

C. Muscle contraction: structure and function of actin and myosin microfilaments

I. General information about the organization of striated muscle

- **Myocyte or muscle fiber** : A myocyte or muscle fiber is a very elongated muscle cell whose ends are made up of collagen filaments. Each muscle fiber is in contact with a nerve fiber that controls its activity. Muscle fibers have two fundamental properties: excitability under the stimulating action of nerve fibers, and contractility, which is the ultimate result of stimulation. When a muscle fiber contracts, its length decreases, causing its ends to move closer together.
- **Myofibril** : Myofibrils are contractile fibers, actin and myosin, located inside the muscle cell. A myofibril is composed of darker and lighter areas. The darker areas are actually protein filaments called myosin, and the lighter areas are protein filaments called actin. By cutting the myofibril between two light areas, we obtain a sarcomere.
- **The sarcomere** : is the unit between two Z bands consisting of :
 - Band I: light area composed of actin filaments.
 - Band A: dark area composed of actin and myosin filaments.
 - Band H (middle of band A) composed of myosin filaments.
 - Thin filaments are actin filaments and thick filaments are myosin filaments.

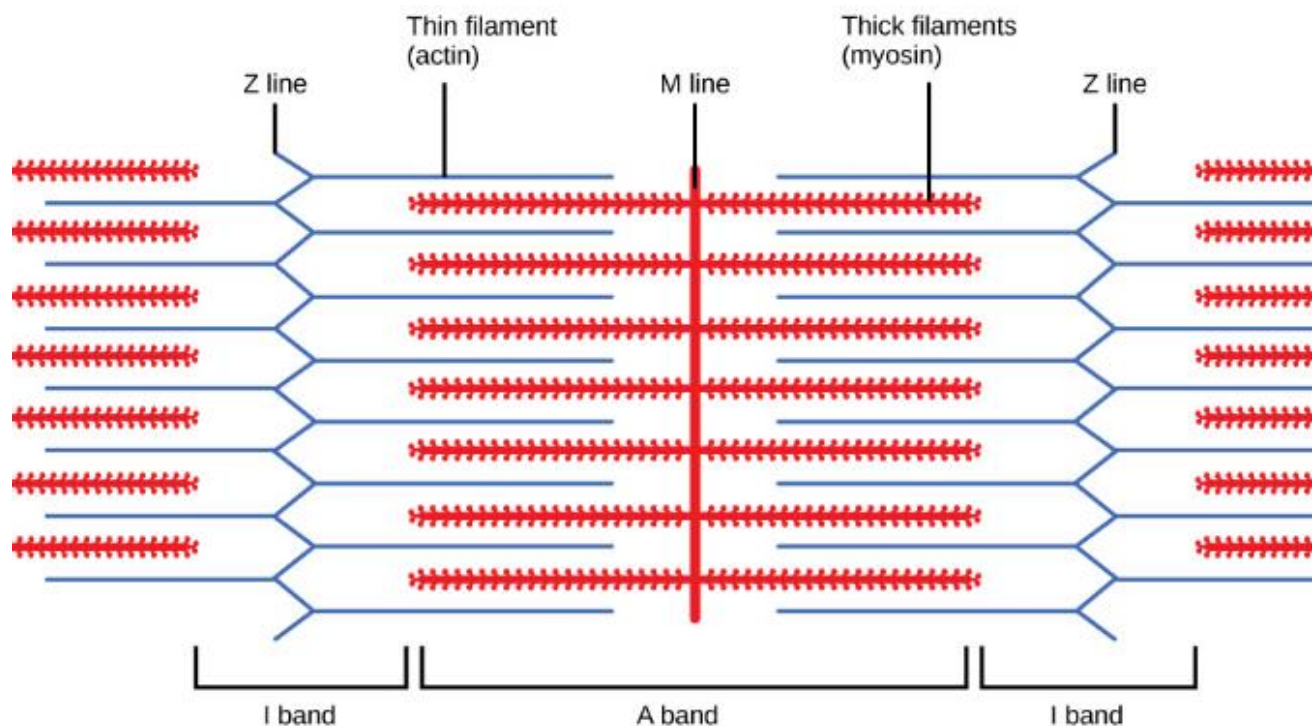


Figure III. 1. The sarcomere [27].

II. Structure of thin and thick filaments

II.1. Fine filaments

The thin filaments have a diameter of approximately 7 nm and are composed of several types of molecules: actin, tropomyosin, and troponin.

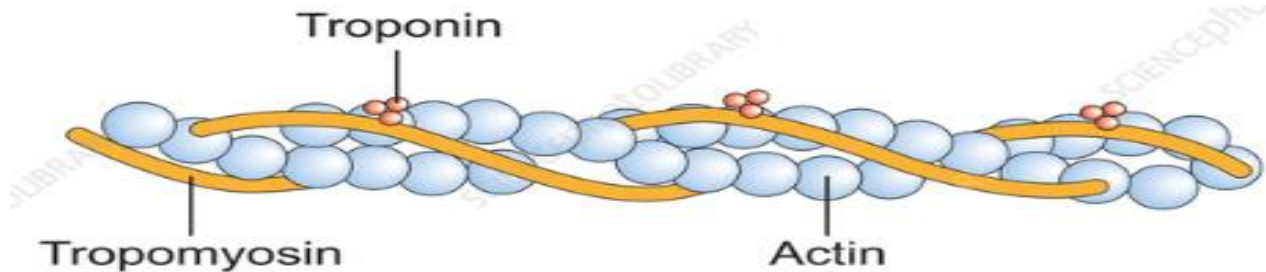


Figure III. 2. Structure of a thin actin filament [28].

-Monomeric actin (or G-actin for globular): is a globular molecule weighing 42 kDa that can polymerize to form filaments (F-actin for filamentous). Actin filaments are composed of two linear chains that wind around each other to form a double helix.

-Tropomyosin: is an elongated homodimeric or heterodimeric protein, each monomer consisting of 284 amino acids adopting an alpha helix structure that winds around each other to form a superhelix. It binds to actin by fitting into the grooves of the double helix formed by actin. At rest, myosin molecules are also in contact with tropomyosin. At each end of a tropomyosin molecule, i.e., an interval corresponding to seven actin molecules, a troponin molecule binds to tropomyosin.

-Troponin: is a molecule composed of three chains called troponin-T, troponin-I, and troponin-C. Each chain has a different function:

- Troponin-T is responsible for the troponin-tropomyosin bond.
- Troponin-I inhibits the ATPase activity of myosin;
- Troponin-C has four binding sites for calcium which, when occupied, inhibit the action of troponin I.

II.2. Thick filaments

Thick filaments have a diameter of approximately 15 nm and are mainly composed of a single molecular species, myosin.

Myosin is an elongated molecule composed of two heavy chains (approximately 200 kDa each) and four light chains (approximately 20 kDa each). Each heavy chain consists of an elongated, fibrillar C-terminal tail in an alpha helix, an N-terminal globular head with ATPase activity associated with two light chains, and a deformable neck domain connecting the two ends. The globular head and cervical region form heavy meromyosin, while the caudal fibrillar region forms light meromyosin. The

elongated tails of two heavy myosin chains wrap around each other in a superhelix, with the two globular heads lying side by side.

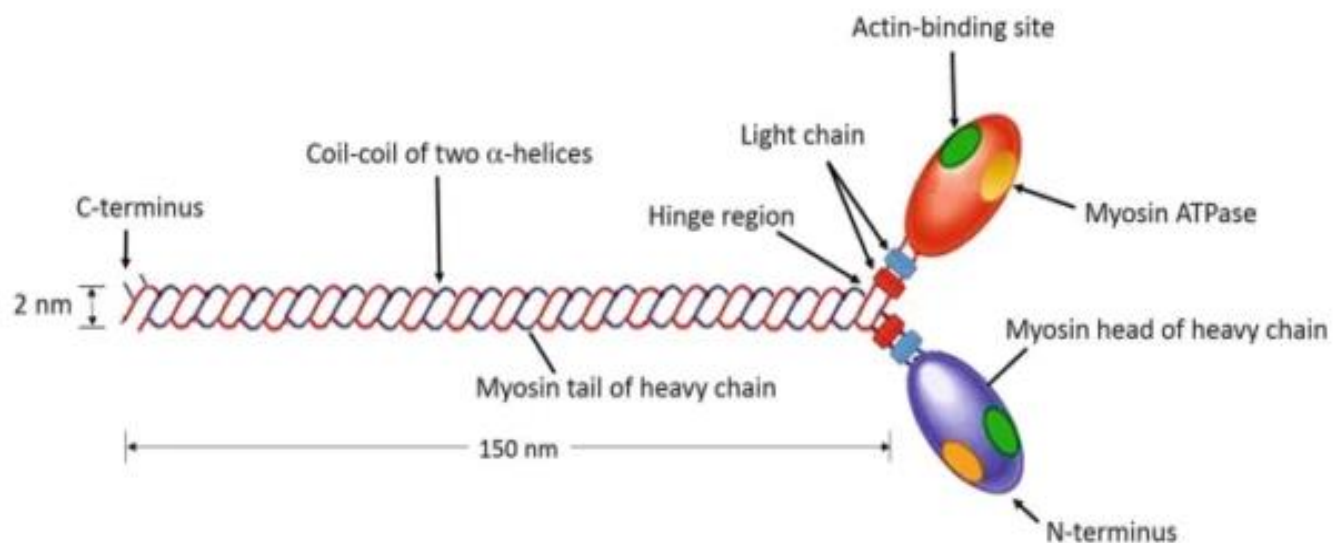


Figure III. 3. Structure of the myosin molecule [28].

Several hundred myosin molecules assemble to form a thick filament. The tail ends of these molecules are arranged parallel to each other. The globular heads project beyond the periphery of this filament and are therefore available to attach to actin filaments. Since the myosin molecules are arranged in two head-to-tail groups, the central part of the filament (corresponding to the M band) is denuded (devoid of globular heads).

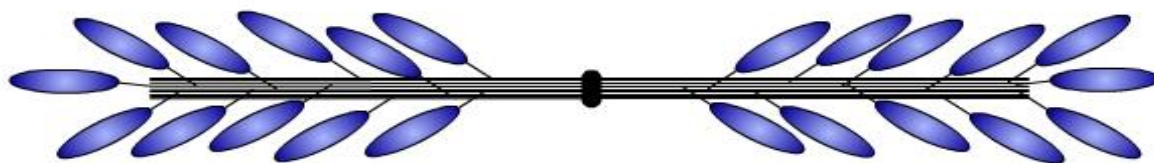


Figure III. 4. Structure of a thick myosin filament [28].

III. Sarcomere shortening

The interaction between actin and myosin, in the presence of ATP, allows the thin filaments to slide mechanically over the thick filaments. This sliding causes sarcomeric shortening and explains muscle contraction. During contraction, only the length of the A bands (+ M band) remains unchanged. Conversely, H bands and I decrease in thickness in the same proportions.

Everything happens at the interaction zone between the myosin heads and the actin filaments. At rest, the TnI subunit of troponin is bound to actin, and the tropomyosin filament interposes itself between the myosin head and actin.

Contraction is triggered by Ca^{++} ions. The binding of Ca^{++} to the TnC subunit of troponin causes the bond between the TnI unit and actin to break and changes the conformation of the molecule. Tropomyosin shifts slightly, allowing actin-myosin contact and lifting the inhibition of the ATPase activity of the myosin head. The hydrolysis of an ATP molecule into ADP provides the energy necessary to mobilize the myosin head, which interacts with actin, pulling on the actin filament (by approximately 7 to 10 nm).

This activity is cyclical. Only a few myosin heads are involved in each contraction cycle. The phenomenon is rapidly reversible. The binding of a new ATP molecule to myosin breaks the bond. The phenomenon can be repeated if Ca^{++} is still present. When no ATP is available, the actin-myosin bond is stable. This explains rigor mortis after death.

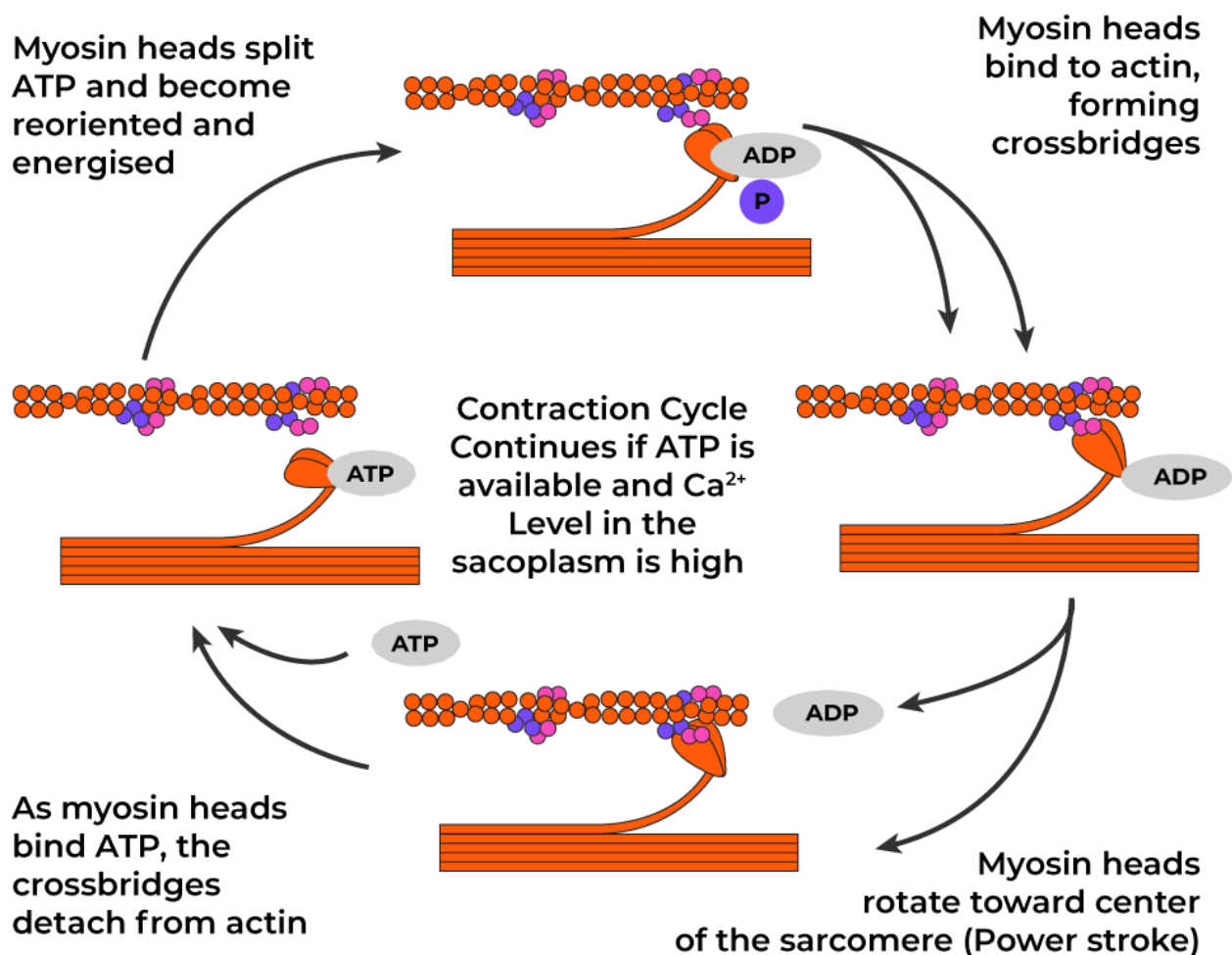


Figure III. 5. Steps of muscle contraction [27].