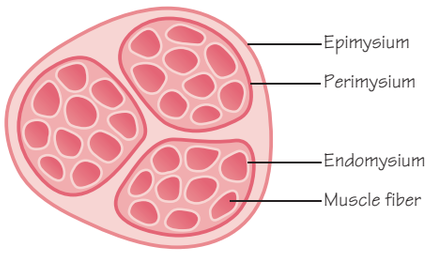
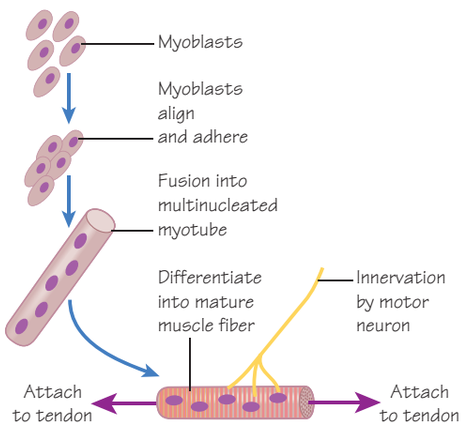
8 Skeletal muscle

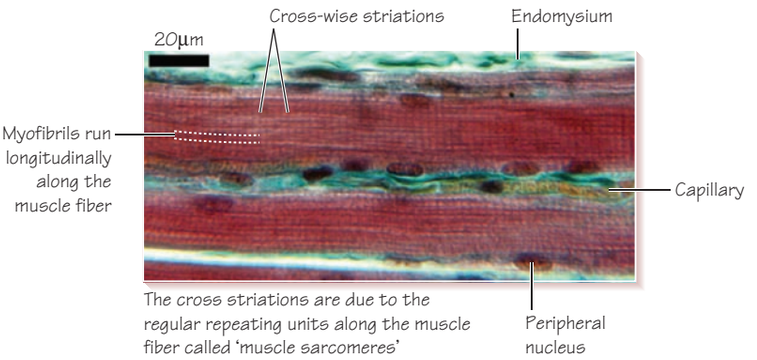
(a) Diagram of a cross section through a muscle fibre: three layers of connective tissue



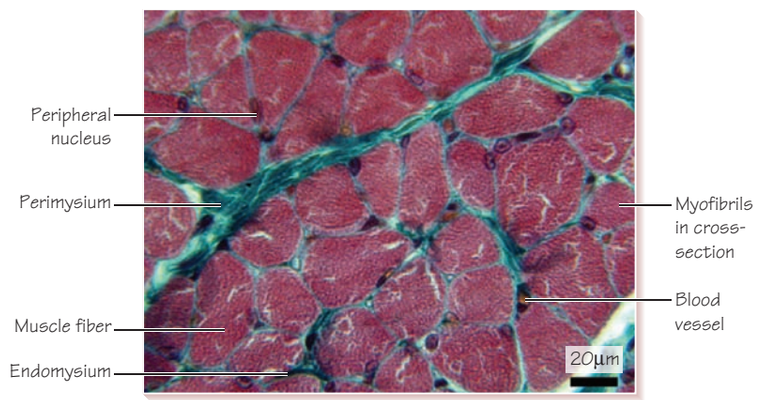
(b) Skeletal muscle fibers are formed by fusion of many myoblasts



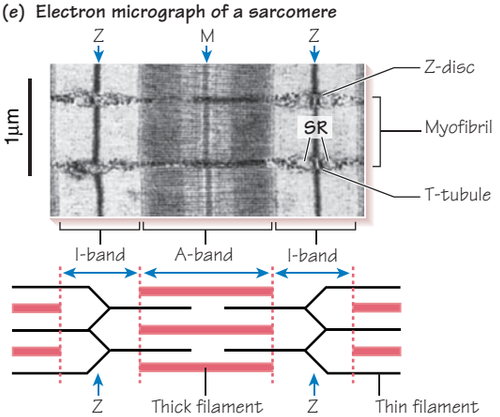
(c) Skeletal muscle (LS)



(d) Skeletal Muscle (TS)

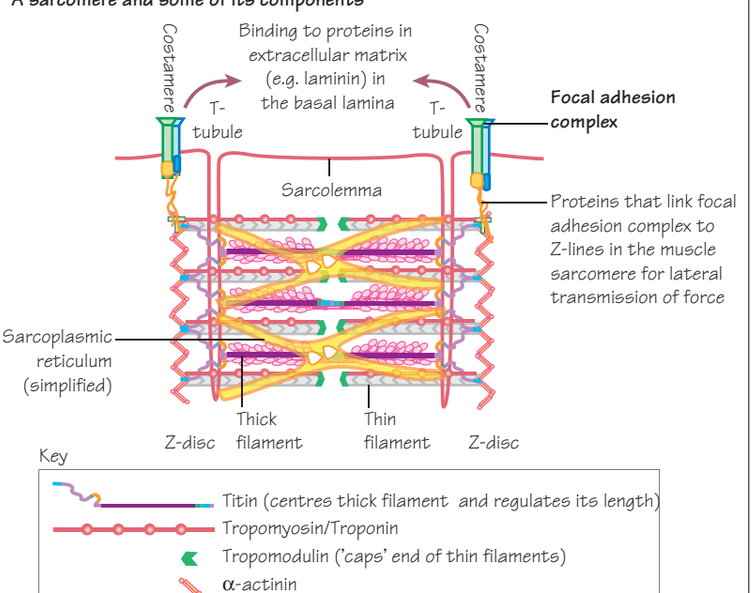


(e) Electron micrograph of a sarcomere



The muscle sarcomere
In cardiac and skeletal muscle cells, thick (myosin-containing) filaments and thin (actin-containing) filaments are organized into regular repeating units called the muscle sarcomere. A single sarcomere extends from one Z-disc to the next. The stripes in H&E stained longitudinal sections shown above (1c) show the end-to-end arrangement of many muscle sarcomeres along the fiber. Reproduced from Skeletal Muscle, Henning Schmalbruch (1986), Springer Verlag. With kind permission of Springer Science+Business Media

(f) A sarcomere and some of its components



Skeletal muscles move joints, support the skeleton, and assist in breathing. They are connected to the skeleton via tendons, and they are all under voluntary control.

Skeletal muscle fibers are arranged into bundles (fascicles) and muscle contains three connective tissue layers (Fig. 8a):

- **epimysium:** an outer layer around the muscle;
- **perimysium:** surrounds each fiber bundle (fascicle);
- **endomysium:** surrounds each fiber.

Each muscle fiber is also surrounded by its own basal lamina.

Muscle structure and contraction

Skeletal muscle fibers are the largest cells in the body, with a single cell stretching from one end of the muscle to the other. Given the lengths of skeletal muscles, this means a single fiber (up to about 100 µm in diameter) can be several centimeters long.

Skeletal muscle fibers can be this large, because they contain thousands of nuclei, which are required to maintain a cell of this size. Thus muscle fibers are single, **multinucleated** cells. The **nuclei** are found at the **cell periphery**, and there is approximately one nucleus every 35 µm along the fiber length.

Multinucleated skeletal muscle fibers are formed by the fusion of many mononucleated cells (myoblasts) together during development, and growth (Fig. 8b).

In longitudinal sections, muscle fibers have a stripy appearance (Fig. 8c). These stripes result from the arrangement of repeating units called **sarcomeres** in series along the fiber. In skeletal muscle, sarcomeres are about 2.5 µm long. A fiber, 30 cm long, contains 120 thousand sarcomeres arranged end to end.

Sarcomeres are arranged longitudinally in structures called myofibrils (Fig. 8c), which are about 1 µm thick. Myofibrils pack together laterally in the muscle fiber, with their Z-lines aligned and connected to each other. The myofibrils can also be seen in cross-section (Fig. 8d) as punctate structures.

At the plasma membrane, the Z-lines are connected to structures called **costameres** by a number of different proteins. Transmembrane proteins (e.g., integrins) in the costameres bind to extracellular proteins in the basal lamina (e.g., laminin). This series of lateral connections enables force to be transmitted laterally through to the extracellular matrix (Fig. 8f).

The structure of the sarcomere can be seen more clearly by electron microscopy (Fig. 8e). Each sarcomere is bordered by a structure called the Z-disc. Myosin and actin are organized into thick and thin filaments, respectively, in the muscle sarcomeres (Fig. 8f).

During contraction, each sarcomere shortens by about 0.1 to 0.2 µm, and this is summed along the length of the fiber, such that the ends of the muscle shorten by a few centimeters.

Longitudinally, muscle fibers are connected via tendons at the ends of the muscles to the skeleton, to generate movement of joints.

Diseases such as congenital myopathies can affect the normal organization of actin into thin filaments. This results in a decrease in muscle mass, as well as disorganized muscle sarcomeres. This disease can result in severe muscle weakness, such that babies born with a severe form of this condition are unable to breathe unaided.

Activation of muscle contraction

Muscle fibers are innervated by nerves, which form a connection with the muscle fiber called the neuromuscular junction (NMJ; see Chapter 11).

Acetylcholine released by the NMJ binds to receptors in the postsynaptic membrane of the skeletal muscle fibers, resulting in their depolarization. Skeletal muscle (and cardiac muscle) contains **T-tubules**, which are invaginations of the plasma membrane or sarcolemma). The t-tubules are in direct contact with the internal membrane system called the **sarcoplasmic reticulum** (SR) at structures known as triads. Proteins, such as the ryanodine receptor, span between the T-tubules and the SR to facilitate this connection. The SR contains the main internal store of Ca^{2+}. When skeletal or cardiac muscle is stimulated to contract, T-tubules are depolarized, and Ca^{2+} is released from the SR into the cytoplasm. Ca^{2+} release is facilitated by the ryanodine receptor.

Once released into the cytoplasm, Ca^{2+} binds to a subunit of troponin (troponin-C), which is present on the thin, actin-containing filaments. This results in the movement of tropomyosin around the thin filament, which exposes sites on actin to which myosin cross-bridges bind. The cross-bridges then bind to actin and generate force or movement, using ATP hydrolysis to power their motion. The muscle relaxes, when Ca^{2+} levels fall back to low levels, which is achieved by pumping Ca^{2+} back into the SR.

Mutations in the ryanodine receptor cause the disease, malignant hyperthermia. In this disease, patients suffer symptoms that include muscle contractures, increased heart rate, and rapid increase in body temperature, when under general anesthesia using volatile anesthetics. This can result in the death of a patient while under anesthesia.

Muscle damage and repair

Muscle fibers are terminally differentiated and do not undergo mitosis. However, 'satellite' cells, which are skeletal muscle 'stem cells', can repair damaged muscle fibers. These cells lie under the basal lamina of the muscle fibers. When the muscle is damaged, they are stimulated to divide to generate new myoblasts, which fuse and repair the damaged muscle fiber. Skeletal muscle is most susceptible to damage as a result of eccentric exercise (actively contracting a muscle, during lengthening).