Muscular System

10

Dipak Banerjee, Pradip Kumar Das, and Joydip Mukherjee

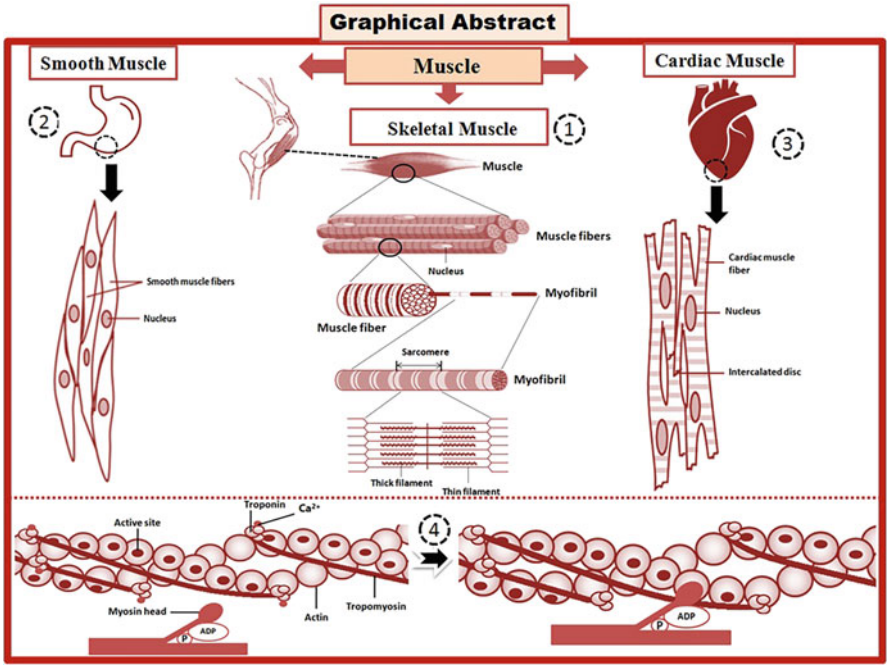
Abstract

Muscle is a soft tissue, having a special ability for contraction. The contraction of the muscle fibers creates force and that causes movement of body as well as visceral organs. Three types of muscles, namely skeletal, cardiac, and smooth muscles, are present in the body. The skeletal muscle is voluntary, while the cardiac muscle and smooth muscle are involuntary. Muscle fibers have some special properties, i.e., excitability, contractility, extensibility, and elasticity. The skeletal muscle fibers have a long cylindrical structure with many nuclei located in the periphery. The active contractile unit of muscle is known as sarcomere. Each myofibril contains several types of protein cells, called myofilaments. During contraction, action potential propagates through the sarcolemma and travels down the T-tubules causing the sarcoplasmic reticulum to release Ca^{2+} ions to the sarcoplasm. The myosin head then attaches to the binding site of the G-actin molecule, and the formation of crossbridges occurs. The following power stroke occurs, which forces and leads to the shortening of muscle fiber. Muscle relaxation occurs when the release of the neurotransmitter stops at the neuromuscular junction. In smooth muscle, cells are small and have one central nucleus. No neuromuscular junctions exist; instead, varicosities transmit the nerve impulse to cells. Contraction and relaxation are slower than the skeletal muscle, and less energy is required for contraction. Cardiac muscle cells are small and branched and have a single nucleus. An intercalated disc is present at the junction between two cells. Gap junction located at the intercalated disc spreads action potential from one cell to another.

D. Banerjee (✉) · P. K. Das · J. Mukherjee
Department of Veterinary Physiology, West Bengal University of Animal & Fishery Sciences, Kolkata, West Bengal, India

P. K. Das et al. (eds.), *Textbook of Veterinary Physiology*, https://doi.org/10.1007/978-981-19-9410-4_10

Graphical Abstract



Description of the graphic: (1) Skeletal muscle fibers have a long cylindrical structure with many nuclei located in the periphery. The active contractile unit of muscle is known as sarcomere. Each myofibril contains several types of protein cells, called myofilaments. (2) In smooth muscle, cells are small and have one central nucleus. Two types of smooth muscles are single-unit smooth muscle and multiunit smooth muscle. (3) Cardiac muscle cells are small and branched and have a single nucleus. An intercalated disc is present at the junction between two cells. Gap junction located at the intercalated disc spreads action potential from one cell to another. (4) During contraction of skeletal muscle, action potential propagates through the sarcolemma and travels down the T-tubules causing the sarcoplasmic reticulum to release Ca^{2+} ions to the sarcoplasm. The myosin head then attaches to the binding site of the G-actin molecule, and the formation of crossbridges occurs

Keywords

Skeletal muscle · Cardiac muscle · Smooth muscle · Muscle contraction · Muscle fibers · Crossbridge

Learning Objectives

- Functions, properties, and types of muscle tissues
- Microscopic structure of a skeletal muscle
- Major phases of skeletal muscle contraction and relaxation and their neural control
- Sources of energy for skeletal muscle contraction, mechanism of muscle fatigue, and rigor mortis
- Structure and contraction mechanisms of smooth and cardiac muscle
- Different muscular disorders of domestic animals

10.1 Basic Characteristics of Muscle

Muscle is a soft contractile tissue, originated from the embryonic mesodermal layer. Muscle consists of muscle cells or muscle fibers. Contraction of muscle fibers generates force and that causes motion (i.e., locomotion or movement of visceral organs). The word "muscle" derived from the Latin word "musculus," which means "little mouse." It may be due to the shape of muscles like mouse, or contracting muscles look like mouse moving under the skin. Muscle fibers contain contractile filaments myosin (also known as thick filament) and actin (also known as thin filament). These protein filaments slide over one another and produce contraction. According to structure, situation, and function, muscles are generally classified into skeletal muscle (attached to bones), smooth muscle (present in the visceral organs), and cardiac

muscle (found in heart). On the basis of action, muscles are classified into voluntary and involuntary muscle. Muscles which can be controlled by animal's own will are voluntary muscle like skeletal muscle, whereas muscles which are not under voluntary control are called involuntary muscle like smooth and cardiac muscle. Depending on the presence of striation, muscles can be classified into striated and nonstriated muscles. Skeletal muscle and cardiac muscle are striated muscles, whereas smooth muscle is a nonstriated muscle. The energy for muscle contraction is provided by ATP molecules, which are generated mainly through oxidation of fats and carbohydrates, but anaerobic reactions also occur.

10.1.1 Functions of Muscle

1. ***Movement of body or locomotion***: The major function of muscular tissue is locomotion or movement of body. The movement is of two types, i.e., gross movement and fine movement. Gross movement includes large, coordinated movements like walking, running, and swimming. Fine movement includes smaller movements, which occur in the limbs. The movements are mainly under voluntary control, but some movements are reflexive.
2. ***Maintenance of posture of the animal***: Skeletal muscles maintain the body in the right position when an animal is in sitting or standing condition. Posture of an animal depends on strong and flexible muscles, whereas stiff, weak, or rigid muscles result in abnormality in posture. This abnormality in posture for a long time may cause pain in joint and muscles.
3. ***Joint stability***: Tendons help in joint stability. Tendons of knee and shoulder joint are very important for stabilization, and muscles of the abdomen, back, and pelvic region are also involved in stabilization of the body and help in different activities.
4. ***Respiration***: Breathing process in animals depends on the contraction of respiratory muscles, mainly diaphragm and intercostal muscles. During inspiration, contraction of diaphragm results in movement of air into the lungs down the pressure gradient, whereas during expiration, relaxation of the diaphragm leads to increase in pressure which pushes air out of the lungs. Forced breathing or deep breathing requires help from other muscles, like muscles of abdomen, back, and neck.
5. ***Circulation***: Cardiac muscle helps in contraction and relaxation of heart, which results in circulation of blood throughout the body. Smooth muscles are present in blood vessels and regulate the constriction and relaxation of blood vessels, blood flow, as well as blood pressure.
6. ***Digestion***: In the gastrointestinal tract (GI tract), contraction of the smooth muscle helps in the movement of the food particle by a wavelike motion called peristalsis. This process also helps in the mixing of food particles with stomach acid and enzymes. Smooth muscles also help to pass the undigested food out of the body as feces.
7. ***Urination***: In the urinary system, smooth as well as skeletal muscles are there and the muscles along with nerves work together to hold and release urine from the urinary bladder. Some abnormal cases of urinary system like poor bladder control or retention of urine are caused by damage of the nerves that carry signals to the muscles.
8. ***Parturition***: During parturition, contraction of uterine smooth muscles helps in expulsion of fetus as well as fetal membrane. Oxytocin hormone initiates the contraction process.
9. ***Vision***: Muscles adjacent to the eye control the movements of eyeball. These muscles around eyes also help the eyes to maintain a stable image, scan the surrounding area, and track moving objects.
10. ***Protection of organ***: Muscles provide protection to different parts of the body, bones, as well as visceral organs. Muscle absorbs shock and protects a visceral organ or bone.
11. ***Thermoregulation***: Muscular system has a significant role in thermoregulation. During heat stress, relaxation of smooth muscles of blood vessels results in increased peripheral circulation and quick loss of heat from the surface of the body. However, during cold stress, contraction of smooth muscles of blood vessels reduces peripheral blood circulation and helps in the reduction of heat loss and maintaining body temperature. During cold stress, shivering thermogenesis also helps in body temperature maintenance.
12. ***Communication***: Muscles help in communication between animals as well as between birds by making sounds and different types of activities.

Except these functions discussed above, muscles are also involved in different physiological functions. These functions are discussed in details later in this chapter (in the discussion portion of individual muscles).

10.1.2 Properties of Muscle Tissue

Muscle fibers have some special properties, which help them to carry out their functions and differentiate them from other types of cells in the body.

The properties are excitability, contractility, extensibility, and elasticity:

1. ***Excitability***: The ability of muscle cells to respond to a stimulus is known as excitability. The stimuli are

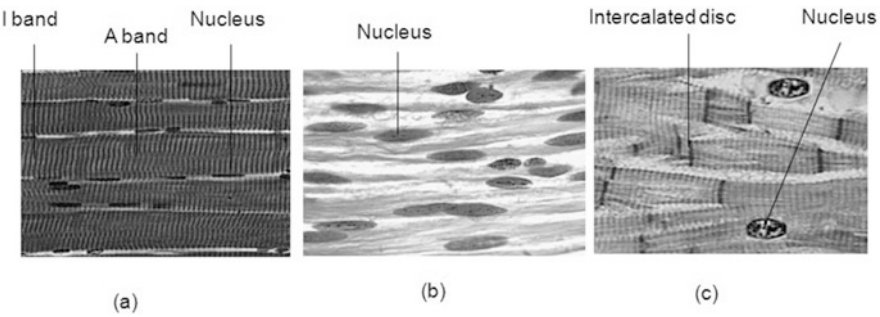


Fig. 10.1 Histological structure of three types of muscles. (**a**) Skeletal muscle. Muscle fibers showing striations with multiple peripherally located nucleuses. (**b**) Smooth muscle. No striations are present. Each cell contains single centrally located nucleus. (**c**) Cardiac muscle. Muscle fibers are branched having intercalated disc and one nucleus per cell

neurochemical, mechanical, and chemical in nature. When the muscle fibers are properly stimulated, then the muscle will respond to the stimulus.

2. ***Contractility***: Contractility is the ability of a muscle to contract and generate pulling force when properly stimulated.
3. ***Extensibility***: Muscle cells can lengthen in response to stretch, which is called extensibility. This property is more evident in smooth muscle compared to skeletal muscle.
4. ***Elasticity***: It is the ability of muscle fiber to recoil to its original resting length once stretched.

10.1.3 Types of Muscles

Three types of muscles are there in the body, i.e., skeletal muscle, smooth muscle, and cardiac muscle.

1. ***Skeletal muscle***: Skeletal muscles are mainly attached with bones (via tendons), maintain posture of the animal, and control the movement or locomotion. Some skeletal muscles are directly attached with other muscles or skin like in the face where different muscles control facial expression.
   Skeletal muscle is under voluntary control and innervated by somatic motor neurons but can maintain posture or balance even in subconscious state. Muscle fibers are striated, elongated, and tubular in shape with multiple nuclei located peripherally (Fig. 10.1).
2. ***Smooth muscle***: Smooth muscle is present in the walls of visceral organs, like organs of digestive system, respiratory system, blood vessels, glands, uterus, eye, and skin. Smooth muscles regulate the functions and movement of such systems, such as movement of food through GI tract via peristalsis or expulsion of fetus during parturition, propel urine, dilate/constrict pupils, regulate blood flow, etc. In some locations, they are autorhythmic like in GI tract. Smooth muscle is controlled involuntarily by endocrine and autonomic nervous systems. No striation is present in the muscle, and cells are uninucleated (Fig. 10.1).
3. ***Cardiac muscle***: Cardiac muscle is located only in the heart, controls the cardiac contractions, and pumps blood all over the body. Like skeletal muscle, cardiac muscle is also striated. The contraction is slow and rhythmic and involuntary. Cells are branched, and intercalated discs are present. Lengths of cardiac myocytes are lesser than skeletal muscle fiber and contain 1–2 centrally located nuclei (Fig. 10.1 and Table 10.1).

10.2 Skeletal Muscle

Skeletal muscles are attached to the bones, are voluntary in nature, and have striations, so they are also called striated muscle. About 40% of the body weight is comprised of skeletal muscle. The major function of skeletal muscle is the movement or locomotion.

Constant little contractions of the skeletal muscle are essential to hold the body upright in any position, even at rest. Skeletal muscles also maintain skeletal stability and protect the skeletal structure from any damage. They act as an external barrier to the body and protect the bones as well as visceral organs from external shock or trauma. They also support the weight of the organs. They also help in the generation of heat by shivering thermogenesis (Fig. 10.2).

10.2.1 Skeletal Muscle: Gross and Microscopic Structure

During embryonic development, embryonic stem cells produce immature muscle cells known as myoblasts (blast = "precursor") (Fig. 10.3). Later, several myoblasts fuse together to produce one long muscle cell or muscle fiber and so each muscle fiber contains multiple nuclei.

Table 10.1 Comparison between skeletal, cardiac, and smooth muscles

	Skeletal muscle	Smooth muscle	Cardiac muscle
Location	Attached to bones	Present in the walls of visceral organs, blood vessels, eye, glands, uterus, skin	Present in the heart
Functions	Responsible for different types of movement like body movement and locomotion, posture, communication, facial expression, and breathing	Propel urine, mix food in digestive tract, dilate/ constrict pupils, and regulate blood flow	Helps in cardiac contractions and pumps blood all over the body. Involuntary and controlled by autonomic nervous systems and hormones
Appearances	Fibers are striated and tubular with peripherally located multiple nucleus	Nonstriated, smooth appearance, and mononucleated cells	Striated mononucleated cells
Control	Voluntary in nature and controlled by somatic motor neurons	Controlled involuntarily by endocrine and autonomic nervous systems	Involuntary, controlled by autonomic nervous system
Contraction	Both contraction and relaxation are very fast	Slow contraction and relaxation, can maintain for extended period	Moderate contraction and relaxation
Fatigue	Easily fatigue	Do not fatigue	Do not fatigue

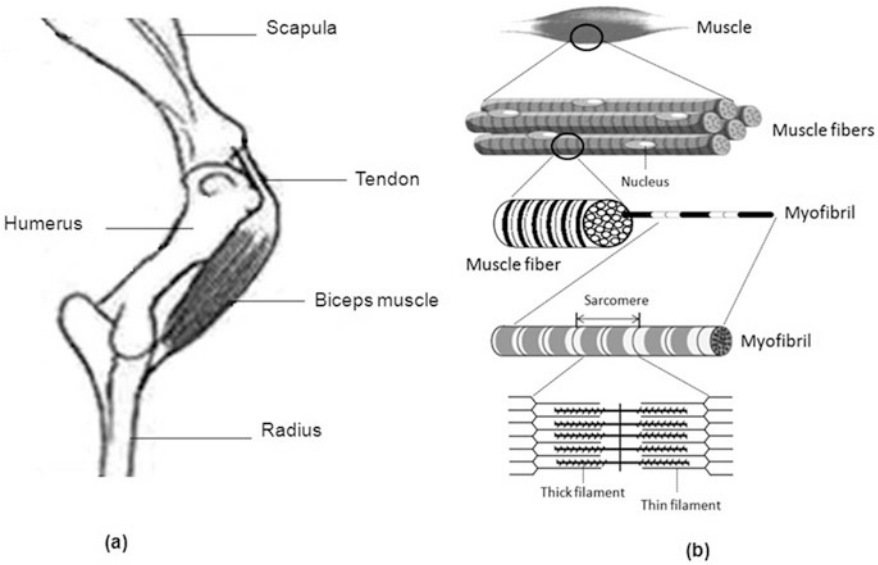


Fig. 10.2 (**a**) Biceps muscle of horse. (**b**) Structure of skeletal muscle. Muscle fibers are long cylindrical with multiple nucleuses. Myofibrils are bundles of rodlike contractile elements made up of myofilaments—thick and thin filaments. The muscles are striated due to the regular arrangement of thick and thin filaments

Each muscle fiber is enclosed by a fine layer of loose (areolar) connective tissue called endomysium ("endo"—inside) (Fig. 10.4). Several muscle fibers form a bundle known as fascicles. In fascicles, blood vessels and nerves are present. Fascicles are covered by a connective tissue known as perimysium ("peri"—around). The fascicles are bundled together and form a muscle. The entire muscle is enclosed by a layer of dense fibrous connective tissue called epimysium ("epi"—outside, and "mysium"—muscle).

Different layers of connective tissue extend away from the ends of the muscle fibers themselves and form the tendons or aponeurosis, which connects muscles to bone. Each muscle fiber is covered by its plasma membrane, known as sarcolemma.

The cytoplasm or sarcoplasm contains a huge amount of glycogen (polysaccharide of glucose), which is utilized for energy. Myoglobin, which is a red color pigment, is also present in sarcoplasm. The major portion of the sarcoplasm (almost 80% of the intracellular space) is occupied by myofibrils, which are rodlike cylindrical contractile proteins. Myofibrils run longitudinally. Around 100–1000 myofibrils are present in each muscle fiber. Myofibrils are compactly

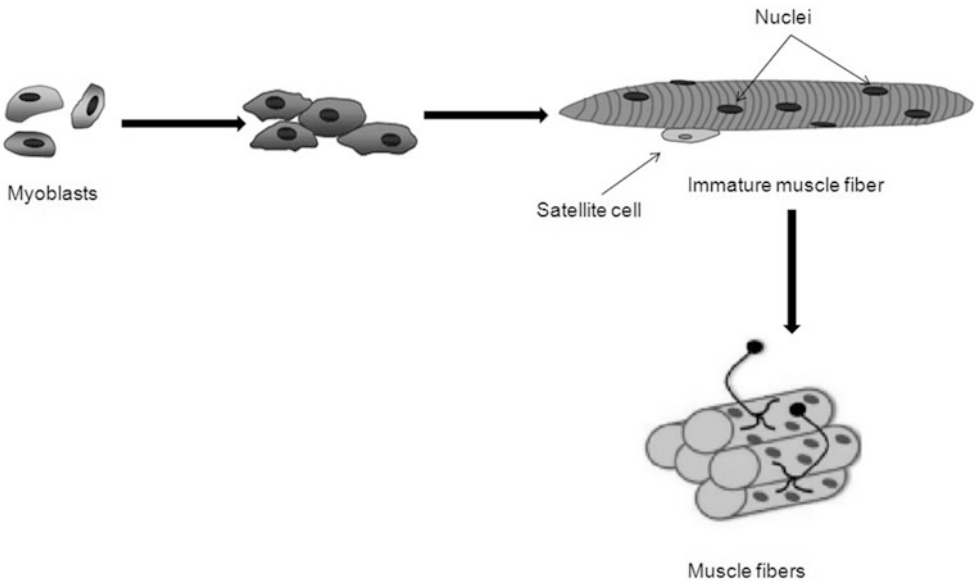


Fig. 10.3 Development of skeletal muscle fiber. During embryonic stage, a number of uninucleated myoblasts fuse to each other and form multinucleated skeletal muscle cell or muscle fiber. Cells which do not fuse remain as satellite cells and function as muscle stem cells

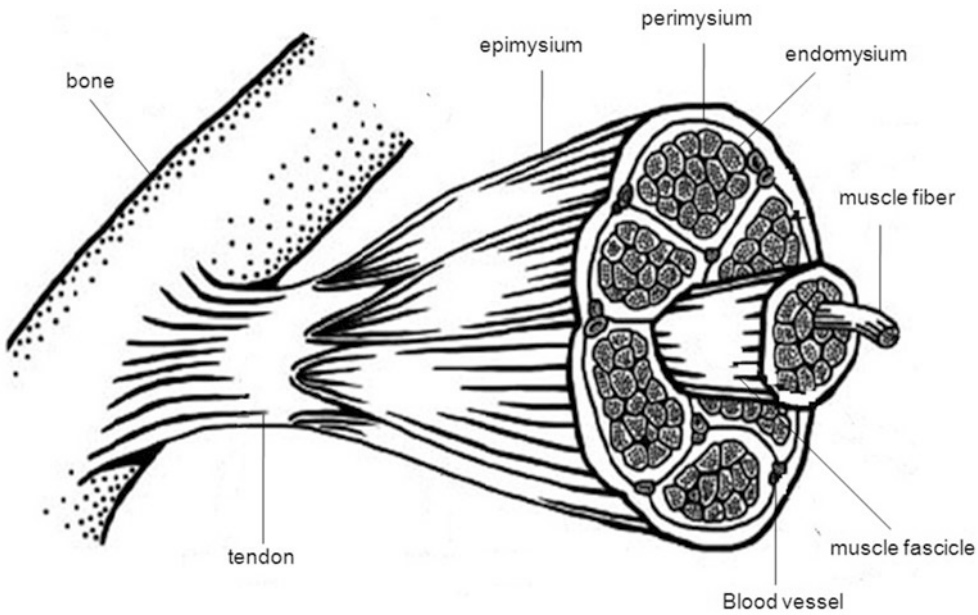


Fig. 10.4 Cross section of skeletal muscle. Individual fiber is surrounded by **endomysium**. A number of muscle fibers form a **fascicle** which is surrounded by **perimysium**. Several fascicles form a muscle, and the entire muscle is covered by **epimysium**. All the connective tissue layers of muscle unite at the end and form a **tendon**, which helps in the attachment of muscle with **bone**

packed, and the cell organelles remain sandwiched between them. The nuclei get pressed to the periphery of the cell just under the sarcolemma.

10.2.1.1 Description of a Single Muscle Fiber of Skeletal Muscle

An individual muscle cell or muscle fiber has the following parts:

1. ***Sarcolemma***: Sarcolemma is the plasma membrane of individual muscle fiber. Sarcolemma is enclosed by the basement membrane and endomysium (Fig. 10.4). It is an excitable membrane. Sarcolemma has many properties similar with nerve cell membrane. Regular invaginations are seen in the sarcolemma, which form tubes that remain around the myofibrils, known as transverse tubules or T-tubules. During muscle contraction, action potential spreads through the sarcolemma, and through T-tubules, it reaches the sarcoplasmic reticulum.
2. ***Sarcoplasm***: The cytoplasm in the muscle fiber is known as sarcoplasm. Like that of other cells, different cell organelles are present in the sarcoplasm. Large numbers of glycosomes are present in the sarcoplasm. Small fat droplets and large amount of myoglobin are also present. Myofibrils fill the sarcoplasm. Mitochondria are present in between the myofibrils, near the Z line and A bands.

3. ***Sarcoplasmic reticulum***: Sarcoplasmic reticulum (SR) is the smooth endoplasmic reticulum (SER) present in the muscle fiber (Fig. 10.5). They form a network of tubes surrounding the myofibrils and remain closely associated with myofibrils. SR stores the Ca^{2+}. During muscle contraction, this stored Ca^{2+} ions are released out from the SR to the sarcoplasm and reabsorbed during relaxation. The membrane of SR has "pumps" (active transport) for the transport of Ca^{2+}. Along with the "pumps," the SR membrane has special types of openings, or "gates," for transport of Ca^{2+} ions. During relaxation of muscle, these gates remain closed and Ca^{2+} ions are unable to pass through the membrane, and the Ca^{2+} concentration is very high in SR and very low in the sarcoplasm. During muscle contraction, when an impulse reaches the sarcolemma, it propagates through the T-tubule to SR membrane. The action potential initiates the opening of Ca^{2+} "gates" and Ca^{2+} comes out of the SR into the sarcoplasm.
4. ***Transverse tubules***: Transverse tubules or T-tubules are narrow tubelike structures formed due to invaginations of the sarcolemma (Fig. 10.5). These tubules extend into the interior of the muscle fiber and encircle each myofibril but never open inside the muscle fiber and form sarcotubular system. They carry action potentials deep into the muscle fiber. The T-tubules are present at the junction between the A and I bands. SR remains parallel to the myofibrils. SR of skeletal muscles forms right-angle enlargements at the junctions of A and I bands near the T-tubules. These enlargements of the SR are called terminal cisternae ("end sacs"). One T-tubule along with two terminal cisternae is known as the triad. Triad plays a very important function in skeletal muscle contraction. The membrane of T-tubule has a number of voltage-dependent proteins, known as dihydropyridine (DHP) channels or L-type calcium channels. But these channels do not allow calcium to move through them. They are physically associated with the calcium-release channels on the terminal cisternae called ryanodine receptor channels (RyR). When action potential comes to sarcolemma and sarcolemma becomes depolarized, the DHP channel identifies the depolarization and causes opening of the RyR channels, resulting in the release of calcium from the terminal cisternae of the SR.

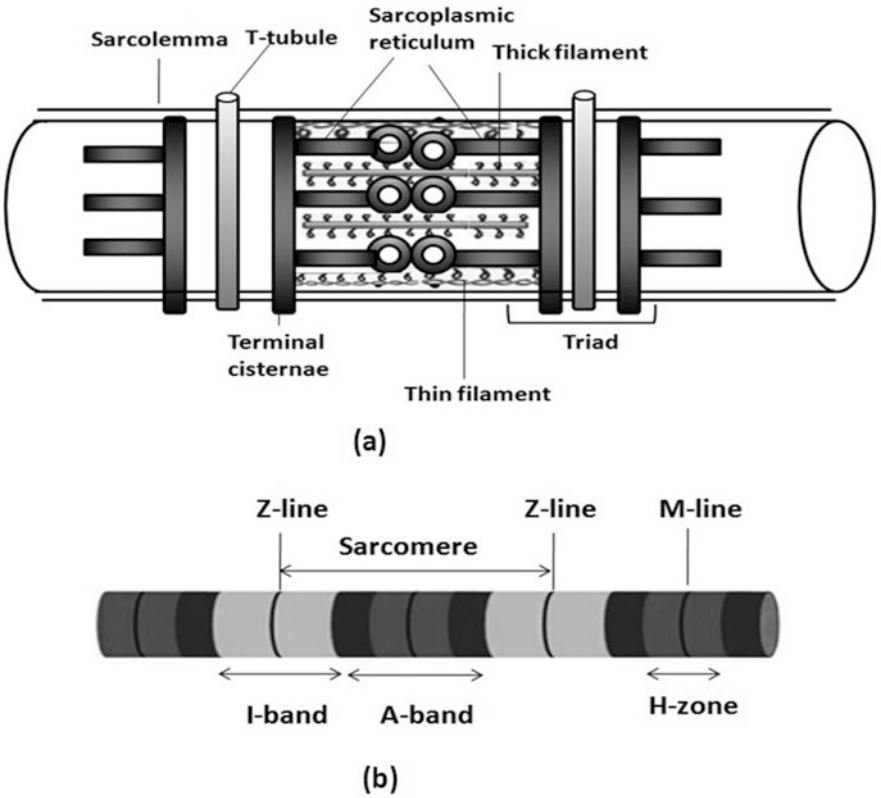


Fig. 10.5 Skeletal muscle fiber. (**a**) Muscle fiber containing sarcoplasmic reticulum and T-tubules. One T-tubule along with two terminal cisternae forms the triad. (**b**) Sarcomere of muscle fiber (the sarcomere is the unit of skeletal muscle fiber, which is the length between two consecutive Z-lines). Z-disc or Z-line: It is a line that separates two adjacent sarcomeres; **A band**: they are dark band known as anisotropic bands or A bands (includes overlapping myosin and actin filaments). **I bands**: the area where only actin filaments are present; the light bands are known as isotopic bands or I bands. **H zone**: a lighter zone in the middle of each dark band or **A band** (the area where only myosin filaments are present). **M-line**: a darker line at the middle of each H zone (central line of the sarcomere where myosin filaments are anchored)

5. ***Myofibril***: Myofibrils are bundles of rodlike contractile elements made up of myofilaments. Almost 80% of the muscle volume is occupied by myofibrils. They are composed of different types of proteins, which form the myofilaments. Contractile elements are present in the myofilaments which help in contraction. The functional contractile unit of skeletal muscle is known as sarcomere ("sarc" means muscle, "mere" means part). Sarcomere is the region of a myofibril between two consecutive Z-lines (Fig. 10.5). The striated appearance in skeletal muscle is produced due to regular, organized arrangement of myofilaments. So light and dark striations are present in each cell. The dark areas in muscle fiber are known as anisotropic bands or A bands, and the light areas are called isotopic bands or I bands. Each myofibril contains several varieties of protein molecules, called myofilaments. The larger or thick myofilaments are made up of the protein, myosin, and the smaller thin myofilaments are chiefly made up of the protein, actin.
   Z-disc or Z-lines are fine dense lines that appear in the middle of each I band. Z-line separates two adjacent sarcomeres from each other. In the middle of each dark band or A band, a lighter zone is present known as H zone (H for "helle"—"bright"). Each H zone has a darker line known as M-line (M for "middle"), which runs right down the middle of the A band. Sarcomere of muscle fiber: Sarcomere is the unit of skeletal muscle fiber, which is the length between two consecutive Z-lines. Z-disc or Z-line: It is a line that separates two adjacent sarcomeres; A bands are dark band known as anisotropic bands or A bands (include overlapping myosin and actin filaments). I bands are the area where only actin filaments are present; the light bands are known as isotopic bands or I bands. H zone is a lighter zone in the middle of each dark band or A band (the area where only myosin filaments are present). M-line is a darker line at the middle of each H zone (central line of the sarcomere where myosin filaments are anchored).
6. ***Myofilaments***: Myofilaments are fine stringlike contractile filaments of myofibrils; they consist of thick filament (myosin) and thin filament (actin). Myosin and actin are contractile proteins, which interact with each other to generate force, resulting in shortening of muscle fiber. Two major regulatory proteins troponin and tropomyosin bind to actin and regulate the attachment of myosin head with actin during muscle contraction.

Thick filaments: Thick myofilaments are mainly made up of the protein, myosin (myosin II). Each thick myofilament is approximately 15 nm in diameter composed of about 300 myosin molecules. Each myosin is made up of six protein subunits, two heavy chains and four light chains. The shape of heavy chains is similar to a golf club, with a long shaft-like structure connected to globular myosin head (Fig. 10.6). The heavy chains of myosin are twisted over one another forming a double-helix structure.

The link between the head and the shaft of the myosin molecules remains as a hinge, and so it is known as hinge region. This hinge region is able to bend and generate power stroke during muscle contraction. The centers of the thick filaments are comprised of the shaft portions of the heavy chains. Each head of myosin has two light chains. Each myosin head has a binding site for actin and an ATPase, which hydrolyzes ATP during muscle contraction.

Thin filaments: The thin filaments contain three different proteins, i.e., actin, tropomyosin, and troponin (Fig. 10.7). Each actin molecule has an active site for attachment with myosin head during muscle contraction. Other two proteins, tropomyosin and troponin, are

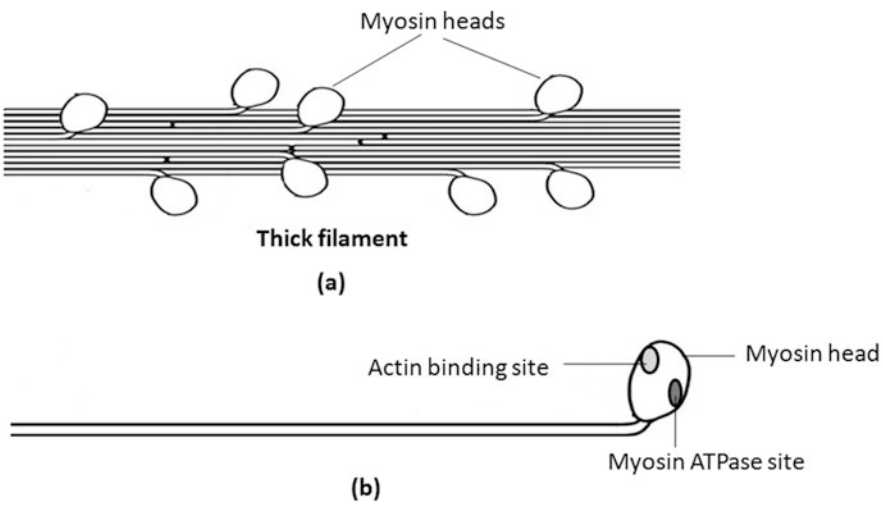


Fig. 10.6 Thick filament and myosin heavy chain. (**a**) Half of the myosin molecules have their heads remain towards one end of the thick filament, and the other half remain in the opposite direction. The heads of the myosin bind to the active sites on the actin during muscle contraction. (**b**) Myosin heavy chain, with a long shaft-like structure connected to globular myosin head. Myosin head has a binding site for actin and an ATPase, which hydrolyzes ATP during muscle contraction

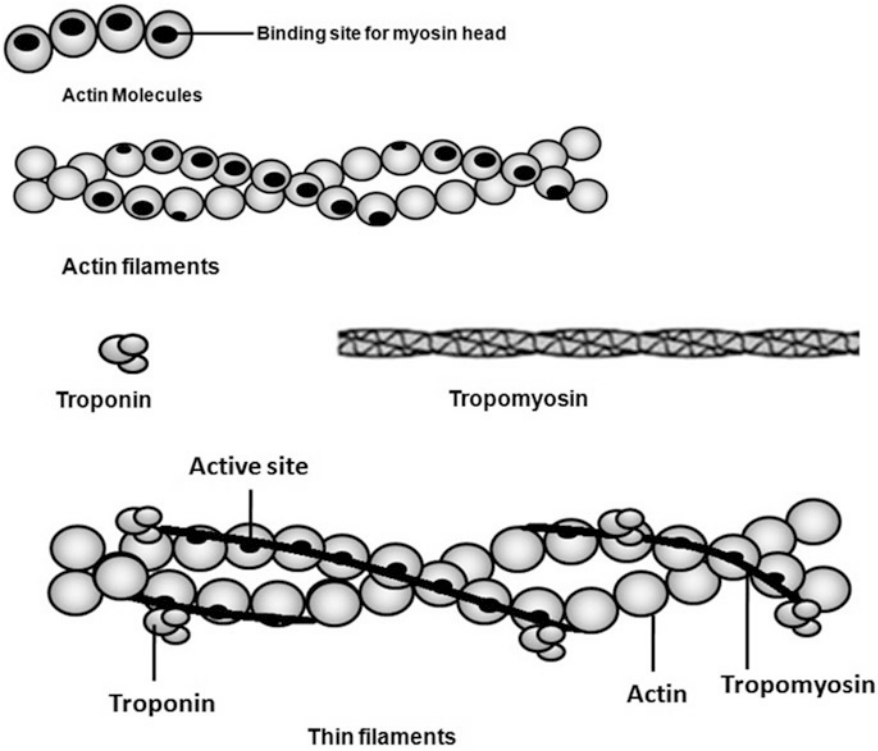


Fig. 10.7 Thin filaments: actin, troponin, and tropomyosin. Strings of globular actin (G-actin) twisted over one another like a double-helical structure. Tropomyosin made up of coiled-coil dimer and the two strands run diametrically opposite to each other along the actin filaments and cover the active sites on actin. Troponin is a complex of three different globular protein subunits, i.e., troponin C, troponin T, and troponin I

regulatory subunits which are bound to actin. Actin is a globular protein called globular actin or G-actin (free monomeric units). Each F-actin (filamentous actin which is the polymer form) is formed by two strings of globular actin (G-actin) twisted over one another like a double-helical structure, which looks like twisting two strands of pearls with each other where individual G-actin molecule is like a pearl necklace. Tropomyosin is another component of thin filament. It is a long threadlike polypeptide that remains parallel to each F-actin strand and covers the active sites of each G-actin molecule when the muscle remains in relaxed state, whereas during contraction, tropomyosin is replaced from its position and the active site on the actin is exposed to which myosin head binds. Tropomyosin has a structural similarity with that of the myosin tail, being a coiled unit of two protein chains. Tropomyosin made up of coiled-coil dimer and the two strands run diametrically opposite to each other along the actin filaments. Another component of thin filament troponin is a complex of three different globular protein subunits, i.e., troponin C, troponin T, and troponin I.

Troponin C has a receptor for Ca^{2+} ions and binds to calcium ions (released from the sarcoplasmic reticulum) on activation of the muscle contraction. Another subunit troponin T is the tropomyosin-binding subunit of troponin, which binds with tropomyosin and keeps it in this position on F actin strands. Troponin I binds to actin, holds the troponin-tropomyosin complex in proper position, and inhibits binding of myosin head with actin. It inhibits the interaction between myosin and actin.

During skeletal muscle contraction, Ca^{2+} binds to troponin C, which results in a conformational change in the entire complex, and tropomyosin is released from its position and myosin-binding sites on the G-actin subunits become exposed for attachment with myosin.

Titin or connectin is another important structural protein that functions like a big rubber band in muscles. It is a long elastic protein that runs within the thick filament and extends from the Z-disc to the M. Titin is the third most abundant protein in the muscle after myosin and actin. It is the largest known protein in the body and has around 30,000 amino acids. Titin acts as a molecular spring in the skeletal muscle and prevents overstretching as well as damage of muscle. Titin helps to return the muscle to its normal length when the muscle is stretched.

Dystrophin is another muscle protein, which connects the cytoskeleton of a muscle fiber to the extracellular matrix through the cell membrane. Dystrophin is located between the sarcolemma and the outermost myofilaments. Mutation of the gene coding for dystrophin is one of the major causes of a class of muscle diseases collectively known as muscular dystrophy (MD).

As a complex structure, sarcomere contains a number of proteins; few of them are listed in Table 10.2.

Table 10.2 Different proteins present in the sarcoplasm of vertebrate striated muscles and their properties

Sl no.	Sarcoplasmic protein	Molecular weight and subunits	Location	Functions	Related diseases
1	Actin	42 kDa, globular monomer	Thin filament (~360 molecules), helical polymer	Filament formation, myosin ATPase activation, filament sliding. Binds myosin, tropomyosin, troponin, nebulin, α-actinin	FHC, NM
2	α-Actinin	190 kDa (homodimer 2 × 95 kDa); CH, spectrin-like, EF hand domains	Z filaments linking actin and titin filaments	Integrates Z-line. Binds actin, titin, CapZ, myopalladin, myozenin, myotilin, ZASP/Cypher, synemin	
3	Cap Z (β-actinin)	68 kDa, heterodimer (36 and 32 kDa subunits) 1 per filament	Caps barbed end of thin filament, in Z-line	Length stabilization. Binds actin, α-actinin	
4	Desmin/vimentin	~55 kDa, α-helical core, nonhelical ends	Surrounds and runs between Z-lines	Sarcomere strengthening and connection with each other and cell membrane	Desmin myopathy
5	FATZ (calsarcin-2, myozenin)	32 kDa	Z-line	Binds α-actinin, γ-filamin, telethonin	
6	γ-Filamin	CH domain, Ig repeats	Z-line	Binds myozenin, myotilin	
7	MM creatine kinase	86 kDa, dimer (2 × 43 kDa)	Line M4 and M4′ of M-line	Buffers [ATP], bridges thick filaments	
8	M protein	165 kDa, Ig and Fn domains	Line M1 of M-line	Bridges thick filaments. Binds myosin	
9	Myomesin	185 kDa, Ig and Fn domains	M-line	Binds myosin and titin	
10	Myopalladin	145 kDa	Z-line	Anchors nebulin in Z-line. Binds α-actinin, nebulin, and CARP	
11	Myopodin	80–95 kDa	Z-line	Bundles actin filaments. It is a zyxin-binding protein, has capabilities to regulate cell growth and motility	
12	Myosin	~520 kDa, hexamer, 2 heavy chains (223 kDa), 4 light chains (~20 kDa)	Thick filament (~300 molecules), helical polymer	Filament formation, ATPase, filament sliding, modulation of contraction. Binds actin, titin, MyBPs, M protein, myomesin	FHC
13	MyBP-C (-X) and MyBP-H	140 kDa (C, X), 86 kDa (H) modular (Ig and Fn domains)	Stripes 3–11 (C, X), 3 (H), 43 nm apart in each half of A band	Myofibrillogenesis, filament stabilization, modulation of contraction. Binds myosin, titin	FHC
14	Myotilin	57 kDa	Z-line	Binds α-actinin, γ-filamin	MD
15	Nebulin (nebulette)	800 kDa (nebulette 109 kDa), single chain. Modular (35-amino acid actin-binding modules)	Extends from Z-line (C terminus) to filament tip (N-terminus)	Thin-filament length determination and stabilization. Binds actin, tropomyosin, tropomodulin, myopalladin	NM
16	Nestin	220–240 kDa, IF protein	Z-line periphery, with desmin	Similar to synemin but mainly in developing muscle	
17	Paranemin	180 kDa, IF protein	Z-line periphery, with desmin	Similar to synemin	
18	Plectin	High molecular weight, α-helical coiled coil	IFAP, at and between Z-lines	Connects Z-line IFs to actin filaments, cell membrane, and organelles. Binds actin, IFs	MD
19	Skelemin	~200 kDa, modular structure, splice variant of myomesin	Periphery of M line	Connects myofibrils at M-line. Binds myosin, IFs, and integrins	
20	Synemin	230 kDa	Z-line periphery; co-polymer with desmin	Links between Z-lines and cell membrane. Binds α-actinin, vinculin	
21	Syncoilin	64 kDa, IF protein	Z-line and sarcolemma	Links IFs to sarcolemma via dystrophin complex.	
22	Telethonin (T-cap)	19 kDa	Z-line, at N-terminus of titin	Binds titin, myozenin, cell membrane K channel	MD
23	Titin (connectin)	~3 MDa (single polypeptide). Modular (Ig and Fn domains, PEVK segment)	Extends from Z-line (N-terminus) to M-line (C-terminus)	Developmental sarcomeric template, muscle elasticity. Binds myosin, MyBP-C, α-actinin, myomesin, telethonin	FHC
24	Tropomodulin (Tmod)	40 kDa, monomer, 1 or 2 per filament	Caps pointed end of thin filament	Thin-filament length stabilization. Binds actin, nebulin, tropomyosin	
25	Tropomyosin	65 kDa, coiled-coil dimer of 2 α-helices (32 kDa each)	Thin filament, ~50 molecules 38 nm repeat	Filament stabilization and regulation. Binds actin, troponin, nebulin, tropomodulin	FHC, NM

(continued)

Table 10.2 (continued)

Sl no.	Sarcoplasmic protein	Molecular weight and subunits	Location	Functions	Related diseases
26	Troponin	80 kDa, complex of TnC (18 kDa), TnI (20–24 kDa), TnT (31–36 kDa)	Thin filament, one per tropomyosin, 38 nm repeat	Regulation of contraction. Binds actin, tropomyosin	FHC
27	ZASP/Cypher	~32 kDa, PDZ-motif protein	Z-line	Binds actinin	Myopathy

Source: Craig and Padrón (2004)
KEY: *CH* calponin homology, *MD* muscular dystrophy, *NM* nemaline myopathy, *FHC* familial hypertrophic cardiomyopathy

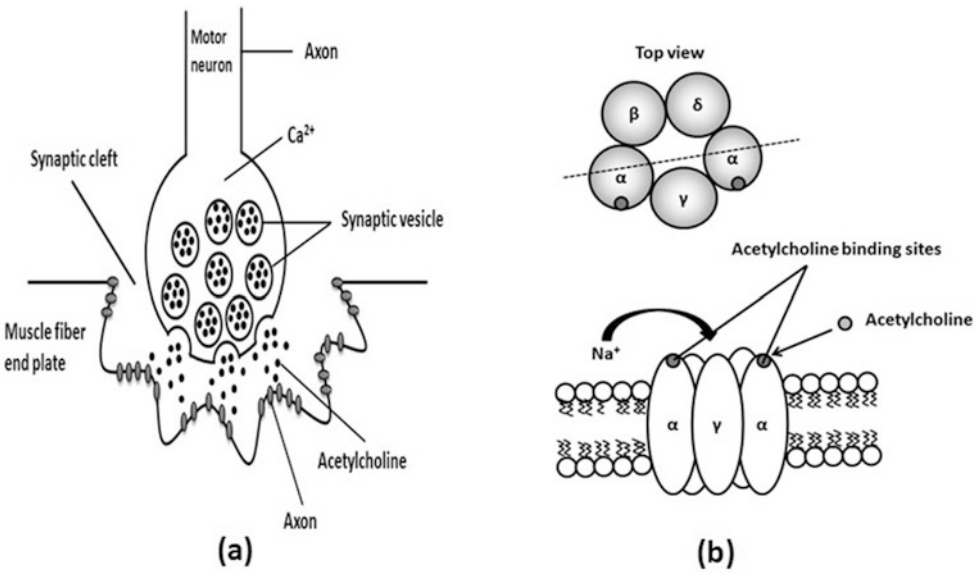


Fig. 10.8 Neuromuscular junction and acetylcholine receptor channel. (**a**) Neuromuscular junction and (**b**) acetylcholine receptor channel: The nicotinic acetylcholine receptor is a ligand-gated ion channel, composed of five subunits arranged symmetrically around a central conducting pore. Upon binding acetylcholine, the channel opens and allows diffusion of sodium (Na^+) and potassium (K^+) ions through the conducting pore

10.2.2 Neuromuscular Junction

Nerve impulse or action potential travels through a motor neuron to a skeletal muscle fiber to trigger the contraction of that muscle. The site attachment between the nerve ending and the skeletal muscle is known as neuromuscular junction. It is like that of the synapse between two neurons. This junction is a chemical synapse formed by an axon terminal of the neuron and motor end plate of a skeletal muscle fiber (Fig. 10.8). The motor neuron can have a number of terminal branches; each of these nerve endings attaches with a separate muscle fiber.

10.2.3 Motor Unit

In the muscle, motor neuron forms many branches and each branch innervates a single muscle fiber. The neuron along with the muscle fiber (innervated by that motor neuron) is known as the motor unit. The size of the motor unit depends on the function of that muscle it innervates. Muscles of limbs and postural muscles are attached with largest motor units, in which one axon supplies many muscle fibers, whereas the smallest motor units, in which one axon may supply only a few muscle fibers, are seen in association with eye movements.

During contraction of a muscle, a number of motor units frequently work together and act like a group and these motor units within a muscle are called motor pool. These muscle fibers within a motor unit are of same type and contract together when activated. The number of motor units also controls the force of contraction.

The terminal branch of the axon does not actually make contact with the muscle fiber but is separated from it by a gap of approximately 50 nm wide called synaptic cleft.

The membrane of nerve terminal releases neurotransmitter (acetylcholine), which has a receptor on postsynaptic membrane. The nerve ending has membrane-bound vesicles containing neurotransmitter. These vesicles are synthesized from the cell body of the neuron and come to nerve ending as an empty bag of proteins.

In the nerve endings, the membrane has choline transporter, which transports choline from outside of the neuron to inside (Fig. 10.9). Then in the nerve endings, mitochondria synthesize acetyl-CoA, and this acetyl-CoA attaches with choline with the help of the enzyme choline acetyl transferase

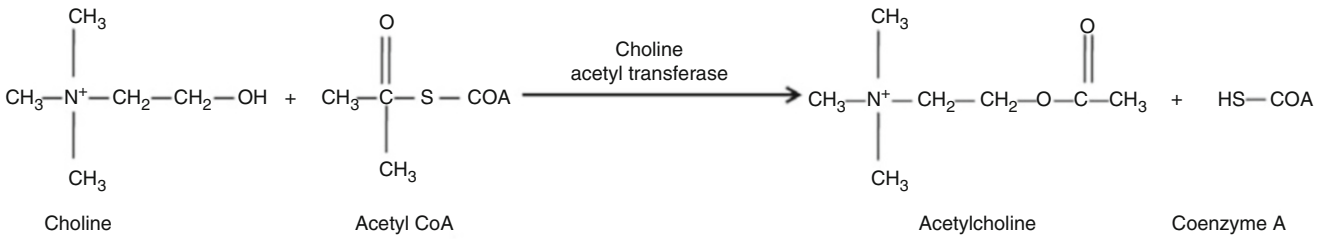


Fig. 10.9 Molecular pathway of acetylcholine synthesis

and forms acetylcholine. The enzyme choline acetyl transferase is also synthesized from the cell body of the neuron.

Then acetylcholine enters into the synaptic vesicles through the transporter on the membrane of the vesicle and is stored in the synaptic vesicle.

10.2.4 Transmission of Action Potential Through Neuromuscular Junction

1. Nerve impulses or action potential travels from the brain or spinal cord to initiate the muscle contraction of skeletal muscle. An action potential propagates through the motor neuron and reaches the axon terminal.
2. During this propagation of action potential through the membranes of nerve endings, the voltage-gated sodium channel opens. This results in the influx of Na^{2+} inside the nerve endings.
3. As Na^{2+} enters inside the nerve ending, the charges of the membrane change from the resting membrane potential to depolarization, and it activates the depolarization-sensitive calcium channel. Now voltage-gated calcium channels open and Ca^{2+} diffuses into the terminal.
4. The axon terminal contains membrane-bound synaptic vesicles, which are filled with the neurotransmitter acetylcholine (ACh).
   Calcium entry causes the synaptic vesicles to release acetylcholine neurotransmitter through exocytosis process. The membrane of synaptic vesicles contains a calcium-sensitive protein called synaptobrevin, which is an intrinsic membrane protein of small synaptic vesicles. Synaptobrevin is a specific secretory organelle of neurons, which accumulates neurotransmitters and participates in their calcium-dependent release by exocytosis.
   Another calcium-sensitive protein is also present on the membrane of nerve endings called syntaxin (syntaxins are a family of membrane-integrated Q-SNARE proteins participating in exocytosis). As soon as the calcium ions bind with the calcium-sensitive protein, i.e., syntaxin on presynaptic membrane, they transform into active configuration and then calcium-sensitive protein on synaptic vesicle, i.e., synaptobrevin attached with it, and a fusion of membrane of synaptic vesicle with the membrane of axon terminal occurs. Then the membrane is dissolved at the site of attachment and results in the release of acetylcholine in the synaptic cleft through exocytosis.
5. Acetylcholine diffuses across the synaptic cleft and binds to the acetylcholine receptors on the motor end plate, which is a ligand-gated cation channel (Fig. 10.9).
   Acetylcholine moves from nerve membrane to motor end plate through the synaptic cleft. On the motor end plate, there are receptors (also called nicotinic cholinergic receptor) for acetylcholine attachment (the channel composed of pentameric proteins 2 α, β, γ, and δ). There are two attachment sites for acetylcholine on a single channel.
6. ACh binding causes ligand-gated cation channels to open. These ion channels are permeable to both Na^+ and K^+.
7. Na^+ enters the muscle fiber, and K^+ exits the muscle fiber. More Na^+ moves inside, and K^+ goes outside. The greater influx of Na^+ relative to outward flux of K^+causes the membrane potential to less negative and the local potential is generated which is also called motor end plate potential.
8. Then the entry of more number of Na^+ ions changes the end plate potential to threshold potential.
   Then this threshold potential causes opening of voltage-gated Na channel nearer to motor end plate. Then more number of Na^+ ions enter inside the cell through the voltage-gated Na^+ channel, and as a result, an action potential generation occurs which propagates along the sarcolemma.
9. The action potential travels across the sarcolemma and is propagated down the T-tubules. The T-tubules are filled with extracellular fluid, high in sodium (Na^+) and low in potassium (K^+) ions.
10. Before the discussion of spreading of action potential and starting of muscle contraction, let us describe how the stimulation of the ACh receptors is terminated.

For relaxation of muscle, ACh should be removed from the synaptic cleft. It is initiated when ACh is cleaved (split) by an enzyme called acetylcholinesterase, which remains in the synaptic cleft. Acetylcholinesterase splits ACh into acetate (acetyl) and choline.

The acetate diffuses out of the synaptic cleft and choline, which is an essential nutrient in the vitamin B group (B4), and is taken up by the axon terminal, where it is recycled to make more acetylcholine.

10.2.5 Muscle Contraction

A series of molecular events occur during muscle contraction known as the crossbridge cycle. The following steps occur during contraction (Fig. 10.10).

10.2.5.1 Crossbridge Formation

The action potential spreads through the sarcolemma, and it reaches the T-tubules. The action potential triggers SR. The resultant change in potential causes the voltage-gated channels in the T-tubule to respond. In the T-tubule, these channels are known as dihydropyridine channels (DHP) or L-type Ca^{2+} channels. They are mechanically linked to ryanodine receptor channels (RyR), which are calcium channels located in the membrane of sarcoplasmic reticulum. When the membrane potential changes, then the DHP channel opens and Ca^{2+} ions come out of the sarcoplasmic reticulum and diffuse into the sarcoplasm. Then Ca^{2+} ions bind to the troponin C. The binding of Ca^{2+} ions causes conformational change in troponin. Then tropomyosin which covers the active site of the actin moves from its position, which results in the exposure of active site of G-actin molecule. Now myosin head attaches with the binding site on G-actin molecule and the formation of crossbridges occurs.

10.2.5.2 Power Stroke Generation

When muscle remains in relaxed state, the myosin head is "cocked." ADP and phosphate (Pi) remain attached with myosin head. As the myosin head is attached with actin, the Pi detaches from the myosin head and energy is released. This energy results in bending of myosin head. The bending or power stroke forcefully pulls the actin past the myosin. ADP is also released from the myosin during the power stroke. Myosin heads pull the thin filament towards the middle and sarcomere shortens.

10.2.5.3 Crossbridge Detachment

For considerable shortening of muscle fiber, the myosin heads must be detached from the actin and reattached with the next actin molecule. When another ATP attaches with myosin head, the attachment of myosin head with actin becomes weaker and myosin head detaches.

10.2.5.4 Reactivation of Myosin Heads

The ATPase present in the myosin heads hydrolyzes the ATP into ADP and Pi, which causes the head to "recock" (the recovery stroke), preparing it for the next power stroke.

The hydrolysis of ATP releases energy which re-energizes the myosin head for the next power stroke. During muscle contraction, each myosin molecule undergoes the entire

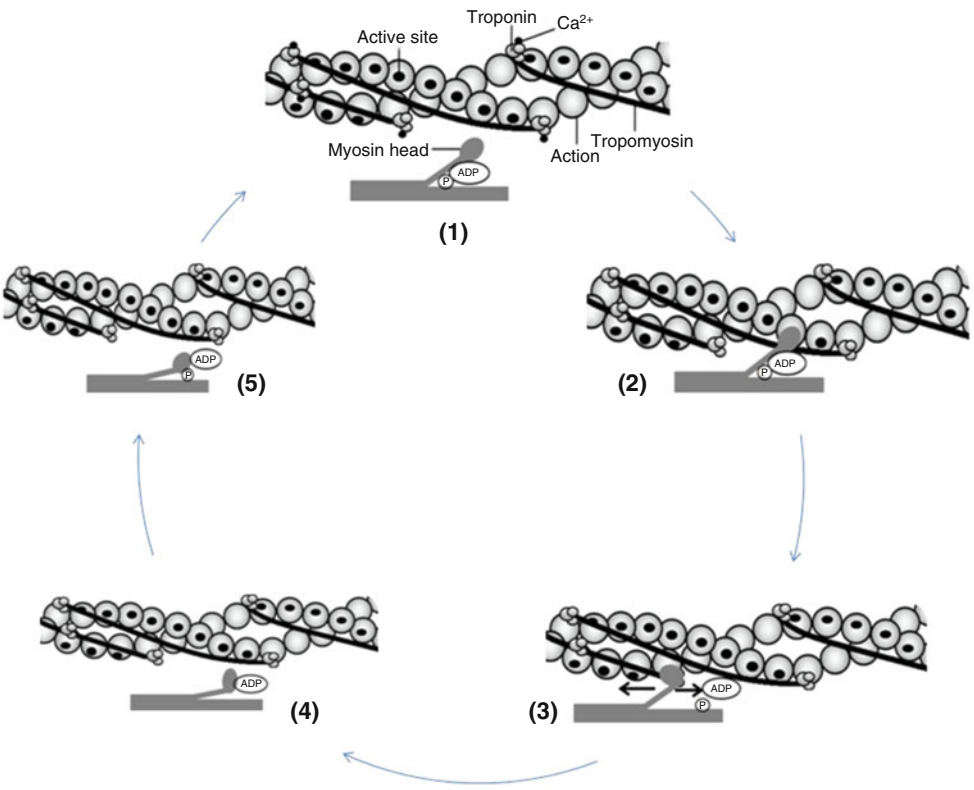


Fig. 10.10 Pathway of skeletal muscle contraction. (1) The active site on the actin is exposed as Ca ions bind to troponin. (2) The myosin head forms a crossbridge with actin. (3) During the power stroke, the myosin head bends, and ADP and phosphate are released. (4) A new molecule of ATP attaches to the myosin head, causing the crossbridge to detach. (5) ATP hydrolyzes to ADP and phosphate, which returns the myosin to the "cocked" position

crossbridge cycle numerous times, so the process is known as crossbridge cycling. The crossbridge cycle will repeat as long as the active site in actin is exposed. As the cycle repeats, the sliding of thin filaments over the thick filaments occurs and Z-lines come closer, resulting in shortening of sarcomere. This shortening causes the whole muscle to contract. As long as Ca^{2+} is present and the active sites are exposed, the process will continue.

10.2.6 Muscle Relaxation

During relaxation of muscle, the release of neurotransmitter (acetylcholine) stops. The remaining acetylcholine is broken down into acetate and choline by acetylcholinesterase. This stops the release of Ca^{2+} from the sarcoplasmic reticulum (SR). Then Ca^{2+} ions diffuse away from troponin C and are pumped back into sarcoplasmic reticulum (SR) by the ATP-dependent Ca^{2+} pump in SR membrane.

Tropomyosin returns back to its original position and covers the active site on the individual G-actin molecules. This prevents crossbridges from reforming. A new ATP binds to the myosin head. Binding of actin and myosin stops, and relaxation of muscle fiber takes place.

Know More. . .. . .
The sliding filament model of muscle contraction explains the fact that when skeletal muscle fibers contract, the individual proteins (actin and myosin) do not shorten. Rather, they slide over each other. ATP is necessary for detachment of myosin heads from actin. Also it is interesting that when a sarcomere contracts, both the H zone and the light I band shrink in width, while the dark A band does not appear to narrow.

10.2.7 Muscle Tone

Muscle always maintains a tension or resistance to stretch (Fig. 10.11). This tension or resistance to stretch is called muscle tone. Skeletal muscles are seldom completely relaxed, or flaccid, even at that time of rest when a muscle does not produce any movement. During rest, little contraction is present in the muscle fibers, which are essential for maintaining the posture, balance of the body, generating the reflexes, and controlling functions of different organs. Muscle tone is also seen in cardiac and smooth muscles. A complex interaction of nervous system and muscles is required for the activation of a few motor units at a time.

That is why muscles not at all fatigue completely because some motor units can recover from fatigue when others are active. The absence of the skeletal muscle tone results in the absence of low-level contractions that lead to loss of resistance to passive stretching muscle. This type of muscle tone is called hypotonia. Hypertonia occurs due to any damage of central nervous system (CNS), such as the cerebellum, or due to loss of innervations to the skeletal muscle. Hypotonic muscles show a flaccid appearance and exhibit functional impairments, such as weak reflexes.

Excessive muscle tone is called hypertonia, which results in hyperreflexia (excessive reflex responses). Hypertonia often occurs due to the damage of upper motor neurons in the CNS. Hypertonia is seen in muscle rigidity or spasticity. This type of condition is seen in neurological disorders in the body like Parkinson's disease.

10.2.8 Types of Muscle Contraction

Force (tension) and length (shortening) are two important variables for description of skeletal muscle contraction. The force which is exerted by a muscle on an object during contraction is known as muscle tension, whereas the force that is exerted by an object to a muscle is known as load (weight of the object). On the basis of the force of contraction and change of muscle length, muscle contractions are of two types.

10.2.8.1 Isometric Contraction

When the tension of muscle increases but the length of the muscle remains the same, then the contraction is known as an isometric contraction (iso = same, metric = length). In this type of contraction, muscle provides force but no movement occurs at the joint and muscle length remains unchanged. Isometric contractions of muscles are very important for maintaining posture or stabilizing a joint. Examples of activities where muscles use isometric contraction include pushing an object that was initially stationary or holding a weight in a certain place above the ground.

10.2.8.2 Isotonic Contraction

When the muscle length changes but the muscle tension remains unchanged, then the contraction is known as an isotonic contraction (tonic = tension). Isotonic contraction is seen during walking, running, and different types of activities.

Based on the pattern of muscle length changes, the isotonic contraction is classified into concentric and eccentric contractions.

If the entire muscle shortens during contraction, then it is called concentric contraction. For example, during lifting a weight, the concentric contraction of the biceps muscle causes the arm to bend at the elbow and lifting the weight towards the shoulder.

If the total length of a muscle increases when tension is produced, then the contraction is called eccentric contraction.

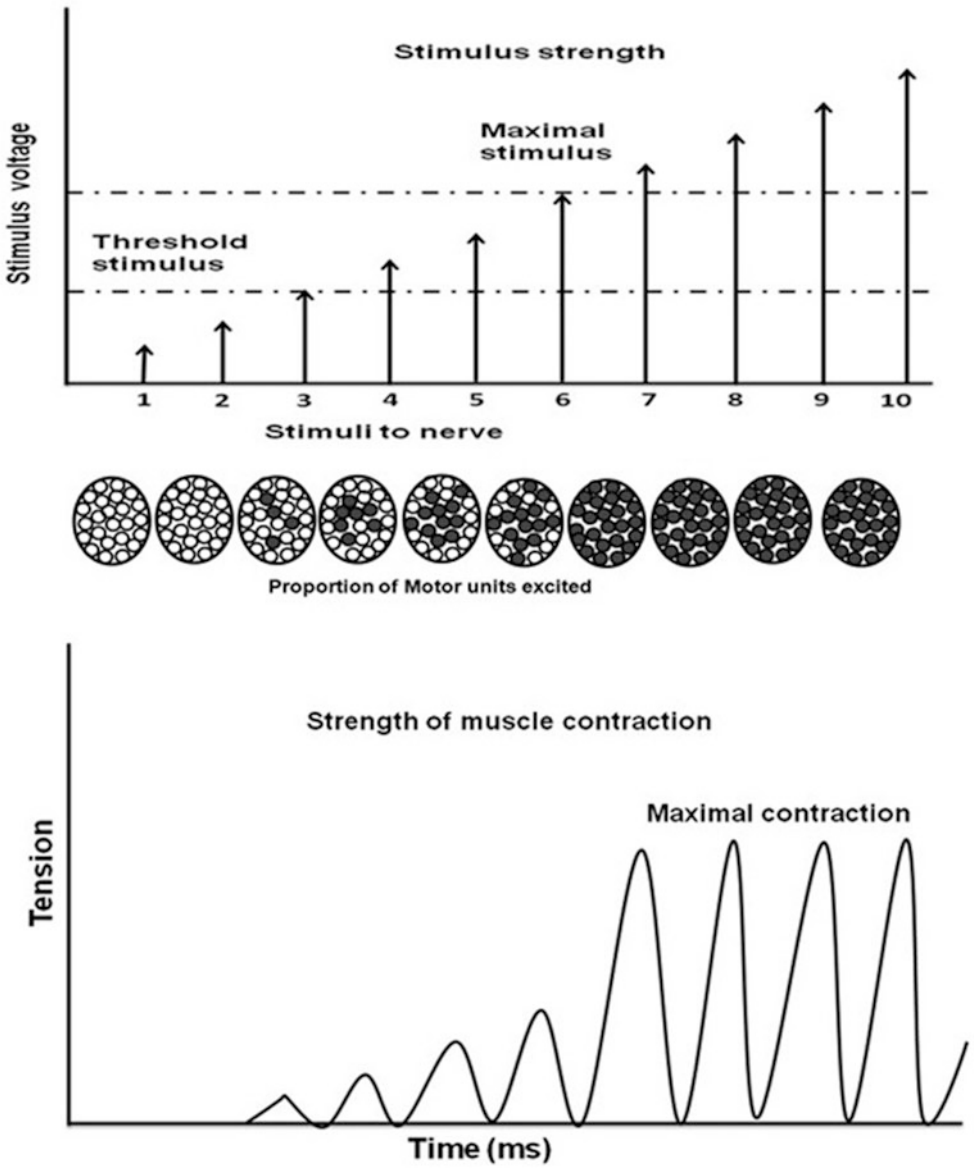


Fig. 10.11 Multiple motor unit recruitment and stimulus intensity. Stimulating the whole nerve with higher and higher voltage produces stronger contractions. More motor units are being recruited called multiple motor unit summation

For example, the lowering phase of a biceps curl shows an eccentric contraction. In eccentric contraction, muscles are able to generate greater forces than in isometric or concentric contractions.

10.2.9 Muscle Twitch

Muscle contraction due to a single action potential is known as twitch contraction (Fig. 10.12). When a single action potential travels through the motor neuron and reaches the muscle fiber of that unit, it initiates the contraction of that single muscle fiber. This isolated contraction is known as muscle twitch. The duration of muscle twitch depends on the type of the muscle, and it can last for a few milliseconds to 100 ms.

Myogram is the graphical representation of the phenomena of muscular contractions (Fig. 10.13). A single muscle twitch has three phases, i.e., latent period or lag phase, contraction phase, and relaxation phase. The first phase is called latent period or lag phase (1–2 ms), which is the short time between the application of stimulus and starting of muscle contraction. During this period, propagation of action potential in the sarcolemma occurs and Ca^{2+} ions are released from the SR for binding with the troponin C. Then tropomyosin moves from its position, myosin head is attached with the actin, crossbridges are formed, and as a result shortening of the muscle fiber occurs. The last phase of twitch is the relaxation phase.

During relaxation phase, muscle contraction stops, Ca^{2+} ions are pumped back to the SR by calcium pump, and muscle returns back to its original resting length. The

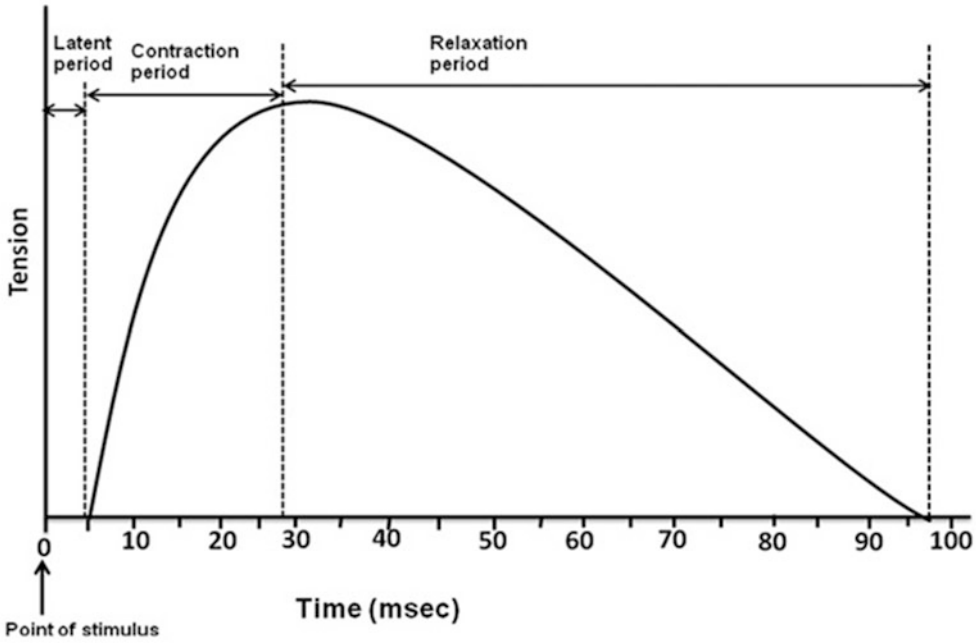


Fig. 10.12 A myogram of a muscle twitch. A single muscle twitch has three phases, i.e., a latent period between the point of stimulus and the starting of contraction, a contraction phase when tension increases, and a relaxation phase when tension decreases

duration of twitch varies between different types of muscle and ranges from 10 to 100 ms.

The **refractory period** is the time immediately after application of a stimulus. If a stimulus is applied during the contraction stage of the muscle, then muscle will not respond to this second stimulus.

10.2.9.1 Factors Influencing Force of Muscle Contraction

Based on the type of work, muscles can generate different levels of force during contraction. Some actions need much more force generation, whereas some work requires less force like lifting a heavy load requires more force compared to lifting a light object.

10.2.10 Multiple Motor Unit Summation or Recruitment

Different ranges of motor units are prudent in a skeletal muscle, and nervous system has a wide range of control over the muscle (Fig. 10.13). Small motor units are innervated by smaller motor neurons with lower threshold. These motor units generate relatively small degree of contractile strength (tension).

Larger motor units are also present with bigger motor neurons having higher threshold. These neurons activate larger muscle fibers and are used when more strength is required. So, increased activation of motor units results in increase in muscle contraction, which is known as recruitment. Motor unit summation is the recruitment of extra motor units within a muscle to develop additional force. The summation of motor units occurs until sufficient force is developed by recruitment of more numbers of motor units within that muscle to move a load. The maximum contraction is generated when all the motor units within a muscle are activated.

The muscle contraction becomes progressively stronger due to recruitment of more number of muscle fibers. In some skeletal muscles, the largest motor units can generate a contractile force of 50 times greater than the smallest motor units in that muscle. The greater the load an animal is carrying, the more number of motor units are activated.

However, at the time of generation of the maximum force, animals are only able to use about 1/3 of total motor units at one time. All muscle fibers do not fire at the same time, which helps in the generation of maximum force and prevents the muscles from fatigue. When muscle fibers begin to fatigue, they are replaced by other fibers, resulting in maintenance of the force. However, under extreme conditions, animals are able to recruit even more motor units at a time to perform a heavy work.

10.2.10.1 Wave Summation

In a muscle fiber, the tension depends on the rate of firing action potential by a motor neuron to that muscle. If the muscle is stimulated before the end of previous twitch, the second twitch will be stronger, and this phenomenon is called wave summation (Fig. 10.14). Wave summation occurs when a given set of muscle fibers is stimulated repeatedly without complete relaxation. The second stimulus causes the release of more number of Ca^{2+} ions from the SR. These Ca^{2+} ions are utilized for the activation of additional sarcomeres while

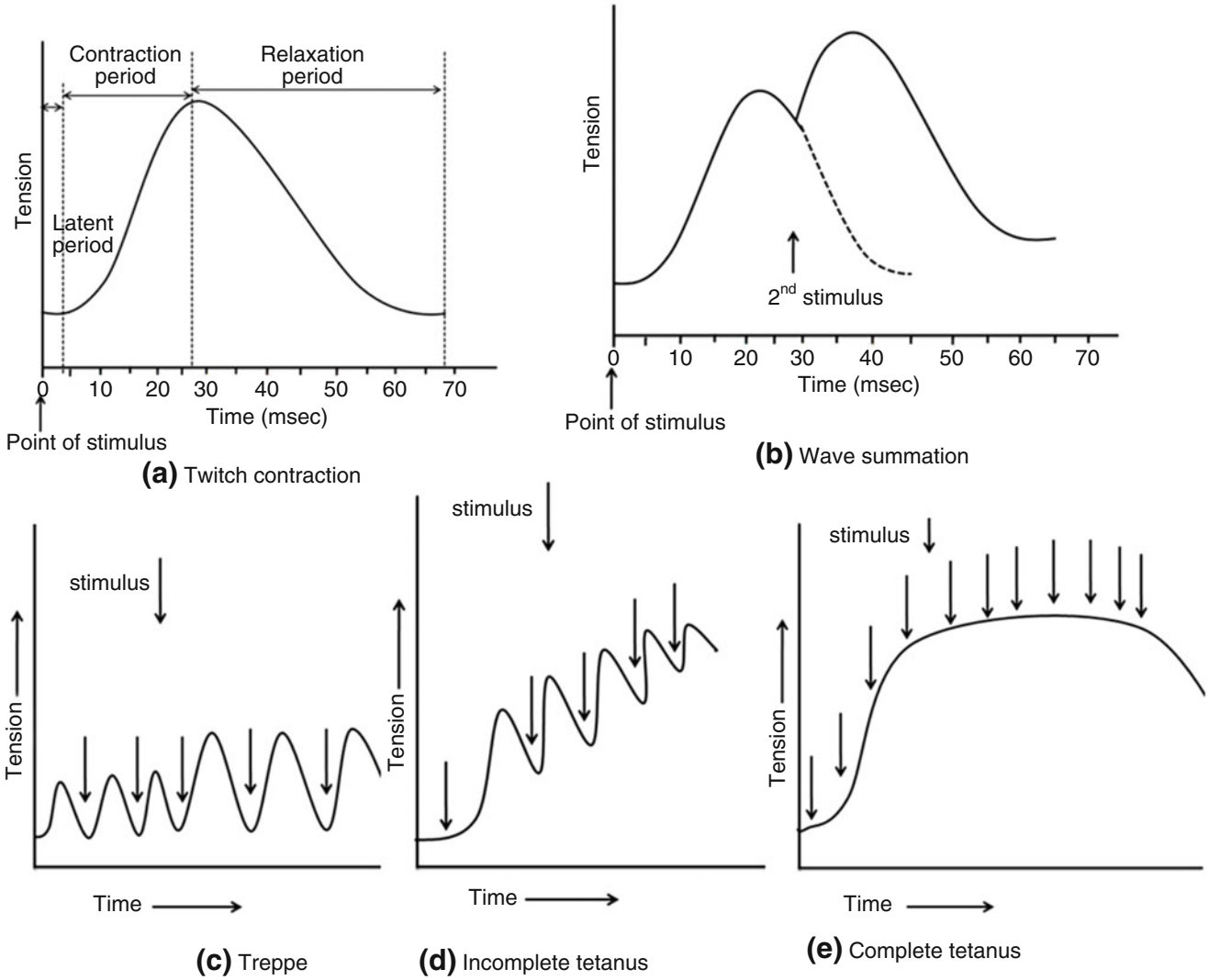


Fig. 10.13 Multiple motor unit summation or recruitment. (**a**) Twitch contraction, (**b**) wave summation, (**c**) treppe, (**d**) incomplete tetanus, (**e**) complete tetanus

the muscle is still contracting from the first stimulus. So, summation results in greater contraction of the motor unit.

10.2.10.2 Treppe

When a muscle is stimulated with repeated stimuli and the stimuli are given just after the completion of the previous contraction, then the tension of the muscle increases in a graded manner till a maximum height is reached, which looks like a staircase (Fig. 10.14). This phenomenon is known as treppe or staircase effect. The frequency of stimuli should be just below the tetanizing frequency.

In this condition, due to a steady stream of signals from the motor neuron, the concentration of Ca^{2+} ions in the sarcoplasm becomes very high.

10.2.10.3 Incomplete Tetanus

If a muscle is given repeated stimuli during contraction phase, then the contraction mechanism will start repeatedly before any relaxation has occurred. Increasing the frequency of motor neuron signaling increases summation, and tension in the motor unit keeps on rising until it reaches a peak. The tension at this time is several times more than the tension of a

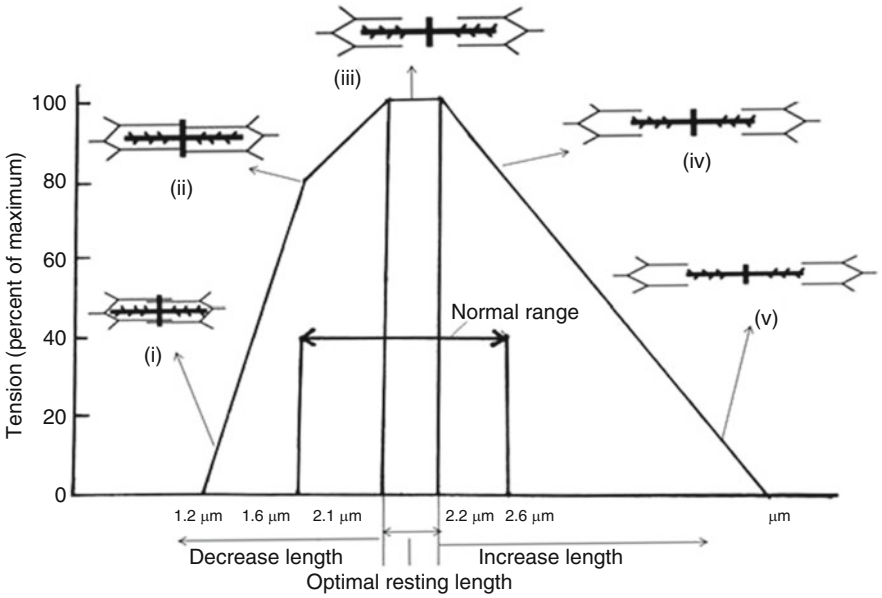


Fig. 10.14 A schematic depicting the sarcomere length-tension relationship

single muscle twitch. This state of muscle is called incomplete or unfused tetanus. During incomplete or unfused tetanus, the muscle goes through quick cycles of contraction with a short relaxation phase for each contraction.

Incomplete tetanus occurs due to repeated stimulus, when there are phases of incomplete relaxation between the summated stimuli (Fig. 10.14).

10.2.10.4 Complete Tetanus

If the frequency of the stimuli is very high and the muscle will not get time for relaxation, then the phenomenon is called complete tetanus (Fig. 10.14). In complete tetanus, the relaxation phases are absent and the contractions become continuous. In complete tetanus, the individual responses fuse and form one continuous contraction. Tetany is the sustained contraction resulting from high-frequency stimulation.

During tetanus, the concentration of Ca^{2+} ion remains very high in the sarcoplasm and that allows nearly all of the sarcomeres to form crossbridges and shorten, and the contraction continues uninterrupted (until the muscle becomes fatigue and is not able to produce tension).

10.2.11 Length-Tension and Force-Velocity Relationship

10.2.11.1 Sarcomere Length-Tension Relationship

A direct relationship is there between the initial length of muscle fibers and the tension in the muscle or force of contraction.

The initial length of the sarcomere influences the force of the contraction, which a muscle can generate (Fig. 10.14). If the sarcomere length is optimum, the isometric tension is maximum due to the position of thin and thick filaments forming maximum number of crossbridges in sarcomere. If the initial sarcomere length is very short, then the thick filaments will already be pushing up against the Z-disc. In this situation, there is no chance of further shortening of the sarcomere as the latter is already short and muscle will not be able to generate much force.

Similarly, if the muscle is stretched very high, then the myosin heads can no longer be able to contact the actin and less force will be generated.

So, maximum force is produced if the muscle is stretched to the point which allows every myosin head to contact with the actin and when the sarcomere has the maximum distance to shorten, i.e., the thick filaments are at the very ends of the thin filaments. This is applicable only in isometric contraction. During dynamic contraction, length-tension relationship must be combined with force-velocity relationship to determine the effect that both length and velocity have on muscle tension.

10.2.11.1.1 Application of Length-Tension Relationship

When applying to muscle joint system, sarcomere length is not same throughout. So, at a particular joint position, there are sarcomeres at many different lengths corresponding to different points of length-tension relationship. During movement, torque produced at joint is not only due to muscle force but also due to function of moment arm (MA) of muscle. So,

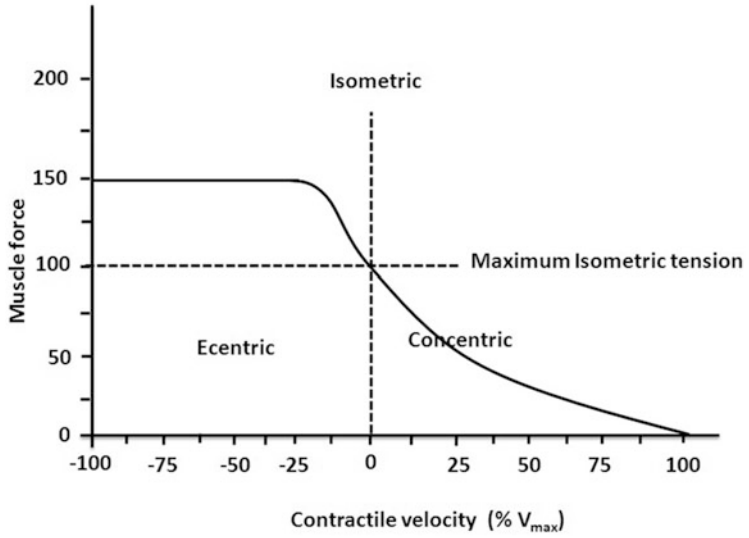


Fig. 10.15 A schematic depicting muscle force-velocity curve

at particular joint position, muscle length may be short but has long MA, maintaining higher torque.

10.2.11.2 Force-Velocity Relationship

The speed of shortening of myofilaments also affects the tension development. Speed of shortening depends on the type and length of muscle fiber. Force-velocity relationship describes the relation between the velocity of muscle contraction and the force produced (concentric and eccentric muscle contraction) (Fig. 10.15). The force which is generated during muscle contraction is the function of velocity of contraction.

For example, in concentric contraction, if speed decreases, the tension increases.

In isometric contraction, the shortening speed is 0, but the tension reduced is more than concentric contraction. In eccentric contraction, as the lengthening speed increases, the tension increases and then plateaus.

10.2.12 Skeletal Muscle Energetics and Metabolism

Muscle contractions require plenty of energy. The major portion of this energy is utilized for the crossbridge cycles, and some portion is also utilized for propelling the Ca^{2+} ions back into the SR from the sarcoplasm during relaxation of the muscle and propelling Na^{+} and K^{+} ions through the sarcolemma.

ATP is the instant source of energy (ATP → ADP + Pi + energy) for muscle contraction. Continuous supply of ATP is required for muscle contraction. For muscle contractions, there are four different ways through which muscles get the ATP.

1. ***Cytosolic stored ATP***: Very little amount of ATP remains inside the muscle fiber as stored ATP. This cytosolic stored ATP can instantly provide energy for contraction and does not require oxygen. Very little amount of ATP is stored in muscle fibers, which can provide energy for muscle contraction for a few seconds. So, it is not enough for long-term contraction. This cytosolic ATP provides energy for contraction of eye muscles which contract constantly and quickly but for a very little period.
2. ***Creatine phosphate***: Muscles cannot obtain ATP from the blood or other tissues. They can produce it as per need. ADP (2 molecule), inorganic phosphate (Pi), and energy from other chemical sources are required to generate a single molecule of ATP by rephosphorylation of ADP.
   When the cytosolic stores of ATP are utilized, muscle fiber initiates another rapid energy source, i.e., creatine phosphate (CP). Creatine phosphate is a high-energy compound, which can rapidly transfer its phosphate to an ADP molecule for synthesis of one molecule of ATP (Fig. 10.16). The process is called phosphagen system, and it does not require oxygen. Creatine kinase or creatine phosphokinase (CPK) enzyme catalyzes the reaction. Creatine kinase enzyme is present on the M-line of the muscle fiber.
   But the energy available from the stored creatine phosphate is also limited, which is sufficient for another 5–8 s. This source is also termed as the immediate energy source and is a very important source of energy for activities like jumping, hitting, and throwing.

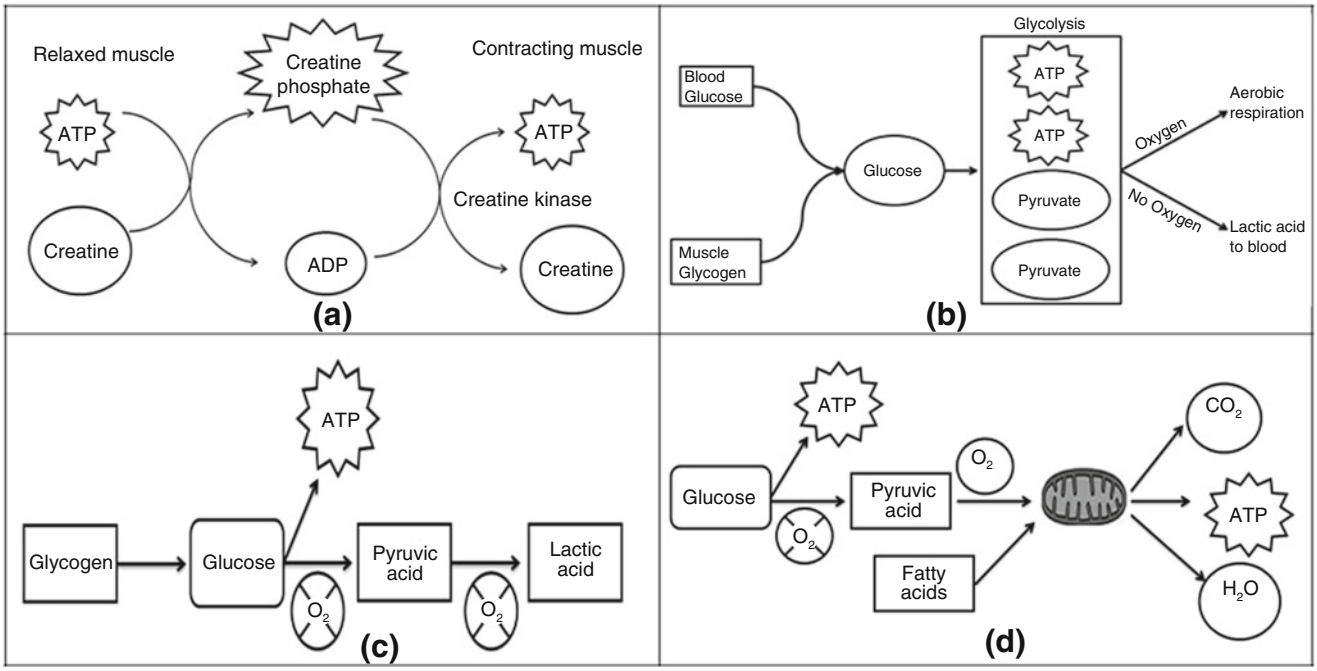


Fig. 10.16 Sources of energy for muscle contraction. (**a**) Molecular pathway of creatine phosphate synthesis. At the time of muscle contraction when muscles require ATP, the reaction is represented by the above equation that runs from left to right. When the muscle is at rest and excess ATP is available, the reaction is represented by the above equation that proceeds from right to left. (**b**) Glycolysis pathway. (**c**) Anaerobic mechanism (glycolysis and lactic acid formation). (**d**) Aerobic or oxidative respiration

Know More. . .. . .
Creatine phosphate or phosphagen system is rapidly replenished during recovery. It requires about 30 s to replenish about 70% of the phosphagens and 3–5 min to replenish 100%. During intermittent work (short periods of activity followed by rest periods), much of the phosphagen can be replenished during the recovery period and thus be used over and over again.

3. ***Glycolysis***: Glycolysis is the metabolic pathway which breaks down glucose into pyruvate and a hydrogen ion (H^+). Glucose molecules reach the muscle tissues through blood. Glucose is also produced in muscle cells through breakdown of stored glycogen (Fig. 10.16). The glycolysis in skeletal muscle generates ATP molecules required for contraction. Glycolysis which occurs in the absence of oxygen is called anaerobic glycolysis, which is the main source of ATP during anaerobic activity. Glycolysis process is very fast and can supply energy for intensive muscular activity, but it can supply energy for about a minute before the muscles begin to fatigue.
   Glycolysis occurs in the cell cytosol and can produce molecules 2 ATP by converting a glucose molecule into pyruvate. In anaerobic glycolysis, the pyruvic acid is converted to lactic acid. The accumulation of lactic acid reduces the pH and makes it more acidic, which produces the stinging feeling in muscles during exercise. This slows down further anaerobic respiration and brings fatigue. Now when the activity of the muscle slows down, oxygen becomes available and lactate is converted back into pyruvate.
4. ***Aerobic or oxidative respiration***: The different mechanisms discussed above are able to supply ATP for about a minute.
   But the different activities like walking and running which continue for a long duration require a constant supply of ATP. So, in these activities where constant ATP is required, the cells utilize aerobic or oxidative respiration occurring in the mitochondria (Fig. 10.16). This aerobic respiration can supply adequate ATP to the muscle cells for hours, but this process of metabolism is slower than anaerobic mechanisms and is not fast enough for intense activity.
   It is an important source of energy for muscle contractions of athlete animal and for endurance exercise required of migrating animals, where repetitive skeletal muscle contractions continue for hours or days. Though glucose can be used as an energy source for aerobic respiration, the primary fuel for muscle contractions during prolonged endurance exercise is fatty acids rather

than glucose. These fatty acids are broken down to acetyl-CoA and enter the citric acid cycle and produce ATP.

Muscle contractions are 50–70% efficient in regard to completion of a work, and the nonwork portion is dissipated as heat. This heat source is very important for the maintenance of body temperature. During cold stress, shivering results in the production of heat in the body.

10.2.13 Muscle Fatigue

If a muscle is used exhaustively, then the performance of the muscle decreases progressively, which mostly recovers after a period of rest. This phenomenon is known as muscle fatigue. This process is temporary and reversible state of muscle. When a muscle is contracted for a long time, then muscle fatigue occurs. If fatigue starts in a muscle, then the force of the muscle decreases and the response of that muscle to stimuli reduces and as a result the activity levels decrease. In fatigue condition, the muscle is unable to contract optimally. Muscle fatigue starts at the time of heavy muscular activity or exercise. As the muscle starts fatigue, the speed and force of contraction reduce, relaxation time prolongs, and a period of rest is required to restore normal function. The factors which influence the muscle fatigue are the following:

1. ***Ionic imbalance within the muscle***: Muscle contraction requires Ca^{2+} ions to interact with troponin for exposing the actin-binding site to myosin head. If deficiency of Ca^{2+} occurs in the body, then muscles do not get the required Ca^{2+} ions for contraction.
2. ***Nervous fatigue and loss of desire***: The contraction of a muscle is controlled by nerves. In central fatigue or "psychological fatigue," brain feels tired. This leads to fatigue.
3. ***Metabolic fatigue***: Depletion of ATP or glycogen results in fatigue due to unavailability of energy. Metabolites like Mg^{2+} ions induce fatigue by inhibiting the release of Ca^{2+} ions or reducing sensitivity of troponin to Ca^{2+} ions.
4. ***Exercise and aging***: With aging of animal, the levels of ATP, CTP, and myoglobin decrease and it reduces the muscle's ability to function. Training and exercise increase the metabolic capacity of a muscle, which delays the onset of muscle fatigue.
5. ***Lactic acid accumulation***: Lactic acid is the by-product of anaerobic respiration, which strongly contributes to muscle fatigue.

10.2.13.1 Effects of Muscle Fatigue

Muscle fatigue causes different types of sign and symptoms in the body like muscle pain, burning, fast breathing, vomiting, and stomach pain.

10.2.13.2 Types of Muscle Fatigue

There are two types of fatigue, i.e., central fatigue and peripheral fatigue:

Central fatigue—It occurs due to the decrease in the capacity to voluntarily activate a muscle during a maximal effort. It occurs due to a decrease in motor unit recruitment levels or a reduction in motor unit firing rates or both.

Peripheral fatigue—It occurs due to the decrease in the capacity of a muscle to produce force even if it is receiving signals from the nervous system.

10.2.14 Types of Skeletal Muscle Fiber

Skeletal muscle fibers can broadly be classified into type I or slow-twitch fibers and type II or fast-twitch fibers on the basis of their contraction speed and fatigue resistance. The relative proportions of these types of muscle fibers are basically determined by genetic factors and influenced by physiological, hormonal, and nutritional factors.

1. ***Slow-twitch muscle fibers***: The slow-twitch muscle fibers are also known as type I muscle fibers. They have myoglobin content and are red in color. Their contraction speed is less than the other types of muscle fibers. The muscle fibers are smaller and produce tension slowly. Their capacity to produce force or power is less. But the main advantage is that these types of muscle fibers are slow to fatigue. They have high myosin ATPase activities, capillary density, and mitochondrial density and have low power. Slow-twitch fibers depend on oxygen for energy, and they can continue the activity for long duration. These types of muscle fibers are generally associated with endurance activities, and highly active animals or athlete animals have higher proportion of these types of muscle fibers in the body.
2. ***Fast-twitch muscle fibers***: Fast-twitch muscle fibers are also known as type II muscle fibers. The speed of contraction is faster than the type I muscle fibers. The duration of contraction is short. Type II muscle fibers are more powerful than type I muscle fibers and are associated with activities such as lifting a heavy weight, which requires more power. This type of fibers gives major strength to the

animal, but they become fatigue very quickly. These fast-twitch fibers can be further classified into fast-twitch oxidative-glycolytic fibers (type IIa) and fast-twitch glycolytic fibers (type IIb) in rodents and pigs. In large mammals including humans and ruminants, type IIx replaces type IIb as the dominant fast-twitch fibers.

***Type IIa muscle fibers*—Type IIa muscle fibers** depend on oxidative glycolysis for energy and produce lactic acid. But the duration of contraction is very short. Animals that are associated with powerful activities have higher proportions of type IIa fibers in their muscles.

Fast-twitch glycolytic (type IIx) fibers—Type IIx muscle fibers are faster and more powerful than type IIa muscle fibers. They also fatigue very quickly. They are associated with the activities of very short duration and which require more power.

In cheetahs and domestic cats, several muscles have high proportion of type IIx fibers and low proportion of type I fibers. In beagle dogs, the percentage of type IIa fibers is very high (Table 10.3).

10.2.15 Rigor Mortis

The word rigor mortis came from two Latin wards, i.e., "rigor" means "stiffness" and "mortis" means "of death." Rigor mortis or postmortem rigidity of muscles is an important sign of death of an animal. It starts a few hours after death. After death of the animal, the muscles become rigid, it is difficult to move or manipulate the body, and the state is irreversible. In the muscle, continuous actin-myosin interaction is seen in rigor mortis. After death of the animal, cellular respiration stops and results in stop of synthesis of adenosine triphosphate (ATP). So, ATP is not available for relaxation of muscle and muscle remains in contraction state.

10.2.15.1 Mechanism of Rigor Mortis

1. Absence of ATP → no reuptake of Ca^{2+} into the SR as Ca^{2+} uptake also requires ATP-dependent Ca^{2+} pump → Ca^{2+} level of sarcoplasm ↑ → continued binding of Ca^{2+} to troponin C → abnormal, rigid, and uninterrupted contraction.
2. No ATP → no relaxation, a new molecule of ATP must attach to the myosin head for detachment of actin-myosin interaction → thus, when no ATP is present, then myosin heads cannot detach themselves from actin.

In humans, rigor mortis starts after about 3–4 h after death. It reaches maximum stiffness after about 12 h and gradually dissipates until approximately 48–60 h (3 days) after death. The onset of rigor mortis depends on the ambient temperature. The warm conditions can speed up the process of rigor mortis. Rigor mortis ends when contractile proteins of the muscle like other body tissues undergo autolysis caused by enzymes released by lysosomes.

10.2.15.2 Factors Affecting Rigor Mortis

Ambient temperature: Cold temperature inhibits rigor mortis and the onset of rigor becomes slower, whereas hot temperature accelerates the process and faster onset and faster progression of rigor mortis occur.

Activity before death: Anaerobic exercise before death accelerates the rigor mortis process because lack of oxygen to muscle buildup of lactic acid and higher body temperature accelerate rigor. Sleep before death slows the process as fully oxygenated muscles exhibit rigor more slowly.

Body mass: In obese animals, the rigor mortis process is slow because fats store oxygen. In thin animals, the process is fast as the body loses oxygen quickly.

Table 10.3 Comparison between three types of muscle fibers

Characteristics	Type I	Type IIA	Type IIX
Myosin ATPase activity	Slow	Fast	Fast
Fiber length	Small	Medium	Large
Duration of contraction	Long	Short	Short
Fatigue	Slow	Quick	Very quick
Energy utilization	Aerobic/oxidative	Both	Anerobic/glycolytic
Capillary density	High	Medium	Low
Availability mitochondria	High numbers	Medium numbers	Low numbers
Color of the fiber	Red (contain myoglobin)	Red (contain myoglobin)	White (no myoglobin)
Force production	Low	High	Very high

10.3 Smooth Muscle and Cardiac Muscle

10.3.1 Smooth Muscle

Smooth muscle is involuntary and nonstriated. Smooth muscle is present mainly in the visceral organs, so this type of muscle is also known as visceral muscle. They are found in GI tract, urinary tract, blood vessels, airways, different glands, inside eye, etc.

Smooth muscle helps in many vital functions in the body like passage of food bolus in the digestive tract through peristalsis, elimination of execratory products through urinary system, and regulation of blood flow through the blood vessels. Smooth muscle is under the control of autonomic nervous system and endocrine system. Muscle cells are small and spindle shaped with one centrally located nucleus. No neuromuscular junction is present, and instead of that, varicosities help in the transmission of nerve impulse to the cells. The contraction and relaxation are slower than the skeletal muscle. In some organs, smooth muscles have pacemaker cells. Less energy is required for their contraction, and they become fatigue slowly.

10.3.1.1 Cellular Structure

Smooth muscle fibers are small and spindle shaped with one centrally located nucleus (Fig. 10.17). The average diameter of fibers is 2–10 mm. The elasticity is more in smooth muscle than striated muscle. Elasticity is very important for visceral organs like urinary bladder. In smooth muscle, myofibrils are absent and thick and thin filaments are not arranged in sarcomere pattern; that is why they are nonstriated.

Smooth muscle fibers contain three types of filaments, i.e., thick myosin filaments, thin actin filaments, and intermediate filaments. Thick myosin filaments are longer in smooth muscle than skeletal muscle. Thin filaments actin and tropomyosin are present, but troponin is absent. During contraction, calcium ions attach with calmodulin instead of troponin. The intermediate filaments do not directly participate in contraction, and they only form part of cytoskeletal framework that supports cell shape. Dense bodies are button shaped and present throughout the cell. Dense bodies contain the same protein found in Z-lines. Actin filaments are attached with these dense bodies.

Sarcoplasmic reticulum stores Ca^{2+} ions, which are essential for contraction. Cells are usually arranged in sheets within muscle and organized into two layers (longitudinal and circular) of closely apposed fibers, which have essentially the same contractile mechanisms as skeletal muscle.

10.3.1.1.1 Structural Differences: Smooth Muscle with Striated Muscle

Smooth muscle is nonstriated, and myofibrils and sarcomeres are absent. Thick and thin filaments are not arranged like skeletal muscle. Thick filaments are scattered throughout sarcoplasm, whereas thin filaments are attached to dense bodies. T-tubule is absent. Loose network of sarcoplasmic reticulum is present in the cytoplasm. Troponin is not present in smooth muscle, and instead of troponin C calcium ions attach with calmodulin during contraction. In single-unit smooth muscle, muscle cells are attached with one another with gap junctions. Gap junction is an electrical junction, which helps in the transmission of nerve impulse from one cell to another. In smooth muscle, connective tissues never unite to form tendon. Thick and thin filaments are arranged in slightly diagonal chains, which are attached to the plasma membrane or dense bodies. During contraction, when action potential reaches the cells, thick and thin filaments slide past each other. In smooth muscle, neuromuscular junction is absent. Instead of neuromuscular junction, varicosities help in the transmission of nerve impulse to the smooth muscle cells.

10.3.1.2 Types of Smooth Muscle

Smooth muscle can be broadly classified into single-unit smooth muscle and multiunit smooth muscle.

1. ***Single-unit smooth muscle***: In single-unit smooth muscle, muscle cells are connected to each other through gap junctions (Fig. 10.18).
   Through these gap junctions, action potential transmits from one cell to another. The cells are stimulated in a

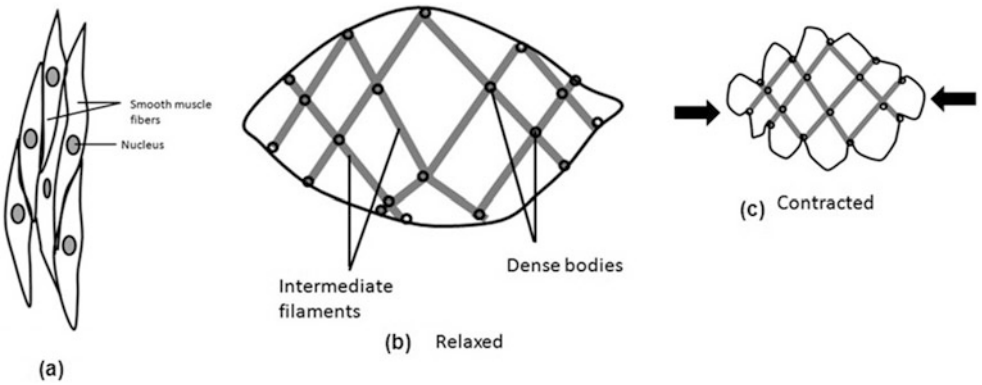


Fig. 10.17 Smooth muscle tissue. (**a**) The cells are spindle shaped with a centrally located nucleus. Anatomy of a relaxed (**b**) and contracted (**c**) smooth muscle cell

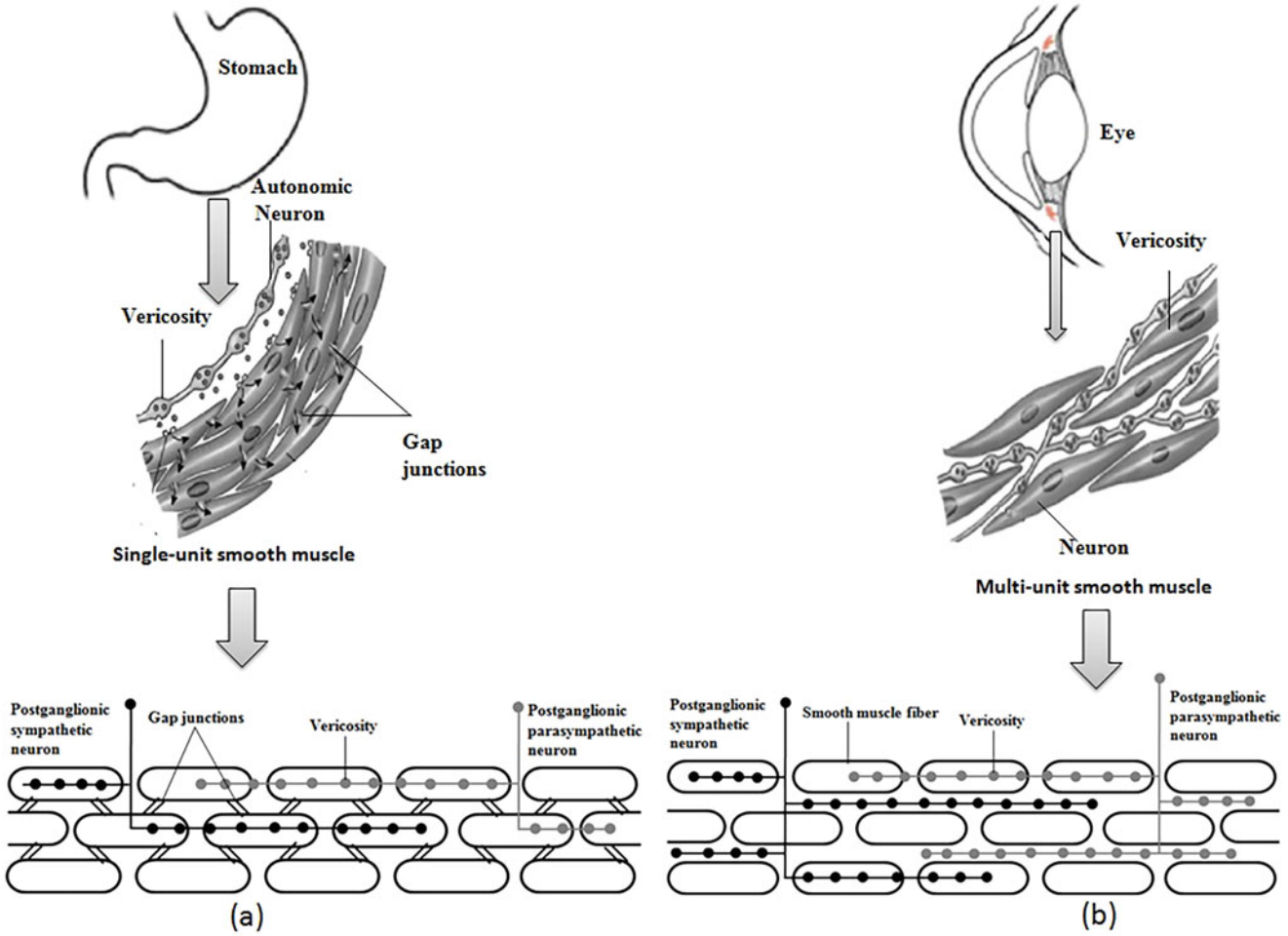


Fig. 10.18 Single-unit smooth muscle and multiunit smooth muscle. (**a**) Innervations of a single-unit smooth muscle through varicosities. (**b**) Innervations of multiunit smooth muscle through varicosities

synchronous pattern from only one synaptic input, and action potential spreads to all the cells and contraction of all the cells occurs at a time like a functional syncytium. Single-unit smooth muscle is myogenic with pacemaker potentials.

2. ***Multiunit smooth muscle***: In multiunit smooth muscle, each cell receives its own synaptic input through single varicosity (Fig. 10.18). This allows for the multiunit smooth muscle to have a much finer control. No gap junction is present. So, cells are not electrically connected and hence selective activation of muscle fibers occurs. Multiunit smooth muscle is neurogenic.

10.3.1.3 Function of Smooth Muscle

Smooth muscle is involved in the movement of different visceral organs and glands; thus, smooth muscle serves a variety of functions in the body.

The basic functions of smooth muscle are the following:

1. Smooth muscle in gastrointestinal tract helps in the movement of the food bolus through peristalsis.
2. The smooth muscles in blood vessels regulate the blood flow and blood pressure through vascular resistance.
3. In urinary system, smooth muscle regulates the urine flow and smooth muscle in urinary bladder regulates the micturition.
4. Smooth muscle of reproductive tract helps in gamete transport, and contraction of uterus helps in parturition.
5. The contraction of smooth muscle of air passages of respiratory tract regulates the diameter bronchiole and passage of air.
6. The contraction of integument causes piloerection and helps in shivering thermogenesis during cold stress.
7. The smooth muscles in eye regulate the dilation and constriction of the pupil and regulate the entry of light

through pupil. Smooth muscles in eye also change the shape lens as required.

10.3.1.3.1 Innervations of Smooth Muscle

Smooth muscles are innervated by postganglionic autonomic neurons. In smooth muscle, neurotransmitter remains in varicosities. When an action potential reaches the varicosity through the axon the neurotransmitter releases from the varicosities and attached with the receptors on the plasma membrane of muscle fibers. In single-unit smooth muscle, the innervation is restricted to a few fibers in the muscle and action potential is transmitted from one cell to another through gap junctions.

10.3.1.3.2 Stimuli Initiate Smooth Muscle Contraction

Different stimuli which influence the smooth muscle contraction are the following:

1. The spontaneous electrical activity in the plasma membrane of the smooth muscle fiber
2. Release of neurotransmitter by autonomic neurons
3. Different hormones
4. Some local changes in the chemical composition like paracrine agents, acidity, oxygen, osmolarity, and ion concentrations of extracellular fluid surrounding the muscle fibers
5. Stretch

10.3.1.4 Mechanism of Smooth Muscle Contraction

When an action potential reaches the sarcolemma through the neurotransmitter released from the varicosities, it causes the depolarization of membrane of smooth muscle cell (Fig. 10.19).

The depolarization of membrane or activation of neurotransmitter results in entry of Ca^{2+} ions through the L-type voltage-gated calcium channel located in the plasma membrane. This increase in Ca^{2+} ions stimulates the release of Ca^{2+} ions from sarcoplasmic reticulum by the way of ryanodine receptors and IP3.

This process is known as Ca-induced Ca release. Then the Ca^{2+} ions bind with calmodulin, which results in the activation of calmodulin. Now the activated calmodulin activates the enzyme myosin light-chain kinase (MLCK). MLCK phosphorylates the light chains in myosin heads and increases myosin ATPase activity. Then myosin binds with actin.

Now crossbridge cycling occurs, which leads to muscle tone. The ATPase activity is less in smooth muscle than in skeletal muscle. That is why the speed of contraction is slow in smooth muscle.

10.3.1.5 Mechanism of Smooth Muscle Relaxation

Smooth muscle contraction ends with the dephosphorylation of myosin light chains.

Unlike skeletal muscle, the depolarization in smooth muscle occurs during its activation. That is why simply reducing calcium ion concentration will not produce the relaxation of smooth muscle. Here, myosin light-chain phosphate is responsible for dephosphorylation of myosin light chain, which ultimately leads to relaxation of smooth muscle.

In smooth muscle, action potentials are slower and they can last for a long time. This may be due to slow opening of calcium channels. Repolarization of smooth muscle is also slow as potassium channels are also slow to react. Some smooth muscle cells act as pacemaker cells and generate action potential. These types of cells are seen in the intestines. It has been seen that in some smooth muscles, they contract without any action potential.

In multiunit smooth muscle, action potentials generally do not occur. Like in smooth muscle, iris depolarization occurs by norepinephrine and ACh, which is known as junctional potential. These neurotransmitters cause the contraction of smooth muscle. The junctional potential results in an influx of calcium through L-type channels into the cell.

Sometimes, the neurotransmitters activate a G-protein, which activates phospholipase C generating IP3. IP3 then initiates the release of calcium from the sarcoplasmic reticulum. Smooth muscle contraction is required to last for a long time. If the contraction occurs like skeletal muscle, then the energy demand will be high for this type of sustained contraction and muscle will become fatigue as intracellular ATP is depleted.

But this phenomenon does not occur because of a special mechanism known as latch state, which allows the smooth muscle to maintain high tension at low energy consumption. The smooth muscle tone remains high even if there is decrease in myosin light-chain kinase.

10.3.2 Cardiac Muscle

Cardiac muscle is only present in the heart. They are striated like skeletal muscle but involuntarily. Cardiac muscle is mainly controlled by autonomic nervous system and endocrine glands. The pacemaker cells of heart generate action potential, and the heart beats rhythmically. Heart supplies blood through the body, and it is possible because of well-organized contraction of cardiac muscle cells.

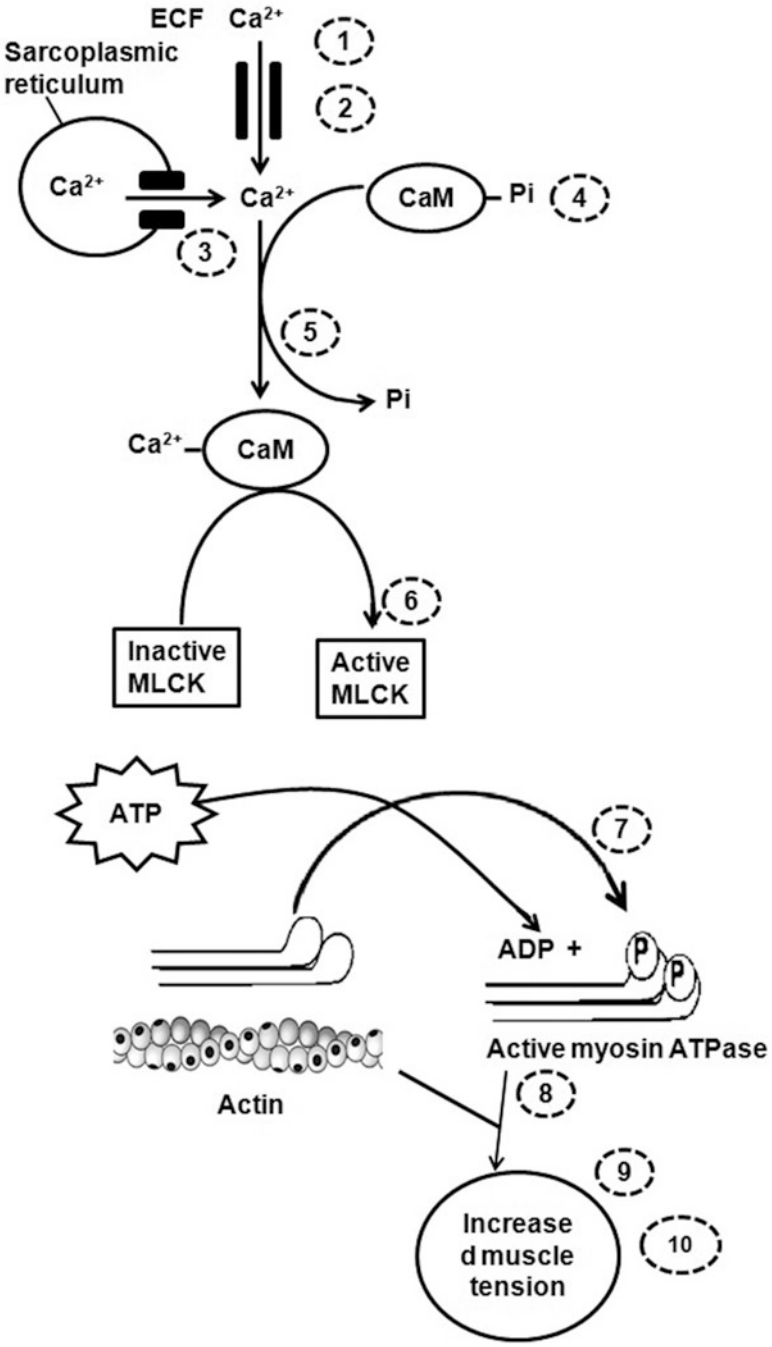


Fig. 10.19 Mechanism of smooth muscle contraction. (**1**) Depolarization of cell membrane or activation of hormone/ neurotransmitter, (**2**) opening of L-type voltage-gated calcium channels, (**3**) calcium-induced calcium release from sarcoplasmic reticulum, (**4**) increased intracellular calcium level, (**5**) calcium binds with calmodulin, (**6**) activation of myosin light-chain kinase (MLCK), (**7**) phosphorylation of myosin light chain, (**8**) increase in myosin ATPase activity, (**9**) myosin-P binds actin, (**10**) crossbridge cycling leads to muscle tone

10.3.2.1 Basic Organization of Cardiac Muscle Cells

Like skeletal muscle, cardiac muscle is also striated, and the organizations of sarcomeres are also similar with actin and myosin filaments (Fig. 10.20). But some differences are also there in the structures and arrangement of the muscle fibers, which allow their coordinated function. The cells of cardiac muscle are smaller than the cells of skeletal muscle and exhibit branching. The cells are interconnected to each other by intercalated discs and form functional syncytia. Intercalated disc has two types of membrane junctions, i.e., desmosomes and gap junctions. Desmosomes are mechanical junctions between the cardiac muscle cells. Gap junctions are electrical junctions which connect one cell to another and allow the propagation of action potential between cells. Action potential is generated from the cardiac cells, and the electrical impulse spreads from one cell to another through the gap junction. So, all the cardiac cells become excited at a time and contract as a single syncytium. The thick and thin filaments are arranged like that of skeletal muscle, which gives a striated appearance. Repeated dark and light bands, i.e., A bands and I bands, are seen when viewed under

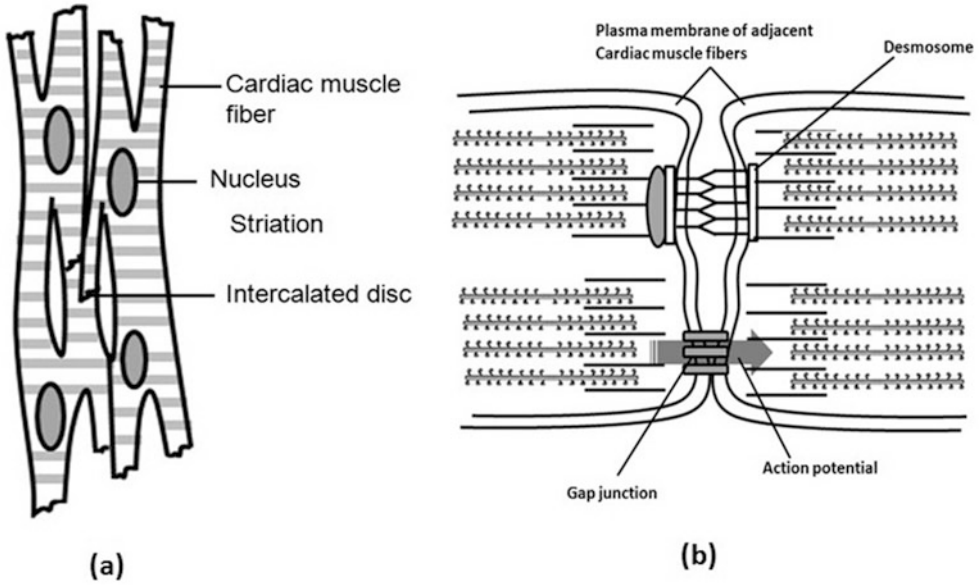


Fig. 10.20 Cardiac muscle tissue. (**a**) Cardiac muscle cells are branched and are interconnected to each other by intercalated discs. (**b**) Intercalated disc

electron microscope. The Z-lines are present at the lateral border of the sarcomere. Thin filaments are composed of actin, troponin, and tropomyosin. Thick filaments are made up of myosins, which extend from the center of the sarcomere towards the Z-lines. The amount of connective tissue is more in cardiac muscle than in the skeletal muscle. This high amount of connective tissue prevents not only muscle rupture, but also overstretching of the heart.

10.3.2.2 Mechanism of Contraction

Like that of skeletal muscle, cardiac muscle contraction is thin filament regulated, with an elevation in intracellular Ca^{2+} required to promote actin-myosin interaction (Fig. 10.21). Action potential transmits through the plasma membrane of cardiac contractile cells. Then it travels down to T-tubule. The action potential causes opening of plasma membrane L-type Ca^{2+} channel in the T-tubules. Ca^{2+} enters cytosol from T-tubules. Increase of cytosolic Ca^{2+} concentration leads to release of large amount of Ca^{2+} from SR through ryanodine release channels. This process is called Ca^{2+}-induced Ca^{2+} release. Increase in cytosolic Ca^{2+} causes binding of Ca^{2+} to troponin C.

This binding of Ca^{2+} with troponin C results in a conformational change in the troponin-tropomyosin complex, tropomyosin is removed from its position, and the active site on actin becomes exposed. Now myosin head binds with actin and crossbridge formation occurs like skeletal muscle. Thin filaments slide inward between thick filaments.

Cardiac muscle can regulate the rise in intracellular Ca^{2+} ions, and by this process, force of contraction is regulated. In heart, all the muscle cells are activated during contraction, so recruiting more muscle cells is possible.

Moreover, tetany of cardiac muscle cells would prevent any pumping action and thus be fatal. Consequently, the heart relies on different means of increasing the force of contraction, including varying the amplitude of the intracellular transient Ca^{2+}.

10.3.2.3 Mechanism of Relaxation

In cardiac muscle, relaxation starts due to re-accumulation of Ca^{2+} by the SR through the action of the SR Ca^{2+} pump (SERCA). It plays an important role in the relaxation process and decreases the cytosolic Ca^{2+}, but the process is more complex in cardiac muscle.

The refractory period in cardiac muscle is long, and the plateau phase is also prolonged. Because of these reasons, cardiac muscle never tetanizes.

10.3.2.4 Cardiac Muscle Metabolism

Like skeletal muscle, myosin uses energy in the form of ATP during contraction. So, the ATP pool is continuously replenished. The source of this ATP is aerobic metabolism, including the oxidation of fats and carbohydrates. During ischemic condition, the creatine phosphate pool, which converts ADP to ATP, may decrease and like skeletal muscle the creatine phosphate pool is small.

10.3.2.5 Cardiac Muscle Hypertrophy

Regular exercise such as regular running causes hypertrophy of individual cardiac muscle cells, which ultimately results in increased heart size.

This is an example of "physiological hypertrophy," and it is beneficial for the animal. In contrast to this, pathological hypertrophy is also seen. If heart is remaining in constant

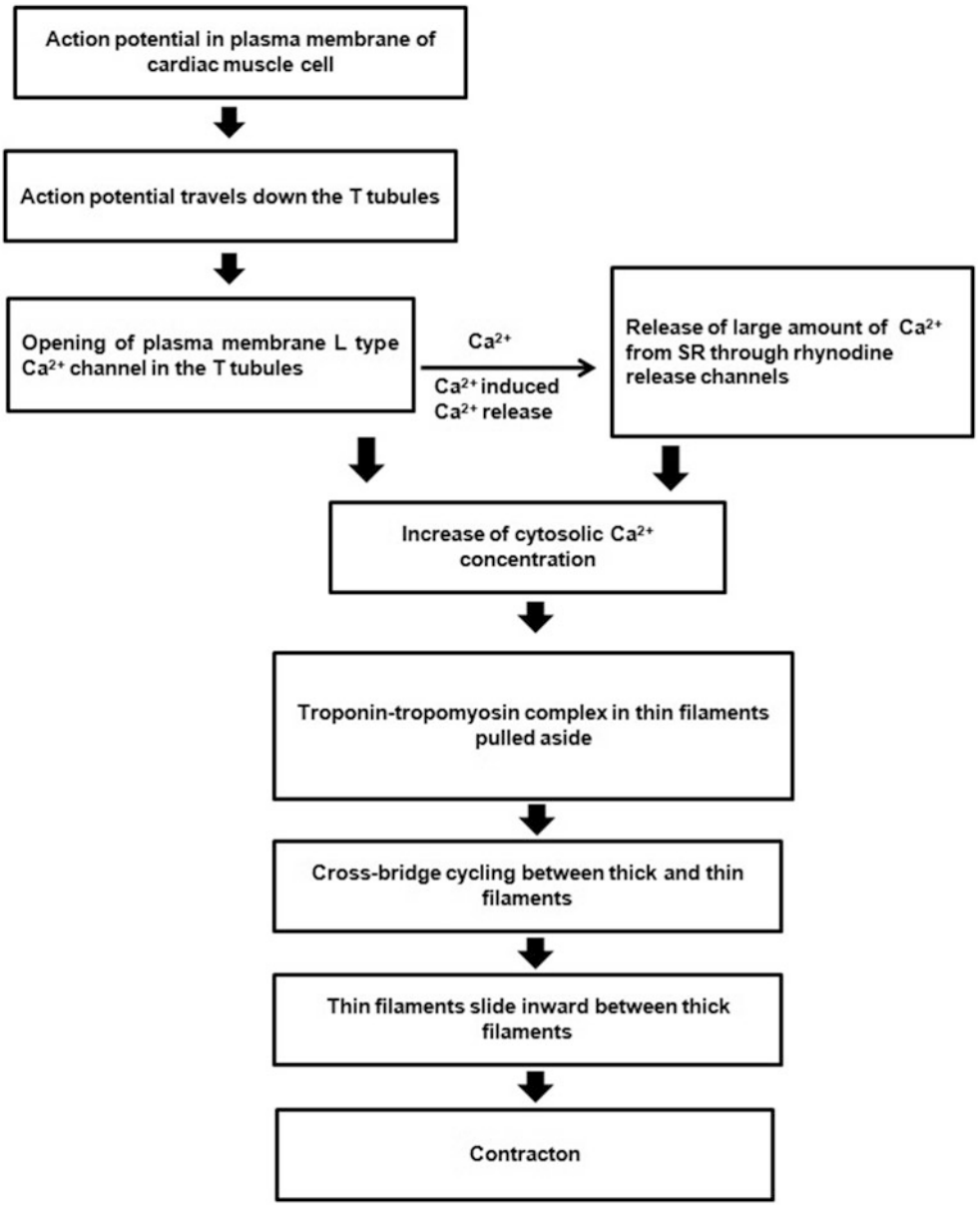


Fig. 10.21 Mechanism of cardiac muscle contraction

chronic pressure overload, it may undergo either concentric left ventricular hypertrophy or dilated left ventricular hypertrophy, with impaired functional consequences.

10.3.3 Muscular Disorders of Domestic Animals

Different diseases influence the typical structure and functions of muscle. Various infections, toxins, or congenital origin causes primary muscular dysfunctions, leading to complete paralysis, paresis, or ataxia. But the major cause of the muscular disorder is dysfunction of the nervous system, e.g., rhinopneumonitis, tetanus, protozoal myelitis, and canine distemper. Some disorders that affect the neuromuscular junction, like hypocalcemia, hypermagnesemia, and myasthenia gravis, can lead to muscular weakness, fatigue, and paralysis. Some antibiotics, toxins (e.g., venoms, botulinum toxins, tetanus toxins), and some muscle-relaxing drugs also affect the neuromuscular junction. The disorder in muscle membrane and muscle fiber is known as myopathies. The disorders in muscle membrane may occur due to hereditary problems (e.g., congenital in goats, myotonia) or acquired (e.g., hypothyroidism, vitamin E and selenium deficiency, hypokalemia). In muscle fiber, various diseases happen, like polymyositis, muscular dystrophy, white muscle disease, and eosinophilic and myositis myopathy.

Muscle trauma is prevalent in the horse and may be from external or extreme activities leading to muscle rupture. In horses, fibrotic myopathy in the rear limb is a mechanical lameness caused due to the trauma and subsequent fibrosis or

ossification of the muscle. Different laboratory tests, viz. determining serum enzyme levels, histopathological examination, and electromyographic studies, are used to diagnose muscular diseases.

Learning Outcomes

- The muscle is a contractile tissue consisting of muscle cells or muscle fibers. Contraction of muscle fibers generates force, and that causes motion. Three types of muscles are there in the body, i.e., skeletal muscle, smooth muscle, and cardiac muscle. Skeletal muscles are mainly attached to bones, smooth muscle is present in the walls of visceral organs, and cardiac muscle is located in the heart.
- The skeletal muscle fibers have a long cylindrical structure with many nuclei located in the periphery. The active contractile unit of muscle is known as the sarcomere. Each myofibril contains several types of protein cells called myofilaments.
- During contraction, action potential propagates through the sarcolemma and travels down the T-tubules causing the sarcoplasmic reticulum to release Ca^{2+} ions. The myosin head then attaches to the binding site of the G-actin molecule, and the formation of crossbridges occurs. Muscle relaxation occurs when the release of the neurotransmitter stops at the neuromuscular junction.
- Smooth muscle fibers are tiny and spindle shaped with one centrally located nucleus. Smooth muscle fibers contain three types of filaments, i.e., thick myosin filaments, thin actin filaments, and intermediate filaments. During contraction, calcium ions attach with calmodulin instead of troponin. The intermediate filaments do not directly participate in contraction, and they only form part of the cytoskeletal framework that supports cell shape.
- Cardiac muscles are striated like skeletal muscle but involuntarily, mainly controlled by the autonomic nervous system and endocrine glands. The cardiac muscle cells are smaller than the cells of skeletal muscle and exhibit branching. The cells are interconnected by intercalated discs and form functional syncytia. Like skeletal muscle, cardiac muscle contraction is thin filament regulated, with an elevation in intracellular Ca^{2+} required to promote actin-myosin interaction.

Exercises

Objective

Q1. What is the layer of connective tissue that separates the muscle tissue into small sections?
Q2. What is the name of loose connective tissue that surrounds individual muscle fibers?
Q3. Where are the crossbridges involved in muscle contraction located?
Q4. During smooth muscle contraction, Ca^{2+} is attached to which protein?
Q5. What is the zone's name in the central portion of A band of skeletal muscle where thin filaments are absent?
Q6. Into what does the neuron release its neurotransmitter at the neuromuscular junction?
Q7. What type of muscle is found in the eyes' irises and the blood vessels?
Q8. What is the function of varicosities?
Q9. What is a T-tubule?
Q10. What is titin?
Q11. What are the principal proteins of muscle contraction?
Q12. What is sarcomere?

Subjective Questions

Q1. What is rigor mortis?
Q2. What is muscle atrophy?
Q3. What is muscle hypertrophy?
Q4. What is muscle fatigue?
Q5. Differentiate between the single-unit and multiunit smooth muscle.
Q6. Differentiate between isotonic and isometric contraction.
Q7. Describe the energy sources for skeletal muscle contraction.
Q8. Describe the events of skeletal muscle contraction (flow diagrammatically).
Q9. Describe different types of skeletal muscle fibers.
Q10. Explain—Cardiac muscle cannot be tetanized in vivo.

Answer to Objective Questions

A1. Perimysium
A2. Endomysium
A3. On the myosin myofilaments
A4. Calmodulin
A5. H zone
A6. Synaptic cleft
A7. Multiunit smooth muscle
A8. Varicosities innervate the smooth muscle
A9. The T-tubules are an invagination of the muscle cell's sarcolemma
A10. Titin is a molecular spring attached to thin filaments
A11. Actin and myosin
A12. The sarcomere is the portion between two successive Z-lines

Keywords for the Answer to Subjective Questions

A1. The word rigor mortis came from two Latin words, i.e., "rigor" means "stiffness" and "mortis" means "of death." Rigor mortis or postmortem rigidity of muscles is an important sign of animal death.

A2. Muscle atrophy is the decrease in the size of the muscle due to a reduction in muscle mass.

A3. Muscle hypertrophy is the increase in the size of the muscle due to increase in muscle mass.

A4. If a muscle is used exhaustively, then the muscle's performance decreases progressively and mostly recovers after a period of rest. This phenomenon is known as muscle fatigue.

A5. In a single unit of smooth muscle, the muscle cells are connected through gap junctions. Through these gap junctions, action potential transmits from one cell to another.

Each cell receives its synaptic input through single varicosity in multiunit smooth muscle. No gap junction is present. So, cells are not electrically connected, and selective activation of muscle fibers occurs.

A6. Isotonic contraction: When the muscle length changes but the muscle tension remains unchanged, the contraction is known as an isotonic contraction (tonic = tension). Isotonic contraction is seen during walking, running, and different types of activities.

Isometric contraction: When the muscle's tension increases but the muscle's length remains the same, then the contraction is known as an isometric contraction (iso = same, metric = length). In this type of contraction, muscle provides the force, but no movement occurs at the joint and muscle length remains unchanged.

A7. Sources for skeletal muscle contraction: (1) cytosolic stored ATP, (2) creatine phosphate, (3) glycolysis, and (4) aerobic or oxidative respiration.

A8. Events of skeletal muscle contraction: crossbridge formation; power stroke generation; crossbridge detachment; reactivation of myosin heads.

A9. Types of skeletal muscle fiber: (1) slow-twitch muscle fibers or type I muscle fibers; (2) fast-twitch muscle fibers or type II muscle fibers: type IIa muscle fibers, fast-twitch glycolytic (type IIX) fibers.

A10. Cardiac muscle cannot be tetanized due to the long refractory period of its action potential.

Further Reading

Allen DG, Lamb GD, Westerblad H (2008) Skeletal muscle fatigue: cellular mechanisms. Physiol Rev 88:287–332

Basmajian JV (1978) Muscle alive: their functions revealed by electromyography. Williams & Wilkins

Bradley K (2012) Cunningham's textbook of veterinary physiology, 5th edn. Elsevier

Cooper R (1980) EEG technology. Butterworths, London

Craig R, Padrón R (2004) Molecular structure of the sarcomere. Chapter 7. In: Engel AG, Franzini-Armstrong C (eds) Myology, 3rd edn. McGraw-Hill, Inc., New York, pp 129–166

Frandson RD, Lee WW, Dee FA (2009) Anatomy and physiology of farm animals, 7th edn. Wiley–Blackwell

Goto M, Kawai M, Nakata M, Itamoto K, Miyata H, Ikebe Y, Tajima T, Wada N (2013) Distribution of muscle fibers in skeletal muscles of the cheetah (Acinonyx jubatus). Mamm Biol 78(2):127–133

Gunning P, O'Neill G, Hardeman E (2008) Tropomyosin-based regulation of the actin cytoskeleton in time and space. Physiol Rev 88:1–35

Klemm WR (1969) Animal electroencephalography. Academic, New York

Luna VM, Daikoku E, Ono F (2015) "Slow" skeletal muscles across vertebrate species. Cell Biosci 5:62

Reece WO (2015) Dukes' physiology of domestic animals, 13th edn. Wiley Blackwell

Schiaffino S, Reggiani C (2011) Fiber types in mammalian skeletal muscles. Physiol Rev 91:1447–1531

Scott W, Stevens J, Binder-Macleod SA (2001) Human skeletal muscle fiber type classifications. Phys Ther 81:1810–1816

Smith RF (1978) Fundamentals of neurophysiology. Springer

Swenson MJ, Reece WO (2005) Duke's physiology of domestic animals. Panima

Talbot J, Maves L (2016) Skeletal muscle fiber type: using insights from muscle developmental biology to dissect targets for susceptibility and resistance to muscle disease. Wiley Interdiscip Rev Dev Biol 5: 518–534

Wan JJ, Qin Z, Wang PY, Sun Y, Liu X (2017) Muscle fatigue: general understanding and treatment. Exp Mol Med 49:e384