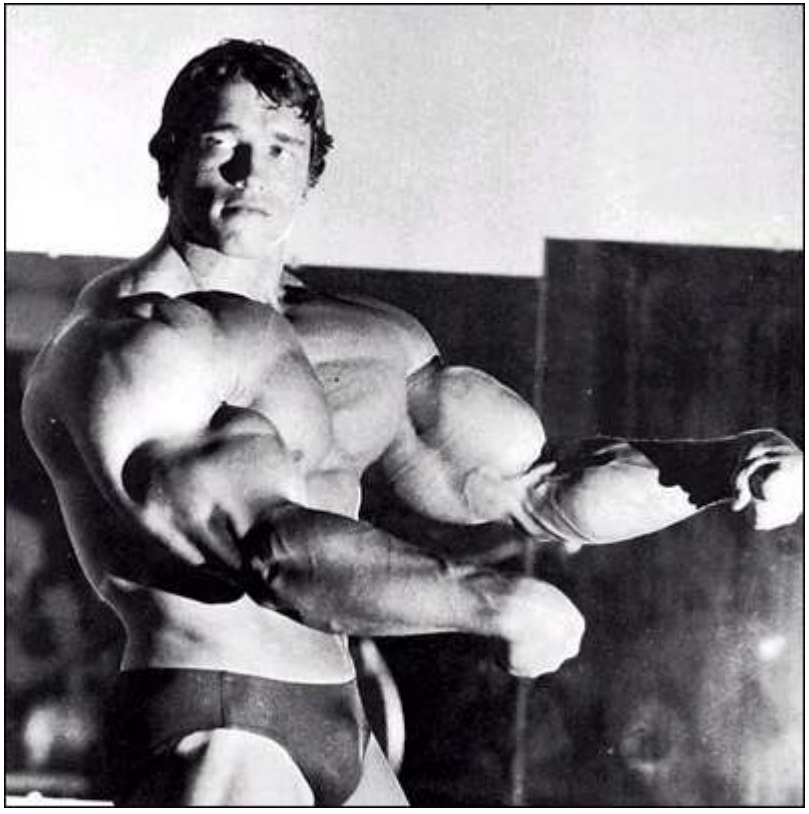
Muscle



Ch. 6: Contraction of Skeletal Muscle

- 40% skeletal muscle + 10% smooth and cardiac muscle
- Ch. 7: Excitation of Skeletal Muscle
- Ch. 8: Contraction and Excitation of Smooth Muscle

Physiological Anatomy of Skeletal Muscle

- Fig. 6.1: Organization of skeletal muscle
  - Skeletal muscles are composed of numerous fibers.
- Sarcolemma
  - Consists of cell membrane of muscle fiber
  - True cell membrane = *plasma membrane*
  - Outer coat made up of a thin layer of polysaccharide material that contains thin collagen fibrils.
  - This surface layer of sarcolemma fuses with a tendon fiber, and tendon fibers into bundles to form the muscle tendons.

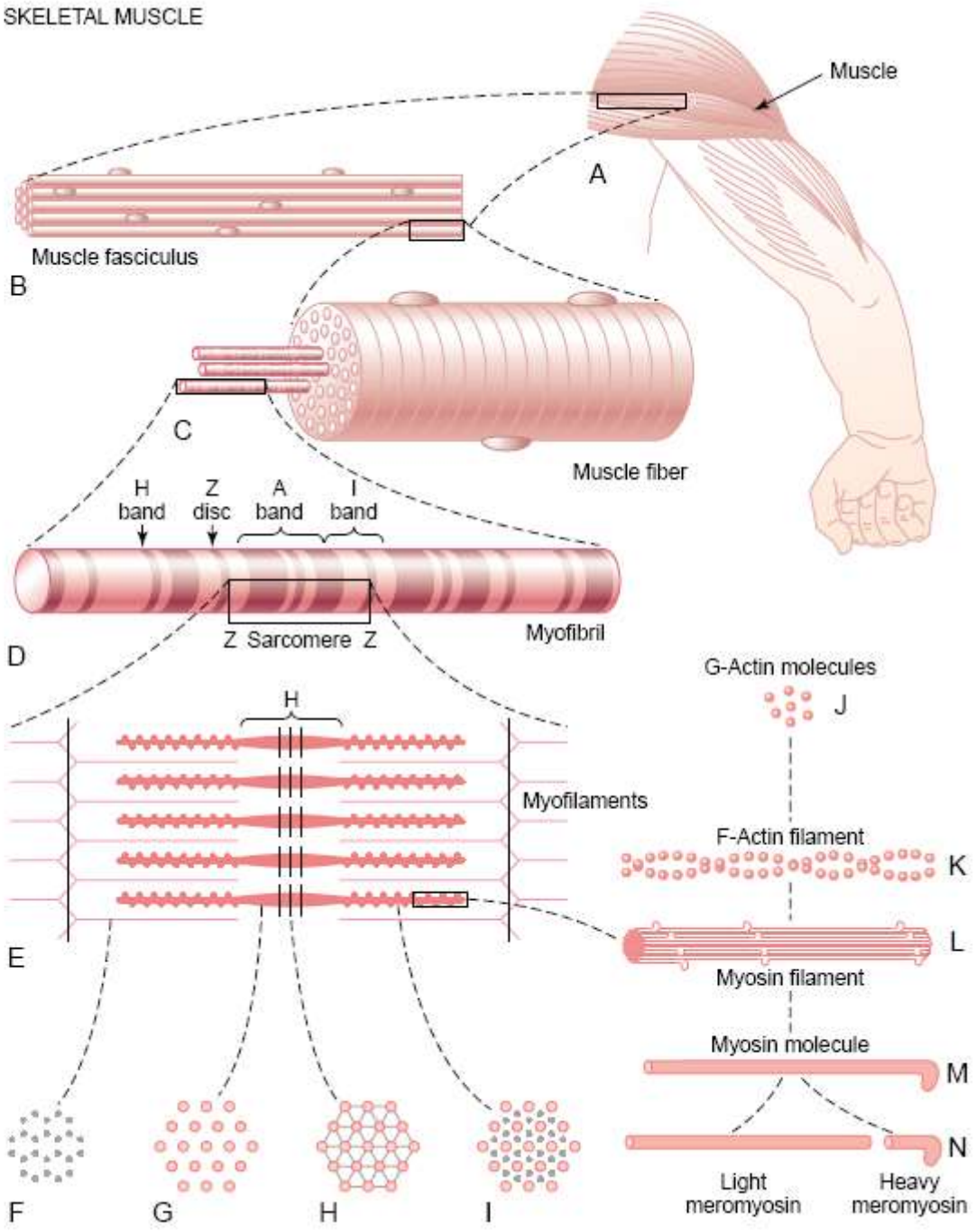


Figure 6–1

Organization of skeletal muscle, from the gross to the molecular level. *F*, *G*, *H*, and *I* are cross sections at the levels indicated. (Drawing by Sylvia Colard Keene. Modified from Fawcett DW: Bloom and Fawcett: A Textbook of Histology. Philadelphia: WB Saunders, 1986.)

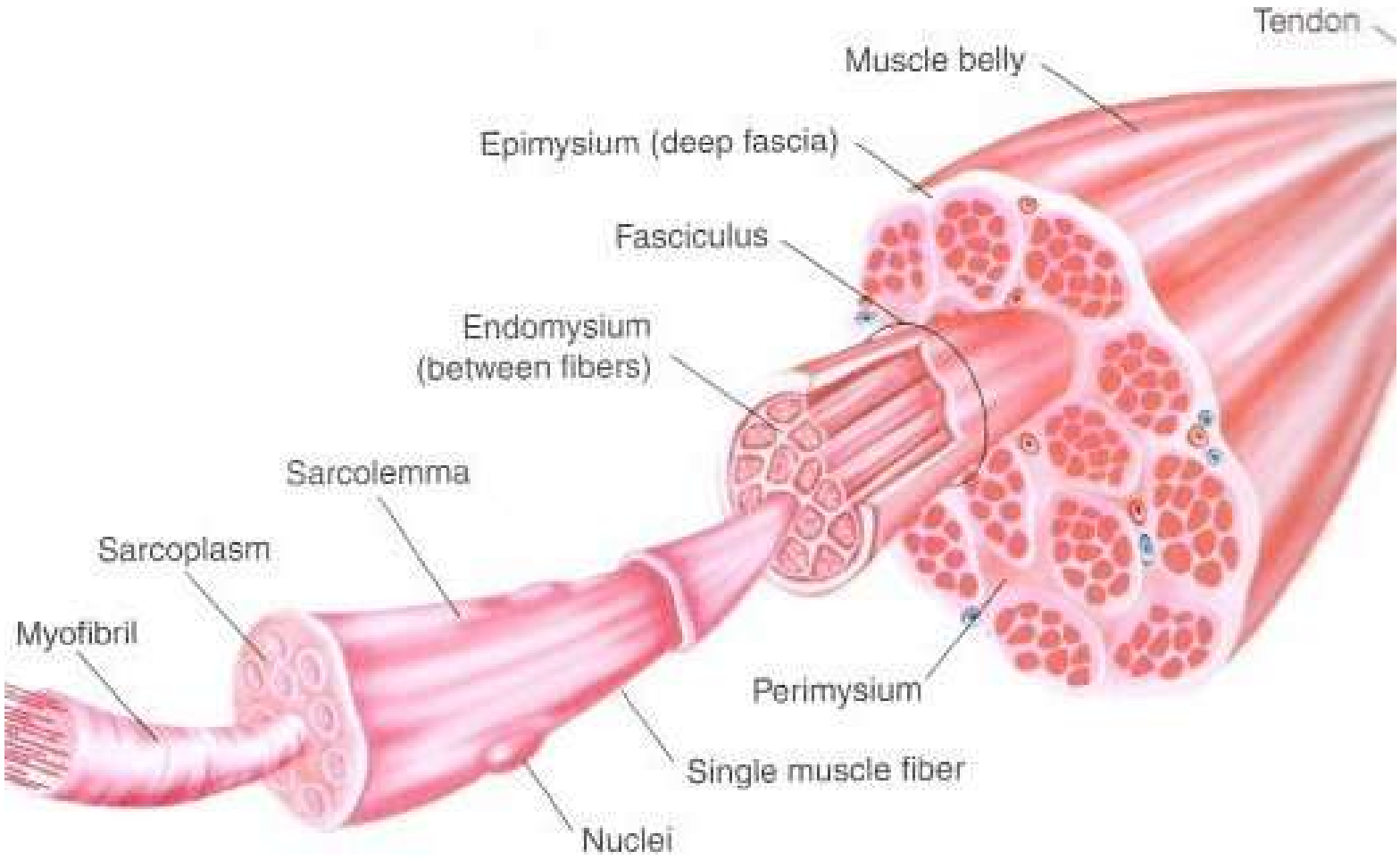
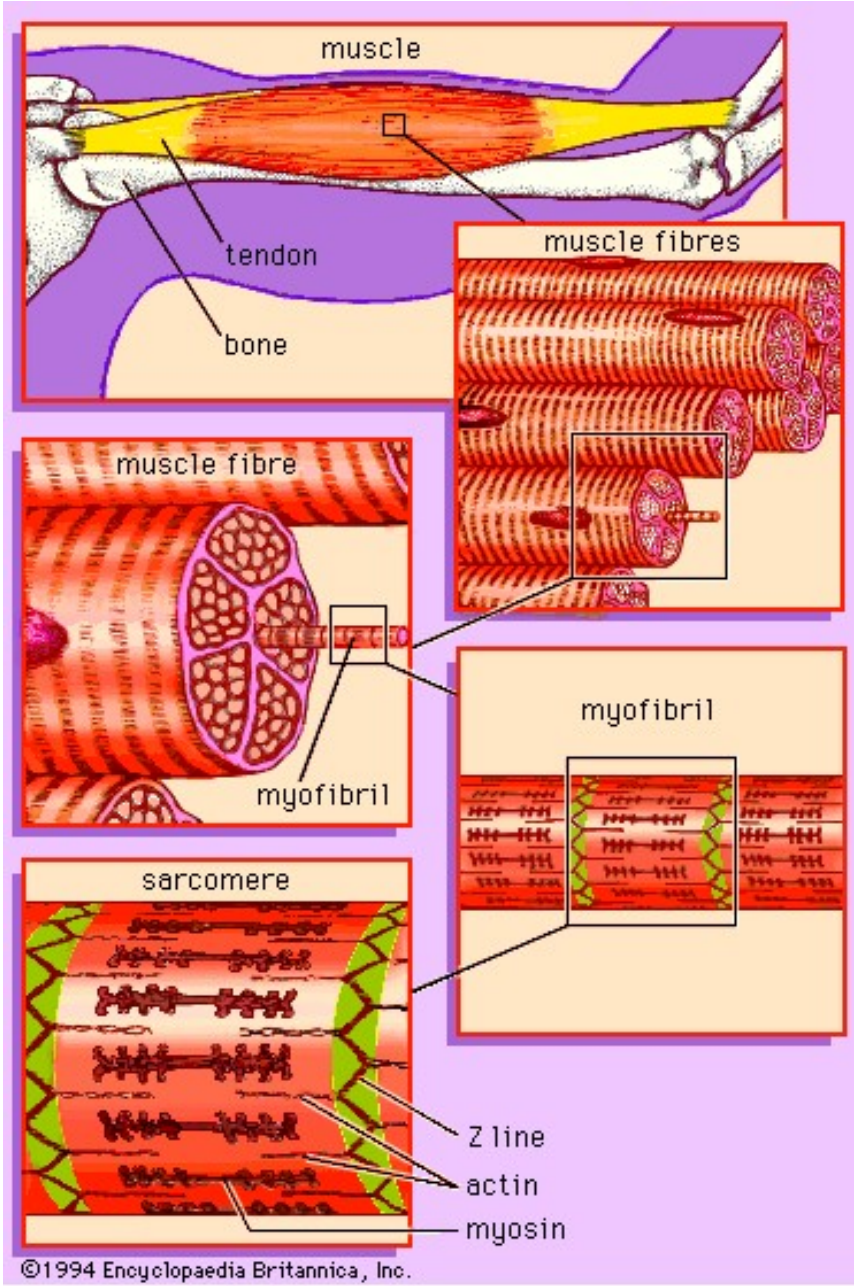
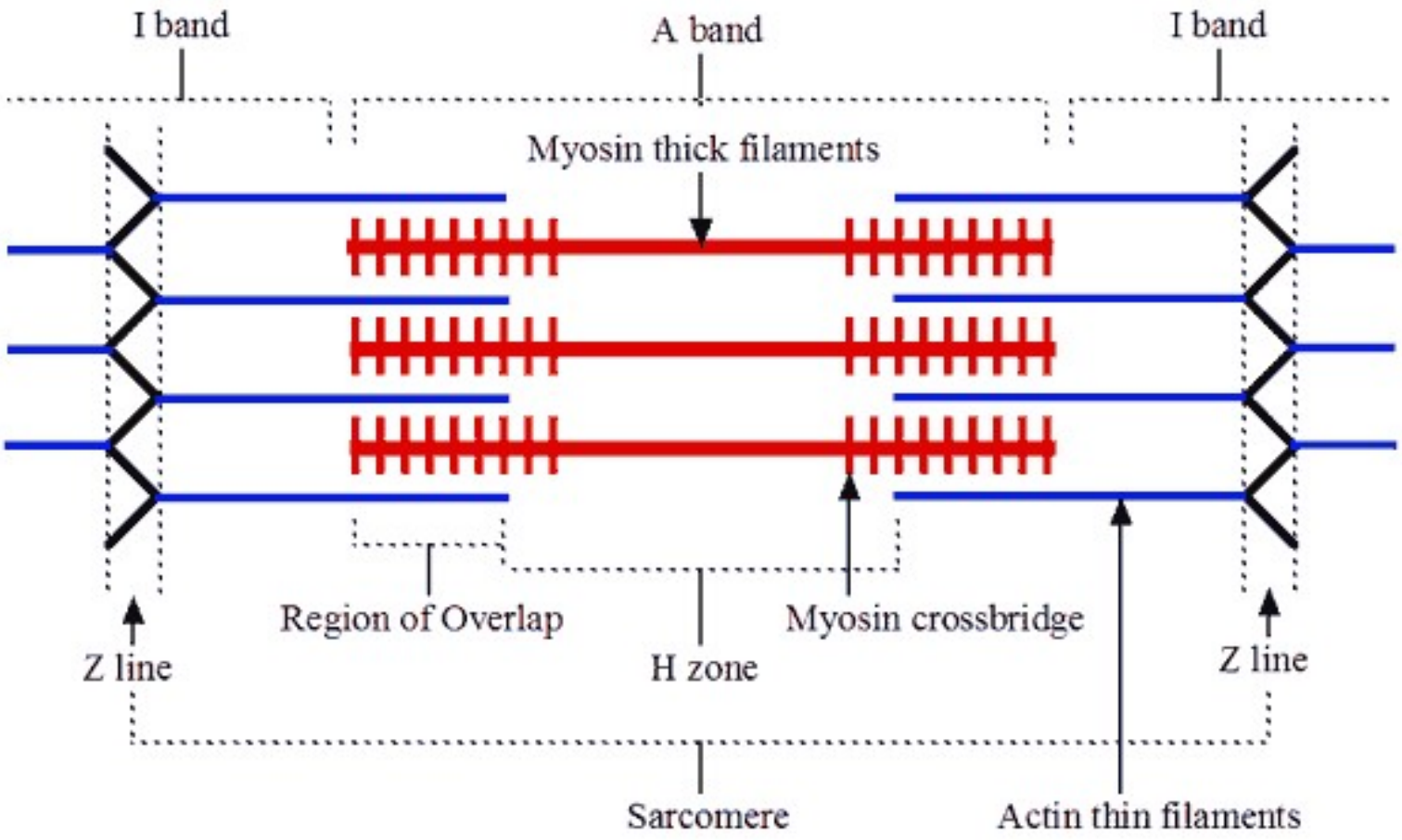


Figure 1: Muscle belly split into various component parts (from Essentials of Strength Training & Conditioning, National Strength & Conditioning Association)


muscle
tendon
bone
muscle fibres
muscle fibre
myofibril
myofibril
sarcomere
Z line
actin
myosin
©1994 Encyclopaedia Britannica, Inc.

- Myofibrils
  - Each muscle fiber contains several hundred to several thousands myofibrils (Fig. 6-1C)
  - Each myofibril is composed of about 1500 myosin filaments and 3000 action filaments, that are responsible for actual muscle contraction (Fig. 6-2)
  - Check Actin and Myosin filaments
  - Fig. 6-1E, myosin and action filaments partially interdigitate and cause the myofibrils to have alternate light and dark bands (Fig. 6-2)
  - I (Isotropic) Band: only actin filaments
  - A (Anisotropic) Band
  - Z Disk
  - Two successive Z-Disk: Sarcomere
  - Fig. 6-4: relaxed and contracted muscle


I band
A band
I band
Myosin thick filaments
Region of Overlap
H zone
Myosin crossbridge
Z line
Z line
Sarcomere
Actin thin filaments

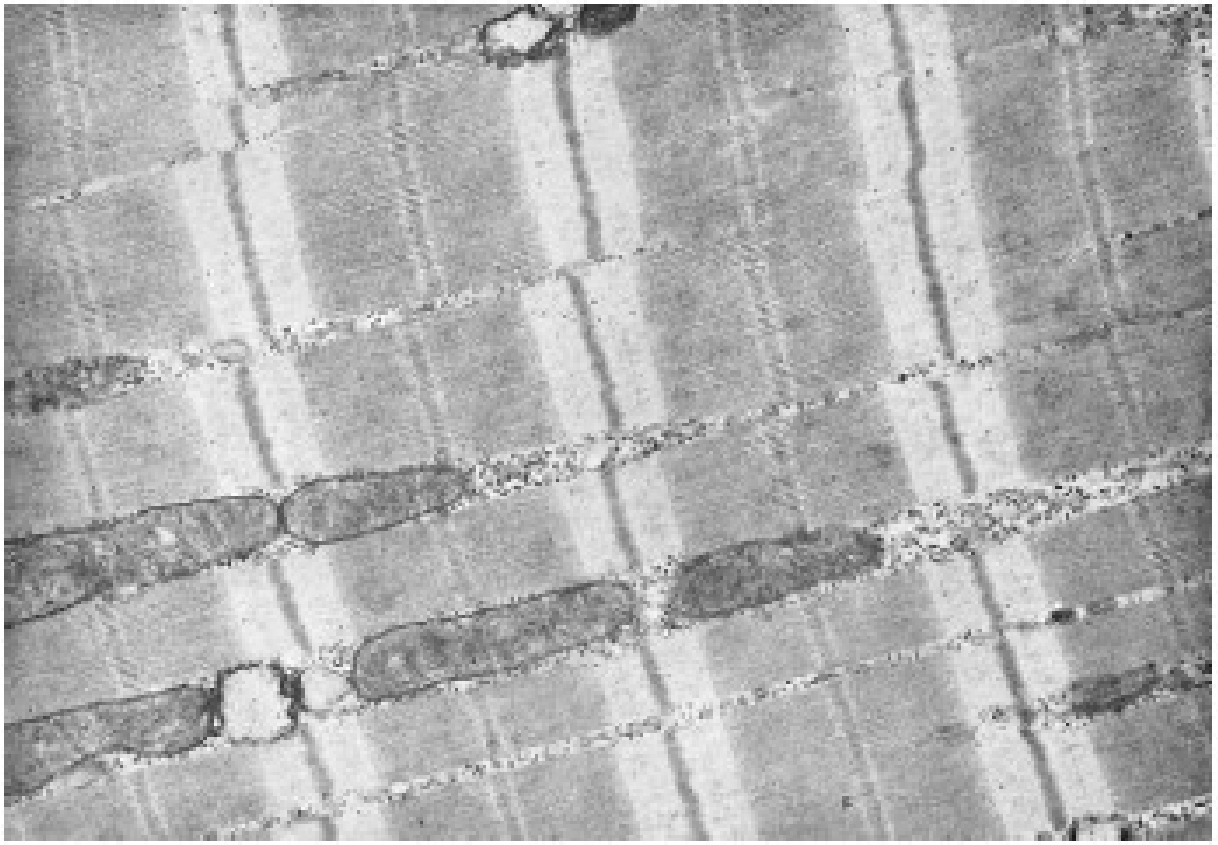
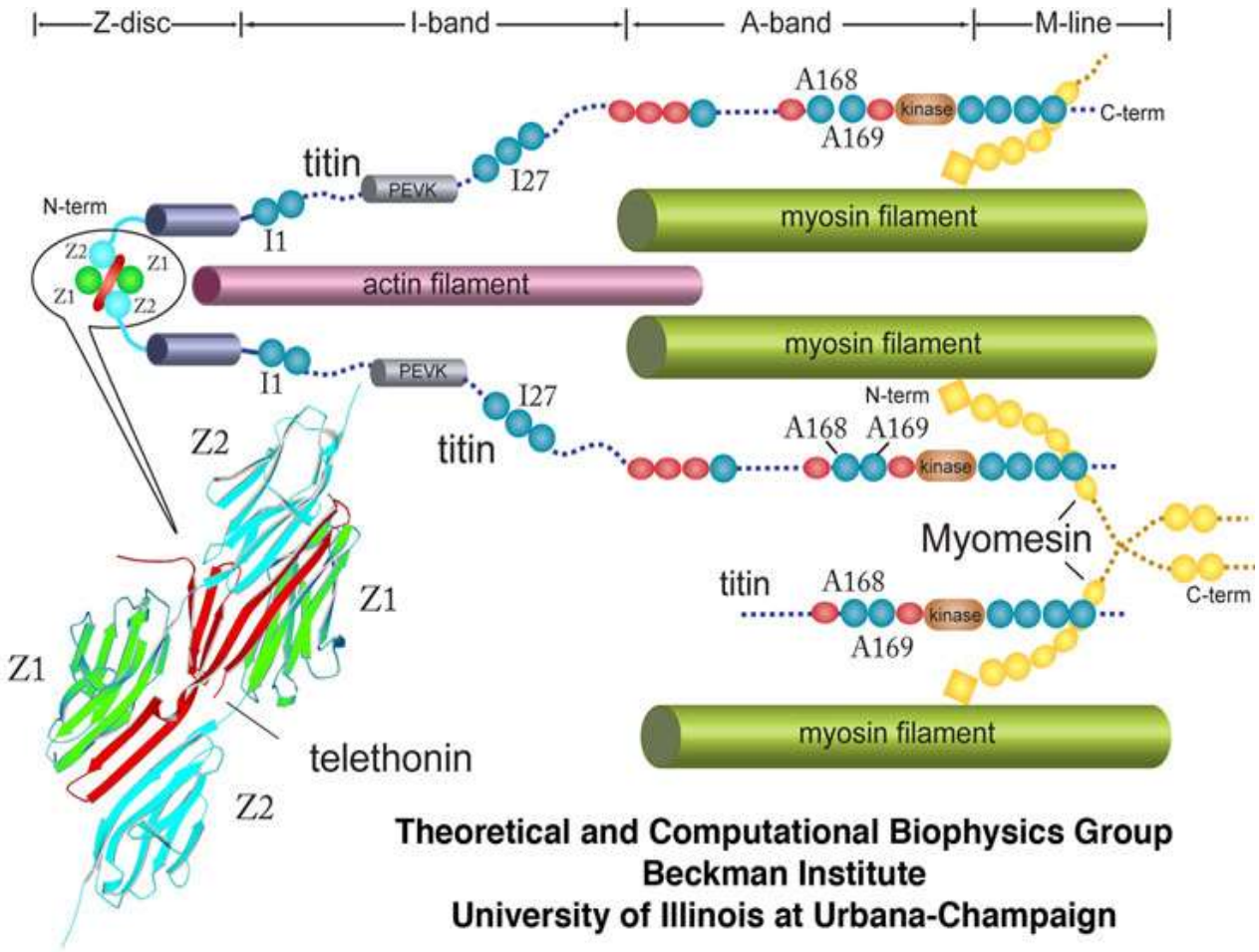


Figure 6–2

Electron micrograph of muscle myofibrils showing the detailed organization of actin and myosin filaments. Note the mitochondria lying between the myofibrils. (From Fawcett DW: The Cell. Philadelphia: WB Saunders, 1981.)

- What keeps myosin and actin in place?
  - Titin filamentous molecules
  - One of the largest protein molecules
  - Filamentous = very springy



- Sarcoplasm
  - Myofibrils are suspended in an intracelluar matrix called sacoplasm
  - This fluid contains potassium, magnesium, phosphate, multiple protein enzymes
  - Also a lot of mitochondria
- Sarcoplasmic Reticulum
  - In sarcoplasm, extensive endoplasmic reticulum called sarcoplasmic reticulum.
  - Very important in controlling muscle contraction discussed in Ch. 7
  - Fig. 6-3, picture

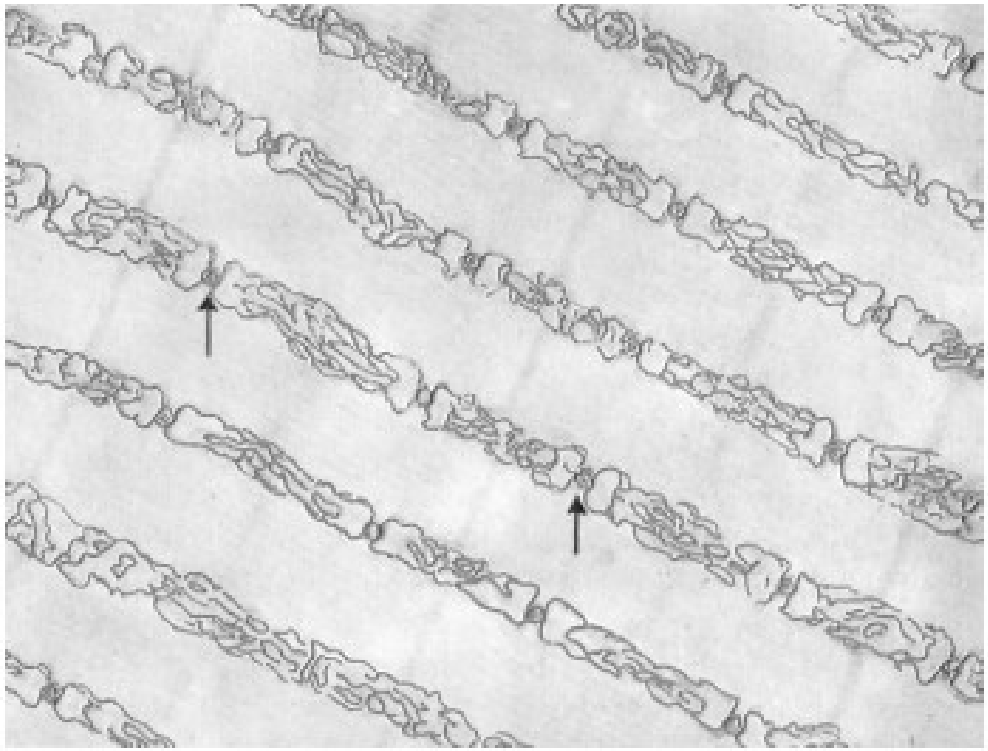


Figure 6–3

Sarcoplasmic reticulum in the extracellular spaces between the myofibrils, showing a longitudinal system paralleling the myofibrils. Also shown in cross section are T tubules *(arrows)* that lead to the exterior of the fiber membrane and are important for conducting the electrical signal into the center of the muscle fiber. (From Fawcett DW: The Cell. Philadelphia: WB Saunders, 1981.)

General Mechanism of Muscle Contraction

1. An action potential travels along a motor nerve to its endings on muscle fibers.

2. At each ending, the nerve secretes a small amount of the neurotransmitter substance *acetylcholine.*

3. The acetylcholine acts on a local area of the muscle fiber membrane to open multiple “acetylcholinegated” channels through protein molecules floating

4. Opening of the acetylcholine-gated channels allows large quantities of sodium ions to diffuse to the interior of the muscle fiber membrane. This initiates an action potential at the membrane.

5. The action potential travels along the muscle fiber membrane in the same way that action potentials travel along nerve fiber membranes.

General Mechanism of Muscle Contraction

6. The action potential depolarizes the muscle membrane, and much of the action potential electricity flows through the center of the muscle fiber. Here it causes the sarcoplasmic reticulum to release large quantities of calcium ions that have been stored within this reticulum.

7. The calcium ions initiate attractive forces between the actin and myosin filaments, causing them to slide alongside each other, which is the contractile process.

8. After a fraction of a second, the calcium ions are pumped back into the sarcoplasmic reticulum by a Ca++ membrane pump, and they remain stored in the reticulum until a new muscle action potential comes along; this removal of calcium ions from the myofibrils causes the muscle contraction to cease.

Molecular Mechanism of Muscle Contraction

- Sliding mechanism of contraction
  - Fig. 6-4
  - Sliding filament mechanism
  - What causes the actin filaments to slide inward among the myosin filaments? Mechanical forces generated by the cross-bridges.
  - Under resting, the forces are inhibited.
  - Action potential initiates contraction (more details coming)

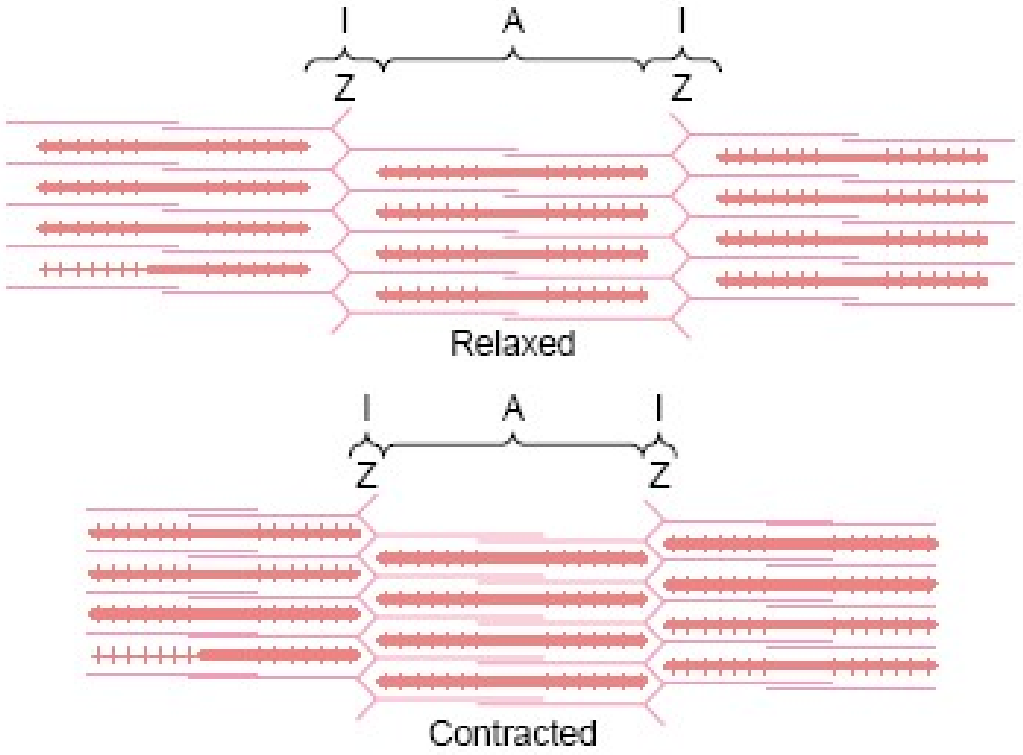
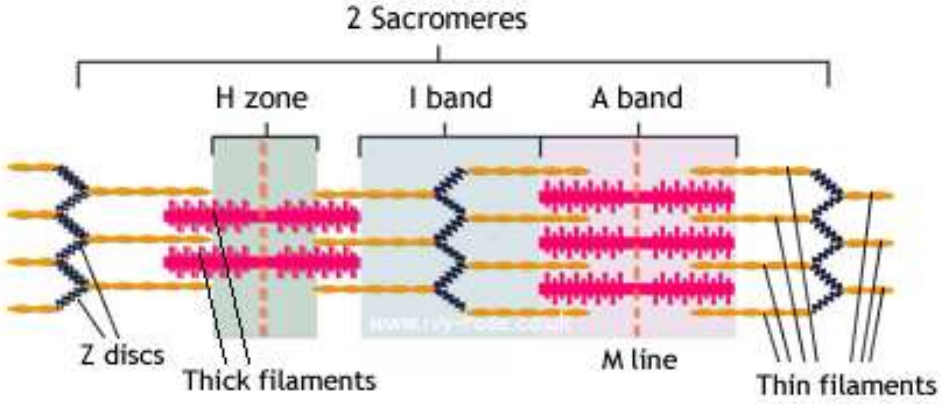


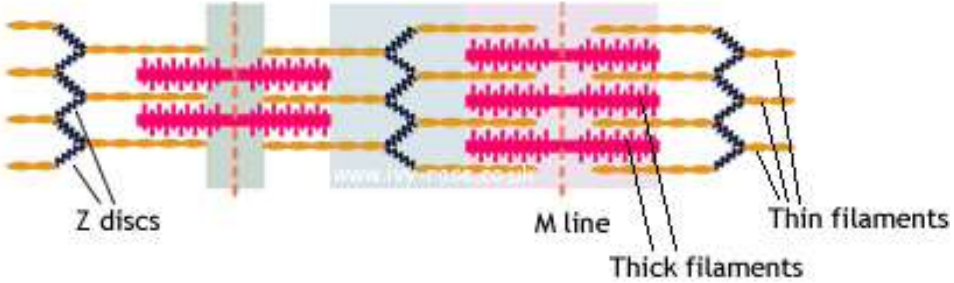
Figure 6–4

Relaxed and contracted states of a myofibril showing *(top)* sliding of the actin filaments *(pink)* into the spaces between the myosin filaments *(red)*, and *(bottom)* pulling of the Z membranes toward each other.

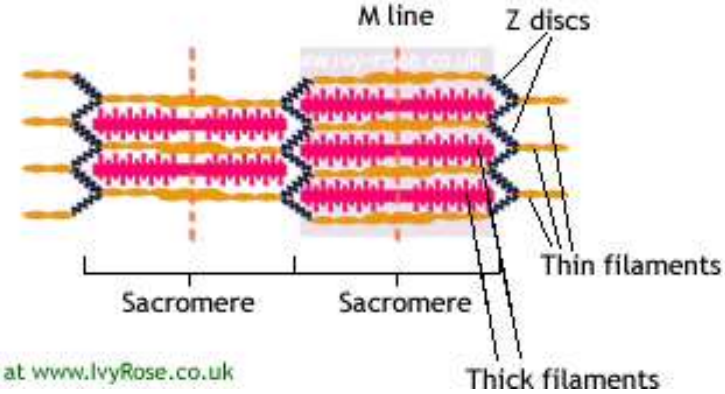
Relaxed Muscle :



Partially Contracted Muscle :



Fully Contracted Muscle :



- Molecular characteristics of the contractile filaments
  - Myosin Filaments
    - Multiple myosin molecules
    - Fig. 6-5A myosin molecule
    - Fig. 6-5B
    - Twisted structure
  - ATPase Activity of the Myosin Head
    - Myosin head functions as an ATPase enzyme.
    - The head to cleave ATP and to use the energy derived from the ATP's high-energy phosphate bond to energize the contraction process

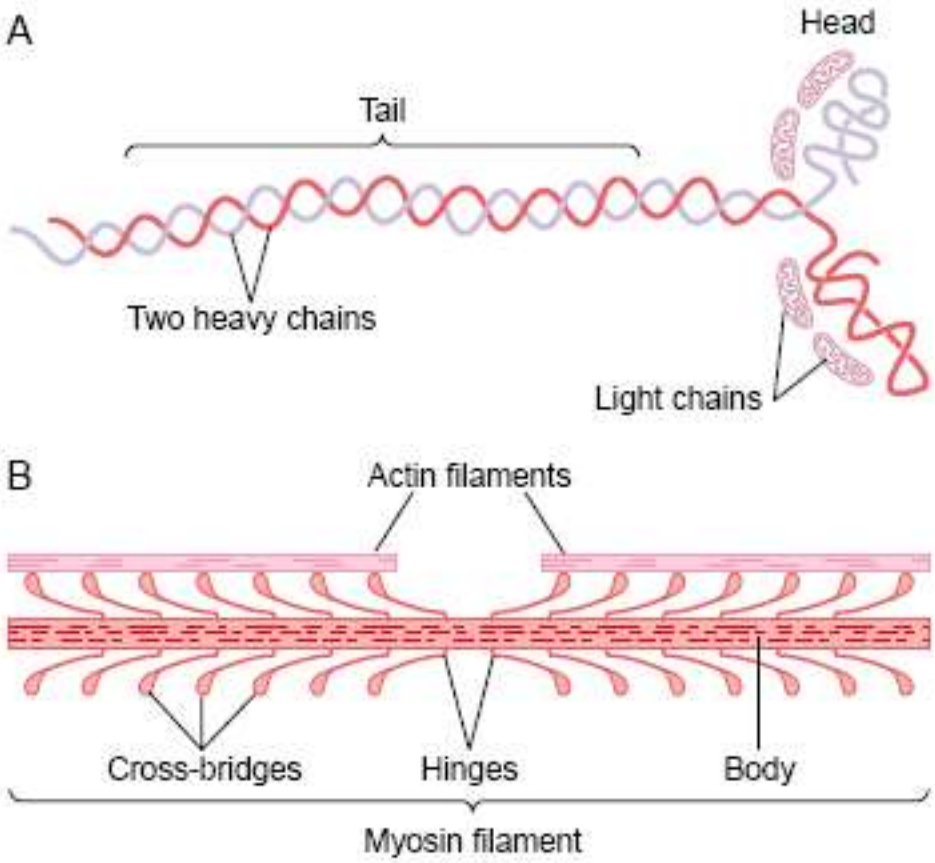
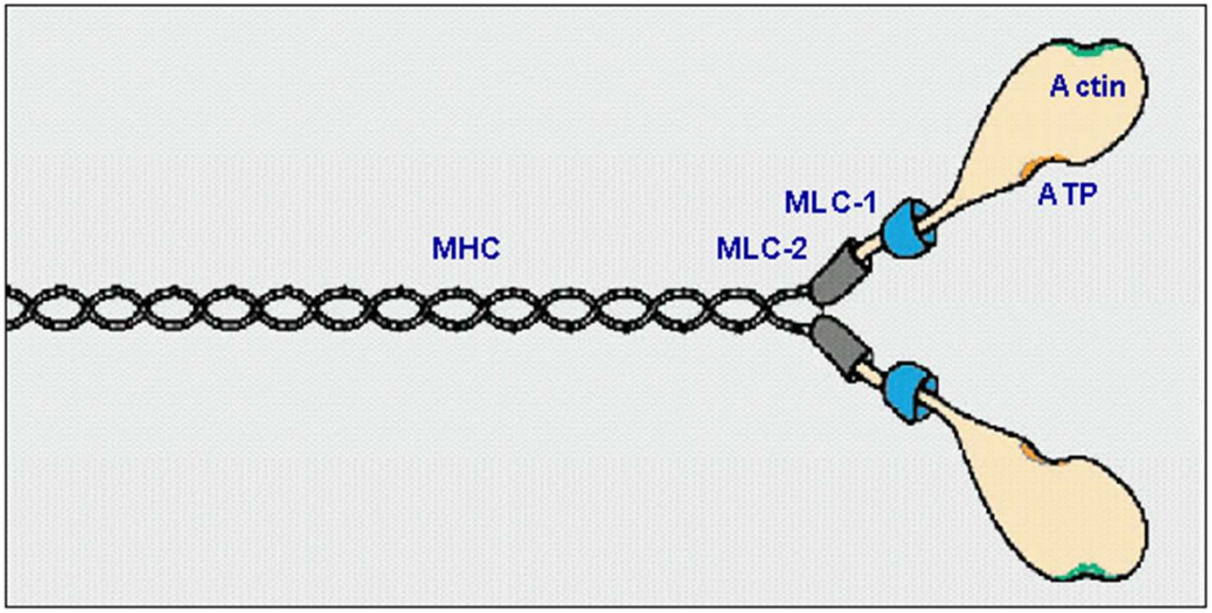
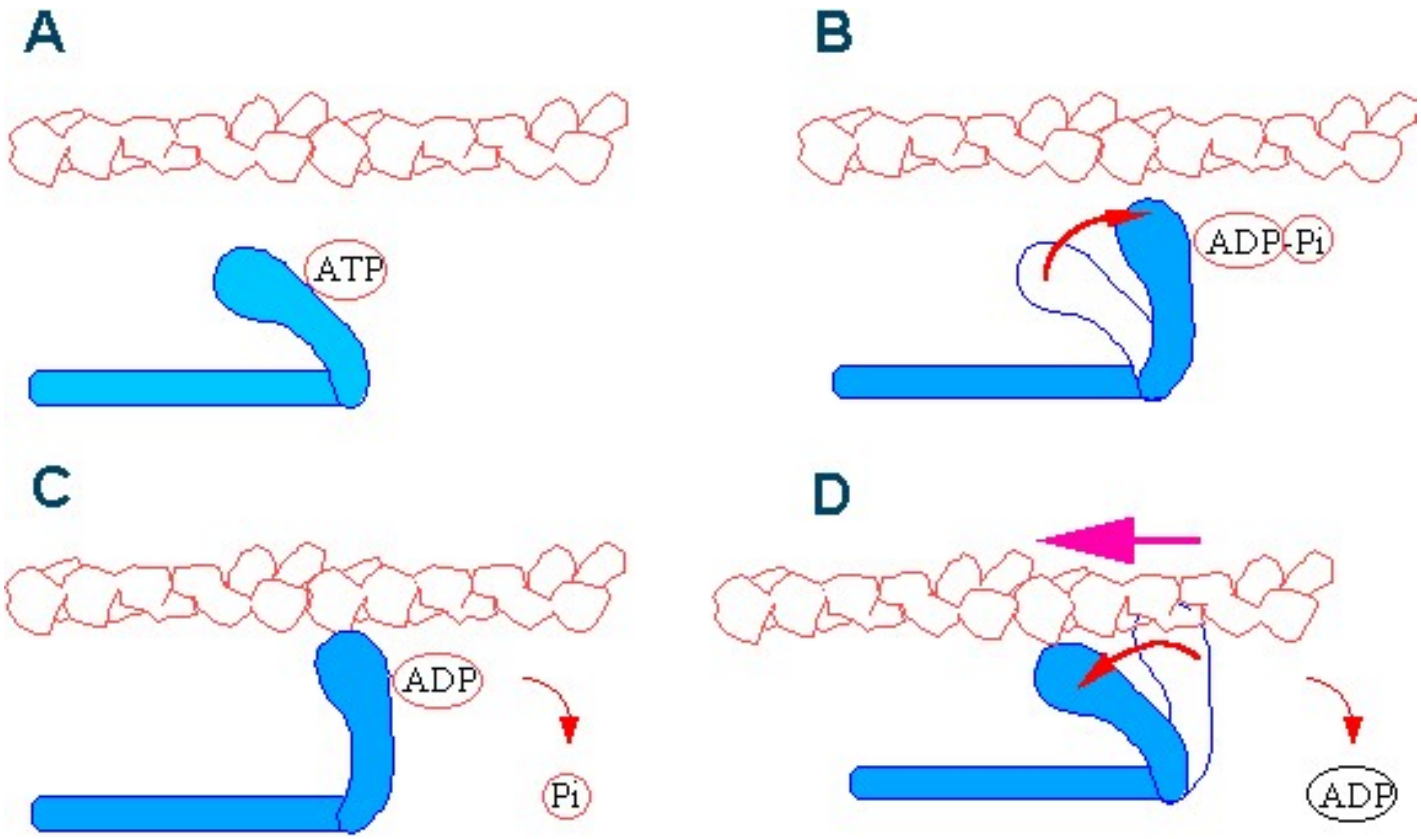


Figure 6–5

A, Myosin molecule. *B*, Combination of many myosin molecules to form a myosin filament. Also shown are thousands of myosin *cross-bridges* and interaction between the *heads* of the cross-bridges with adjacent actin filaments.

Myosin filament





The Myosin Cross-bridge Cycle. A. ATP binding to a cleft at the "back" of the head causes a conformation which cannot bind actin. B. As the ATP is hydrolysed, the head swings back about 5nm to the "cocked" position the ADP and phosphate (Pi) remain bound. C+D. The force generating stages. When the Pi leaves the myosin, the head binds the actin and the "power stroke" is released as the head bind actin. ADP is released to continue the cycle. At this stage the head in bound to actin in the "rigor" or tightly bound state.

- Actin filaments (Fig. 6-6)
  - Three protein components: actin, tropomyosin, and troponin
  - Backbone is a double-stranded F-actin protein molecules
  - Actin filaments are inserted into the Z discs.
  - Tropomyosin: in the resting state, tropomyosin molecules on the top of the active sites, no attraction occurs between actin and myosin
  - Troponin
    - Three loosely bound protein molecules
    - Plays a specific role in controlling muscle contraction
    - Troponin I: strong affinity for actin
    - Troponin T: for tropomyosin
    - Troponin C: for calcium ions

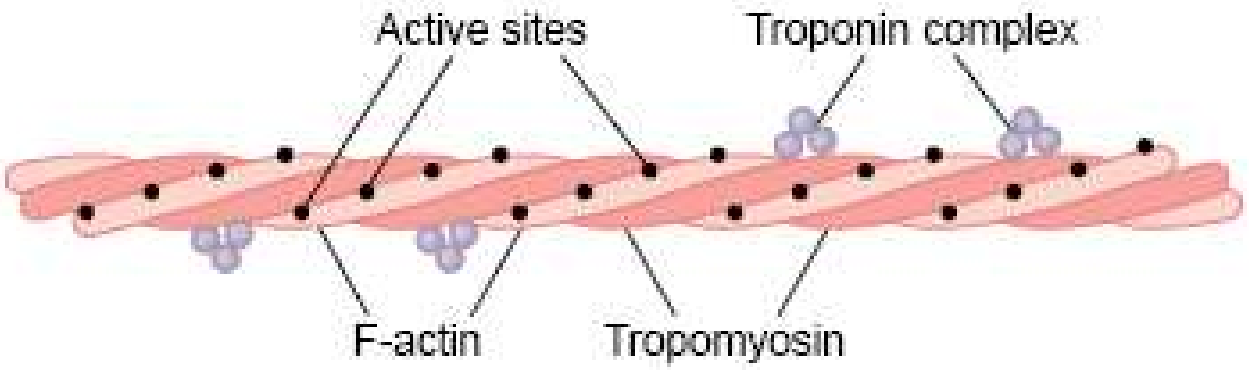
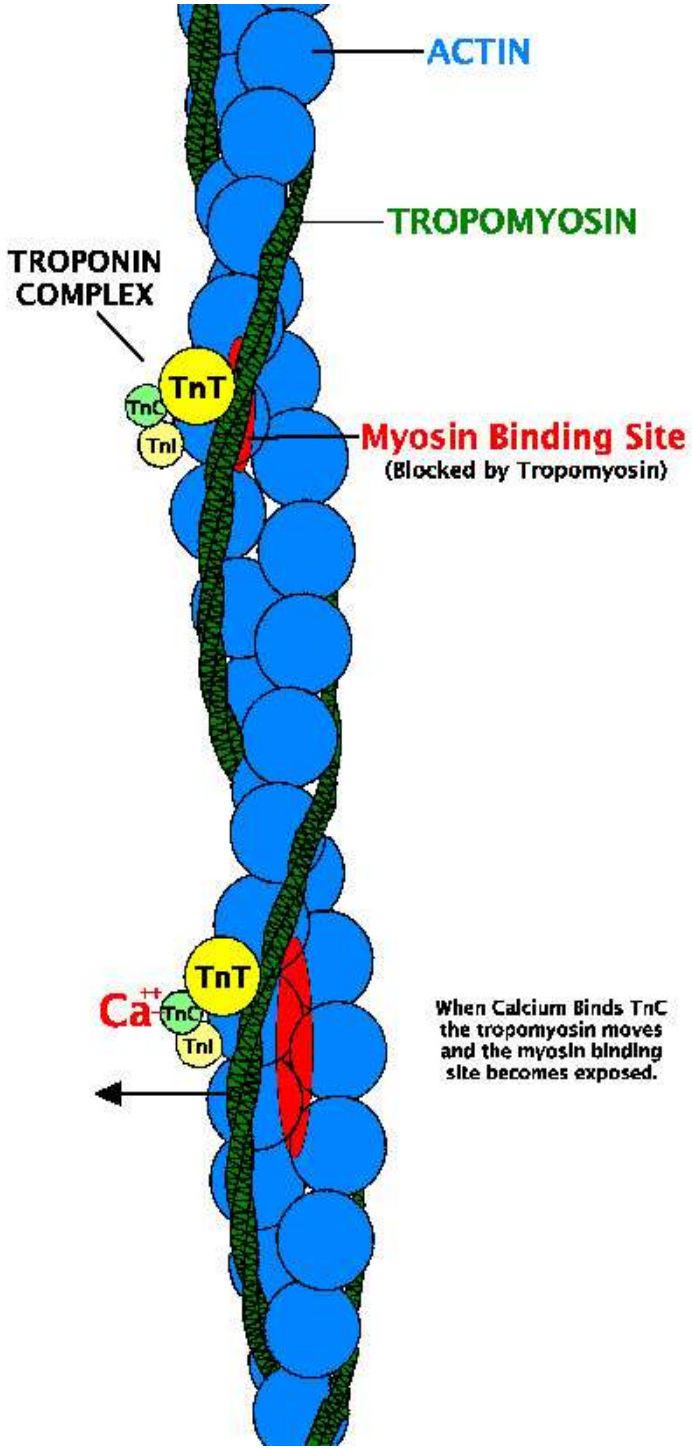


Figure 6–6

Actin filament, composed of two helical strands of *F-actin* molecules and two strands of *tropomyosin* molecules that fit in the grooves between the actin strands. Attached to one end of each tropomyosin molecule is a *troponin* complex that initiates contraction.

- Interaction of myosin, actin filaments, and calcium ions to cause contraction
  - Inhibition of the actin filament by the troponin-tropomyosin complex; activation by calcium ions
    - Without the troponin-tropomyosin complex, actin filaments bind strongly with the head of myosin molecules.
    - If with troponin-tropomyosin complex, there is no binding occurs
    - Therefore, active site on actin of the relaxed muscle are inhibited by the complex. Thus no contraction
    - With calcium ions, the inhibitory effect of the complex is inhibited.
    - Calcium combines with Troponin C, the troponin complex transforms => Expose the active site => Then Attach to the myosin heads. => Contraction occurs.
    - Is it true? Do not know yet.


ACTIN
TROPOMYOSIN
TROPONIN COMPLEX
TnT
TnC
TnI
Myosin Binding Site
(Blocked by Tropomyosin)
TnT
Ca++
TnC
TnI
When Calcium Binds TnC the tropomyosin moves and the myosin binding site becomes exposed.

- Interaction of myosin, actin filaments, and calcium ions to cause contraction
  - Interaction between the activated actin filament and the myosin cross-bridges – the **walking-along** theory of contraction
    - With activation of the actin filament by calcium, the heads of the cross-bridges from the myosin become attached to the active sites of the actin, then contraction begins.
    - Fig. 6-7, theory of walk along.
    - Power stroke mechanism (important)
  - ATP as the source of energy for contraction – chemical events in the motion of the myosin heads.
    - Fenn effect: the greater the amount of work performed by the muscle, the greater the amount of ATP is cleaved.

ATP as the Source of Energy for Contraction—Chemical Events in the Motion of the Myosin Heads.

1. Before contraction begins, the heads of the crossbridges bind with ATP. The ATPase activity of the myosin head immediately cleaves the ATP but leaves the cleavage products, ADP plus phosphate ion, bound to the head. In this state, the conformation of the head is such that it extends perpendicularly toward the actin filament but is not yet attached to the actin.
2. When the troponin-tropomyosin complex binds with calcium ions, active sites on the actin filament are uncovered, and the myosin heads then bind with these, as shown in Figure 6–7.
3. The bond between the head of the cross-bridge and the active site of the actin filament causes a conformational change in the head, prompting the head to tilt toward the arm of the cross-bridge. This provides the *power stroke* for pulling the actin filament. The energy that activates the power stroke is the energy already stored, like a “cocked” spring, by the conformational change that occurred in the head when the ATP molecule was cleaved earlier.

ATP as the Source of Energy for Contraction—Chemical Events in the Motion of the Myosin Heads.

4. Once the head of the cross-bridge tilts, this allows release of the ADP and phosphate ion that were previously attached to the head. At the site of release of the ADP, a new molecule of ATP binds. This binding of new ATP causes detachment of the head from the actin.

5. After the head has detached from the actin, the new molecule of ATP is cleaved to begin the next cycle, leading to a new power stroke. That is, the energy again “cocks” the head back to its perpendicular condition, ready to begin the new power stroke cycle.

6. When the cocked head (with its stored energy derived from the cleaved ATP) binds with a new active site on the actin filament, it becomes uncocked and once again provides a new power stroke.

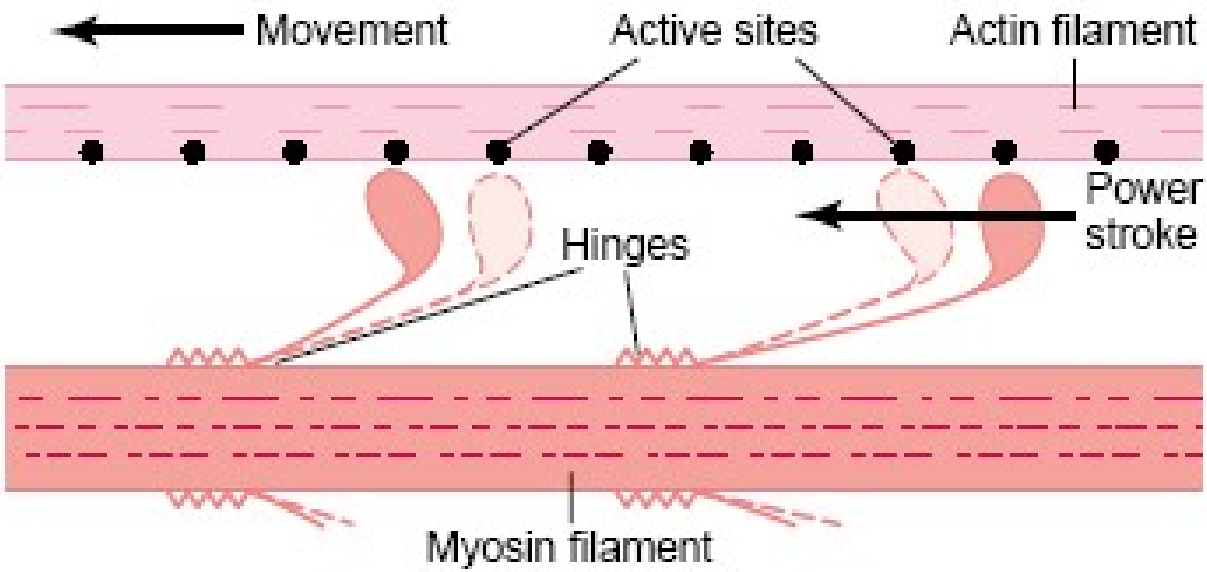


Figure 6–7

"Walk-along" mechanism for contraction of the muscle.

Muscle Contraction

- https://www.youtube.com/watch?v=gJ309LfHQ3M