Theme: Electrical Communication of Cells

Contraction of Muscle

Lecture notes

The contraction of muscle

Muscles are composed of highly specialized cells that can generate force and produce movement. In skeletal muscle, the effectors are responsible for voluntary actions ranging from speaking to running. Smooth muscle and cardiac muscle underlie the functions of the visceral systems such as the cardiovascular, urogenital and gastrointestinal systems.

In skeletal muscle, individual muscle cells (muscle fibres) are arranged anatomically and mechanically in parallel so that muscle cells function independently, and the total force generated by a muscle is equal to the sum of the forces generated by individual cells. The musculoskeletal system is arranged so that most gravitational loads are borne by the skeleton and ligaments. **The nervous system coordinates the activity of different parts of muscle tissue to produce useful movements and postures.**

Structural Organisation of Skeletal muscle

Skeletal muscle is composed of numerous parallel elongated cells referred to as muscle fibres that are 10 – 100 microns in diameter, vary in length with the length of the muscle, and often extending the entire length of the muscle (Fig. 1). They are multinucleated cells, bounded by an excitable membrane called the **sarcolemma**. Individual muscle fibres contain many parallel **myofibrils** which are one micron (1μm) in diameter and are surrounded by the **sarcoplasm** (the cytoplasm of the muscle cell) which is rich in glycogen, ATP, creatine phosphate and glycolytic enzymes. Each myofibril is further subdivided into **thick** and **thin filaments**. The functional unit of the myofibril is called the sarcomere and repeats along the fibril axis. A sarcomere consists of the region between two consecutive Z lines and is the fundamental contractile unit of muscle.

The sarcoplasmic reticulum is an elaborately anastomosing tubular network running parallel to the myofilaments. The sarcoplasm is analogous to the endoplasmic reticulum found in most cells. The dilated ends of the sarcoplasmic reticulum are called **lateral sacs**. Passing between adjacent segments of the sarcoplasmic reticulum at the level of the A-I junction, a separate continuous tubular structure, the **transverse tubule** (t-tubule) extends into the muscle fibre. T-tubules are extensions of the sarcolemma (and are therefore continuous with the ECF), and they conduct a wave of depolarization from the sarcolemma deep into the muscle fibre allowing deep lying myofibrils to be activated. The functions of the sarcoplasmic reticulum are the release of calcium during muscle contraction and the sequestration and storage of calcium during muscle relaxation (Fig. 2).

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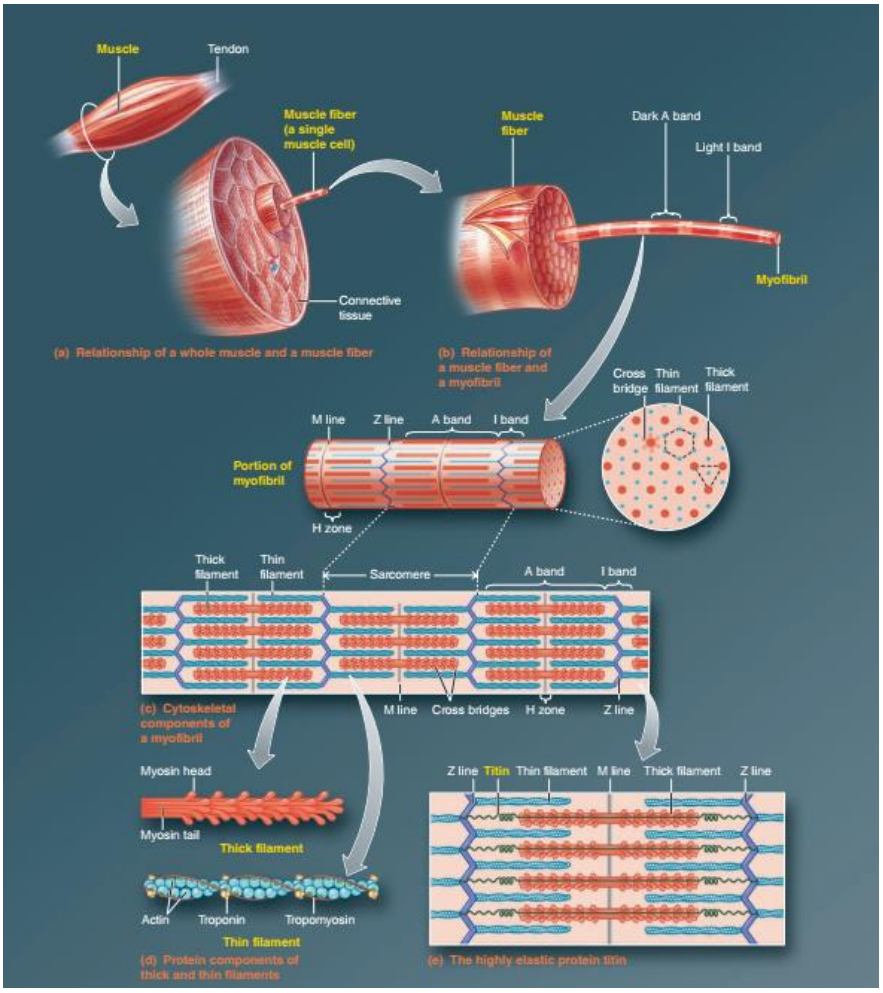

Figure 2: The organisation of skeletal muscle. (Sherwood page 253 6th edition).

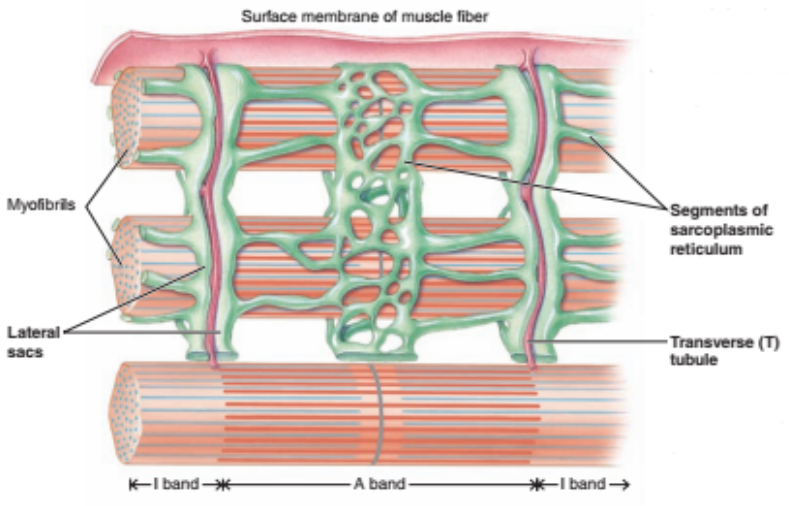

Figure 1:Sarcoplasmic reticulum and T tubules. (Sherwood, page 259 6th edition).

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Proteins of the contractile elements

Thin filaments

Thin filaments are composed primarily of three types of protein: actin, tropomyosin, and troponin in the ratio of 7:1:1. The Z line consists of actinin and the M line contains M-protein. Actin contains the binding sites for other actin monomers, myosin, tropomyosin, and troponin (Fig. 3).

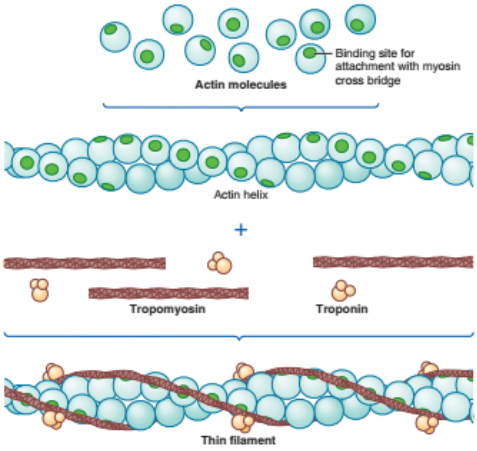

Figure 3: Thin filament. (Sherwood page255, 6th edition)

Thick filaments and myosin

Myosin (approx. 540 kilodalton (kd)) is made up of six polypeptide chains: two identical heavy chains (each 230 kd) and four light chains (~20 kd). The molecule consists of a double-headed globular region joined to a very long rod. The rod is a two-stranded-helical coil formed by the heavy chains. In each head, two different light chains are bound to the heavy chain (Fig. 4). Myosinis split by trypsin into two fragments, called light meromyosin (LMM) and heavy meromyosin(HMM). LMM forms filaments, lacks ATPase activity, and does not bind to actin. LMM is a two-stranded-helical rod for its entire length of 850 A. HMM hydrolyses ATP, binds to actin, but does not form filaments. It is the force-generating unit of muscle contraction and consists of a short rod attached to two globular domains, the myosin heads.

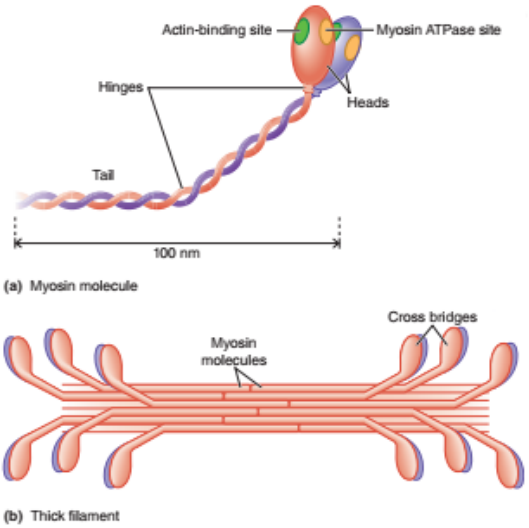

Figure 4: Thick filament (Sherwood pg 255, 6th edition)

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Muscle contraction, the interaction of actin and myosin: the sliding filament model

The sliding filament model states that muscle contraction is the result of two overlapping sets of filaments sliding past each other. The thin filaments at each end of the sarcomere move in opposite directions towards the centre and between the thick filaments to which they are linked by cross-bridges (Fig. 5). The power stroke in contraction is driven by conformational changes in the myosin S1 head which result in cyclical formation and dissociation of complexes between actin and the S1 heads of myosin.

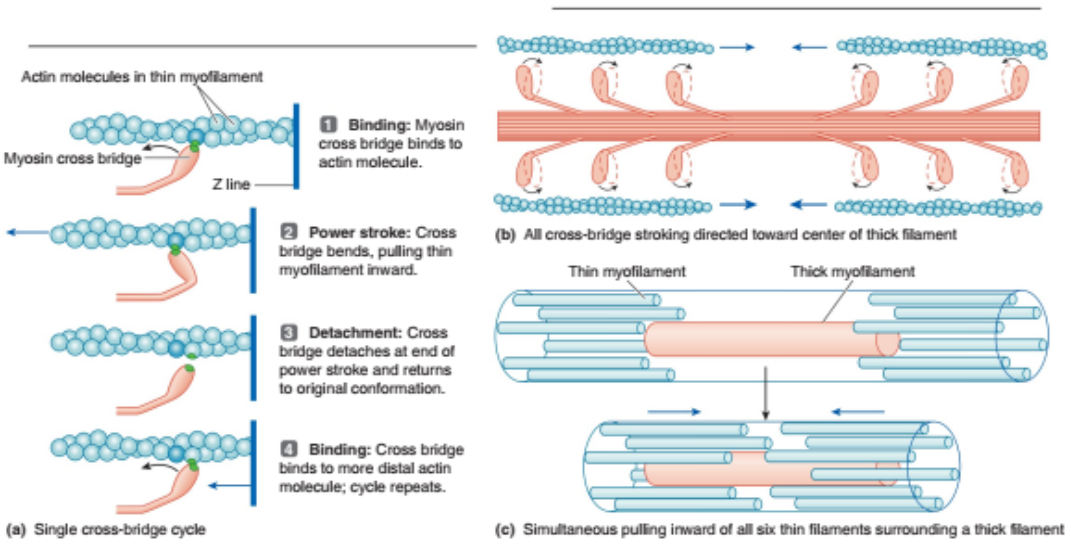

Figure 5: Sliding filament model of contraction (Sherwood page 257, 6th edition)

Excitation-contraction coupling

Stimulation of the nerve supplying a muscle sets up a process which starts on the sarcolemma and ends in the contractile machinery i.e. cross-bridge activity and contraction via increased availability of calcium. The entire process can be summarized as follows. Stimulus → depolarization of the sarcolemma → action potential initiated and propagated along the T- tubules → calcium released from sarcoplasmic reticulum system → calcium ions diffuse and attach to the active sites on TN-C → Inhibitory effect of TN-I on the interaction of actin and myosin is removed → Thin filaments slide along thick filaments shortening the sarcomere. This series of events is fully reversible under normal conditions. Following repolarization the sarcoplasmic reticulum takes up calcium ions and as the concentration of calcium ions falls they dissociate from their binding sites on TN-C resulting in conformational changes in the troponin complex which allows tropomyosin to cover the cross-bridge binding sites on actin. An action potential in a skeletal muscle fibre lasts 1 - 2 msec and is completed before any signs of mechanical activity begin. After a **latent period,** during which the events of excitation- contraction coupling are occurring, mechanical activity commences. This activity following a single action potential may last 100 ms or more.

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The neuromuscular junction

The nerve cells that innervate skeletal muscle are called **motor neurons** or somatic efferent neurons. They have their cell bodies in the brain stem or anterior horn of the spinal cord. These are myelinated, large diameter, high velocity conducting nerve fibres. Each motor axon divides into many branches as it approaches the muscle, each of which forms a single junction with a muscle fibre. Each motor neuron is connected to several muscle fibres (but each muscle fibre is innervated by only a single motor neuron). The motor neuron plus the muscle fibre it innervatesis called a **motor unit**. When the motor neuron of a motor unit fires an action potential, all the muscle fibres in that unit are activated. The region of the muscle membrane which lies directly under the terminal portion of the axon is known as the **motor endplate** and the entire junction, including axon terminal and motor endplate is known as a **neuromuscular junction**.

The mechanics of muscle contraction

Skeletal muscles account for 40-45% of an animal's body weight. The force developed by an uncontrolled maximal contraction of a whole muscle is of little practical use in the movements of animals. Therefore, the force and movement generated in a given circumstance by a given muscle depends upon the time-integrated individual activities of its component motor units. For fine control of movement one or more motor units are employed. As more force is required the number of stimuli carried by each motor unit is increased, along with the **recruitment** of additional motor units. The grading of muscular activity is the result, therefore, of asynchronous firing of the motor units of a whole muscle. It should be noted that no muscle acts alone even in the simplest movement i.e. a variety of muscles which are described as agonists, synergists,and antagonists are involved in each action. The force generated by a contracting muscle on an object is known as the **muscle tension** and the force generated by the object is **the load**.

The single muscle twitch

The contraction - relaxation of a skeletal muscle in response to a single action potential is called a **twitch**. There is a brief lag between the arrival of the action potential and the initiation of tension development known as the **latent period**.

Summation and tetanus

If a skeletal muscle is stimulated and a second stimulus is applied before relaxation is complete, a second traction is **fused** to the first contraction. This is called summation. If the stimulus is repeated at a sufficiently high rate, the muscle will not relax between each stimulus, but rather will remain in a contracted state which is referred to as **tetanus**. The plateau of such a tetanic contraction exceeds the peak of a single twitch and, in fact, represents the maximum contraction of which the muscle is capable. If stimulation is continued until **fatigue** sets in the muscle will then gradually relax. If stimulation is discontinued before fatigue sets in the tetanized muscle relaxes immediately.

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The Motor Unit

The single motor neuron and the group of muscle fibres which it innervates is, as we have seen, called a motor unit (Fig. 6). This is the smallest point of the muscle that can be made to contract independently. The number of muscle fibres in this unit varies in different muscles, from 2 to 3 to more than 1000; the size of the unit is correlated with the precision with which the tension developed by the muscle is graded. Generally, muscles controlling fine movements and adjustments (e. g. those attached to the ossicles of the ear and of the eyeball, larynx and pharynx) have the smallest number of muscle fibres per motor unit. The muscles that move the eye have less than 10 fibres per unit, on the other hand, large coarse acting muscles have motor units with many fibres, e.g. gastrocnemius has more than 2000. Even the largest bundles of muscle fibres are quite small, and so a strong contraction of a skeletal muscle requires the participation of many motor units.

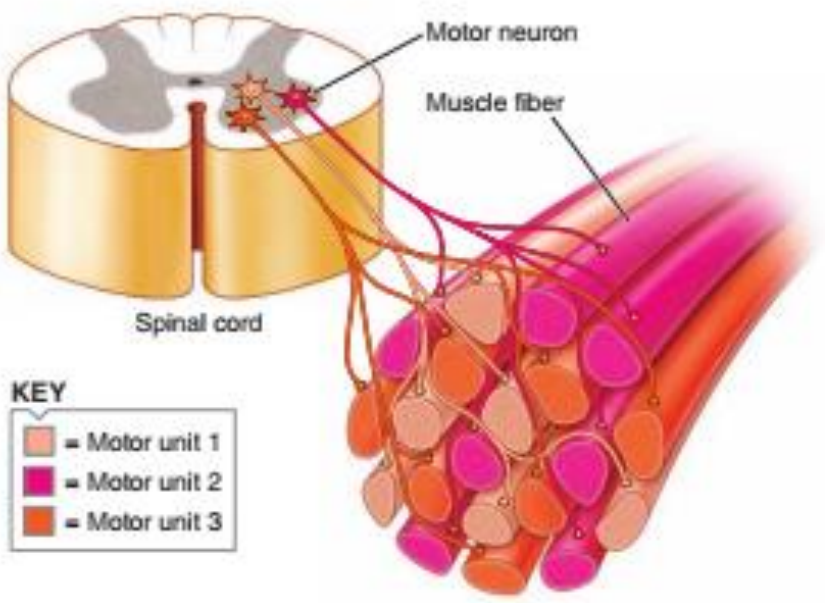

Figure 6: Motor units Sherwood pg. 266, 6th edition

Reflex control of skeletal muscle movement

Spinal Reflexes

Motor neurons can be activated by voluntary or reflex pathways (see Fig. 7 and 8). The 'simplest' reflex is the excitatory monosynaptic stretch reflex between the muscle spindle and the motor neurons. The monosynapticstretch reflex produced by slower muscle stretch may also be of use in controlling muscle length in postural control. The reflex arc is under the control of the gamma-motor neurons (the neurons that regulate the sensitivities of the muscle spindles to stretch). The stretch reflex can be modified or adapted to suit the prevailing motor control condition. An example of a stretch reflex is the **Knee Jerk Reflex** which is also called the patellar tendon reflex (Fig. 8). In a clinical setting, this reflex is activated by striking the distal patellar tendon with a reflex hammer, causing the muscle spindles of the quadriceps muscle to stretch. In the reflex arc, afferent neurons from the muscle spindles relay the excitatory signal directly to the alpha motor neurons supplying the same muscle causing the contraction of the quadriceps muscle without the involvement of any interneuron. At the same time, inhibitory signals are relayed directly to the hamstring muscle (antagonistic muscle) causing it to relax also without the involvement of an interneuron.

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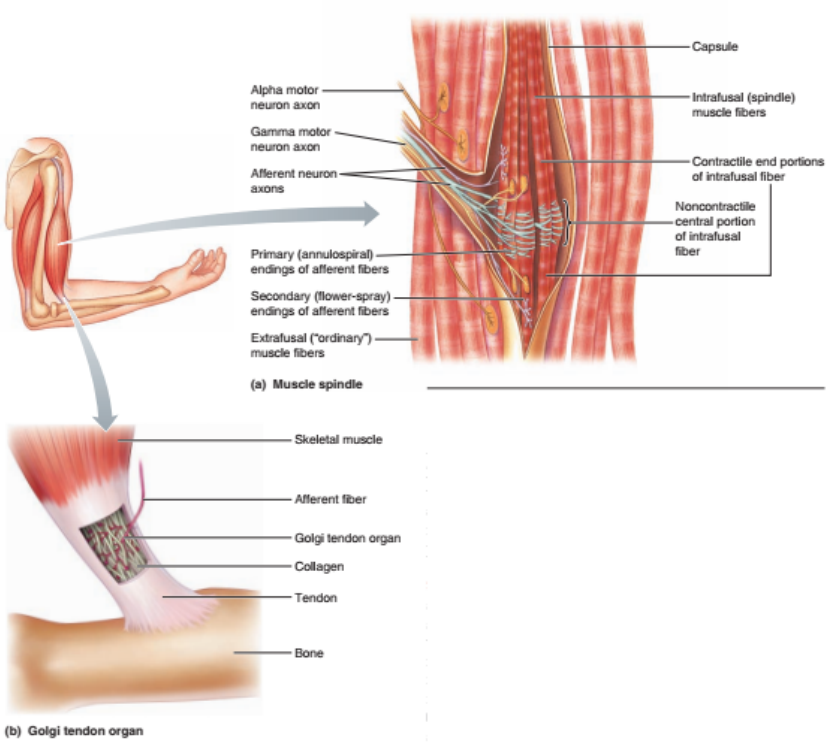

Figure 7:Receptors in skeletal muscle

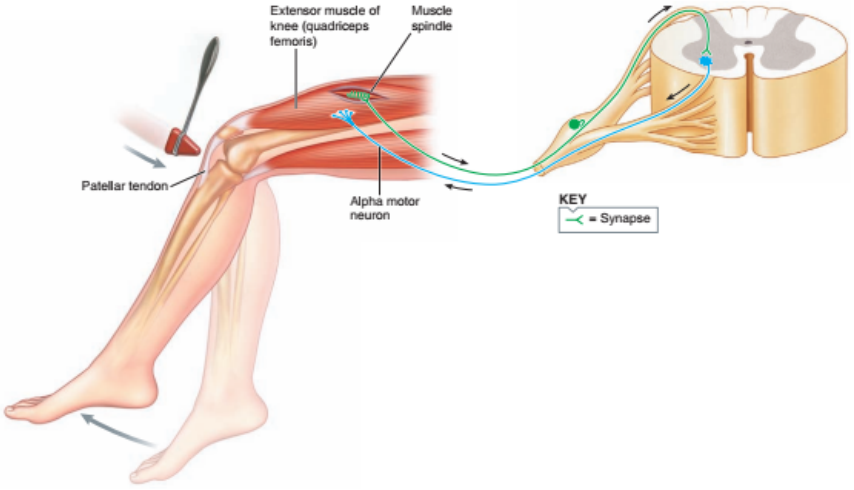

Figure 8: A simple stretch reflex