

# SKELETAL SYSTEM ANATOMY & PHYSIOLOGY

# osms.it/skeletal-system-anatomy-physiology

# SKELETAL BASICS

- 206 bones in skeleton
- Separated into axial, appendicular skeleton

### **Axial skeleton**

 Vertical axis of body; 80 bones (22 in skull, 33 vertebrae, 24 ribs, 1 sternum)

### Appendicular skeleton

• Supports limbs; pectoral girdle (clavicles, scapulae) holds humeri, pelvic girdle (hip bones) holds femora; 126 bones (4 in shoulders, 6 arms, 54 hands, 2 hips, 8 legs, 52 feet)

### TYPES OF BONES

### Long bones

- Length > width
- Humerus, radius, ulna (in arms); metacarpals, phalanges (hands, fingers); femur, tibia, fibula (legs); metatarsals, phalanges (feet, toes)
- Primarily responsible for height

#### **Short bones**

- Similar length, width
- Carpal bones (in wrists); tarsal bones (ankles)
- Support hands, feet

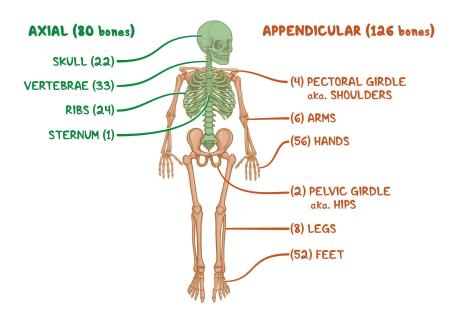


Figure 48.1 Overview of skeleton.

#### Flat bones

- Thin, sometimes curved
- Skull bones; scapulae, sternum, ribs
- Protect vital organs

#### Sesamoid bones

- Embedded in tendons, shaped like giant sesame seeds
- Pisiform bone (in wrists); patella (knees)
- Support, protect, give additional leverage to tendons

## Irregular bones

• Facial bones; mandible; vertebrae; sacrum, COCCYX

### SURFACE FEATURES OF BONES

# Sites of muscle, ligament attachment

- Tubercle, tuberosity: small bumps on bone, serve as attachment sites for muscles; large tubercle → tuberosity; deltoid tuberosity (on humerus)
- Process: bony prominence; xiphoid process (sternum)
- Crest: narrow ridge; iliac crest (ilium)

#### **Projections**

- Part of joints
- Condyle: rounded, articular projection; lateral, medial condyles (femur); epicondyle → raised portion on/above condyle (lateral, medial epicondyles)
- Ramus: arm-like section: mandibular ramus (mandible)

### Openings, passageways, depressions

- Foramen: holes in bone, allow blood vessels/nerves through; foramen magnum (in occipital bone of skull)
- Canal/meatus: tunnels, allow blood vessels/ nerves through; optic canal (sphenoid bone); external auditory meatus (temporal bone of ear)
- Sinuses, cavities: empty spaces within/ between bones; nasal cavity, paranasal sinuses
- Fossa: depressions where other structures rest; hypophyseal fossa (sphenoid bone)

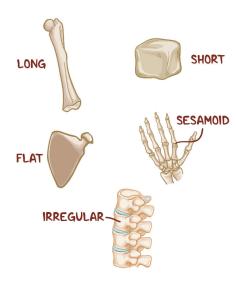


Figure 48.2 Types of bones.

# STRUCTURE OF BONE

### Cortical/compact bone

- Surrounded by periosteum
- Contains pipe-like structures called osteons
- Osteons contain hollow centers (Haversian canals) for nerves, blood cells; connected laterally by Volkmann's canals
- Osteon walls made of bone matrix (type I collagen reinforced with hydroxyapatite), produced by osteoblast cells
- Some osteoblasts get trapped in bone matrix → mature into osteocytes → repair old/broken bone
- Osteoclast cells secrete enzymes → break down bone matrix → release calcium, phosphate into blood

### Trabecular/spongy bone

- Similar material to cortical bone
- Looser structure; branching rods called trabeculae
- Contains bone marrow, consists of hematopoietic stem cells ("red marrow"), adipocytes/fat cells ("yellow marrow")
  - Appendicular bones often contain red marrow at tips, yellow marrow in hollow medullary cavity (center)
  - Axial bones mostly red marrow

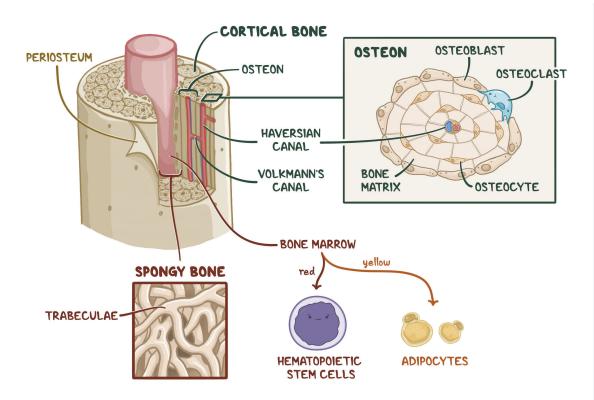


Figure 48.3 Bone cross-section showing structure which consists of cortical bone and spongy bone. Spongy bone contains two types of bone marrow, each made up of a different kind of cell.

# CARTILAGE

# osms.it/cartilage

# WHAT IS CARTILAGE?

- Strong, flexible connective tissue
  - Comprises part of nose, ears
  - Provides cushioning between joints
  - Supports/connects body parts (e.g. costal cartilage connects ribs to sternum)
- Perichondrium: connective tissue that wraps around cartilage
  - Outer laver contains fibrous connective tissue, blood vessels
  - □ Inner layer contains chondroblasts → secrete proteins that make extracellular matrix

- Extracellular matrix: protein fibers (collagen for strength; elastin for flexibility) suspended in viscous gel (water, proteoglycan aggregates)
  - Chondrocytes: chondroblasts trapped in lacunae (small holes) of matrix; maintain, repair extracellular matrix
  - Proteoglycan aggregates: hyaluronan (long chain of hyaluronic acid molecules) with hundreds of proteoglycans (proteins + long chains of glycosaminoglycan sugars—GAGS) branching off

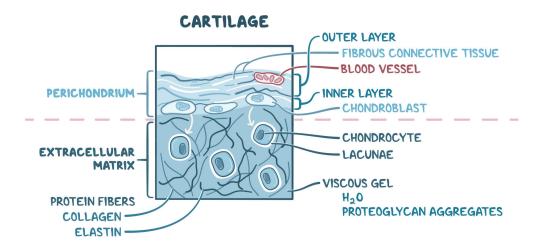


Figure 48.4 Cross-section through cartilage showing its histological structure. Perichondrium wraps around extracellular matrix. Chondroblasts originally in perichondrium become chondrocytes as they become trapped in the extracellular matrix.

## **TYPES**

Three main cartilage types

### Elastic cartilage

- Least common type
- ↑ chondrocyte density; ↓ protein fiber density (mostly loose elastin fibers, some type II collagen fibers)
- Softest, most flexible cartilage
- Ear pinnae, throat epiglottis

### Hyaline cartilage

- Most common type
- Medium chondrocyte density; medium protein fiber density (mostly type II collagen fibers, some loose elastin fibers)
- Stronger, but less flexible cartilage; \( \) friction surface
- Embryonic skeleton (eventually replaced by bone); nose; larynx walls; tracheal, costal cartilages; growth plates; articular cartilages

### **Fibrocartilage**

- ↓ chondrocyte density; ↑ protein fiber density (mostly type I collagen fibers)
- Most tensile strength; resistant to compression, stretching; ↓ flexible
- Meniscus of knee, spinal intervertebral discs

### PROTEOGLYCAN AGGREGATE

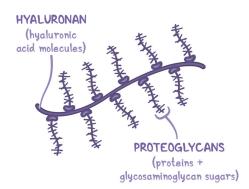


Figure 48.5 Proteoglycan aggregate, found in viscous gel of the extracellular matrix.

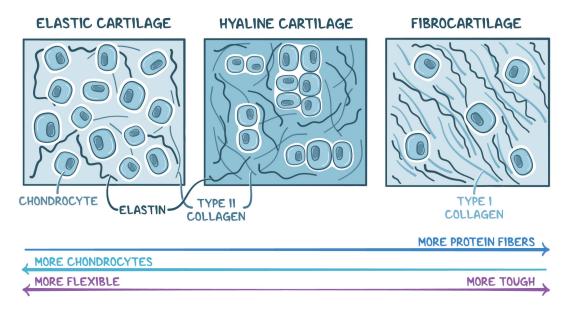


Figure 48.6 Histology, characteristics of the three main cartilage types.

# **GROWTH PATTERNS**

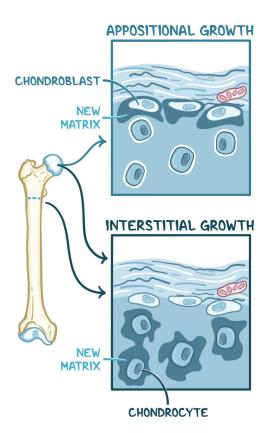
- Two cartilage growth patterns
- Both growth patterns present in growing bones of children, teenagers (e.g. femur)
  - Chondrocytes in growth plate →
    interstitial growth → cartilage lengthens
    → osteoblasts turn cartilage into bone
  - Articular cartilage on tips of bone experience both appositional, interstitial growth

## Appositional growth

 Chondroblasts secrete new matrix on existing surfaces → cartilage expands, widens

## Interstitial growth

 Chondrocytes secrete new matrix within cartilage → cartilage grows in length



**Figure 48.7** The two cartilage growth patterns. Both types of growth occur in articular cartilage. In the growth plate, only interstitial growth occurs.

# **BONE REMODELING & REPAIR**

# osms.it/bone-remodeling-repair

### **BONE REPAIR**

- Old bone removed/resorbed (broken down) before new tissue replaces it
  - 1. Osteoblasts sense microcracks, secrete receptor activator of nuclear factor κβ ligand (RANKL)
  - 2. RANKL binds to RANK receptors on monocytes  $\rightarrow$  causes them to fuse, form multinucleated osteoclast cells
  - 3. Osteoclasts secrete lysosomal enzymes (mostly collagenase) → digest collagen in bone matrix → create surface holes

- (Howship's lacunae), hydrochloric acid → dissolves hydroxyapatite into soluble calcium, phosphate
- 4. Osteoblasts secrete osteoprotegerin → deactivates RANKL, slows down osteoclast activity (before osteoclast apoptosis), osteoid seam (mostly collagen) → fill in Howship's lacunae
- 5. Calcium, phosphate deposit on seam forming hydroxyapatite
- 6. Some osteoblasts get trapped within lacunae → turn into osteocytes

# **BONE REPAIR** RANK OSTEOPROTEGERIN RANKL **OSTEOBLAST** 00000 MONOCYTE **APOPTOSED OSTEOCLAST MICROCRACKS** CALCIUM + PHOSPHATE OSTEOCLAST **HYDROXYAPATITE** OSTEOID SEAM LYSOSOMAL **ENZYMES** (e.g. collagenase) HCI COLLAGEN **OSTEOCYTE** HOWSHIP'S HYDROXYAPATITE LACUNA Y CALCIUM + PHOSPHATE

Figure 48.8 Summary of bone repair.

### REMODELING FACTORS

- Hormonal
  - Parathyroid hormone enhances bone resorption
  - Calcitonin inhibits bone resorption
  - Vitamin D (→ ↓ calcitonin) enhances bone resorption
- Mechanical (physical stress)
  - Wolff's law: bones that bear more weight remodel more

# FIBROUS, CARTILAGE, & SYNOVIAL JOINTS

# osms.it/fibrous-cartilage-synovial-joints

# TYPES

- Classification based on movement of three main groups
  - Fibrous joints: no movement
  - Cartilaginous joints: some movement
  - Synovial joints: freely movable

### FIBROUS JOINTS

- Synarthrosis/fixed joints
- Bones are connected by ligaments

## Three main categories (based on location)

- Sutures: junctions between adjacent skull bones; Sharpey's fibers connect bones; fixed (non-fused in babies → partially movable)
- Gomphoses: peg-and-socket joints for teeth; periodontal ligaments connect roots of teeth to sockets; slightly movable
- Syndesmoses: remaining fibrous joints; connected by interosseous membrane (e.g. between radius, ulna); slightly movable

# FIBROUS JOINTS

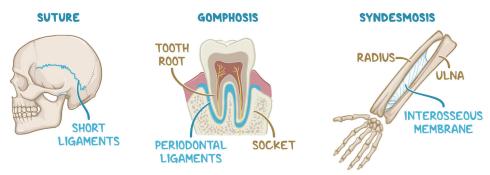


Figure 48.9 Three main categories of fibrous joints.

### CARTILAGINOUS JOINTS

- Hyaline cartilage connects bones, stretches to allow some movement
- Synchondrosis: costochondral joint, where cartilage attaches rib to sternum; growth plates between bone diaphysis, epiphysis
- Symphysis: symphysis pubis in pelvic bone (fibrous cartilage)
  - ↑ strength, ↓ flexibility

### SYNOVIAL JOINTS

- Joint capsule connects bones
  - Composed of outer fibrous capsule, inner synovial membrane
  - Filled with synovial fluid: lubricates joint, absorbs shock; made of hyaluronic acid, lubricin, proteinases, collagenases
  - Articular cartilage covers tips of bones (same function)
- Allow for abduction, adduction, rotation about axis

# Six main categories (based on structure, movement)

- Hinge joints: allow movement only in one axis (e.g. between humerus, ulna)
- Pivot joints: allow for rotation (e.g. between head of radius, groove of ulna)
- Plane (gliding) joints: allow flat bones to glide across one another (e.g. in carpal, tarsal bones)
- Ball and socket joints: allow all movements (e.g. shoulder joint)
- Condyloid (ellipsoid) joints: allow most movements, but not rotation (e.g. metacarpophalangeal, metatarsophalangeal joints)
- Saddle joints: allow most movements, with limited rotation (e.g. carpometacarpal joint)

## **CARTILAGINOUS JOINTS**

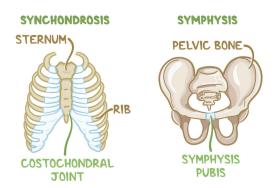


Figure 48.10 The two categories of cartilaginous joints (with examples).

### JOINT CAPSULE

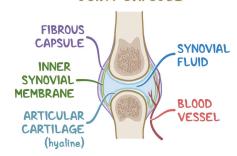


Figure 48.11 Synovial joint cross-section showing joint capsule.

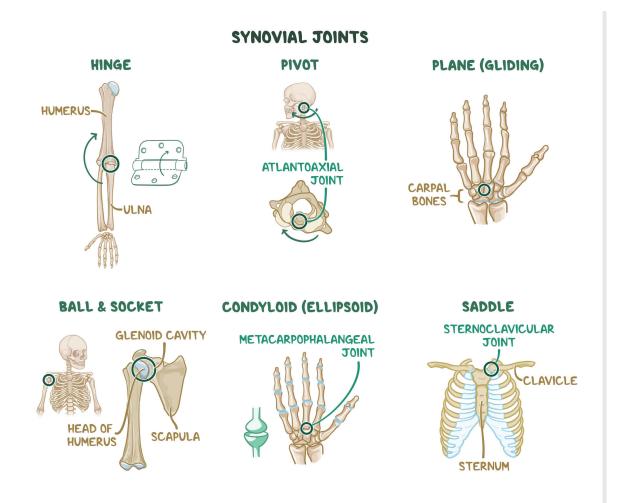


Figure 48.12 The six categories of synovial joints (with examples). Joints circled in green.



# NOTES **MUSCLES**

# **MUSCULAR SYSTEM ANATOMY &** PHYSIOLOGY

# osms.it/muscle-anatomy-physiology

- Three types of muscle cell/tissue
  - Skeletal, cardiac, smooth
- Differ in location, innervation, cell structure
  - All cells excitable, extensible, elastic

## SKELETAL MUSCLE

- Attaches to bone/skin; mostly voluntary; maintains posture, stabilizes joints, generates heat
- Most muscles consist of belly (contracts), tendons

### Connective tissue

- Layers of connective tissue separate muscle belly
  - Epimysium: wrapped around muscle
  - Perimysium: wrapped around fascicles in muscle
  - Endomysium: wrapped around muscle fibers/cells (e.g. myocytes in fascicles)

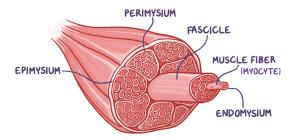


Figure 49.1 Cross section of skeletal muscle illustrating connective tissue layers, fascicles, muscle fibers.

- Combine at end to form tendons
  - Origin attaches to stationary bone; insertion attaches to moving bone

### **Myocytes**

- Long cylindrical cells with multiple nuclei
- Cell membrane → sarcolemma
- Cytoplasm → sarcoplasm
  - Contains smooth endoplasmic reticulum → sarcoplasmic reticulum (stores calcium)
- Transverse tubules (T tubules) project from sarcolemma to center of muscle
- Long filaments called myofibrils fill sarcoplasm, contain thin actin filaments, thick myosin filaments (arranged into sarcomeres)

## Motor signals

- Brain's motor signals control skeletal
- Motor neurons release acetylcholine receptors onto sarcolemma → rapid ion shifts across sarcolemma, down T tubules → calcium enters myocyte → sarcoplasmic reticulum releases calcium into sarcoplasm  $\rightarrow$  actin, myosin bind  $\rightarrow$ sarcomeres contract → myocyte contracts → sarcoplasmic reticulum grabs calcium → muscle relaxes

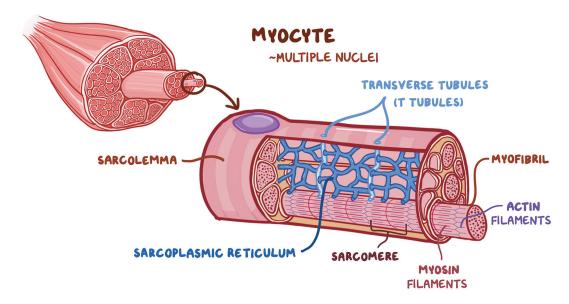


Figure 49.2 Composition of a myocyte.

## CARDIAC MUSCLE

- Involuntary, striated muscle; found only in heart walls
- Shorter than skeletal muscle: branched and interconnected
- 1–2 central nuclei per fiber
- Numerous mitochondria provide resistance to fatique
- Pacemaker cells demonstrate automaticity; generate action potentials

### Intercalated discs

- Composed of gap junctions and desmosomes
  - Gap junctions: areas of low resistance, allows fast signal propagation between cardiomyocytes (coordinated contraction of cells)
  - Desmosomes: anchor the cells together; keeps cells from pulling apart during contraction
  - Allows heart to work as a unit (functional syncytium; syn = together, citos = cell

### T tubules/transverse tubules

- Invaginate from sarcolemma
- Also serve faster propagation
  - Help conduct signal deeper into cell, enabling more synchronized contraction
  - Run along Z bands, communicate with sarcoplasmic reticulum (Ca2+ storage)

#### Thick and thin filaments

- Like skeletal muscle, cardiac myofibrils contain sarcomeres bounded by Z bands
  - <sup>a</sup> Z bands: perpendicular to myofibril, attached to thin filaments
  - Thick filaments lie between Z bands
  - All proteins involved are globular
- Thick, thin filaments slide over each other → contraction

#### Thick filaments

- Myosin: tail with two heads
  - Each head has ATPase, actin binding sites

### Thin filaments

- Actin: globular/G-actin polymerizes into a strand of filamentous/F-actin
  - Two F-actins twist into strand with myosin binding site
- Tropomyosin: site blocker, prevents contraction by disabling attachment of myosin to actin
- Troponin: molecule composed of three subunits:
  - $\,$  □ C: Ca<sup>2+</sup> binding  $\rightarrow$  stops troponin inhibition of actin
  - □ I: Inhibitory → inhibits ATPase
  - ¬ T: → relaxed state attachment of troponin complex to actin; myocardial infarction marker in blood

# **Endomysium (intercellular connective**

- Contains capillaries, nerves
- Provides support, elasticity; separates cells
- Maintained by fibroblasts

# SMOOTH MUSCLE

- Often found in hollow organs (e.g. intestines, bladder, uterus, blood vessels); involuntary muscle
- Smooth muscle cells fusiform, only one nucleus
- No T tubules; invaginations called caveolae
- Thin, thick myofilaments; no sarcomeres → "smooth" appearance

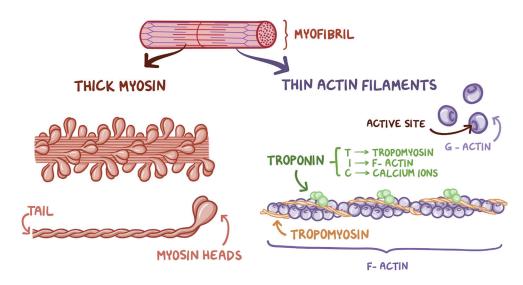


Figure 49.3 Appearance of myosin and actin filaments.

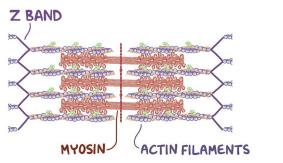


Figure 49.4 Z bands are the boundaries between sarcomeres in skeletal and cardiac muscles.

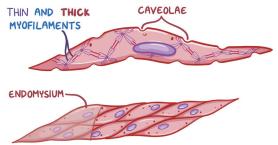


Figure 49.5 Features of smooth muscle cells.

| TYPES OF MUSCLE                            |   |  |  |
|--|---|--|--|
|  | SKELETAL                                    | SMOOTH   | CARDIAC                                  |
| LOCATION                                   | Attached to bones                           | Forms walls of hollow<br>organs<br>Lines blood vessels, glands                                     | Heart                                    |
| NEUROLOGICAL<br>CONTROL                    | Voluntary                                   | Involuntary  | Involuntary                              |
|  | Involuntary (reflexes,<br>shivering)        |  |  |
|  | Innervation: somatic<br>nervous system      | Innervation: autonomic<br>nervous system   | Innervation: autonomic<br>nervous system |
|  | Neurotransmitter: ACh                       | Neurotransmitter: ACh, NE  | Neurotransmitter: ACh                    |
|  |   | Also regulated by hormones<br>(e.g. oxytocin), locally-<br>produced substances (e.g.<br>histamine) |  |
|  |   | Autorhythmicity (e.g.<br>visceral smooth muscle in<br>digestive tract)                             | Autorhythmicity:<br>pacemaker cells      |
|  |   | Contracts in response to being stretched   |  |
| FUNCTIONS                                  | Movement, posture,<br>stabilization of body | Wide distribution  | Propulsion of blood                      |
|  | Shivering thermogenesis                     | Digestive tract: movement of food  |  |
|  | Voluntary control of micturition (external  | Urinary: bladder emptying  |  |
|  | sphincter)                                  | Vascular: vessel diameter  |  |
|  |   | Sensory: pupil size changes  |  |
|  |   | Endocrine: contraction of glands   |  |
| CELL<br>CHARACTERISTICS                    | Long, cylindrical, striated                 | Spindle-shaped   | Cylindrical, striated,<br>branched       |
| NUCLEUS                                    | Multiple                                    | One, centrally located   | One, centrally located                   |
| SPECIAL<br>CELL-TO-CELL<br>CHARACTERISTICS | None  | Gap junctions in some<br>visceral cells  | Intercalated discs                       |
|  |   | visceral cells   | Desmosomes                               |
|  |   |  | Gap junctions                            |

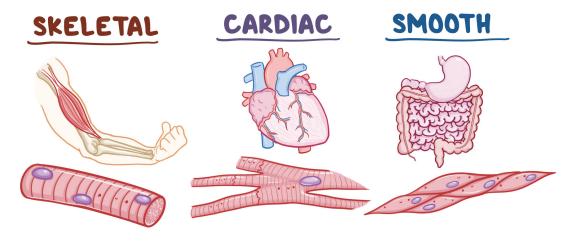


Figure 49.6 An illustration of the three types of muscle: skeletal, cardiac, and smooth.

# **SLOW TWITCH & FAST TWITCH** MUSCLE FIBERS

# osms.it/slow-fast-twitch-muscle-fibers

- Each action potential generates brief muscle contraction (AKA twitch)
- Twitches overlap to create longer, smooth muscle contractions

## Skeletal muscle fibers

- Slow twitch (AKA slow oxidative)
- Fast twitch (AKA fast oxidative, fast alycolytic)
- Slow twitch fibers → slow-functioning ATPases → slower individual twitches
- Fast twitch fibers → fast-functioning ATPases → longer individual twitches

## **SLOW OXIDATIVE FIBERS**

- AKA Type I fibers
- Have aerobic respiration pathway for metabolizing glucose
- Relatively small → weakest contractions
- ↑ blood vessels, ↑ myoglobin → red color AKA "slow red muscle fibers"
- ↑↑ mitochondria supports aerobic respiration
- Generate lots of ATP, use little; ↓ glycogen
- Sustain muscle ability for long time

### **FAST OXIDATIVE FIBERS**

- AKA Type IIa fibers
- Have aerobic respiration pathway for metabolizing glucose
- Larger than slow fibers → stronger contractions
- ↑ blood vessels, ↑ myoglobin → red color AKA "fast red muscle fibers"
- ↑↑ mitochondria supports aerobic respiration
- Generate lots of ATP, use more; ↑ glycogen storage
- Fatigue quickly

# FAST GLYCOLYTIC FIBERS

- AKA Type IIx fibers
- Have anaerobic respiration pathway for metabolizing glucose
- Largest fibers → stronger contractions
- ↓ blood vessels, ↓ myoglobin → white color AKA "white muscle fibers"
- J mitochondria
- Generate little ATP, use lots; ↑↑ glycogen storage
- Fatigue fastest

# SLIDING FILAMENT MODEL OF MUSCLE CONTRACTION

# osms.it/sliding-filament-model

# MECHANISM OF MUSCLE **CONTRACTION AFTER POWER** STROKE

- Thick myosin filaments pull thin actin filaments towards M-line → sarcomere shortens; A-band of the muscle does not change, but H-, I-bands shorten
- At max contraction, almost complete overlap of thick, thin filaments; H-, I- bands almost completely gone

# FACTORS DETERMINING **CONTRACTION FORCE**

### Size of muscle fibers

 Larger muscle fibers → ↑ filaments → ↑ cross-bridges → stronger contraction

### Number of active muscle fibers

↑ muscle fibers → stronger contraction

## Frequency of stimulation (force-frequency relationship)

 ↑ frequency of stimulation → ↑ calcium ions flow from sarcoplasmic reticulum into sarcoplasm → ↑ bind to troponin regulatory proteins on actin filaments → ↑ myosin binding → stronger contraction

### Length of sarcomere

- AKA length-tension relationship
- Longer sarcomere → stronger contraction; directly proportional

### Velocity of muscle shortening

- AKA force-velocity relationship
- Slower contraction  $\rightarrow$  stronger contraction

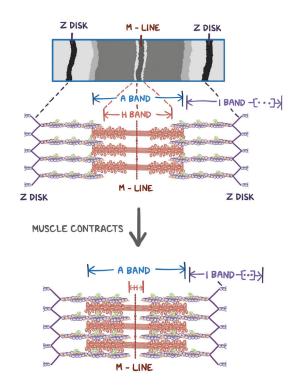


Figure 49.7 The changes that occur when muscle contracts.

# ATP & MUSCLE CONTRACTION

# osms.it/ATP-and-muscle-contraction

### MUSCLE TONE

Force applied to muscles at rest

## MUSCLE TENSION

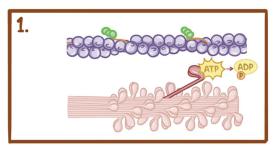
Pulling force when muscles act

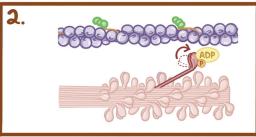
# MUSCLE CONTRACTION

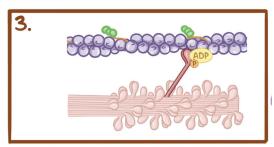
- Action potential travels along sarcolemma, reaches T-tubule, stimulating dihydropyridine (DHP) receptors
- DHP receptor stimulation opens ryanodine receptors
  - AKA calcium channels
- Calcium from sarcoplasmic reticulum flows into sarcoplasm, binds to C-subunits of troponin regulatory proteins
- Troponin changes shape, moving tropomyosin out of the way, allowing actin to be bound by myosin head's cross-bridge formation
- Energy cocks myosin head backwards → high-energy position
- Myosin head can then launch towards M-line, pulling actin filament with it
  - AKA power stroke
- Action potential ends → calcium ions pumped back into sarcoplasmic reticulum → C-subunit of troponin no longer bound → troponin, tropomyosin cover back up actin's active sites → no myosin binding (cross-bridge detaches) → muscle relaxes

# ISOTONIC VS. ISOMETRIC CONTRACTIONS

- Isotonic: muscle length changes but tension stays same
- Isometric: muscle length stays same but tension increases







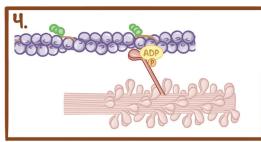


Figure 49.8 Muscle contraction.

- 1: Part of myosin head is an ATPase; it cleaves ATP into ADP and phosphate ion.
- 2: Myosin head uses this energy to tip back into its high-energy position.
- 3: Myosin head binds to active site on actin, triggering release of stored energy in myosin head.
- 4: Power stroke (myosin head launches, pulling actin with it).

# **NEUROMUSCULAR JUNCTION &** MOTOR UNIT

# osms.it/neuromuscular-junction-motor-unit

### **NEUROMUSCULAR JUNCTION**

- Where axon terminal meets muscle fiber
- Presynaptic membrane
  - Membrane of axon terminal
- Postsynaptic membrane
  - AKA motor end plate
  - Membrane of skeletal muscle fiber
- Synaptic cleft
  - Gap between membranes

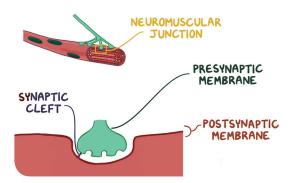


Figure 49.9 Illustration of the neuromuscular junction.

# **ACTION POTENTIAL GENERATION** IN MUSCLE FIBER

- Action potentials in axon terminal stimulate voltage-gated calcium channels in presynaptic membrane → extracellular calcium ions flow into the axon terminal
- Calcium binds to acetylcholine-containing vesicles in axon terminal → vesicles fuse with presynaptic membrane, acetylcholine released into synaptic cleft
- Two acetylcholine molecules bind to one ligand gated ion channel
  - AKA nicotinic receptor
  - On motor end plate → sodium ions flow into muscle

- Positive charge builds up inside muscle fiber → creates end plate potential
  - AKA depolarization
- Resting potential of membrane: -100mV  $\rightarrow$  -60mV
- Voltage-gated sodium channels open up → more sodium ions flow in, generating action potential in muscle fiber

# ACTION POTENTIAL CESSATION IN MUSCLE FIBER

- Action potential in axon stops → voltagegated calcium channels close → influx of calcium ions to axon terminal stops → synaptic vesicles stop fusing with membrane
- Remaining acetylcholine in cleft degraded by acetylcholinesterase into choline, acetate → choline taken back into axon terminal → acetylcholine transferase makes new acetylcholine → acetate diffuses away

### MOTOR UNITS

- One lower motor neuron, fibers it innervates form single motor unit
- On average, one lower motor neuron innervates 150 skeletal muscle fibers
- More precise muscles → smaller motor units; e.g. 10-15 muscle fibers per neuron
- Less precise muscles → larger motor units (e.g. ≤ 2000 muscle fibers per neuron in bicep)

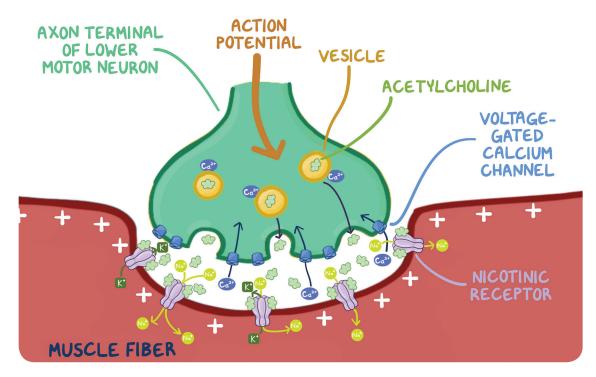


Figure 49.10 Action potential generation in muscle fiber. Influx of sodium ions leads to buildup of positive charge inside muscle fiber. Action potential generated → muscle fiber contracts.

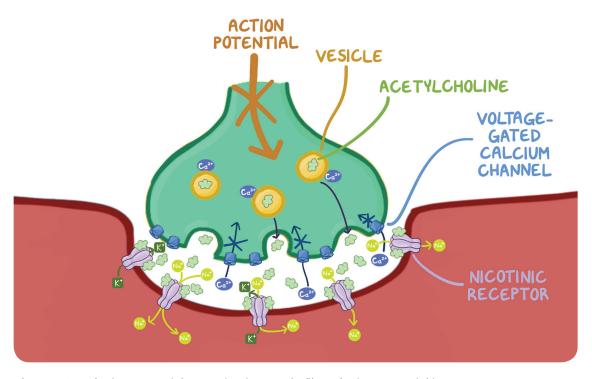


Figure 49.11 Action potential cessation in muscle fiber. Action potential in axons stops  $\rightarrow$ voltage-gated calcium channels close → influx of calcium stops → synaptic vesicles stop fusing with membrane.