Learn and Understand:
• The definition of “cell” changes again
• The contractile unit of muscle is the sarcomere.
• ATP and Ca\(^{2+}\) must be available for muscle to contract and relax.
• Skeletal muscle is stimulated to contract by neurons of the CNS. Nervous system controls force applied.
• Ion movement and changes in electrical potential across the sarcolemma is the ultimate signal for contraction.
• Muscle cells vary in their ability to use sources of energy and their speed of contraction.

Muscle Functions
• Four important functions
  – Movement of bones or fluids (e.g., blood)
  – Maintaining posture and body position
  – Stabilizing joints
  – Heat generation (especially skeletal muscle)
• Additional functions
  – Protects organs, forms valves, controls pupil size, causes “goosebumps”

Special Characteristics of Muscle Tissue
• **Excitability** (responsiveness): ability to receive and respond to stimuli
• **Contractility**: ability to shorten forcibly when stimulated
• **Elasticity**: ability to stretch beyond resting length and recoil

Muscle Tissue
• Nearly half of body’s mass
  – Female skeletal muscle makes up 36% of body mass
  – Male skeletal muscle makes up 42% of body mass, primarily due to testosterone
• Transforms chemical energy (ATP) to directed mechanical energy $\rightarrow$ exerts force
• Three types
  – Skeletal
  – Cardiac
  – Smooth
• Myo, mys, and sarco - prefixes for muscle
Skeletal Muscles

- Each muscle served by one artery, one nerve, and one or more veins
- Connective tissue sheaths of skeletal muscle
  - External to internal
    - Epimysium: dense irregular connective tissue
    - Perimysium: fibrous connective tissue surrounding fascicles
    - Endomysium: fine areolar connective tissue

Skeletal Muscle Fibers: Anatomy

- Long, cylindrical cell up to 30 cm long
- Multiple nuclei
- Sarcolemma
- Sarcoplasm
  - Glycosomes for glycogen storage, myoglobin for $O_2$ storage - amount of each dependent on muscle type
- Modified structures: myofibrils, sarcoplasmic reticulum, and T tubules
Figure 9.2b  Microscopic anatomy of a skeletal muscle fiber.

Sarcolemma  Mitochondrion
Dark A band  Light I band  Nucleus

Thin (actin) filament  Z disc  H zone  Z disc
Thick (myosin) filament

I band  A band  I band  M line

Sarcomere

Figure 9.2d  Microscopic anatomy of the sarcomere

Z disc  Sarcomere  M line  Z disc

Thin (actin) filament

Elastic (titin) filaments

Thick (myosin) filament

Longitudinal section of filaments within the sarcomere of a myofibril

Each thick filament consists of many myosin molecules whose heads protrude at opposite ends of the filament. Myosin heads are present only in areas of myosin-actin overlap.

Each thin filament consists of two strands of actin subunits twisted into a helix plus two types of regulatory proteins (troponin and tropomyosin).

Myosin head
Tropomyosin
Troponin
Actin

Actin-binding sites
ATP-binding site
Heads
Tail
Flexible hinge region
Myosin molecule

Active sites for myosin attachment
Figure 9.5 Relationship of the sarcoplasmic reticulum and T tubules to myofibrils and sarcomeres of skeletal muscle.

### Triad Relationships

- T tubules conduct impulses deep into muscle fiber; every sarcomere
- Integral proteins protrude into intermembrane space from T tubule and SR cistern membranes and connect with each other
- T tubule integral proteins act as voltage sensors and change shape in response to voltage changes
- SR integral proteins are channels that release Ca\(^{2+}\) from SR cisterns when voltage sensors change shape

### Sliding Filament Model of Muscle Contraction

- In relaxed state, thin and thick filaments overlap only at ends of A band
- Actin myofilaments are pulled (slide) over myosin to shorten sarcomeres
  - Actin and myosin do not change length
  - Occurs when myosin heads bind to actin
- Shortening occurs when tension generated by cross bridges on thin filaments exceeds forces opposing shortening
Figure 9.6  Sliding filament model of contraction.

1. Fully relaxed sarcomere of a muscle fiber

2. Fully contracted sarcomere of a muscle fiber

Figure 9.22  Length-tension relationships of sarcomeres in skeletal muscles.
Stimulus for Contraction: Upsetting Ion Concentrations at the Sarcolemma

- Resting membrane potential (RMP) maintained by active transport
  - Just outside the sarcolemma: high Na⁺ concentration, some Cl⁻, some K⁺
  - Just inside the sarcolemma: high K⁺ and negatively-charged proteins
- Action potential (AP) stimulates contraction
  - Changes to membrane permeability resulting in ion movement
  - Voltage change is the stimulus
- Resting potential re-established almost immediately

Polarized Membrane: Resting Membrane Potential

- Unequally-distributed ions
- Membrane is POLARIZED
Ion Channel Role in Maintaining/Upsetting Potential

- **Types**
  - **Ligand-gated.** Ligands are molecules that bind to receptors.
    - Receptor: protein or glycoprotein with a receptor site
    - Example ligand: neurotransmitters
  - **Voltage-gated**
    - Open and close in response to small voltage changes across plasma membrane
- Each is specific for one ion

Resting Potential

What’s missing:
- Open K⁺ channels
- Na⁺/K⁺ pump

Action Potentials

- **Phases**
  - Graded (end plate) potential at NMJ
  - Threshold
  - Depolarization
  - Repolarization
- All-or-none principle
- Propagation
The Nerve Stimulus and Events at the Neuromuscular Junction

- Skeletal muscles stimulated by somatic motor neurons
- Axons of motor neurons travel from central nervous system via nerves to skeletal muscle
- Each axon forms several branches as it enters muscle
- Each axon ending forms neuromuscular junction with single muscle fiber
  - Usually only one per muscle fiber
  - Situated midway along length of muscle fiber
Figure 9.8 When a nerve impulse reaches a neuromuscular junction, acetylcholine (ACh) is released.

1. Nerve impulse arrives at axon terminal
2. Acetylcholine released by synaptic terminal into synaptic cleft
3. ACh diffuses across cleft and binds with nicotinic (excitatory) receptors on sarcolemma opening sodium ion gates
4. Sodium influx depolarizes sarcolemma to threshold
5. Propagation of AP away from NMJ along fiber sarcolemma

Action Potential Propagation

Propagation in one direction only due to refractory period
Excitation-Contraction (E-C) Coupling

- Events that transmit AP along sarcolemma lead to sliding of myofilaments
- AP brief; ends before contraction
  - Causes rise in intracellular Ca\(^{2+}\) which initiates contraction

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

- At low intracellular Ca\(^{2+}\) concentration
  - Tropomyosin blocks active sites
  - Myosin heads cannot attach to actin
  - Muscle fiber relaxed
- At higher intracellular Ca\(^{2+}\) concentrations
  - Ca\(^{2+}\) binds to troponin
    - Troponin changes shape and moves tropomyosin away from myosin-binding sites
    - Myosin heads bind to actin
  - When nervous stimulation ceases, Ca\(^{2+}\) pumped back into SR and contraction ends

Figure 9.12 The cross bridge cycle is the series of events during which myosin heads pull thin filaments toward the center of the sarcomere.
Relaxation

• $\text{Ca}^{2+}$ moves away from troponin-tropomyosin complex causing ‘relaxation’
• $\text{Ca}^{2+}$ **diffuses** out of the myofibril
  – Transformed back into sarcoplasmic reticulum by **active transport**.
• Troponin-tropomyosin complex re-establishes its position and blocks binding sites.
  – Myosin cannot form cross bridges, filaments cannot slide
• **Muscle recoil**
  – Sarcomere elements, connective tissue, antagonistic muscle action and opposing forces, gravity

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**Principles of Muscle Mechanics**

• Same principles apply to contraction of single fiber and whole muscle
• Contraction produces **muscle tension**, force exerted on load or object to be moved
Motor Unit: The Nerve-Muscle Functional Unit

- Each muscle served by at least one motor nerve
  - Motor nerve contains axons of up to hundreds of motor neurons
  - Axons branch into terminals, each of which → NMJ with single muscle fiber
- **Motor unit** = motor neuron and all (four to several hundred) muscle fibers it supplies
  - Smaller number = fine control

![Figure 9.13 A motor unit consists of one motor neuron and all the muscle fibers it innervates.](image)
Motor Unit

- Muscle fibers from motor unit spread throughout muscle so single motor unit causes weak contraction of entire muscle
- Motor units in muscle usually contract asynchronously; helps prevent fatigue

Graded Muscle Responses

- Graded muscle responses
  - Varying strength of contraction for different demands
- Required for proper control of skeletal movement
- Responses graded by
  1. Changing frequency of stimulation
  2. Changing strength of stimulation

Figure 9.15a  A muscle’s response to changes in stimulation frequency.
Response to Change in Stimulus Strength

- **Recruitment** (multiple motor unit summation) controls force of contraction
  - **Subthreshold stimuli** – no observable contractions
  - **Threshold stimulus**: stimulus strength causing first observable muscle contraction
  - **Maximal stimulus** – strongest stimulus that increases contractile force
Figure 9.16 Relationship between stimulus intensity (graph at top) and muscle tension (tracing below).

Frog Gastrocnemius

Muscle Tone

- Constant, slightly contracted state of all muscles
- Due to spinal reflexes
  - Groups of motor units alternately activated in response to input from stretch receptors in muscles
- Keeps muscles firm, healthy, and ready to respond
- Less active when lying down or asleep
Muscle Metabolism: Energy for Contraction

- ATP only source used directly to move and detach cross bridges, calcium pumps in SR, return of Na⁺ & K⁺ after excitation-contraction coupling
- Available stores of ATP depleted in 4–6 seconds
- ATP regenerated by:
  - Direct phosphorylation of ADP by creatine phosphate (CP)
  - Anaerobic pathway (glycolysis → lactic acid)
  - Aerobic respiration

Anaerobic Pathway

- Glycolysis – does not require oxygen
- At 70% of maximum contractile activity
  - Bulging muscles compress blood vessels; oxygen delivery impaired
- Anaerobic respiration yields only 5% as much ATP as aerobic respiration, but produces ATP 2½ times faster
- Anaerobic threshold
  - Point at which muscle metabolism converts to anaerobic
Aerobic pathway

Aerobic cellular respiration

Energy sources: glucose; pyruvic acid; free fatty acids from adipose tissue; amino acids from protein catabolism

Glucose from glycogen breakdown or delivered from blood

Pyruvic acid

Fatty acids

Amino acids

Oxygen use: Required

Products: 32 ATP per glucose, CO$_2$, H$_2$O

Duration of energy provided: Hours

- Produces 95% of ATP during rest and light to moderate exercise; slow
- Series of chemical reactions that require oxygen
- Fuels:
  1. stored glycogen
  2. then bloodborne glucose
  3. pyruvic acid from glycolysis
  4. and free fatty acids
- Aerobic endurance
  - Length of time muscle contracts using aerobic pathways

Figure 9.20 Comparison of energy sources used during short-duration exercise and prolonged-duration exercise.

Muscle Fatigue

- Physiological inability to contract despite continued stimulation
- Occurs when
  - Ionic imbalances (K$^+$, Ca$^{2+}$, P$_i$) interfere with E-C coupling
  - Prolonged exercise may damage SR and interferes with Ca$^{2+}$ regulation and release
- Total lack of ATP occurs rarely, during states of continuous contraction, and causes contractures (continuous contractions)
  - Includes rigor mortis
Excess Postexercise Oxygen Consumption

- To return muscle to resting state
  - Oxygen reserves replenished
  - Lactic acid converted to pyruvic acid
  - Glycogen stores replaced
  - ATP and creatine phosphate reserves replenished
- All require extra oxygen; occurs post exercise

Muscle Fiber Type

- Most muscles contain mixture of fiber types
- Classified according to two characteristics
  - Speed of contraction: **slow or fast fibers**
    - Speed at which myosin ATPases split ATP
    - Pattern of electrical activity of motor neurons
  - Metabolic pathways for ATP synthesis
    - **Oxidative fibers**—use aerobic pathways
      - Slow oxidative fibers; Fast oxidative fibers;
    - **Glycolytic fibers**—use anaerobic glycolysis
      - Fast glycolytic fibers
- All fibers in one motor unit same type
  - Genetics dictate individual's percentage of each
  - Training can aid in development of what you currently have

<table>
<thead>
<tr>
<th>Table 9.2</th>
<th>Structural and Functional Characteristics of the Three Types of Skeletal Muscle Fibers</th>
<th>SLOW OXIDATIVE FIBERS</th>
<th>FAST OXIDATIVE FIBERS</th>
<th>FAST GLYCOLYTIC FIBERS</th>
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<td><strong>Muscle Characteristics</strong></td>
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<td>Speed of contraction</td>
<td>Slow</td>
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<td>Fast</td>
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<tr>
<td>Oxidative ATPase activity</td>
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<td>Fast</td>
<td>Fast</td>
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<td>Primary pathway for ATP synthesis</td>
<td>Anaerobic + aerobic (slow oxidative)</td>
<td>Anaerobic (fast oxidative)</td>
<td>Anaerobic glycolysis</td>
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<td>Mitochondrial content</td>
<td>High</td>
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<td>Glycogen stores</td>
<td>Low</td>
<td>Intermediate</td>
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<td>Recruitment order</td>
<td>First</td>
<td>Second</td>
<td>Third</td>
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<tr>
<td>Rate of fatigue</td>
<td>Slow (fatigue-resistant)</td>
<td>Intermediate (moderately fatigue-resistant)</td>
<td>Fast (fatigue-prone)</td>
<td></td>
</tr>
</tbody>
</table>

| Activities Best Served For | Endurance-type activities, e.g., running or swimming, maintaining posture for extended periods of time | Sprinting, cycling | Short-term intense or powerful movements, e.g., lifting a weight |

<table>
<thead>
<tr>
<th>Structural Characteristics</th>
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<tbody>
<tr>
<td>Color</td>
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<td>Intermediate</td>
<td>Large</td>
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<td>Capillaries</td>
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<td>Few</td>
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