as heat

Heat is dissipated by radiation of heat from the skin and sweating

Force of Muscle Contraction



Length Tension Relationships

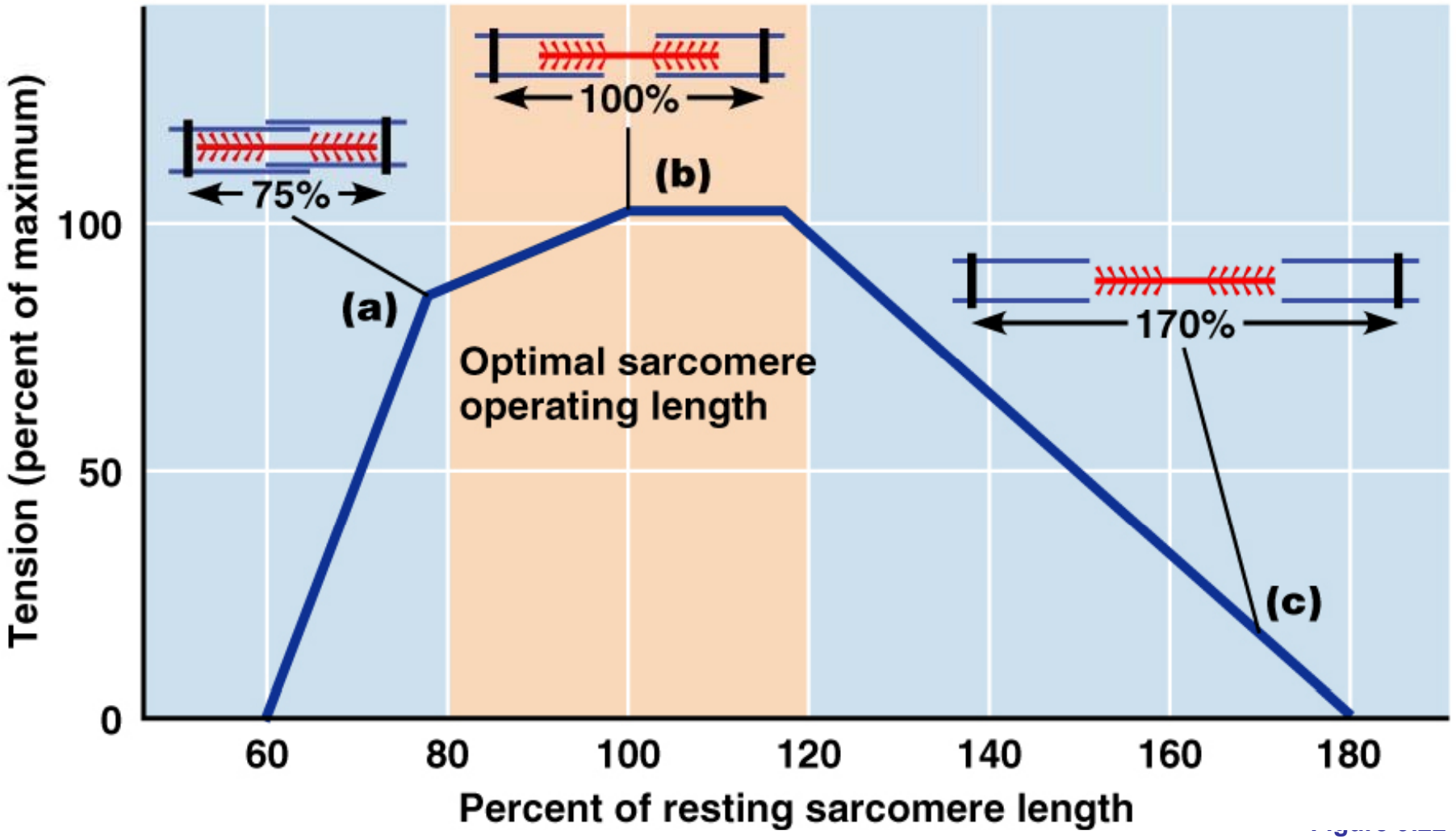


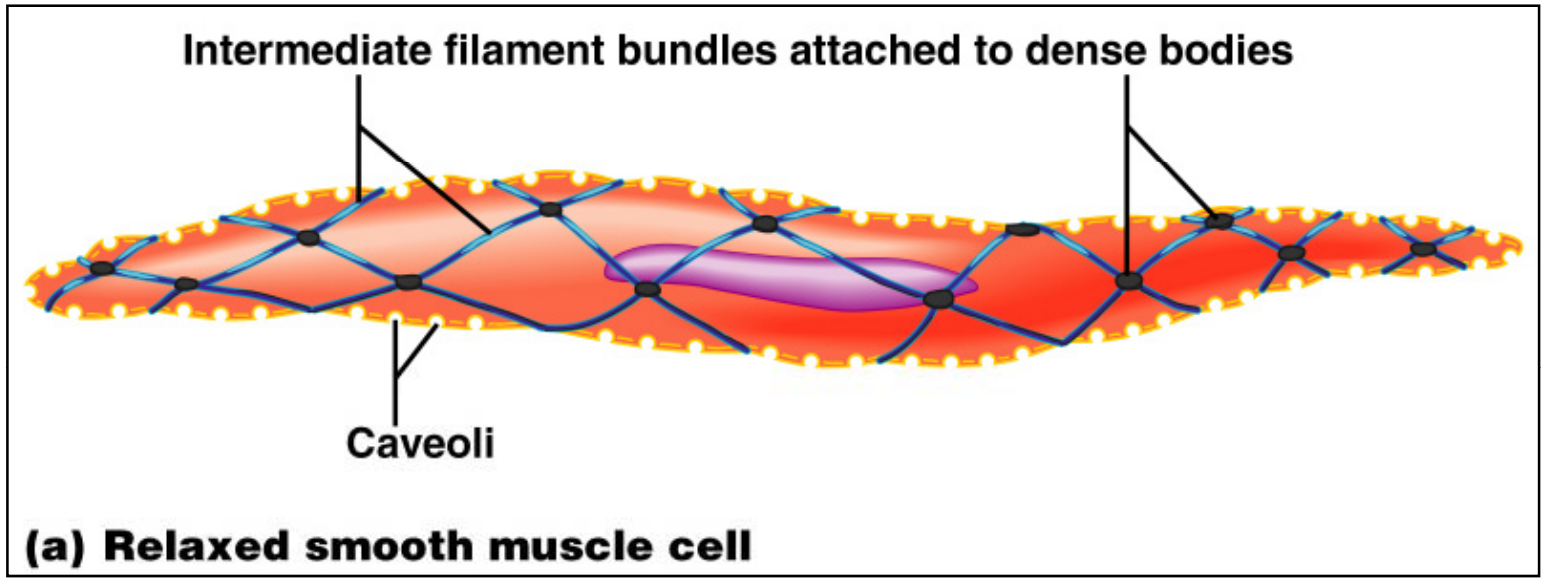
TABLE 9.2 Structural and Functional Characteristics of the Three Types of Skeletal Muscle Fibers

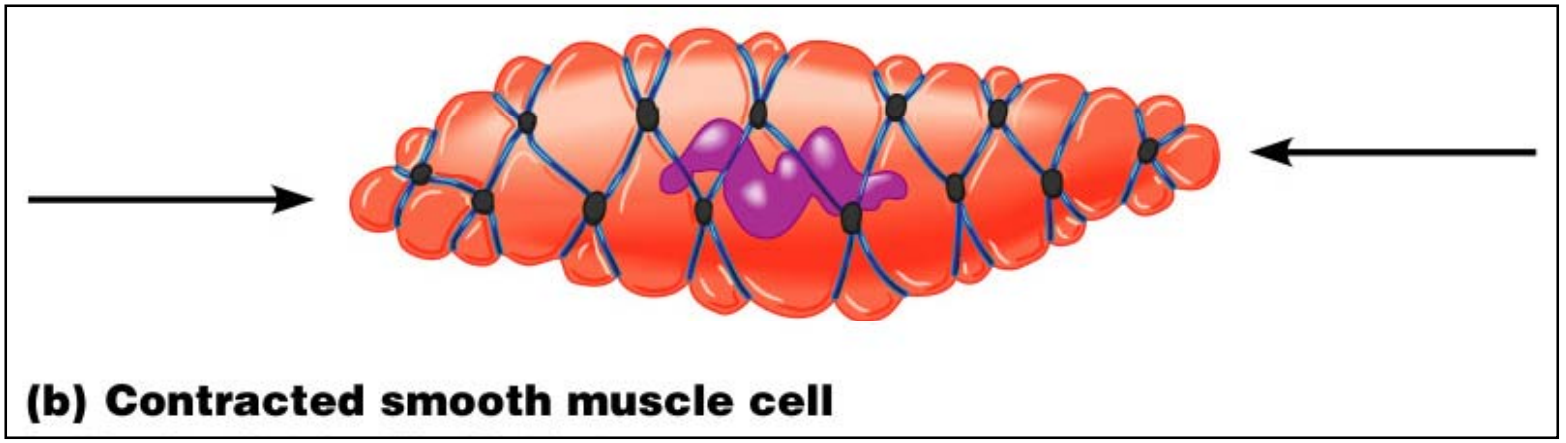
	SLOW OXIDATIVE FIBERS	FAST OXIDATIVE FIBERS	FAST GLYCOLYTIC FIBERS
METABOLIC CHARACTERISTICS			
Speed of contraction	Slow	Fast	Fast
Myosin ATPase activity	Slow	Fast	Fast
Primary pathway for ATP synthesis	Aerobic	Aerobic (some anaerobic glycolysis)	Anaerobic glycolysis
Myoglobin content	High	High	Low
Glycogen stores	Low	Intermediate	High
Recruitment order	First	Second	Third
Rate of fatigue	Slow (fatigue-resistant)	Intermediate (moderately fatigue-resistant)	Fast (fatigable)
ACTIVITIES BEST SUITED FOR			
	Endurance-type activities—e.g., running a marathon; maintaining posture (antigravity muscles)	Sprinting, walking	Short-term intense or powerful movements, e.g., hitting a baseball
STRUCTURAL CHARACTERISTICS			
Color	Red	Red to pink	White (pale)
Fiber diameter	Small	Intermediate	Large
Mitochondria	Many	Many	Few
Capillaries	Many	Many	Few

Myofilaments in Smooth Muscle

- Ratio of thick to thin filaments is much lower than in skeletal muscle
- Thick filaments have heads along their entire length
- There is no troponin complex
- Thick and thin filaments are arranged diagonally, causing smooth muscle to contract in a corkscrew manner
- Noncontractile intermediate filament bundles attach to dense bodies (analogous to *Z* discs) at regular intervals

Myofilaments in Smooth Muscle





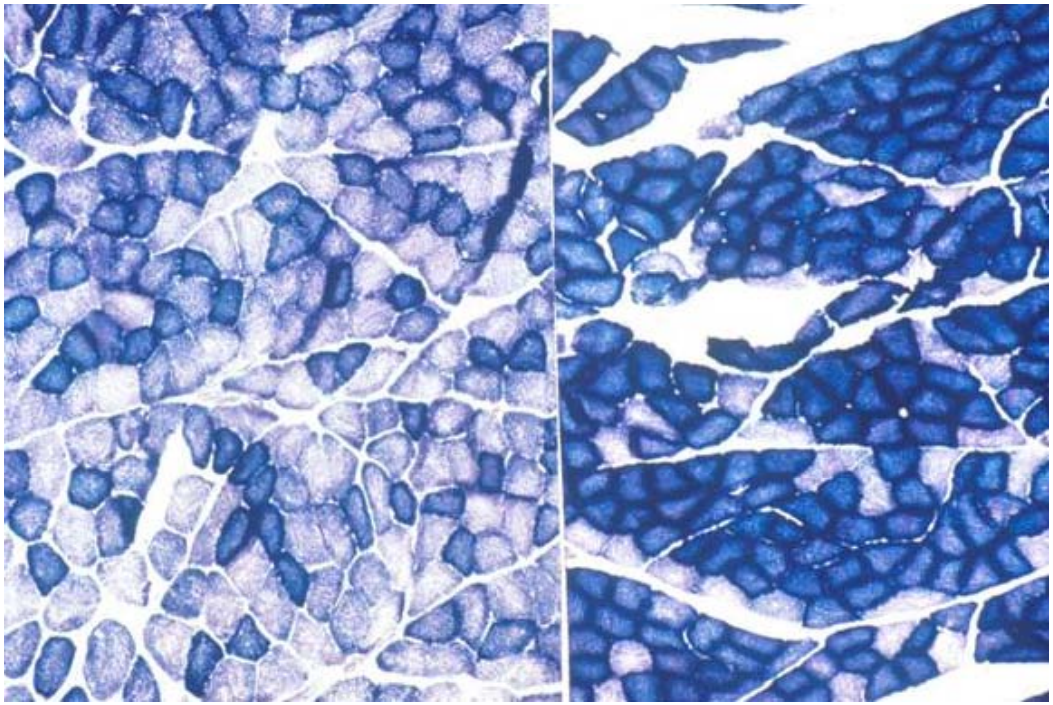
Contraction of Smooth Muscle

- Whole sheets of smooth muscle exhibit slow, synchronized contraction
- They contract in unison, reflecting their electrical coupling with gap junctions
- Action potentials are transmitted from cell to cell
- Some smooth muscle cells:
  - Act as pacemakers and set the contractile pace for whole sheets of muscle
  - Are self-excitatory and depolarize without external stimuli

Endurance training

Little hypertrophy but major biochemical adaptations within muscle fibers.

Increased numbers of mitochondria; concentration and activities of oxidative enzymes (e.g. succinate dehydrogenase, see below).



Control

12-weeks
treadmill running

Succinate dehy-
drogenase (SDH)
activity:
Low activity light
High activity dark

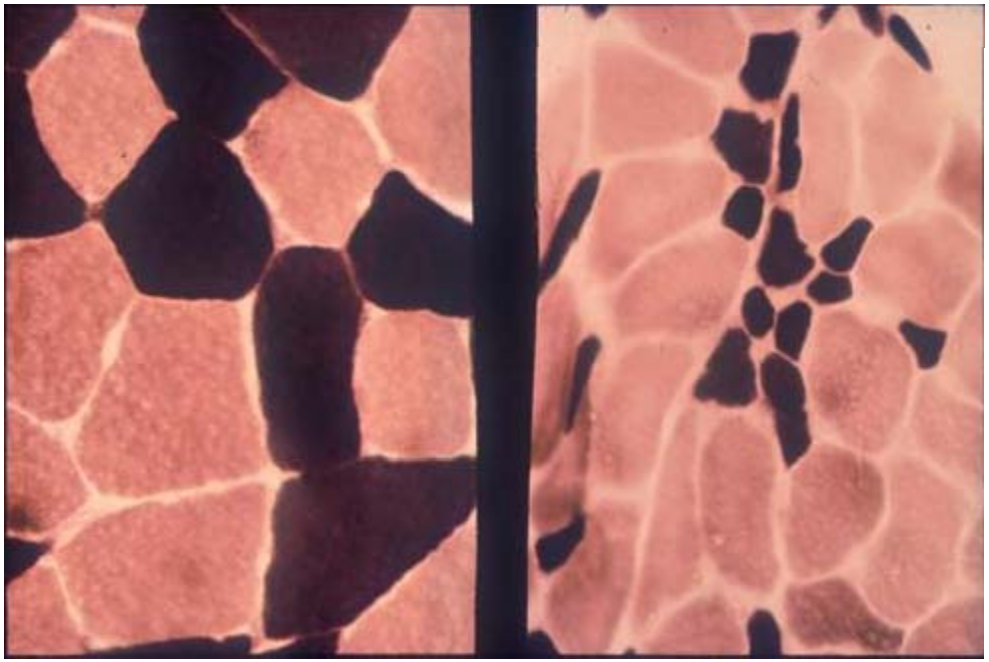
Images courtesy of John Faulkner and Timothy White

Disuse causes atrophy -- USE IT OR LOSE IT!

Individual fiber atrophy (loss of myofibrils) with no loss in fibers.

Effect more pronounced in Type II fibers.

“Completely reversible” (in young healthy individuals).



Control

Prolonged bed rest

ATPase activity:
Type I fibers light
Type II fibers dark

Images courtesy of John Faulkner

Toxins affecting NMJ

1) cobra toxin and curare
   a) block Ach receptors
   b) cause flaccid paralysis, potentially fatal respiratory arrest

2) nerve gas and insecticides
   a) inhibit AchE
   b) cause potentially fatal paralytic convulsions

3) botulism toxin
   a) block Ach release
   b) cause flaccid paralysis; potentially fatal respiratory arrest

4) tetanus toxin
   a) cause excessive Ach release from motor neurons
   b) cause potentially fatal paralytic convulsions ("lockjaw")

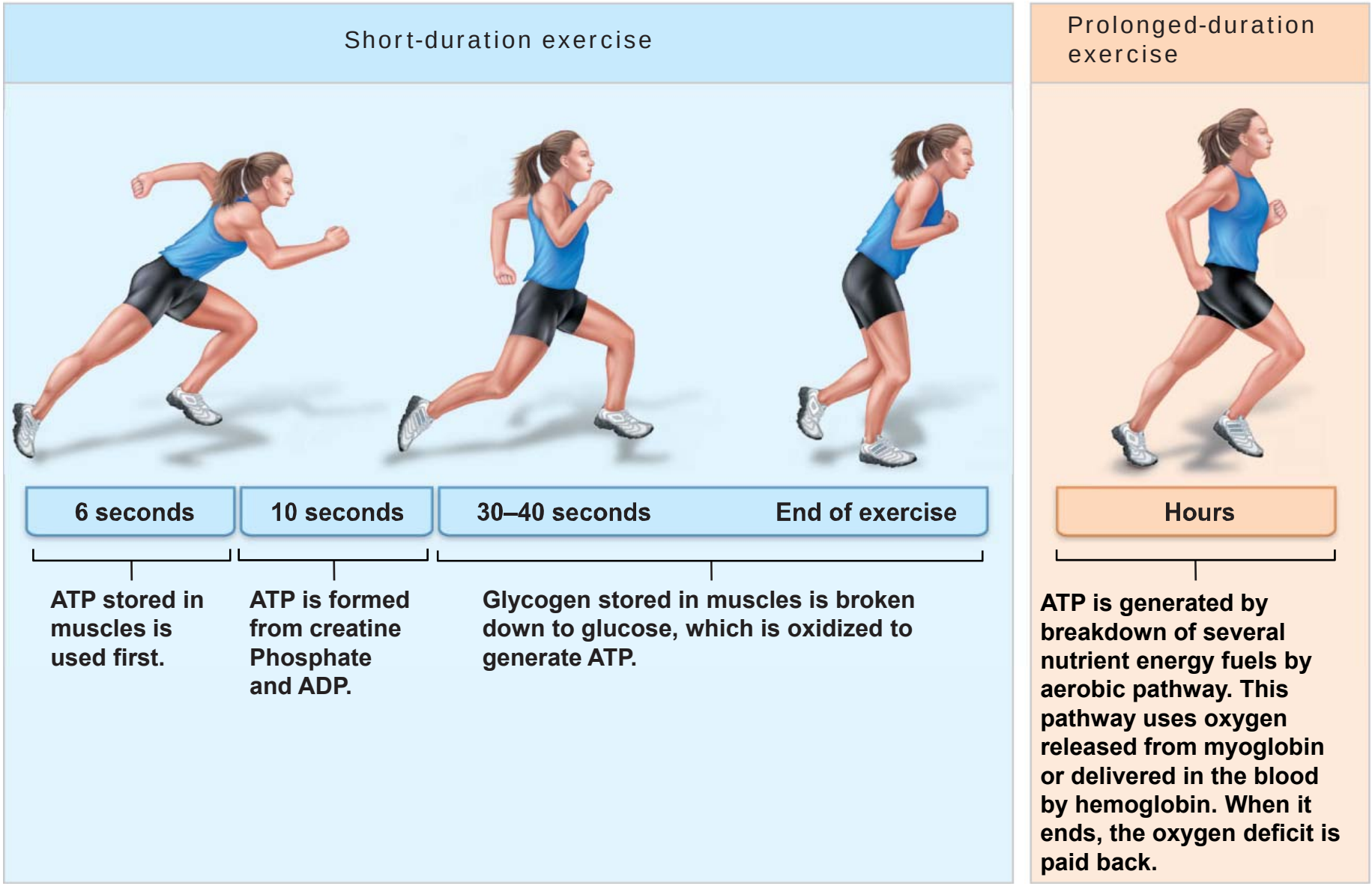

Short-duration exercise
Prolonged-duration exercise
6 seconds
10 seconds
30–40 seconds
End of exercise
Hours
ATP stored in muscles is used first.
ATP is formed from creatine Phosphate and ADP.
Glycogen stored in muscles is broken down to glucose, which is oxidized to generate ATP.
ATP is generated by breakdown of several nutrient energy fuels by aerobic pathway. This pathway uses oxygen released from myoglobin or delivered in the blood by hemoglobin. When it ends, the oxygen deficit is paid back.

Figure 9.20

Muscle Fatigue

- Physiological inability to contract
- Occurs when:
  - Ionic imbalances (K^+, Ca^{2+}, P_i) interfere with E-C coupling
  - Prolonged exercise damages the SR and interferes with Ca^{2+} regulation and release
- Total lack of ATP occurs rarely, during states of continuous contraction, and causes contractures (continuous contractions)

Oxygen Deficit

Extra O_2 needed after exercise for:

- Replenishment of
  - Oxygen reserves
  - Glycogen stores
  - ATP and CP reserves
- Conversion of lactic acid to pyruvic acid, glucose, and glycogen

Heat Production During Muscle Activity

- ~ 40% of the energy released in muscle activity is useful as work
- Remaining energy (60%) given off as heat
- Dangerous heat levels are prevented by radiation of heat from the skin and sweating

TO REVIEW

MEMBRANE EVENTS OF CONTRACTION

I. FACTORS NECESSARY TO HAVE MUSCLE EXCITABILITY

A. Cell membrane must be semipermeable
B. High extracellular concentration of sodium ions(Na+)

1. extracellular sodium ions are 10 times greater than intracellular sodium ions.

C. High intracellular concentration of potassium ions(K+)

1. intracellular potassium is 30 times higher than extracellular potassium

D. Negative intracellular voltage

1.negatively charged protein ions are prevented from exiting muscle cell; combined with the positively charged potassium ions that slowly leak out of the cell, they provide an overall negative charge to the inside of the cell

MUSCLE CONTRACTION

I. <u>MUSCLES CONTRACT ONLY IF STIMULATED</u>

A. stimulus provided by nerve impulse received from motor unit

Note: Makeup of motor unit = the motor neuron, all of its branches and all the muscle cells that it supplies or innervates

NOTE: All components of the motor unit must be intact in order for the muscle to contract.

a.To perform a voluntary muscular activity,neurons from cerebral cortex send an action potential down their axons in the spinal cord.

b. The action potential is relayed over other motor neurons that lie in the spinal cord. Their axons carry the action potential to the neuromuscular or myoneural junction, at the muscle.

NERVE IMPULSE CAUSES CHANGES AT MYONEURAL JUNCTION

_____a. Makeup of myoneural or neuromuscular junction

1) **MOTOR AXON** = that part of the motor neuron that conducts nerve impulses away from the cell body of the motor neuron in the CNS

2) **TERMINAL OR SYNAPTIC END BULB** = ballooned out end of the axon at the place where it meets the muscle cell

3) **SYNAPTIC VESICLE** = stores and releases neurotransmitter

4) **SYNAPTIC CLEFT** = space between synaptic end bulb and motor end plate of muscle cell

3) **MOTOR END PLATE** = Portion of sarcolemma in contact with the terminal or synaptic end bulb

ACETYLCHOLINE RELEASE

a. action of acetylcholine

b. Acetylcholine makes the muscle cell membrane more permeable to sodium.

DEPOLARIZATION OF MUSCLE CELL OCCURS, producing an "action potential" or charge to the inside of the cell.

a. Events in depolarization

1) Na+ moves to inside of cell changing the resting polarity

2) Depolarization causes production of the action potential or "charge" carried along the sarcolemma to the T-Tubules.

Note: As soon as the acetylcholine has initiated an action potential on the sarcolemma, the acetylcholine is destroyed by the enzyme, cholinesterase.

EFFECTS OF CALCIUM WITHIN SARCOPLASM

a. calcium binds to troponin allowing it to change its shape; this removes the blocking action of tropomyosin and leaves active sites on actin exposed.

a. calcium activates the enzyme needed to breakdown ATP into ADP,+ P + ENERGY, thus making available the energy for contraction (sliding of the filaments).

b. calcium initiates the mechanism that allows the actin filaments to slide across the myosin filaments.

HOW SHORTENING OCCURS AT MOLECULAR LEVEL

NOTE: Myosin cross bridges alternately attach to actin and detach, pulling the actin filaments toward the center of the sarcomere. The whole process is powered by the breakdown(hydrolysis) of ATP to ADP plus high energy phosphate.

a. Sliding of actin towards the center draws the "Z" lines toward each other;

1) sarcomere shortens

2) muscle fiber shortens

3) whole muscle shortens

SEQUENCE OF EVENTS LEADING TO RELAXATION OF MUSCLE. FOLLOWING CONTRACTION

1. Calcium ions actively transported back into sarcoplasmic reticulum.

a. Action of Calsequestrin = promotes the calcium pump

2. Lack of calcium ions in cytoplasm stops enzymatic action of myosin.

a. No more ATP broken down by ATP-ASE so no energy available for further contraction.

3. Adenosine diphosphate (ADP) is converted back into Adenosine Triphosphate (ATP)

4. Once the Ca++ is gone from the filaments and the ATP is regenerated, the actin and myosin slide apart and the sarcomere lengthen again. When this happens throughout the muscle cell, the muscle cell is said to relax (regain its resting length).

NOTE: Troponin-tropomyosin binding reoccurs. Remember that calcium normally unbinds the Troponin-tropomyosin complex.

Red Vs White meat

- Red muscle fibers have more mitochondria than white
- Red has more enzymes for oxidative energy metabolism
- Red contract slowly, but sustain contraction for long time
- Bursts of action potentials are 10-20/sec
- Red found in antigravity muscles (leg muscles)
- White rely on anaerobic metabolism
- White can contract rapidly (30-60/sec) and powerfully but will fatigue rapidly
- White muscles are involved in escape reflexes (jumping)
- Alpha motor units in white are bigger, larger diameter, fast conducting axons