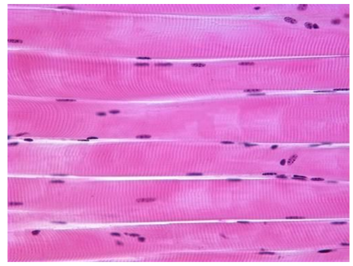
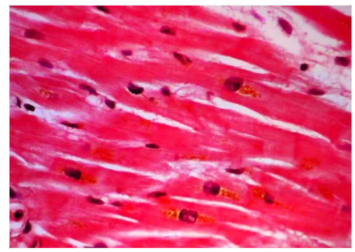
Types of muscle tissue

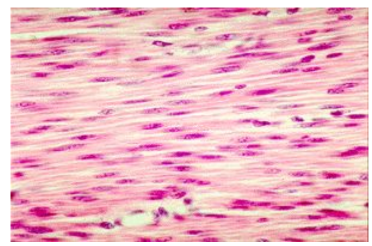
Skeletal
- Attach to and cover bone
- Longest muscle fibers
- Striated and voluntary
- Can contract rapidly
- Tires easily and must rest
- Strong an adaptable



Cardiac
- Only in the heart
- Striated and involuntary
- Pacemaker sets rate of contractions
- Neutral input can increase or decrease heart rate



Smooth
- Walls of hollow, visceral organs
- Nonstriated, involuntary
- Slow and sustained contraction



Skeletal and smooth muscle cells are elongated and are called muscle fibres
Myo, mys and sarco refer to muscles
Muscle contraction depends on actin & myosin muscle filaments (threads)

Characteristics of muscle tissue
- Excitability--responsiveness, (Irritability): “ability to receive and respond to a stimulus” stimulus usually a chemical (NT, hormone, pH), response = action potential along sarcolemma + muscle contraction
- Contractility--ability to shorten forcibly when adequately stimulated
- Extensibility--ability to be stretched or extended
- Elasticity--ability to resume resting length after being stretched

Functions
- Produce movement
    - locomotion, manipulation, blood flow & pressure, respiration, propelling of food and urine (gastrointestinal and ureteral peristalsis
- Maintain posture
    - constantly working against gravity
- Stabilize joint
    - eg: shoulders, knees when moving parts of skeleton
- Generate heat

  - maintenance of body temperature
  - esp: skeletal muscle (at least 40% of body mass)

Nerve and blood supply

One nerve, one artery and one or more vein serve each muscle
Smooth and cardiac muscle cannot contract without nerve stimulation.
Skeletal muscle has a rich supply in blood.

Connective tissue sheaths

- Epimysium is the overcoat
- Perimysium and fascicles around each layer
- Endomysium the shelth within

A muscle fiber or myocyte is a muscle cell, its plasma membrane is the sarcolemma, its intracellular fluid is sarcoplasm and it has 5 or 6 nuclei to support its huge length – 30 cm vs 0.1 mm. This is rather a large cell. Can contain multiple nuclei.

Attachments

The muscle insertion will move towards the muscle origin. Direct or fleshy attachments is when the epimysium is fused to the perimysium. In indirect attachments, connective tissue extends past the tendon or aponeurosis. Indirect is much more common because of its durability.

Microscopic anatomy of a skeletal muscle fiber

- long, cylindrical cell with many oval nuclei (cell membrane is the sarcolemma)
- huge cells (diameters of 10-100 μm & lengths in cm)
- sarcoplasm contains lots of glycogen energy store & myoglobin oxygen store - lots of myofibrils, extensive sarcoplasmic reticulum; T-tubules – hold and release Ca++

- Sarcolemma or the Pm
- Sarcoplasm- cytoplasm
  - Contains large amounts of glycosomes which is glycogen and myoglobin which store oxygen.

Myofibrils

- Each muscle fiber (cell) consists of parallel myofibrils
- ~80% of cell volume (100s to 1000s per cell)
- Made up of sarcomeres linked end to end. Sarcomeres contain myofilaments(Actin and myosin)

<u>Striations</u>

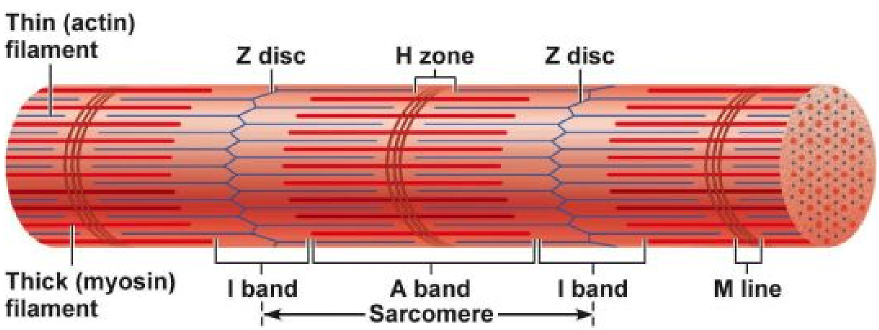
- Repeating dark and light bands. A bands are dark and I bands are light. Each A band has a lighter region called the H zone. Each H zone is bisected by a dark line called the M line. Each I band has a darker area called the Z disc.
-

Sarcomeres

- extend from one Z disc to the next Z; sarcomeres give this muscle type the name “striated muscle”

Myofilaments

- actin: = thin filaments - across I band & partly into A band
- myosin: = thick filaments - entire width of A band
- zones & lines:
- Z disc = anchors thin filaments & connects all myofibrils of a cell (nebulin, connection)
- H zone: area with no thin filaments (relaxed muscle)
- M line: fine strands connecting adjacent thick filaments (desmin)

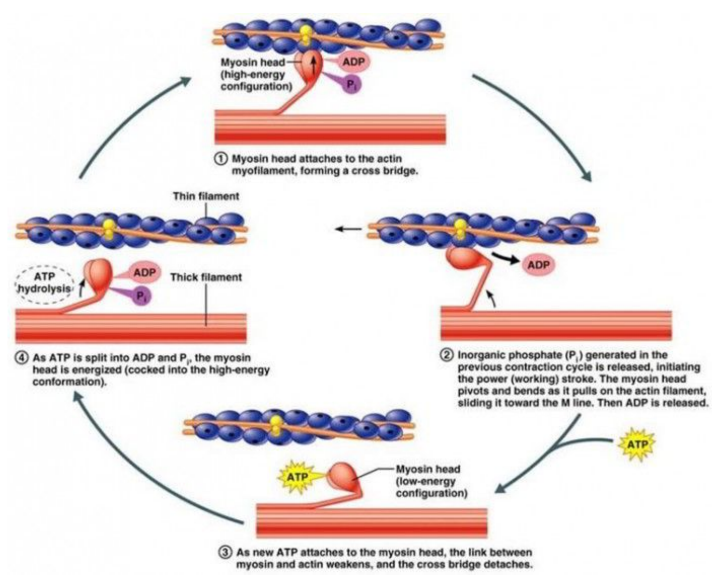


Thick filaments

- rod-like tail (2 heavy chains) + 2 globular heads (ends of heavy chains + 2 light chains = cross bridges)
- cross bridges are the business ends of the thick filaments
- each thick filament = ~200 myosins; arrayed so central part smooth & each end studded with many myosin heads
- myosin heads contain ATPase
- Contain A band and M line

Thin filaments

- binding sites for myosin [crossbridges]
- strands are F-actin; 2 strands wound as a helix
- G stands for globular actin (Where myosin binds)
- “F” stand for Filamentous (Polymerized G strand)
- Tropomyosin: a rod-shaped protein helps to stabilizes
    - stiffen filament
    - blocks crossbridge binding
- Troponin is another type of protein which attaches to the actin



<u>Elastic filament</u>

- Made on giant protein called titin
- Maintains organization
- Helps to reisis excess stretching
- Dystrophin links the thin filaments to the sarcolemma.

Muscular dystrophy is muscle destroying diseases. The most serious is DMD which is sexed linked and commonly occurs in males.

Sarcoplasmic Reticulum

- Smooth ER
- Regulates and store calcium
- Can also be called terminal cisterns.
- Elaborate web of SR around each myofibril inside PM
- Most SR tubules run longitudinally; pairs of terminal cisternae across A-I junctions
- ROLE: regulate intracellular Ca++; storage depot for Ca++ releases it when muscle stimulated to contract

T-Tubules

- Allows for membrane potential to penetrate deepest into the fiber
- Is a continuation of sarcolemma
- at A-I junction sarcolemma penetrates cytoplasm to form hollow elongated tubes; T-tubule = transverse tubule (lumen continuous with ECS)
- triad: group of 3 structures - 2 terminal cisternae + 1 T-tubule (middle)
- T system: thousands (2/sarcomere) of T-tubules in a single muscle cell
- Triads are the T-tubules and SR linked together. It helps to provide contractions.

Sliding filament

- muscle fiber shortens because sarcomeres shorten; filaments remain same length
- thin filaments slide over thick filaments
  - relaxed: only slight overlap of thick & thin filaments
  - contracted: thin filaments penetrate more deeply into A band - Z discs pulled toward thick filaments
- distance between Z discs reduced
- I bands shorten
- H zones disappear
- A bands move closer together, but stay same length
- intracellular [Ca++] low: myosin binding sites on actin blocked by tropomyosin
- Ca++ influx: binds to troponin >> shape change & brief detachment from actin >> moves tropomyosin away from myosin binding sites >> sites are exposed
- single power stroke of all cross bridges 1% shortening; only ½ of myosin heads actively pulling at one time and relaxation occurs as SR reclaims Ca++

How is works

1. Calcium binds to troponin
2. Troponin changes shape
3. Tropomyosin is moved exposing active sites on F-actin
4. Myosin heads bind to active sites on actin molecules
5. ADP and Pi (inorganic phosphate) are released from the thick filament
6. Myosin heads pull on the thin filaments (power stroke) and slide them towards the centre of the sarcomere
7. ATP binds to the thick filament
8. Myosin cross bridges detach from actin
9. ATP is hydrolyzed
10. Myosin heads return to high-energy shape, ready for the next power stroke
11. Cycling continues until calcium ions are sequestered by the SR

Neuromuscular junction & nerve stimulus:

- skeletal muscles stimulated by motor neurons of somatic ns
- 1 NMJ in ~middle of fiber - synaptic cleft; NT is acetylcholine
- events at nerve-muscle synapse identical to those in nerve-nerve synapse

Skeletal muscle contraction

1. Event at the neuromuscular junction.Releases ACh and depolarization called the end plate potential
2. Muscle fiber excitation at which the EEP causes AP
3. Excitation-contraction coupling which releases ca+2 and it binds to troponin.
4. Cross bridge cycling causes the contraction

The result of the events at the neuromuscular junction is a transient change in membrane potential that cause a depolarization which is called end plate potential EPP. During repolarization the muscle is said to be in a refractory period.

Generation of ATP across the sarcolemma

- chemically gated channels: local depolarization AP in all directions
- depolarization/repolarization with Na+, than K+ as for axon
- Na+/K+ pump to restore
- once initiated, AP is unstoppable - all-or-none response of muscle cell
- AP is brief (1-2 msec); contraction can be 100 msec
- acetylcholinesterase (AChE) = enzyme on sarcolemma of NMJ

*What is the **latent period** of excitation-contraction coupling??* *Ca diffusion*

What happens if nerve impulses arrive at the NMJ at high frequency?? *Fusion, tetanus*

Excitation-Contraction coupling

- Is the sequence of events by which transmission of AP along the sarcolemma at which causes the myofilaments to slide.

Steps in E-C coupling

1. Ap propagates along the sarcolemma and down the T tubules
2. Calcium ions are released
3. Calcium binds to troponin and removes the blocking action of tropomyosin
4. Contraction begins

Cross Bridge Cycle

1. Cross bridge formation--Energizing myosin head attaches to an actin myofilament, forming a cross bridge
2. The power (working) stroke- -ADP and P are released and the myosin head pivots and bends, charging to its bent low-energy state. As a result it pulls the actin filament towards the M line
3. Cross bridge detachment--After ATP attaches to myosin an actin weakens and the myosin head detaches ie the cross bridge breaks
4. Cooking of the myosin head--As myosin hydrolyzes ATP to ADP and P, the myosin head returns to its pre stroke high-energy or cocked position

Muscle mechanics

- The principles governing contraction of a single muscle fiber and of a skeletal muscle consisting of a large number of fibers are pretty much the same
- The force exerted by a contracting muscle on an object is called muscle tension. The opposing force exerted on the muscle by weight of the object to be moved is called the load

Motor unit: consists of one or more motor neuron and all the muscle fibers.

- motor nerve (at least 1/muscle)
- hundreds of motor neuron axons
- each axon to many axonal terminals
- each axonal terminal to NMJ of a single muscle fiber (cell)
- avg. no muscle fibers/neuron = 150   (range = 4 to hundreds)
- when neuron fires, all fibers contract

Muscle Twitch

A muscle can be attached to an apparatus at which can produce a myogram which is a recording of contractile activity consisting of one or more recorded tracings. In a lab, muscle twitch is the response of a muscle to a single simulation. Every twitch has three phases;

1. Latent period

   First few ms then E-C coupling occurs.Cross bridging beings but muscle tension hasn't
2. Period of contraction

Cross bridges are activated and myogram tracing peaks. Last 10-100ms

3. Period of relaxation

    Last 10-100ms. Pumps ca2+ into the SR. Muscle tension is 0

Graded Muscle contractions

- Vary in strength
- Can be graded in two ways
    - Increase in frequency of stimulation causes temporal summation. The higher the frequency, the greater the strength of contraction of a given motor unit
    - An increase in strength of simulation causes recruitment. The stronger the more motor units are activated.
- The brain determines the strength of a muscles contraction by changing;
        - The rate of firing of AP along the axon
        - The number of motor neurons that are activated
- 2 types of graded responses:
- 1) change speed of stimulation
- 2) change # of motor units activated

Muscle response to changes in stimulus frequency

- Temporal or wave summation
- Second contraction begins before muscle has relaxed and is greater then the first
- rapid rate of stimuli: each contraction builds on the previous one but AP refractory period is always honoured
- If muscle is stimulated at increasingly faster rate;
    - The relaxation becomes shorter
    - Ca2+ becomes higher
    - Summation gets larger which refers to incomplete tetanus
- tetanus: fused contractions - inter-stimulus interval too short to allow inter-twitch muscle relaxation - eventually followed by muscle fatigue
- primary goal: smooth, continuous contractions

Muscle Response to changes in Stimulus Strength

- Recruitment or multiple motor unit summation.
- A means of increasing strength of contraction
- Stimuli that produce no observable contractions are subthreshold stimuli
- Threshold stimulus: first observable response
- Maximal stimulus: strongest stimulus that produces an increase in contractile force (more motor units recruited)
    - smallest motor units controlled by most excitable neurons
    - more intense stimulation recruits larger motor units
- All units can be recruited simultaneously, but usu staggered result is ???

Muscle Tone

- even relaxed muscle a bit contracted (tone) due to spinal reflexes activated by stretch receptors

Isotonic Contractions

- muscle changes in length & moves load
- Concentric contractions are when the muscle shortens
- Eccentric contractions are when the muscle lengthens
- NB: eccentric contractions are 50% more forceful, use less ATP/O2 & fewer muscle fibers but more prone to delayed-onset soreness than concentric contractions

Isometric Contractions

- isometric: tension increases but muscle remains same length
- Most body movements are a mix of isotonic and isometric contractions
- Realize that in isotonic contractions, the thin filaments are sliding, but in isometric contractions the cross bridges are generating force, but do not move thin filaments

Sources of energy

1. Stored ATP:
    - ATP for cross bridge movement & detachment; Ca++ pump
    - only 4-6 sec stored ATP; regenerated immediately & continuously by (A2-A4)
2. Direct phosphorylation of ADP by creatine phosphate:
    - CP = unique high-energy molecule stored in muscles CP + ADP creatine + ATP
    - enzyme = creatine kinase; but CP reserves quickly gone (CP & ATP = 15-20 sec; @ maximum muscle power)
    - Creatine phosphate is high energy molecule
    - Catalyzes the enzyme creatine kinase
3. Aerobic respiration:
    - high ATP yield but slower (many steps); requires continuous O2/nutrients
    - Aerobic respiration
    - Creates a lot of ATP
    - Uses oxygen
4. Anaerobic glycolysis:
    - only 2 ATP/glucose but O2 not used and is fast
    - usually pyruvic acid then enters aerobic pathway; but if ~70% activity for long period, blood vessels compressed by muscles & aerobic respiration too slow
    - pyruvic acid converted to lactic acid; converted back to pyruvic acid once exercise over; aerobic respiration used to replenish ATP stores anaerobic pathway produces ~5% ATP of aerobic pathway, but is 2.5x faster >> important during vigorous muscle activity
    - Glycolysis and lactic acid form
    - No oxygen

The length at which a muscle can continue to contract is called aerobic endurance. At this point the muscle metabolism converts to anaerobic glycolysis is called anaerobic threshold.

Energy systems used during sports activities:
• weight lifting, diving, sprinting: ATP & CP because it's a short duration of intensity
• tennis, soccer, 100 m swim: almost entirely anaerobic - Because its shifts and short
• marathon runs, jogging: mainly aerobic; but anaerobic may function until aerobic reaches full efficiency
aerobic endurance: length of time a muscle can use aerobic
anaerobic threshold: point at which muscle converts to anaerobic

Muscle Fatigue
• = state of physiological inability to contract; results from a relative deficit of ATP (total absence would cause contractures)
• contributors: build-up of lactic acid, ion imbalances (Na+/K+ pump requires ATP!)

- The following chemical changes can be involved
    - Ionic imbalance
    - Increase in inorganic phosphate
    - Decrease in ATP and increase in Mg
    - Decrease in glycogen
- Lactic acid can cause

Excess postexercise oxygen consumption (EPOC) also known as Oxygen debt

- post exercise need to: replenish O2 reserves, convert lactic acid to pyruvic acid, replace glycogen stores, restock ATP & CP
- liver converts additional lactic acid to glucose/glycogen (Cori cycle)
- oxygen debt: extra amount of oxygen needed to be taken in to accomplish the above (lactic acid indirectly stimulates respiratory centre of brain)
- ATP-driven muscle contraction 20-25% efficient; dissipated by body' s cooling mechanisms

Force of Muscle Contraction

- The number of myosin bridges attaching to actin depends on
    - Frequency of simulation (High frequency high exertion)
    - Number of muscle fiber recruited (More, high force)
    - Size of muscle fibers (Bigger=powerful Hypertrophy=increase in size)
    - Degree of stretch (can create isometric contraction)
- Length-tension relationship
    - Cannot be too far or too close

Muscle Fiber Type

- Speed of contraction
    - Slow fibers and fast fibers
- Pathway for forming ATP
    - Oxidative-Aerobic
    - Glycolytic-Anaerobic

- Slow oxidative
  - Endurance
  - thin cells with slow-acting myosin ATPases - - contract slowly (red = lots of myoglobin); primary energy fuel is fat
  - lots of mitos, capillaries, aerobic enzymes: oxidative
  - fatigue-resistant, but not powerful (thin) -
- Fast oxidative
  - Sprinting or walking
  - Red or pink, intermediate cell size; fast-acting myosin ATPases & contract quickly; high myoglobin content & O2-dependent; fairly fatigue-resistant
- Fast Glycolytic
  - Short-term intense or powerful
  - Large, pale (white), little myoglobin & diameter 2x that of slow oxidative fibers; fast-acting myosin ATPases & contract quickly
  - few mitochondria; lots of glycogen reserves: glycolytic
  - will fatigue, but powerful

Most body muscles have a mixture of fiber types; genetics can alter distributions & subsequent athletic strengths

Aerobic (Endurance) Exercise

- Number of capiliatire increase
- Number of mitochondria increase
- Fibers synthesise more myoglobin
- Slow oxidative

Resistance Exercise

- Increase in muscle fibers
- Fast oxidative or fast glycolytic

Arrangement Muscle Fibers

- small, spindle-shaped cells; one centrally-located nucleus
- Longitudinal layer--parallel
- Circular layer--Circumference
- diameter 2-10 um; length 100-500 um
- cells separated by fine CT; sheets of closely opposed fibers; usually at least 2 sheets with opposite orientations
- alternating contractions of opposing layers provide mixing, peristalsis, expelling
- varicosities instead of NMJs; bulbous swellings of autonomic ns - release NT into wide synaptic cleft near smooth muscle cells - diffuse junctions
- SR less developed than in skeletal muscle; no T tubules; but SR touches sarcolemma & smooth muscle cells have large SA/volume ratio
- no striations, but do have interdigitating thick & thin filaments:

1) ratio of thick:thin=1:13 (smooth) vs 1:2 (skeletal); but smooth muscle myosin has actin-gripping heads along entire length >> strength
2) tropomyosin but no troponin (calmodulin instead)
3) no sarcomeres: thick & thin filaments spiral down smooth muscle cell
4) noncontractile intermediate filaments & dense bodies (attach to thin filaments)

Contraction of Smooth Muscle

Mechanism:

- electrical coupling via gap junctions slow, synchronized contractions
- some smooth muscle cells are pacemaker cells

Mechanism:

1) actin & myosin interact by sliding filament mechanism
2) final trigger is rise in intracellular Ca++
3) sliding process is energized by ATP

- contraction of smooth muscle is slow (30x), sustained, fatigue-resistant (24-h maintenance of tone of blood vessels, visceral organs)
- few mitos; most ATP generated aerobically

Special features of smooth muscle contraction

a) Response to stretch: more stretch (120% resting length) >> more vigorous contraction - stretching can induce brief contraction (gut) or can have stretch relaxation response (filling) What does that accomplish?
Length & tension changes: stretches more than skeletal; can generate more tension than skeletal (contracts in a corkscrew-like manner) (150% vs 60%)
c) Hyperplasia: eg. estrogen & uterine smooth muscle cells
d) Secretory functions: collagen, elastin - make their own CT

Single-unit (unitary) smooth muscle:

- = visceral muscle; more common
  1) contracts as a unit & rhythmically
  2) electrically coupled by gap junctions
  3) often spontaneous action potentials
  4) all other smooth muscle characteristics

Multiunit smooth muscle:

- eg: large airways to lungs, large arteries, arrector pili muscles of skin hair follicles, internal eye muscles for focus
  1) gap junctions, spontaneous, synchronized depolarizations rare
  2) muscle fibers structurally independent of each other
  3) richly supplied with nerve endings, each forms a motor unit with a number of muscle fibers
  4) responds to neural stimulation with graded contractions (still regulated by autonomic ns, hormones)