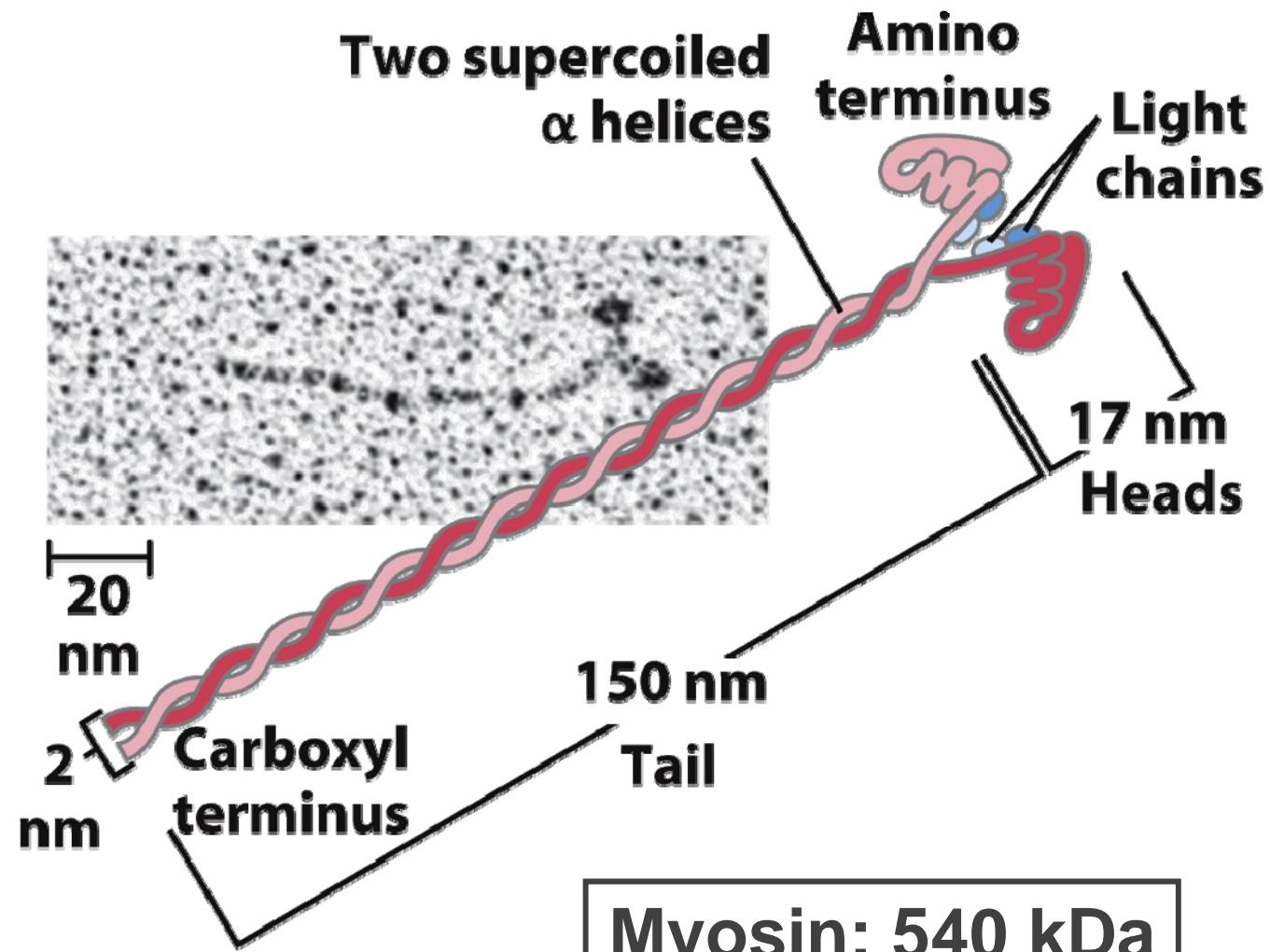
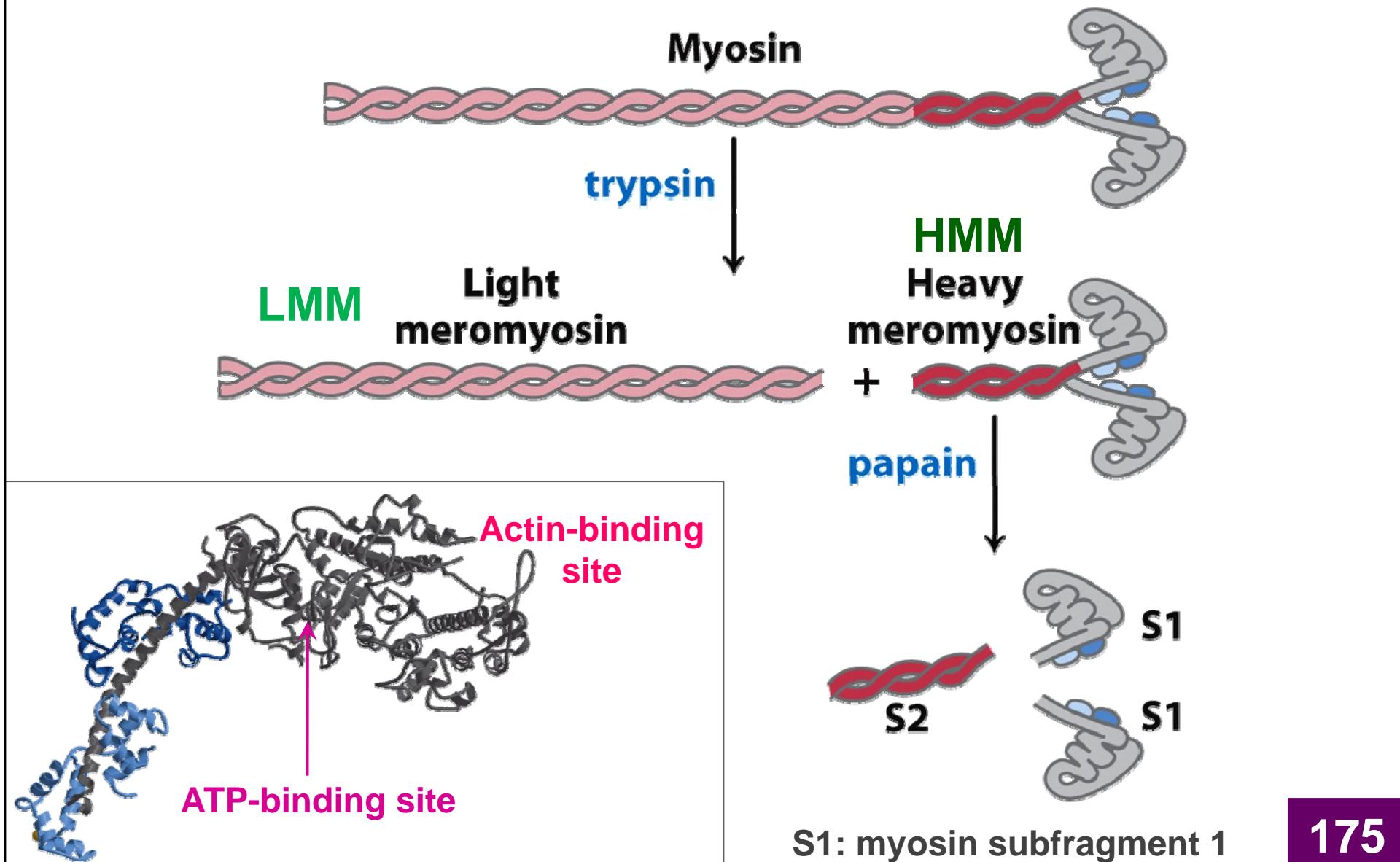


**The Major Proteins
of Muscle Are
Myosin and Actin**

Myosin is composed of two heavy chains and four light chains



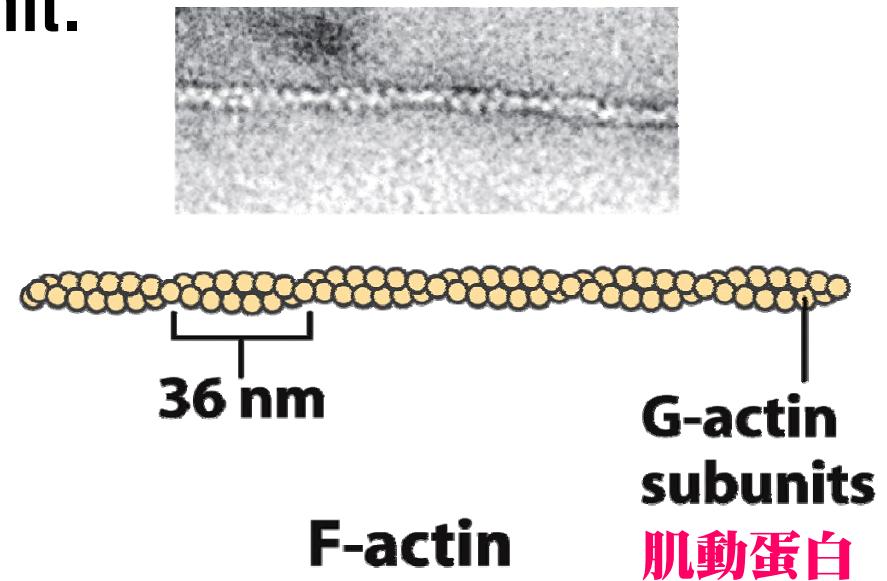
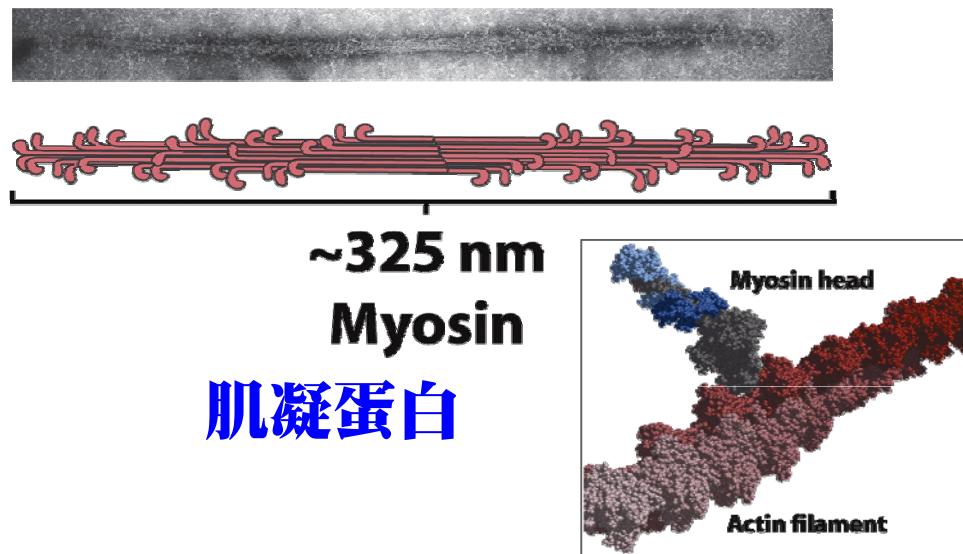
Cleavage with trypsin and papain separates the myosin heads (S1 fragments) from the tails



S1: myosin subfragment 1

Thick filaments and thin filaments in muscle

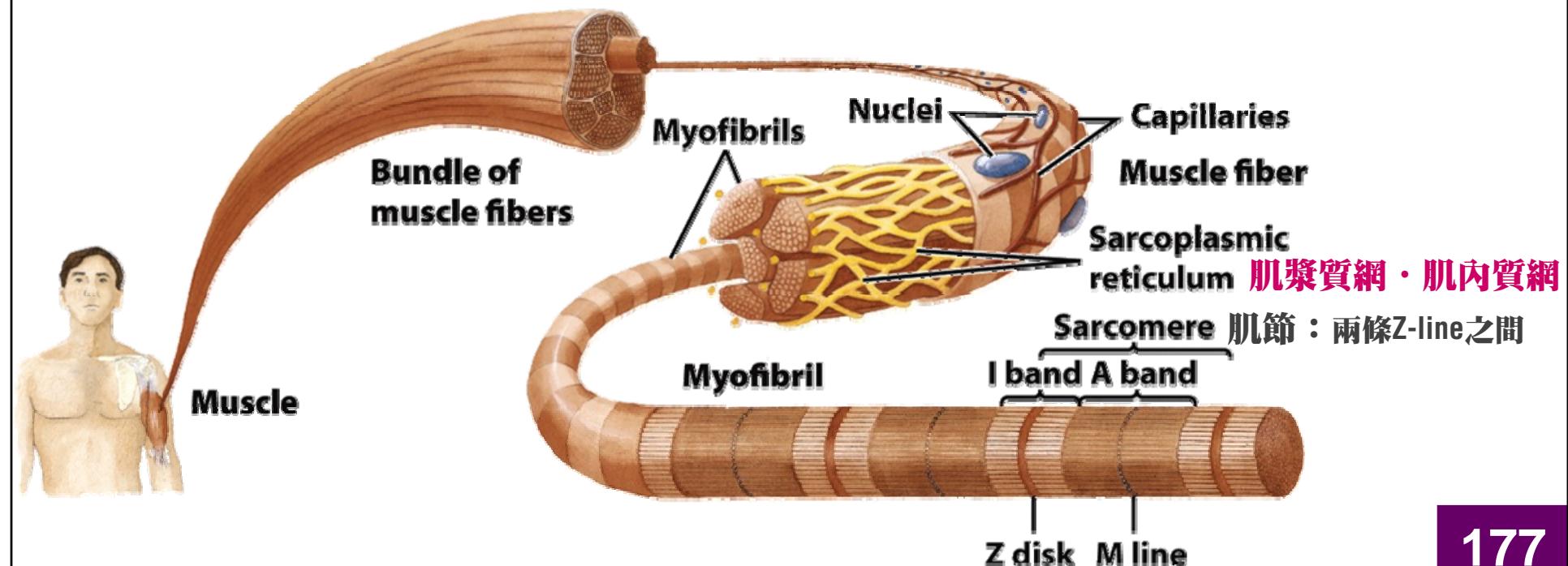
- In muscle cells, molecules of myosin aggregate to form structures called **thick filaments**. These rodlike structures are the core of the contractile unit.



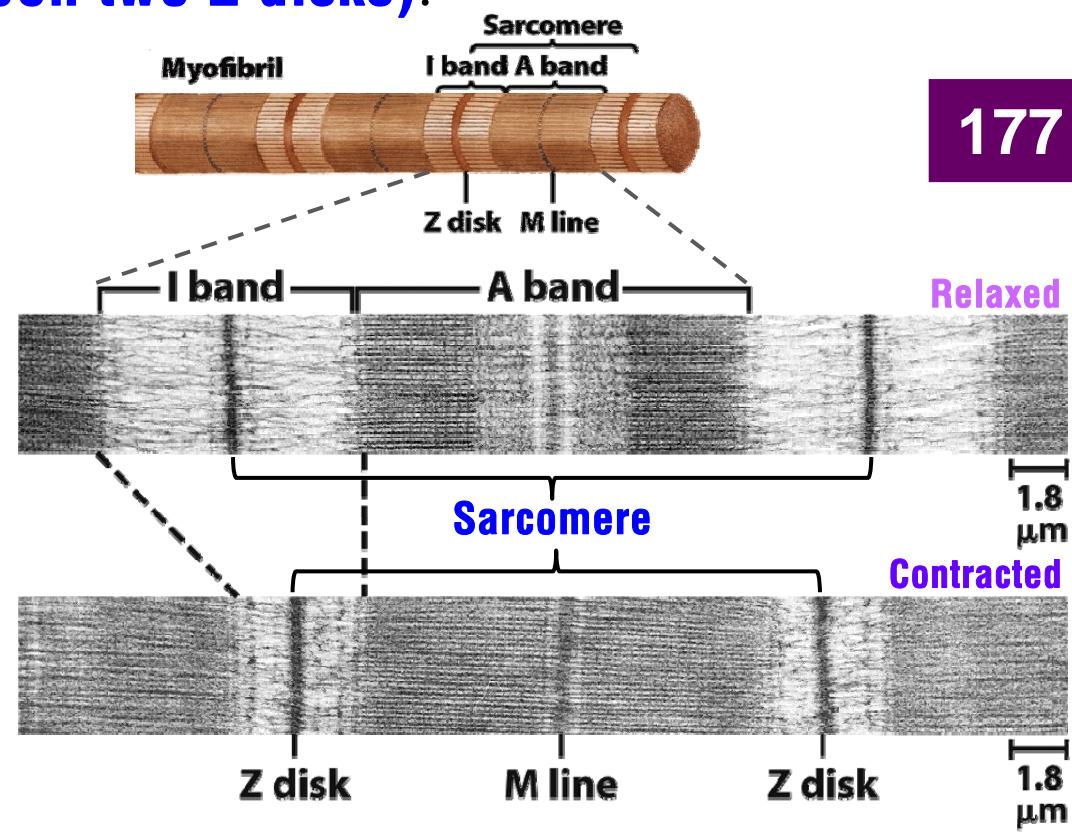
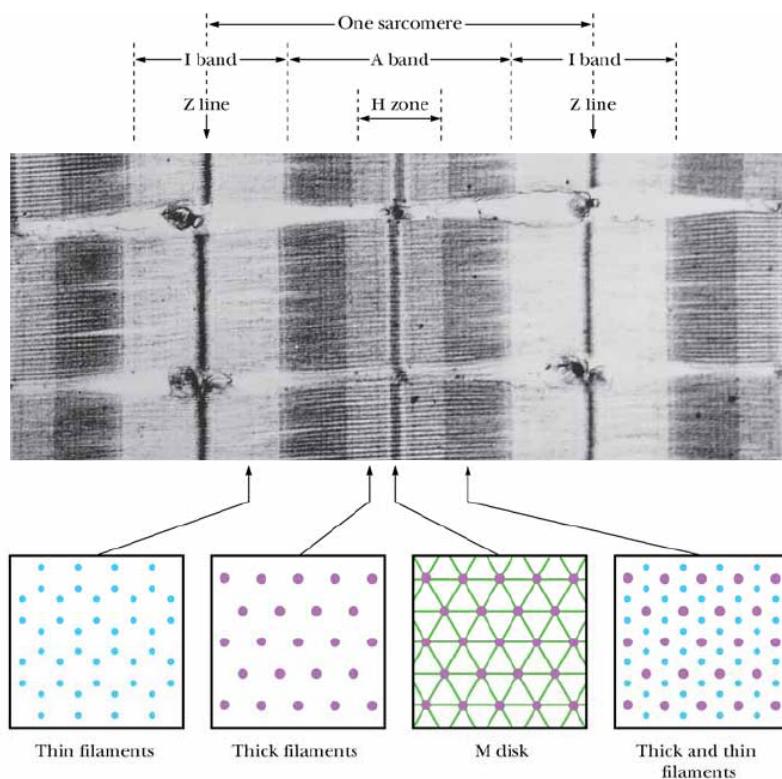
- In muscle, molecules of monomeric actin, called **G-actin complexed to ADP**, associate to form a long polymer called F-actin. The **thin filament** consists of F-actin, along with the proteins troponin and tropomyosin

The components of the muscle fibers

- Skeletal muscle consists of parallel bundles of **muscle fibers (肌纖維)**.
- Each fiber contains about 1,000 **myofibrils (肌原纖維)**, each consisting of a vast number of regularly arrayed thick and thin filaments complexed to other proteins.
- The organization of thick and thin filaments in a myofibril gives it a **striated appearance**.
- A system of flat membranous vesicles, **sarcoplasmic reticulum**, surrounds each myofibril.
- The **sarcoplasmic reticulum** is a specialized endoplasmic reticulum that stores **calcium ions** needed for muscle contraction.

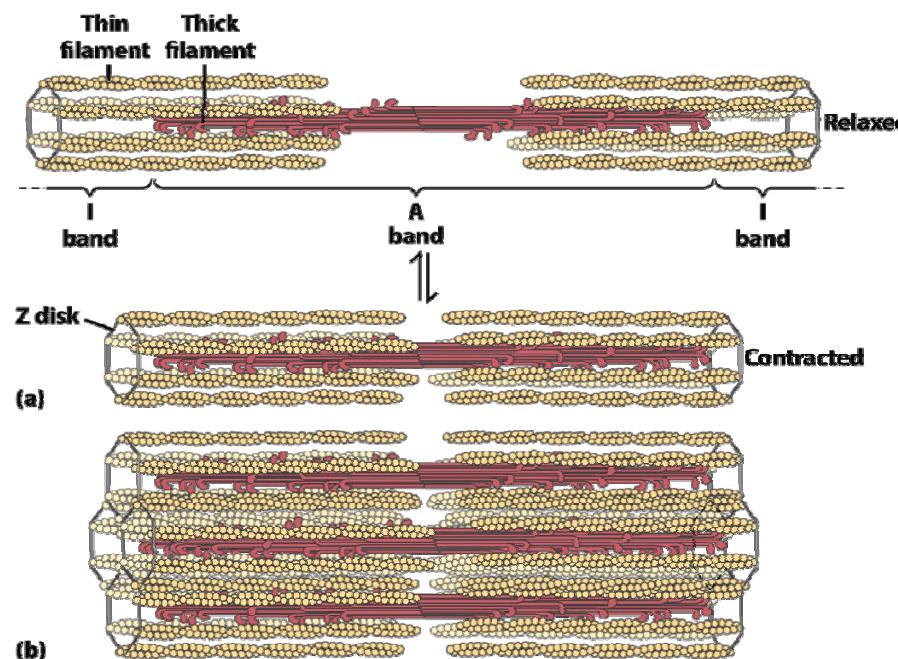


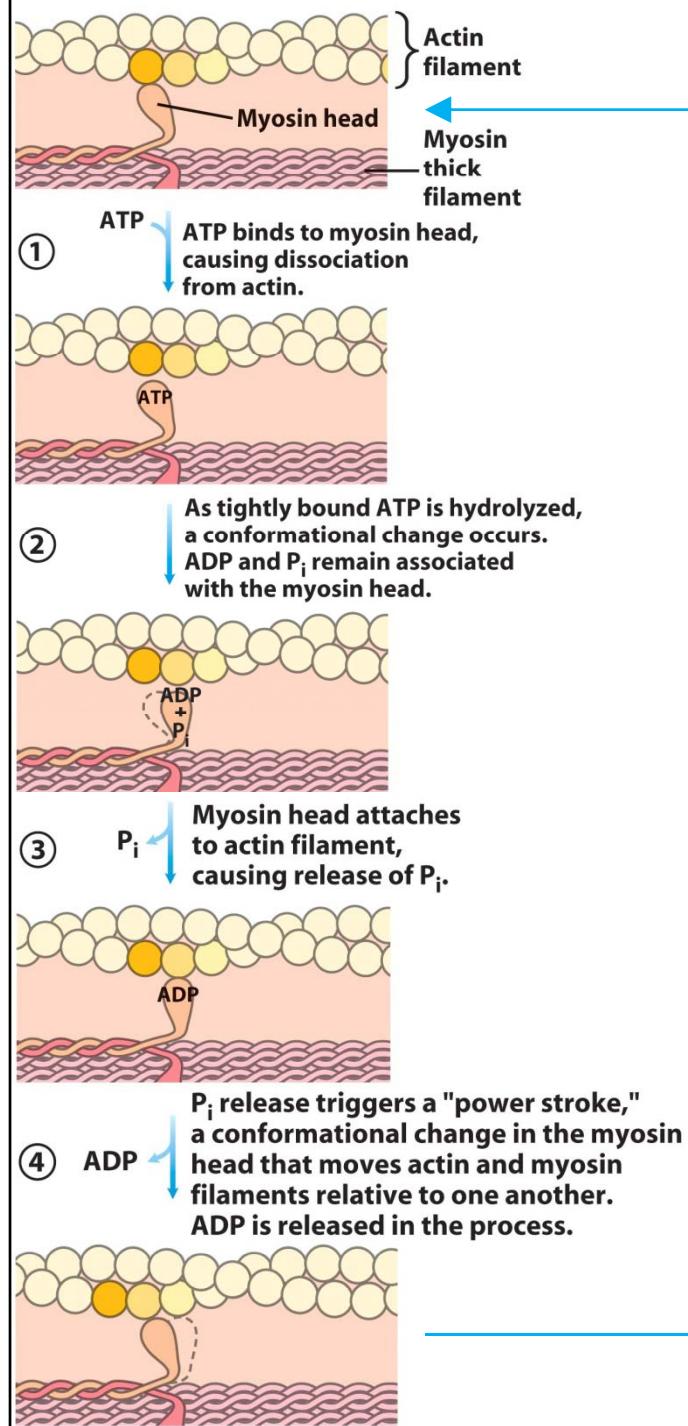
- Muscle fibers reveal alternating regions of **high** and **low** electron density, called the **A bands** and **I bands**.
- The **A band** is bisected by a thin line, the **M line** or **M disk**.
- Bisecting the **I band** is a thin structure called the **Z disk**.
- The entire contractile unit, consisting of bundles of thick filaments interleaved at either end with bundles of thin filaments, is called the **sarcomere** (the region between two Z disks).



Additional components organize the thin and thick filaments into ordered structures

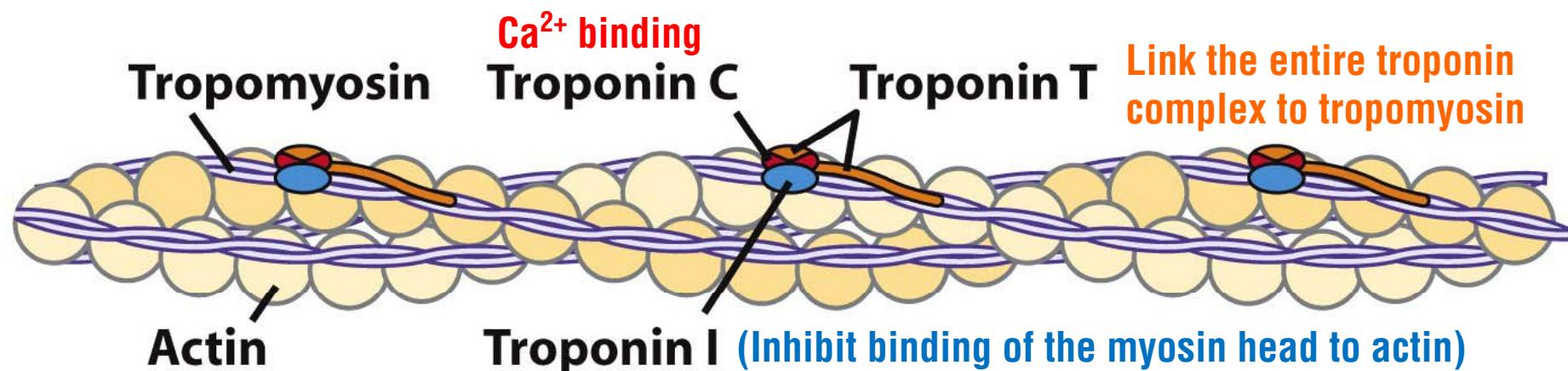
- The **thin actin filaments** are attached at one end to the **Z disk** in a regular pattern. The assembly includes the minor muscle proteins **α -actinin, desmin, and vimentin**.
- Thin filaments also contain a large protein called **nebulin** (伴肌動蛋白).
- M line** contains the proteins **paramyosin, C-protein, and M-protein**.
- Each thick filament is surrounded by six thin filaments**.
- Titins (connectin 肌聯蛋白), the largest single polypeptide chains discovered thus far (26,926 amino acid residues)**, extends from the Z disk to the M line and link the thick filaments to the Z disk, regulating the length of the sarcomere itself and preventing overextension of the muscle.
- Nebulin and titin are believed to act as “molecular rulers”, regulating the length of the thin and thick filaments, respectively.**





- The cycle has four major steps. In step ①, ATP binds to myosin and a cleft in the myosin molecule opens, disrupting the actin-myosin interaction so that the bound actin is released.
- ATP is then hydrolyzed in step ②, causing a conformational change in the protein to a “high-energy” state that moves the myosin head and changes its orientation in relation to the actin thin filament. Myosin then binds weakly to an F-actin subunit closer to the Z disk than the one just released.
- As the phosphate product of ATP hydrolysis is released from myosin in step ③, another conformational change occurs in which the myosin cleft closes, strengthening the myosin-actin binding.
- This is followed quickly by step ④, a “power stroke” during which the conformation of the myosin head returns to the original resting state, its orientation relative to the bound actin changing so as to pull the tail of the myosin toward the Z disk. ADP is then released to complete the cycle.

Regulation of muscle contraction by tropomyosin and troponin



- The interaction between actin and myosin is mediated by a complex of two proteins, **tropomyosin** and **troponin (a Ca²⁺-binding protein)**.
- Tropomyosin binds to the thin filament (F-actin), blocking the attachment sites for the myosin head groups.
- A nerve impulse causes release of **Ca²⁺** from sarcoplasmic reticulum. The released **Ca²⁺** binds to troponin and cause a conformational change in the tropomyosin-troponin complexes, exposing the myosin-binding sites on the thin filaments. Contraction follows.
- Working skeletal muscle requires two types of molecular functions that are common in proteins— binding and catalysis.



optical trapping experiments have shown that *a single cycle or turnover of a single myosin molecule along an actin filament involves an average movement of 4 to 11 nm (40–110 Å) and generates an average force of 1.7 to 4×10^{-12} newton (1.7–4 piconewtons (pN)).* 3~4 pN

hydrolysis of a single ATP molecule? The energy required for a contraction cycle is defined by the “work” accomplished by contraction, and work (w) is defined as force (F) times distance (d):

$$w = F \cdot d \quad 5\text{--}10 \text{ nm}$$

For a movement of 4 nm against a force of 1.7 pN, we have

$$w = (1.7 \text{ pN}) \cdot (4 \text{ nm}) = 0.68 \times 10^{-20} \text{ J}$$

For a movement of 11 nm against a force of 4 pN, the energy requirement is larger:

$$w = (4 \text{ pN}) \cdot (11 \text{ nm}) = 4.4 \times 10^{-20} \text{ J}$$

If the cellular free energy of hydrolysis of ATP is taken as -50 kJ/mol , the free energy available from the hydrolysis of a single ATP molecule is

$$\Delta G = (-50 \text{ kJ/mol}) / 6.02 \times 10^{23} \text{ molecules/mol} = 8.3 \times 10^{-20} \text{ J}$$

Thus, *the free energy of hydrolysis of a single ATP molecule is sufficient to drive the observed movements against the forces that have been measured.*