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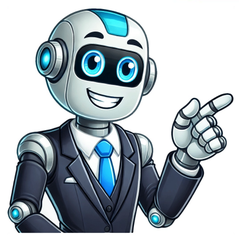

One of three major types of muscle Skeletal muscleDepiction of skeletal muscleDetailsSynonymsSkeletal striated muscle, striated voluntary muscleSystemMuscular systemIdentifiersLatinmuscularis skeletalisMeSHD018482TA21976THH2.00.05.2.00002 Anatomical terminology[edit on Wikidata] Skeletal muscle (commonly referred to as muscle) is one of the three types of vertebrate muscle tissue, the others being cardiac muscle and smooth muscle. They are part of the voluntary muscular system[1] and typically are attached by tendons to bones of a skeleton.[2][3] The skeletal muscle cells are much longer than in the other types of muscle tissue, and are also known as muscle fibers.[4] The tissue of a skeletal muscle is striated – having a striped appearance due to the arrangement of the sarcomeres. A skeletal muscle contains multiple fascicles – bundles of muscle fibers. Each individual fiber and each muscle is surrounded by a type of connective tissue layer of fascia. Muscle fibers are formed from the fusion of developmental myoblasts in a process known as myogenesis resulting in long multinucleated cells. In these cells, the nuclei, termed myonuclei, are located along the inside of the cell membrane. Muscle fibers also have multiple mitochondria to meet energy needs. Muscle fibers are in turn composed of myofibrils. The myofibrils are composed of actin and myosin filaments called myofilaments, repeated in units called sarcomeres, which are the basic functional, contractile units of the muscle fiber necessary for muscle contraction.[5] Muscles are predominantly powered by the oxidation of fats and carbohydrates, but anaerobic chemical reactions are also used, particularly by fast twitch fibers. These chemical reactions produce adenosine triphosphate (ATP) molecules that are used to power the movement of the myosin heads.[6] Skeletal muscle comprises about 35% of the body of humans by weight.[7] The functions of skeletal muscle include producing movement, maintaining body posture, controlling body temperature, and stabilizing joints.[8] Skeletal muscle is also an endocrine organ.[9][10][11] Under different physiological conditions, subsets of 654 different proteins as well as lipids, amino acids, metabolites and small RNAs are found in the secretome of skeletal muscles.[12] Skeletal muscles are substantially composed of multinucleated contractile muscle fibers (myocytes). However, considerable numbers of resident and infiltrating mononuclear cells are also present in skeletal muscles.[13] In terms of volume, myocytes make up the great majority of skeletal muscle. Skeletal muscle myocytes are usually very large, being about 2–3 cm long and 100 µm in diameter.[14] By comparison, the mononuclear cells in muscles are much smaller. Some of the mononuclear cells in muscles[15] are endothelial cells (which are about 50–70 µm long, 10–30 µm wide and 0.1–10 µm thick),[16] macrophages (21 µm in diameter) and neutrophils (12-15 µm in diameter).[17] However, in terms of nuclei present in skeletal muscle, myocyte nuclei may be only half of the nuclei present, while nuclei from resident and infiltrating mononuclear cells make up the other half.[13] Considerable research on skeletal muscle is focused on the muscle fiber cells, the myocytes, as discussed in detail in the first sections, below. Recently, interest has also focused on the different types of mononuclear cells of skeletal muscle, as well as on the endocrine functions of muscle, described subsequently, below. See also: List of skeletal muscles of the human body Front and back views of the major skeletal muscles of the human bodyFront view of major skeletal musclesBack view of major skeletal muscles There are more than 600 skeletal muscles in the human body, making up around 40% of body weight in healthy young adults.[18][19][20] In Western populations, men have on average around 61% more skeletal muscle than women.[21] Most muscles occur in bilaterally-placed pairs to serve both sides of the body. Muscles are often classed as groups of muscles that work together to carry out an action. In the torso there are several major muscle groups including the pectoral, and abdominal muscles; intrinsic and extrinsic muscles are subdivisions of muscle groups in the hand, foot, tongue, and extraocular muscles of the eye. Muscles are also grouped into compartments including four groups in the arm, and the four groups in the leg. Apart from the contractile part of a muscle consisting of its fibers, a muscle contains a non-contractile part of dense fibrous connective tissue that makes up the tendon at each end. The tendons attach the muscles to bones to give skeletal movement. The length of a muscle includes the tendons. Connective tissue is present in all muscles as deep fascia. Deep fascia specialises within muscles to enclose each muscle fiber as endomysium; each muscle fascicle as perimysium, and each individual muscle as epimysium. Together these layers are called mysia. Deep fascia also separates the groups of muscles into muscle compartments. Two types of sensory receptors found in muscles are muscle spindles, and Golgi tendon organs. Muscle spindles are stretch receptors located in the muscle belly. Golgi tendon organs are proprioceptors located at the myotendinous junction that inform of a muscle's tension. Skeletal muscle cells are the individual contractile cells within a muscle, and are often termed as muscle fibers.[3] A single muscle such as the biceps in a young adult male contains around 253,000 muscle fibers.[22] Skeletal muscle fibers are multinucleated with the nuclei often referred to as myonuclei. This occurs during myogenesis with the fusion of myoblasts each contributing a nucleus.[23] Fusion depends on muscle-specific proteins known as fusogens called myomaker and myomerger.[24] Many nuclei are needed by the skeletal muscle cell for the large amounts of proteins and enzymes needed to be produced for the cell's normal functioning. A single muscle fiber can contain from hundreds to thousands of nuclei.[25] A muscle fiber for example in the human biceps with a length of 10 cm can have as many as 3,000 nuclei.[25] Unlike in a non-muscle cell where the nucleus is centrally positioned, the myonucleus is elongated and located close to the sarcolemma. The myonuclei are quite uniformly arranged along the fiber with each nucleus having its own myonuclear domain where it is responsible for supporting the volume of cytoplasm in that particular section of the myofiber.[24][25] A group of muscle stem cells known as myosatellite cells, also satellite cells are found between the basement membrane and the sarcolemma of muscle fibers. These cells are normally quiescent but can be activated by exercise or pathology to provide additional myonuclei for muscle growth or repair.[26] Muscles attach to tendons in a complex interface region known as the musculotendinous junction, also known as the myotendinous junction, an area specialised for the primary transmission of force.[27] At the muscle-tendon interface, force is transmitted from the sarcomeres in the muscle cells to the tendon.[5] Muscles and tendons develop in close association, and after their joining at the myotendinous junction they constitute a dynamic unit for the transmission of force from muscle contraction to the skeletal system.[27] Main article: Muscle architecture Muscle types by fiber arrangement Types of pennate muscle. A – unipennate; B – bipennate; C – multipennate Muscle architecture refers to the arrangement of muscle fibers relative to the axis of force generation, which runs from a muscle's origin to its insertion. The usual arrangements are types of parallel, and types of pennate muscle. In parallel muscles, the fascicles run parallel to the axis of force generation, but the fascicles can vary in their relationship to one another, and to their tendons.[28] These variations are seen in fusiform, strap, and convergent muscles.[4] A convergent muscle has a triangular or fan-shape as the fibers converge at its insertion and are fanned out broadly at the origin.[28] A less common example of a parallel muscle is a circular muscle such as the orbicularis oculi, in which the fibers are longitudinally arranged, but create a circle from origin to insertion.[29] These different architectures, can cause variations in the tension that a muscle can create between its tendons. The fibers in pennate muscles run at an angle to the axis of force generation.[29] This pennation angle reduces the effective force of any individual fiber, as it is effectively pulling off-axis. However, because of this angle, more fibers can be packed into the same muscle volume, increasing the physiological cross-sectional area (PCSA). This effect is known as fiber packing, and in terms of force generation, it more than overcomes the efficiency-loss of the off-axis orientation. The trade-off comes in overall speed of muscle shortening and in the total excursion. Overall muscle shortening speed is reduced compared to fiber shortening speed, as is the total distance of shortening.[29] All of these effects scale with pennation angle; greater angles lead to greater force due to increased fiber packing and PCSA, but with greater losses in shortening speed and excursion. Types of pennate muscle are unipennate, bipennate, and multipennate. A unipennate muscle has similarly angled fibers that are on one side of a tendon. A bipennate muscle has fibers on two sides of a tendon. Multipennate muscles have fibers that are oriented at multiple angles along the force-generating axis, and this is the most general and common architecture.[29] Muscle fibers grow when exercised and shrink when not in use. This is due to the fact that exercise stimulates the increase in myofibrils which increase the overall size of muscle cells. Well exercised muscles can not only add more size but can also develop more mitochondria, myoglobin, glycogen and a higher density of capillaries. However, muscle cells cannot divide to produce new cells, and as a result there are fewer muscle cells in an adult than in a newborn.[30] Further information: Anatomical terms of motion, Anatomical terms of location, and Anatomical terms of muscle There are a number of terms used in the naming of muscles including those relating to size, shape, action, location, their orientation, and their number of heads. By size brevis means short; longus means long; longissimus means longest; magnus means large; major means larger; maximus means largest; minor means smaller, and minimus smallest; latissimus means widest, and vastus means huge.[31] These terms are often used after the particular muscle such as gluteus maximus, and gluteus minimus.[32] By relative shape deltoid means triangular; quadratus means having four sides; rhomboideus means having a rhomboid shape; teres means round or cylindrical, and trapezius means having a trapezoid shape;[32] serratus means saw-toothed; orbicularis means circular; pectinate means comblike; piriformis means pear-shaped; platys means flat and gracilis means slender.[31] Examples are the pronator teres, and the pronator quadratus. By action abductor moving away from the midline; adductor moving towards the midline; depressor moving downwards; elevator moving upwards; flexor moving that decreases an angle; extensor moving that increase an angle or straightens; pronator moving to face down; supinator moving to face upwards;[32] internal rotator rotating towards the body; external rotator rotating away from the body; sphincter decreases the size, and tensor gives tension to; fixator muscles serve to fix a joint in a given position by stabilizing the prime mover whilst other joints are moving. By number of heads biceps two; triceps three and quadriceps four.[32] By location named after the near main structure such as the temporal muscle (temporalis) near to the temporal bone.[31] Also supra- above; infra- below, and sub- under.[19] By fascicle orientation Relative to the midline, rectus means parallel to the midline; transverse means perpendicular to the midline, and oblique means diagonal to the midline.[31] Relative to the axis of the generation of force – types of parallel, and types of pennate muscles. Broadly there are two types of muscle fiber: Type I, which is slow, and Type II which are fast. Type II has two divisions of type IIA (oxidative), and type IIX (glycolytic), giving three main fiber types.[33] These fibers have relatively distinct metabolic, contractile, and motor unit properties. The table below differentiates these types of properties. These types of properties—while they are partly dependent on the properties of individual fibers—tend to be relevant and measured at the level of the motor unit, rather than individual fiber.[34] Various Properties of Different Fiber Types[34] Properties Type I fibers Type IIA fibers Type IIX fibers Motor Unit Type Slow Oxidative (SO) Fast Oxidative/Glycolytic (FOG) Fast Glycolytic (FG) Twitch speed Slow Fast Fast Twitch force Small Medium Large Resistance to fatigue High High Low Glycogen content Low High High Capillary supply Rich Rich Poor Capillary density High Intermediate Low Myoglobin High High Low Red color Dark Dark Pale Mitochondrial density High High Low Oxidative enzyme capacity High Intermediate-high Low Z-line width Intermediate Wide Narrow Alkaline ATPase activity Low High High Acidic ATPase activity High Medium-high Low Slow oxidative (type I) fibers contract relatively slowly and use aerobic respiration to produce ATP. Fast oxidative (type IIA) fibers have fast contractions and primarily use aerobic respiration, but because they may switch to anaerobic respiration (glycolysis), can fatigue more quickly than slow oxidative fibers. Fast glycolytic (type IIX) fibers have fast contractions and primarily use anaerobic glycolysis. The FG fibers fatigue more quickly than the others. Most skeletal muscles in a human contain(s) all three types, although in varying proportions.[35] Traditionally, fibers were categorized depending on their varying color, which is a reflection of myoglobin content. Type I fibers appear red due to the high levels of myoglobin. Red muscle fibers tend to have more mitochondria and greater local capillary density. These fibers are more suited for endurance and are slow to fatigue because they use oxidative metabolism to generate ATP (adenosine triphosphate). Less oxidative Type II fibers are white due to relatively low myoglobin and a reliance on glycolytic enzymes. Fibers can also be classified on their twitch capabilities, into fast and slow twitch. These traits largely, but not completely, overlap the classifications based on color, ATPase, or MHC (myosin heavy chain). Some authors define a fast twitch fiber as one in which the myosin can split ATP very quickly. These mainly include the ATPase type II and MHC type II fibers. However, fast twitch fibers also demonstrate a higher capability for electrochemical transmission of action potentials and a rapid level of calcium release and uptake by the sarcoplasmic reticulum. The fast twitch fibers rely on a well-developed, anaerobic, short term, glycolytic system for energy transfer and can contract and develop tension at 2–3 times the rate of slow twitch fibers. Fast twitch muscles are much better at generating short bursts of strength or speed than slow muscles, and so fatigue more quickly.[36] The slow twitch fibers generate energy for ATP re-synthesis by means of a long term system of aerobic energy transfer. These mainly include the ATPase type I and MHC type I fibers. They tend to have a low activity level of ATPase, a slower speed of contraction with a less well developed glycolytic capacity.[36] Fibers that become slow-twitch develop greater numbers of mitochondria and capillaries making them better for prolonged work.[37] Individual muscles tend to be a mixture of various fiber types, but their proportions vary depending on the actions of that muscle. For instance, in humans, the quadriceps muscles contain ~52% type I fibers, while the soleus is ~80% type I.[38] The orbicularis oculi muscle of the eye is only ~15% type I.[38] Motor units within the muscle, however, have minimal variation between the fibers of that unit. It is this fact that makes the size principal of motor unit recruitment viable. The total number of skeletal muscle fibers has traditionally been thought not to change. It is believed there are no sex or age differences in fiber distribution; however, proportions of fiber types vary considerably from muscle to muscle and person to person.[citation needed] Among different species there is much variation in the proportions of muscle fiber types.[39] Sedentary men and women (as well as young children) have 45% type II and 55% type I fibers.[citation needed] People at the higher end of any sport tend to demonstrate patterns of fiber distribution e.g. endurance athletes show a higher level of type I fibers. Sprint athletes, on the other hand, require large numbers of type IIX fibers. Middle-distance event athletes show approximately equal distribution of the two types. This is also often the case for power athletes such as throwers and jumpers. It has been suggested that various types of exercise can induce changes in the fibers of a skeletal muscle.[40] It is thought that by performing endurance type events for a sustained period of time, some of the type IIX fibers transform into type IIA fibers. However, there is no consensus on the subject.[citation needed] It may well be that the type IIX fibers show enhancements of the oxidative capacity after high intensity endurance training which brings them to a level at which they are able to perform oxidative metabolism as effectively as slow twitch fibers of untrained subjects. This would be brought about by an increase in mitochondrial size and number and the associated related changes, not a change in fiber type. ATPase staining of a muscle cross section. Type II fibers are dark, due to the alkaline pH of the preparation. In this example, the size of the type II fibers is considerably less than the type I fibers due to denervation atrophy. There are numerous methods employed for fiber-typing, and confusion between the methods is common among non-experts. Two commonly confused methods are histochemical staining for myosin ATPase activity and immunohistochemical staining for myosin heavy chain (MHC) type. Myosin ATPase activity is commonly—and correctly—referred to as simply "fiber type", and results from the direct assaying of ATPase activity under various conditions (e.g. pH).[34] Myosin heavy chain staining is most accurately referred to as "MHC fiber type", e.g. "MHC IIa fibers", and results from determination of different MHC isoforms.[34] These methods are closely related physiologically, as the MHC type is the primary determinant of ATPase activity. However, neither of these typing methods is directly metabolic in nature; they do not directly address oxidative or glycolytic capacity of the fiber. When "type I" or "type II" fibers are referred to generically, this most accurately refers to the sum of numerical fiber types (I vs. II) as assessed by myosin ATPase activity staining (e.g. "type II" fibers refers to type IIA + type IIAX + type IIXA ... etc.). Below is a table showing the relationship between these two methods, limited to fiber types found in humans. Subtype capitalization is used in fiber typing vs. MHC typing, and some ATPase types actually contain multiple MHC types. Also, a subtype B or b is not expressed in humans by either method.[41] Early researchers believed humans to express a MHC IIb, which led to the ATPase classification of IIB. However, later research showed that the human MHC IIb was in fact IIx,[41] indicating that the IIB is better named IIX. IIb is expressed in other mammals, so is still accurately seen (along with IIB) in the literature. Non human fiber types include true IIb fibers, IIc, IId, etc. ATPase Vs. MHC fiber types[34][42][43] ATPase type MHC heavy chain(s) Type I MHC Iβ Type IC MHC Iβ > MHC IIa Type IIC MHC IIa > MHC Iβ Type IIA MHC IIa Type IIAX MHC IIa > MHC IIx Type IIXA MHC IIx > MHC IIa Type IIX MHC IIx Further fiber typing methods are less formally delineated, and exist on more of a spectrum. They tend to be focused more on metabolic and functional capacities (i.e., oxidative vs. glycolytic, fast vs. slow contraction time). As noted above, fiber typing by ATPase or MHC does not directly measure or dictate these parameters. However, many of the various methods are mechanistically linked, while others are correlated in vivo.[44][45] For instance, ATPase fiber type is related to contraction speed, because high ATPase activity allows faster crossbridge cycling.[34] While ATPase activity is only one component of contraction speed, Type I fibers are "slow", in part, because they have low speeds of ATPase activity in comparison to Type II fibers. However, measuring contraction speed is not the same as ATPase fiber typing. Almost all multicellular animals depend on muscles to move.[46] Generally, muscular systems of most multicellular animals comprise both slow-twitch and fast-twitch muscle fibers, though the proportions of each fiber type can vary across organisms and environments. The ability to shift their phenotypic fiber type proportions through training and responding to the environment has served organisms well when placed in changing environments either requiring short explosive movements (higher fast twitch proportion) or long duration of movement (higher slow twitch proportion) to survive.[47] Bodybuilding has shown that changes in muscle mass and force production can change in a matter of months.[48] Some examples of this variation are described below.[49] American lobster, Homarus americanus, has three fiber types including fast twitch fibers, slow-twitch and slow-tonic fibers.[50] Slow-tonic is a slow twitch-fiber that can sustain longer contractions (tonic).[51][52] In lobsters, muscles in different body parts vary in the muscle fiber type proportions based on the purpose of the muscle group.[50] In the early development of vertebrate embryos, growth and formation of muscle happens in successive waves or phases of myogenesis. The myosin heavy chain isotype is a major determinant of the specific fiber type. In zebrafish embryos, the first muscle fibers to form are the slow twitch fibers. These cells will undergo migration from their original location to form a monolayer of slow twitch muscle fibers. These muscle fibers undergo further differentiation as the embryo matures.[53] In larger animals, different muscle groups will increasingly require different fiber type proportions within muscle for different purposes. Turtles, such as Trachemys scripta elegans, have complementary muscles within the neck that show a potential inverse trend of fiber type percentages (one muscle has high percentage of fast twitch, while the complementary muscle will have a higher percentage of slow twitch fibers). The complementary muscles of turtles had similar percentages of fiber types.[51] Chimpanzee muscles are composed of 67% fast-twitch fibers and have a maximum dynamic force and power output 1.35 times higher than human muscles of similar size. Among mammals, there is a predominance of type II fibers utilizing glycolytic metabolism. Because of the discrepancy in fast twitch fibers compared to humans, chimpanzees outperform humans in power related tests. Humans, however, will do better at exercise in aerobic range requiring large metabolic costs such as walking (bipedalism).[54] Across species, certain gene sequences have been preserved, but do not always have the same functional purpose. Within the zebrafish embryo, the Prdm1 gene down-regulates the formation of new slow twitch fibers through direct and indirect mechanisms such as Sox6 (indirect). In mice, the Prdm1 gene is present but does not control slow muscle genes in mice through Sox6.[55] In addition to having a genetic basis, the composition of muscle fiber types is flexible and can vary with a number of different environmental factors. This plasticity can, arguably, be the strongest evolutionary advantage among organisms with muscle. In fish, different fiber types are expressed at different water temperatures.[53] Cold temperatures require more efficient metabolism within muscle and fatigue resistance is important. While in more tropical environments, fast powerful movements (from higher fast-twitch proportions) may prove more beneficial in the long run.[56] In rodents such as rats, the transitory nature of their muscle is highly prevalent. They have high percentage of hybrid muscle fibers and have up to 60% in fast-to-slow transforming muscle.[48] Environmental influences such as diet, exercise and lifestyle types have a pivotal role in proportions of fiber type in humans. Aerobic exercise will shift the proportions towards slow twitch fibers, while explosive powerlifting and sprinting will transition fibers towards fast twitch.[47] In animals, "exercise training" will look more like the need for long durations of movement or short explosive movements to escape predators or catch prey.[57] Structure of muscle fibre showing a sarcomere under electron microscope with schematic explanation Diagram of sarcoplasmic reticulum with terminal cisternae and T-tubules Skeletal muscle exhibits a distinctive banding pattern when viewed under the microscope due to the arrangement of two contractile proteins myosin, and actin – that are two of the myofilaments in the myofibrils. The myosin forms the thick filaments, and actin forms the thin filaments, and are arranged in repeating units called sarcomeres. The interaction of both proteins results in muscle contraction. The sarcomere is attached to other organelles such as the mitochondria by intermediate filaments in the cytoskeleton. The costamere attaches the sarcomere to the sarcolemma.[5] Every single organelle and macromolecule of a muscle fiber is arranged to ensure that it meets desired functions. The cell membrane is called the sarcolemma with the cytoplasm known as the sarcoplasm. In the sarcoplasm are the myofibrils. The myofibrils are long protein bundles about one micrometer in diameter. Pressed against the inside of the sarcolemma are the unusual flattened myonuclei. Between the myofibrils are the mitochondria. While the muscle fiber does not have smooth endoplasmic cisternae, it contains sarcoplasmic reticulum. The sarcoplasmic reticulum surrounds the myofibrils and holds a reserve of the calcium ions needed to cause a muscle contraction. Periodically, it has dilated end sacs known as terminal cisternae. These cross the muscle fiber from one side to the other. In between two terminal cisternae is a tubular infolding called a transverse tubule (T tubule). T tubules are the pathways for action potentials to signal the sarcoplasmic reticulum to release calcium, causing a muscle contraction. Together, two terminal cisternae and a transverse tubule form a triad.[58] Main article: Myogenesis Human embryo showing somites labelled as primitive segments All muscles are derived from paraxial mesoderm. During embryonic development in the process of somitogenesis the paraxial mesoderm is divided along the embryo's length to form somites, corresponding to the segmentation of the body most obviously seen in the vertebral column.[59] Each somite has three divisions, sclerotome (which forms vertebrae), dermatome (which forms skin), and myotome (which forms muscle). The myotome is divided into two sections, the epimere and hypomere, which form epaxial and hypaxial muscles, respectively. The only epaxial muscles in humans are the erector spinae and small vertebral muscles, and are innervated by the dorsal rami of the spinal nerves. All other muscles, including those of the limbs are hypaxial, and innervated by the ventral rami of the spinal nerves.[59] During development, myoblasts (muscle progenitor cells) either remain in the somite to form muscles associated with the vertebral column or migrate out into the body to form all other muscles. Myoblast migration is preceded by the formation of connective tissue frameworks, usually formed from the somatic lateral plate mesoderm. Myoblasts follow chemical signals to the appropriate locations, where they fuse into elongated multinucleated skeletal muscle cells.[59] Between the tenth and the eighteenth weeks of gestation, all muscle cells have fast myosin heavy chains; two myotube types become distinguished in the developing fetus – both expressing fast chains but one expressing fast and slow chains. Between 10 and 40 per cent of the fibers express the slow myosin chain.[60] Fiber types are established during embryonic development and are remodelled later in the adult by neural and hormonal influences.[39] The population of satellite cells present underneath the basal lamina is necessary for the postnatal development of muscle cells.[61] The primary function of muscle is contraction.[3] Following contraction, skeletal muscle functions as an endocrine organ by secreting myokines – a wide range of cytokines and other peptides that act as signalling molecules.[62] Myokines in turn are believed to mediate the health benefits of exercise.[63] Myokines are secreted into the bloodstream after muscle contraction. Interleukin 6 (IL-6) is the most studied myokine, other muscle contraction-induced myokines include BDNF, FGF21, and SPARC.[64] Muscle also functions to produce body heat. Muscle contraction is responsible for producing 85% of the body's heat.[65] This heat produced is as a by-product of muscular activity, and is mostly wasted. As a homeostatic response to extreme cold, muscles are signaled to trigger contractions of shivering in order to generate heat.[66] Classes of levers present in the human skeletal muscular system Main article: Muscle contraction When a sarcomere contracts, the Z lines move closer together, and the I band becomes smaller. The A band stays the same width. At full contraction, the thin and thick filaments overlap. Contraction in more detail Contraction is achieved by the muscle's structural unit, the muscle fiber, and by its functional unit, the motor unit.[4] Muscle fibers are excitable cells stimulated by motor neurons. The motor unit consists of a motor neuron and the many fibers that it makes contact with. A single muscle is stimulated by many motor units. Muscle fibers are subject to depolarization by the neurotransmitter acetylcholine, released by the motor neurons at the neuromuscular junctions.[67] In addition to the actin and myosin myofilaments in the myofibrils that make up the contractile sarcomeres, there are two other important regulatory proteins – troponin and tropomyosin, that make muscle contraction possible. These proteins are associated with actin and cooperate to prevent its interaction with myosin. Once a cell is sufficiently stimulated, the cell's sarcoplasmic reticulum releases ionic calcium (Ca^{2+}), which then interacts with the regulatory protein troponin. Calcium-bound troponin undergoes a conformational change that leads to the movement of tropomyosin, subsequently exposing the myosin-binding sites on actin. This allows for myosin and actin ATP-dependent cross-bridge cycling and shortening of the muscle. Excitation contraction coupling is the process by which a muscular action potential in the muscle fiber causes the myofibrils to contract. This process relies on a direct coupling between the sarcoplasmic reticulum calcium release channel RYR1 (ryanodine receptor 1), and voltage-gated L-type calcium channels (identified as dihydropyridine receptors, DHPRs). DHPRs are located on the sarcolemma (which includes the surface sarcolemma and the transverse tubules), while the RyRs reside across the SR membrane. The close apposition of a transverse tubule and two SR regions containing RyRs is described as a triad and is predominantly where excitation–contraction coupling takes place. Excitation–contraction coupling occurs when depolarization of skeletal muscle cell results in a muscle action potential, which spreads across the cell surface and into the muscle fiber's network of T-tubules, thereby depolarizing the inner portion of the muscle fiber. Depolarization of the inner portions activates dihydropyridine receptors in the terminal cisternae, which are close to ryanodine receptors in the adjacent sarcoplasmic reticulum. The activated dihydropyridine receptors physically interact with ryanodine receptors to activate them via foot processes (involving conformational changes that allosterically activates the ryanodine receptors). As the ryanodine receptors open, Ca^{2+} is released from the sarcoplasmic reticulum into the local junctional space and diffuses into the bulk cytoplasm to cause a calcium spark. The sarcoplasmic reticulum has a large calcium buffering capacity partially due to a calcium-binding protein called calsequestrin. The near synchronous activation of thousands of calcium sparks by the action potential causes a cell-wide increase in calcium giving rise to the upstroke of the calcium transient. The Ca^{2+} released into the cytosol binds to Troponin C by the actin filaments, to allow crossbridge cycling, producing force and, in some situations, motion. The sarco/endoplasmic reticulum calcium-ATPase (SERCA) actively pumps Ca^{2+} back into the sarcoplasmic reticulum. As Ca^{2+} declines back to resting levels, the force declines and relaxation occurs.[68] This section does not cite any sources. Please help improve this section by adding citations to reliable sources. Unsourced material may be challenged and removed. (June 2021) (Learn how and when to remove this message) The efferent leg of the peripheral nervous system is responsible for conveying commands to the muscles and glands, and is ultimately responsible for voluntary movement. Nerves move muscles in response to voluntary and autonomic (involuntary) signals from the brain. Deep muscles, superficial muscles, muscles of the face and internal muscles all correspond with dedicated regions in the primary motor cortex of the brain, directly anterior to the central sulcus that divides the frontal and parietal lobes. In addition, muscles react to reflexive nerve stimuli that do not always send signals all the way to the brain. In this case, the signal from the afferent fiber does not reach the brain, but produces the reflexive movement by direct connections with the efferent nerves in the spine. However, the majority of muscle activity is volitional, and the result of complex interactions between various areas of the brain. Nerves that control skeletal muscles in mammals correspond with neuron groups along the primary motor cortex of the brain's cerebral cortex. Commands are routed through the basal ganglia and are modified by input from the cerebellum before being relayed through the pyramidal tract to the spinal cord and from there to the motor end plate at the muscles. Along the way, feedback, such as that of the extrapyramidal system contribute signals to influence muscle tone and response. Deeper muscles such as those involved in posture often are controlled from nuclei in the brain stem and basal ganglia. Main article: Proprioception In skeletal muscles, muscle spindles convey information about the degree of muscle length and stretch to the central nervous system to assist in maintaining posture and joint position. The sense of where our bodies are in space is called proprioception, the perception of body awareness, the "unconscious" awareness of where the various regions of the body are located at any one time. Several areas in the brain coordinate movement and position with the feedback information gained from proprioception. The cerebellum and red nucleus in particular continuously sample position against movement and make minor corrections to assure smooth motion.[citation needed] Main article: Bioenergetic systems (a) Some ATP is stored in a resting muscle. As contraction starts, it is used up in seconds. More ATP is generated from creatine phosphate for about 15 seconds. (b) Each glucose molecule produces two ATP and two molecules of pyruvic acid, which can be used in aerobic respiration or converted to lactic acid. If oxygen is not available, pyruvic acid is converted to lactic acid, which may contribute to muscle fatigue. This occurs during strenuous exercise when high amounts of energy are needed but oxygen cannot be sufficiently delivered to muscle. (c) Aerobic respiration is the breakdown of glucose in the presence of oxygen (O_2) to produce carbon dioxide, water, and ATP. Approximately 95 percent of the ATP required for resting or moderately active muscles is provided by aerobic respiration, which takes place in mitochondria. Muscular activity accounts for much of the body's energy consumption. All muscle cells produce adenosine triphosphate (ATP) molecules which are used to power the movement of the myosin heads. Muscles have a short-term store of energy in the form of creatine phosphate which is generated from ATP and can regenerate ATP when needed with creatine kinase. Muscles also keep a storage form of glucose in the form of glycogen. Glycogen can be rapidly converted to glucose when energy is required for sustained, powerful contractions. Within the voluntary skeletal muscles, the glucose molecule can be metabolized anaerobically in a process called glycolysis which produces two ATP and two lactic acid molecules in the process (in aerobic conditions, lactate is not formed; instead pyruvate is formed and transmitted through the citric acid cycle). Muscle cells also contain globules of fat, which are used for energy during aerobic exercise. The aerobic energy systems take longer to produce the ATP and reach peak efficiency, and requires many more biochemical steps, but produces significantly more ATP than anaerobic glycolysis. Cardiac muscle on the other hand, can readily consume any of the three macronutrients (protein, glucose and fat) aerobically without a 'warm up' period and always extracts the maximum ATP yield from any molecule involved. The heart, liver and red blood cells will also consume lactic acid produced and excreted by skeletal muscles during exercise. Skeletal muscle uses more calories than other organs.[69] At rest it consumes 54.4 kJ/kg (13.0 kcal/kg) per day. This is larger than adipose tissue (fat) at 18.8 kJ/kg (4.5 kcal/kg), and bone at 9.6 kJ/kg (2.3 kcal/kg).[70] This section does not cite any sources. Please help improve this section by adding citations to reliable sources. Unsourced material may be challenged and removed. (June 2021) (Learn how and when to remove this message) The efficiency of human muscle has been measured (in the context of rowing and cycling) at 18% to 26%. The efficiency is defined as the ratio of mechanical work output to the total metabolic cost, as can be calculated from oxygen consumption. This low efficiency is the result of about 40% efficiency of generating ATP from food energy, losses in converting energy from ATP into mechanical work inside the muscle, and mechanical losses inside the body. The latter two losses are dependent on the type of exercise and the type of muscle fibers being used (fast-twitch or slow-twitch). For an overall efficiency of 20 percent, one watt of mechanical power is equivalent to 4.3 kcal per hour. For example, one manufacturer of rowing equipment calibrates its rowing ergometer to count burned calories as equal to four times the actual mechanical work, plus 300 kcal per hour, this amounts to about 20 percent efficiency at 250 watts of mechanical output. The mechanical energy output of a cyclic contraction can depend upon many factors, including activation timing, muscle strain trajectory, and rates of force rise & decay. These can be synthesized experimentally using work loop analysis. Main article: Physical strength Grading of muscle strength Grade 0 No contraction Grade 1 Trace of contraction, but no movement at the joint Grade 2 Movement at the joint with gravity eliminated Grade 3 Movement against gravity, but not against added resistance Grade 4 Movement against external resistance, but less than normal Grade 5 Normal strength Muscle strength is a result of three overlapping factors: physiological strength (muscle size, cross sectional area, available crossbridging, responses to training), neurological strength (how strong or weak is the signal that tells the muscle to contract), and mechanical strength (muscle's force angle on the lever, moment arm length, joint capabilities).[citation needed] Vertebrate muscle typically produces approximately 25–33 N (5.6–7.4 lbf) of force per square centimeter of muscle cross-sectional area when isometric and at optimal length.[71] Some invertebrate muscles, such as in crab claws, have much longer sarcomeres than vertebrates, resulting in many more sites for actin and myosin to bind and thus much greater force per square centimeter at the cost of much slower speed. The force generated by a contraction can be measured non-invasively using either mechanomyography or phonomyography, be measured in vivo using tendon strain (if a prominent tendon is present), or be measured directly using more invasive methods. The strength of any given muscle, in terms of force exerted on the skeleton, depends upon length, shortening speed, cross sectional area, pennation, sarcomere length, myosin isoforms, and neural activation of motor units. Significant reductions in muscle strength can indicate underlying pathology, with the chart at right used as a guide. The maximum holding time for a contracted muscle depends on its supply of energy and is stated by Rohmert's law to exponentially decay from the beginning of exertion. This section needs additional citations for verification. Please help improve this article by adding citations to reliable sources in this section. Unsourced material may be challenged and removed. (March 2016) (Learn how and when to remove this message) Since three factors affect muscular strength simultaneously and muscles never work individually, it is misleading to compare strength in individual muscles, and state that one is the "strongest". But below are several muscles whose strength is noteworthy for different reasons. In ordinary parlance, muscular "strength" usually refers to the ability to exert a force on an external object—for example, lifting a weight. By this definition, the masseter or jaw muscle is the strongest. The 1992 Guinness Book of Records records the achievement of a bite strength of 4,337 N (975 lbf) for 2 seconds. What distinguishes the masseter is not anything special about the muscle itself, but its advantage in working against a much shorter lever arm than other muscles. If "strength" refers to the force exerted by the muscle itself, e.g., on the place where it inserts into a bone, then the strongest muscles are those with the largest cross-sectional area. This is because the tension exerted by an individual skeletal muscle fiber does not vary much. Each fiber can exert a force on the order of 0.3 micronewton. By this definition, the strongest muscle of the body is usually said to be the quadriceps femoris or the gluteus maximus. Because muscle strength is determined by cross-sectional area, a shorter muscle will be stronger "pound for pound" (i.e., by weight) than a longer muscle of the same cross-sectional area. The myometrial layer of the uterus may be the strongest muscle by weight in the female body. At the time when an infant is delivered, the entire uterus weighs about 1.1 kg (40 oz). During childbirth, the uterus exerts 100 to 400 N (25 to 100 lbf) of downward force with each contraction. The external muscles of the eye are conspicuously large and strong in relation to the small size and weight of the eyeball. It is frequently said that they are "the strongest muscles for the job they have to do" and are sometimes claimed to be "100 times stronger than they need to be." However, eye movements (particularly saccades used on facial scanning and reading) do require high speed movements, and eye muscles are exercised nightly during rapid eye movement sleep. The statement that "the tongue is the strongest muscle in the body" appears frequently in lists of surprising facts, but it is difficult to find any definition of "strength" that would make this statement true. The tongue consists of eight muscles, not one. Muscle force is proportional to physiological cross-sectional area (PCSA), and muscle velocity is proportional to muscle fiber length.[72] The torque around a joint, however, is determined by a number of biomechanical parameters, including the distance between muscle insertions and pivot points, muscle size and architectural gear ratio. Muscles are normally arranged in opposition so that when one group of muscles contracts, another group relaxes or lengthens.[73] Antagonism in the transmission of nerve impulses to the muscles means that it is impossible to fully stimulate the contraction of two antagonistic muscles at any one time. During ballistic motions such as throwing, the antagonist muscles act to 'brake' the agonist muscles throughout the contraction, particularly at the end of the motion. In the example of throwing, the chest and front of the shoulder (anterior deltoid) contract to pull the arm forward, while the muscles in the back and rear of the shoulder (posterior deltoid) also contract and undergo eccentric contraction to slow the motion down to avoid injury. Part of the training process is learning to relax the antagonist muscles to increase the force input of the chest and anterior shoulder. Contracting muscles produce vibration and sound.[74] Slow twitch fibers produce 10 to 30 contractions per second (10 to 30 Hz). Fast twitch fibers produce 30 to 70 contractions per second (30 to 70 Hz).[75] The vibration can be witnessed and felt by highly tensing one's muscles, as when making a firm fist. The sound can be heard by pressing a highly tensed muscle against the ear, again a firm fist is a good example. The sound is usually described as a rumbling sound. Some individuals can voluntarily produce this rumbling sound by contracting the tensor tympani muscle of the middle ear. The rumbling sound can also be heard when the neck or jaw muscles are highly tensed.[citation needed] This section does not cite any sources. Please help improve this section by adding citations to reliable sources. Unsourced material may be challenged and removed. (May 2021) (Learn how and when to remove this message) Skeletal muscle fiber-type phenotype in adult animals is regulated by several independent signaling pathways. These include pathways involved with the Ras/mitogen-activated protein kinase (MAPK) pathway, calcineurin, calcium/calmodulin-dependent protein kinase IV, and the peroxisome proliferator γ coactivator 1 (PGC-1). The Ras/MAPK signaling pathway links the motor neurons and signaling systems, coupling excitation and transcription regulation to promote the nerve-dependent induction of the slow program in regenerating muscle. Calcineurin, a Ca^{2+}/calmodulin-activated phosphatase implicated in nerve activity-dependent fiber-type specification in skeletal muscle, directly controls the phosphorylation state of the transcription factor NFAT, allowing for its translocation to the nucleus and leading to the activ

polypeptide tail (only one tail of each pair is shown). The pairs of histones, H2A, H2B, H3 and H4, each have lysines (K) in their tails, some of which are subject to post-translational modifications consisting, usually, of acetylations [Ac] and methylations {me}. The lysines (K) are designated with a number showing their position as, for instance, (K4), indicating lysine as the 4th amino acid from the amino (N) end of the tail in the histone protein. The particular acetylations [Ac] and methylations {Me} shown are those that occur on nucleosomes close to, or at, some DNA regions undergoing transcriptional activation of the DNA wrapped around the nucleosome. As indicated above, after exercise, epigenetic alterations to enhancers alter long-term expression of hundreds of muscle genes.[102] This includes genes producing proteins secreted into the systemic circulation, many of which may act as endocrine messengers.[102] Six sedentary, about 23 years old, Caucasian males provided vastus lateralis (a thigh muscle) biopsies before entering an exercise program (six weeks of 60-minute sessions of riding a stationary cycle, five days per week). Four days after this exercise program was completed, the expression of many genes was persistently epigenetically altered. The alterations altered acetylations and deacetylations of the histone tails located in the enhancers controlling the genes with altered expression.[102] Up-regulated genes were associated with epigenetic acetylations added at histone 3 lysine 27 (H3K27ac) of nucleosomes located at their enhancers. Down-regulated genes were associated with the removal of epigenetic acetylations at H3K27 in nucleosomes located at their enhancers (see Figure "A nucleosome with histone tails set for transcriptional activation"). Biopsies of the vastus lateralis muscle showed expression of 13,108 genes at baseline before the exercise training program. Four days after the exercise program was completed, biopsies of the same muscles showed altered gene expression, with 641 genes up-regulated and 176 genes down-regulated.[102] Williams et al. identified 599 enhancer-gene interactions, covering 491 enhancers and 268 genes (multiple enhancers were found connected to some genes), where both the enhancer and the connected target gene were coordinately either upregulated or downregulated after exercise training.[102] Medicine portal Facioscapulohumeral muscular dystrophy Hill's muscle model In vitro muscle testing Musculoskeletal injury Muscle relaxant Microtrauma Muscle memory Myomere Myotomy Preflexes ^ Birbrair, Alexander; Zhang, Tan; Wang, Zhong-Min; Messi, Maria Laura; Enikolopov, Grigori N.; Mintz, Akiva; Delbono, Osvaldo (21 March 2013). "Role of Pericytes in Skeletal Muscle Regeneration and Fat Accumulation". Stem Cells and Development. 22 (16): 2298–2314. doi:10.1089/scd.2012.0647. ISSN 1547-3287. PMC 3730538. 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