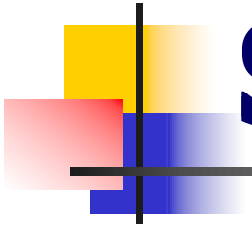
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估.



# Section 4

# Contraction of Muscle

Lei Chen

Email: chenleiqd@hotmail.com

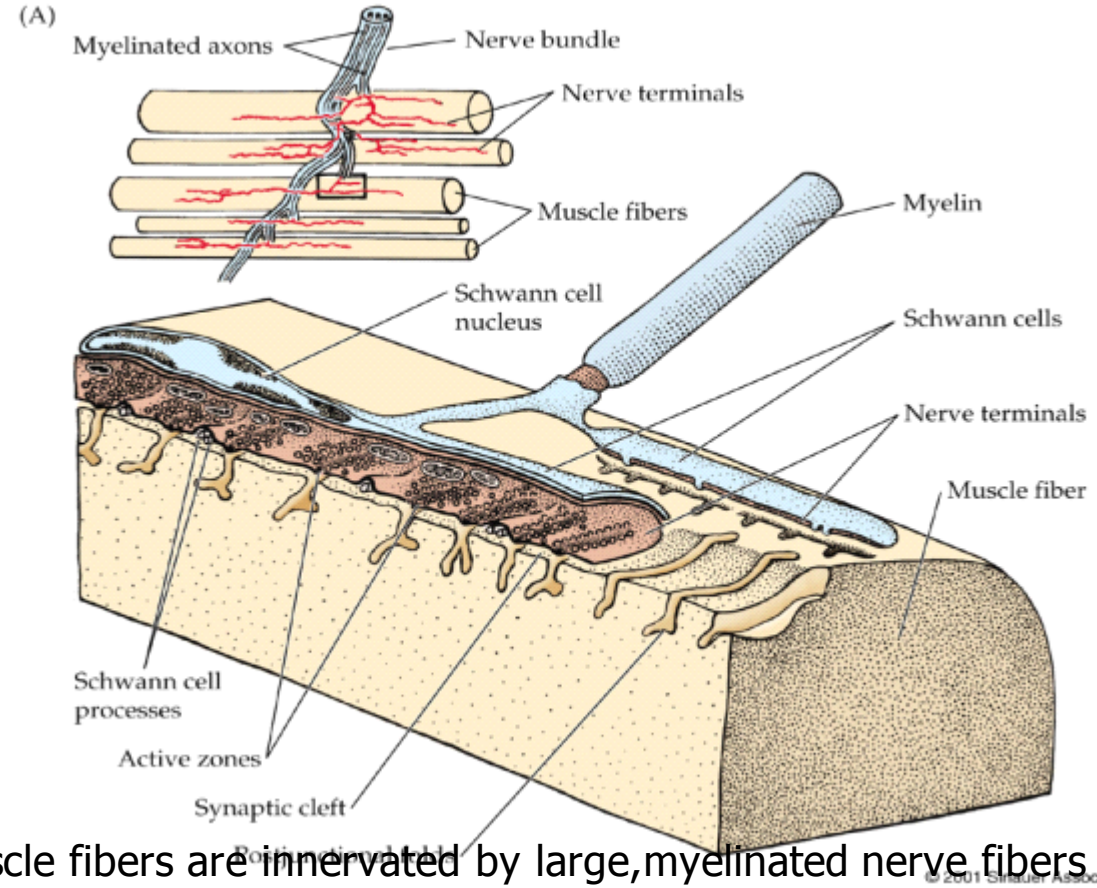
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Striated muscle

- Striated muscle
- Skeletal muscle
- Cardiac muscle
- Smooth muscle

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Neuromuscular junction




- The skeletal muscle fibers are innervated by large,myelinated nerve fibers that originate in the large motoneurons of the anterior horns of the spinal cord.

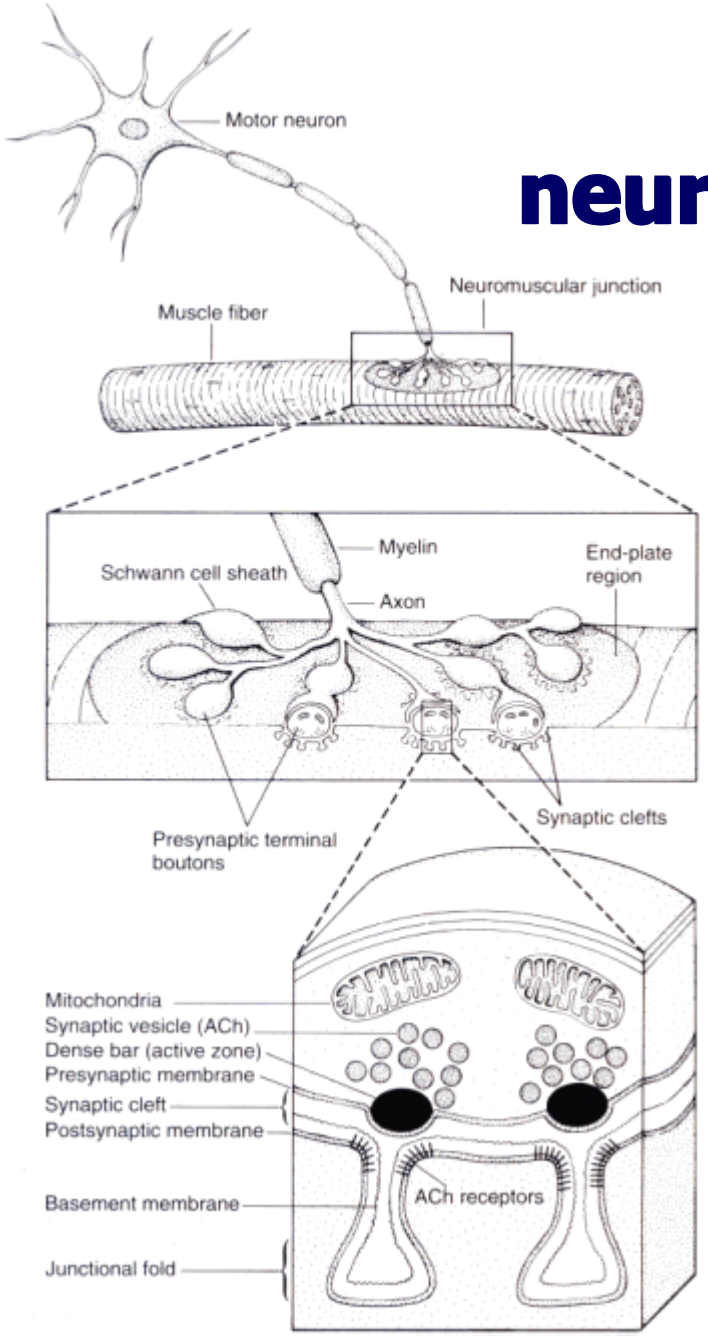
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估.

# Transmission of excitation at neuromuscular junction

- **Anatomy** of neuromuscular junction
- **Major processes** of neuromuscular transmission
- **Factors** affecting the neuromuscular transmission

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Anatomy of neuromuscular junction

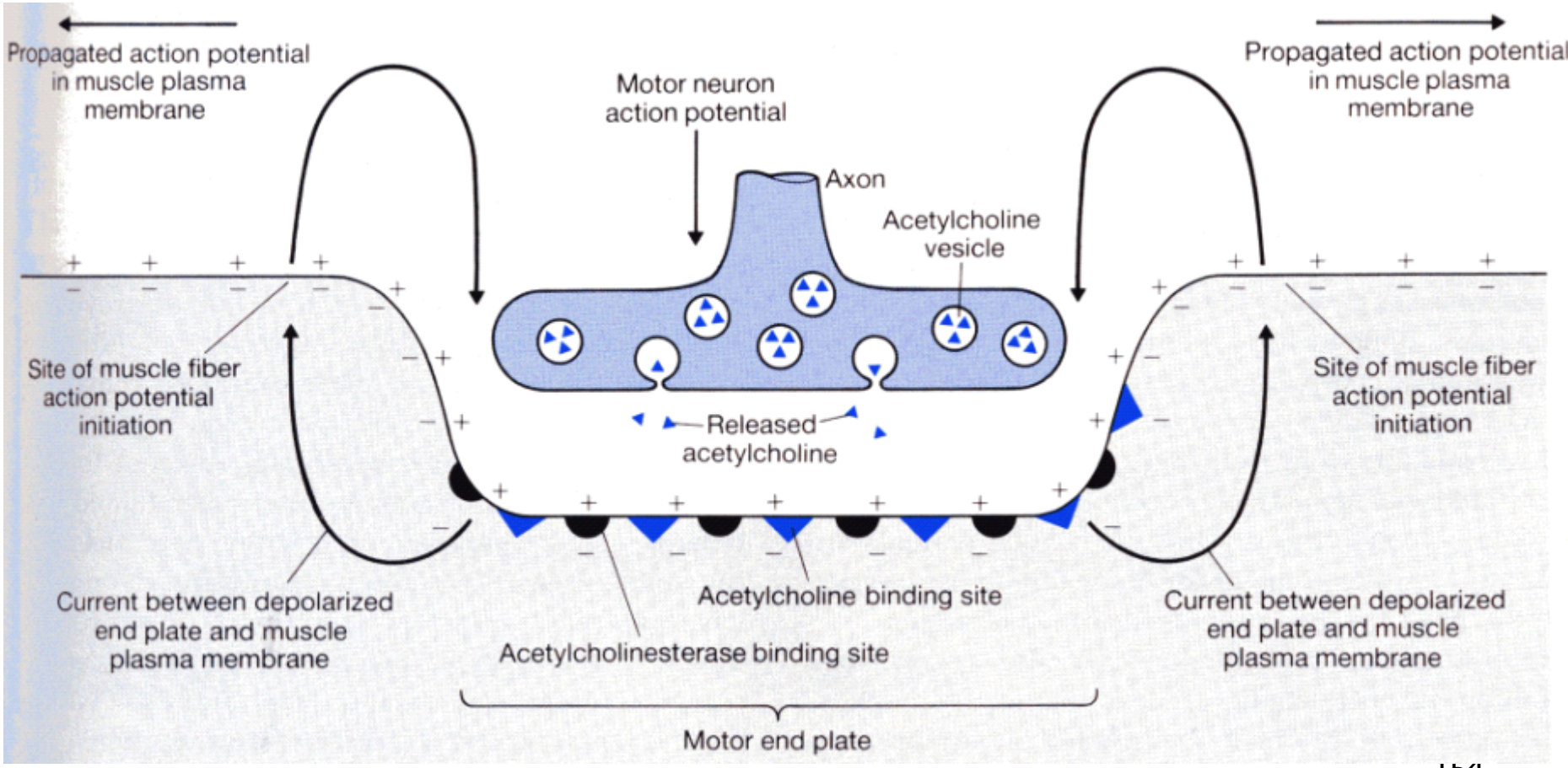



- **Prejunctional membrane**
- **Synaptic vesicle**
- **Junctional cleft**
- **Endplate membrane**

  **Junctional fold**
- **$N_2$-Ach receptor cation channel**
- **Acetylcholinesterase**

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Processes of neuromuscular transmission



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估.

# Sequence of events during transmission

Action potential arrives at prejunctional membrane

↓

Action potential causes calcium channels to open ($Ca^{2+}$ enters )

↓

$Ca^{2+}$ cause synaptic vesicle to move and release Ach

↓

Ach diffuses across junctional cleft

↓

Ach binds to $N_2$ Ach receptor on endplate membrane

↓

$Na^+$, $K^+$ channels open ($Na^+ > K^+$ )

↓

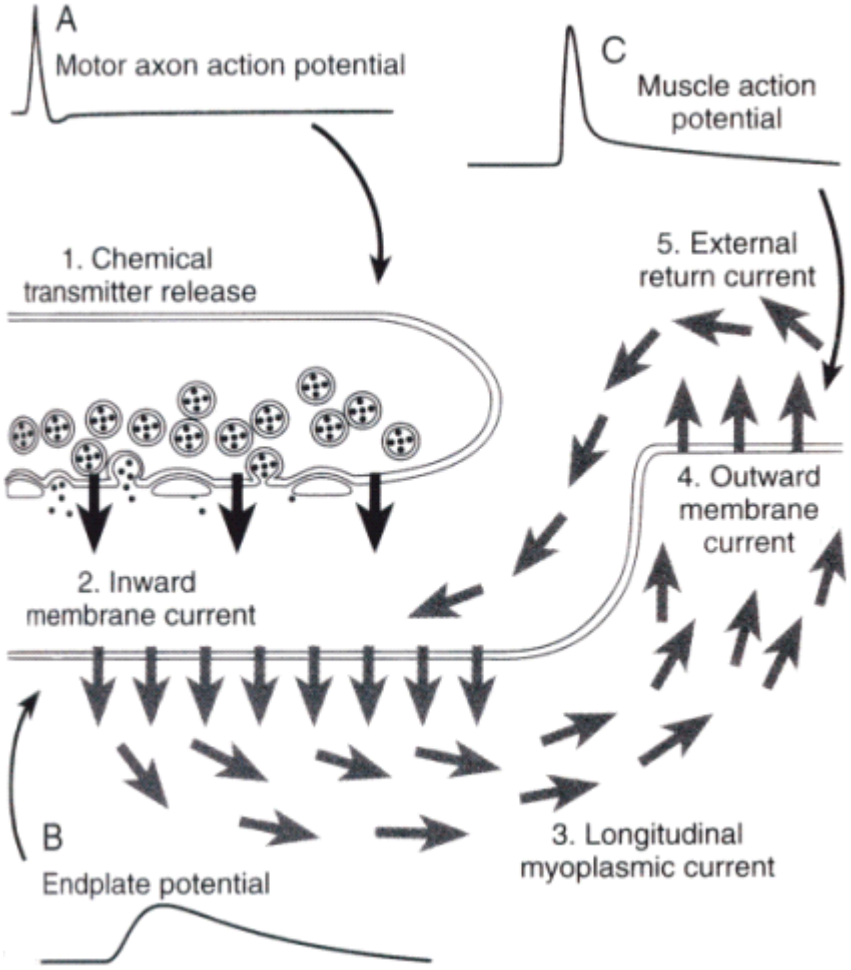
Causes depolarization of the endplate membrane (EPP)

↓

Action potential is produced in the muscle membrane

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

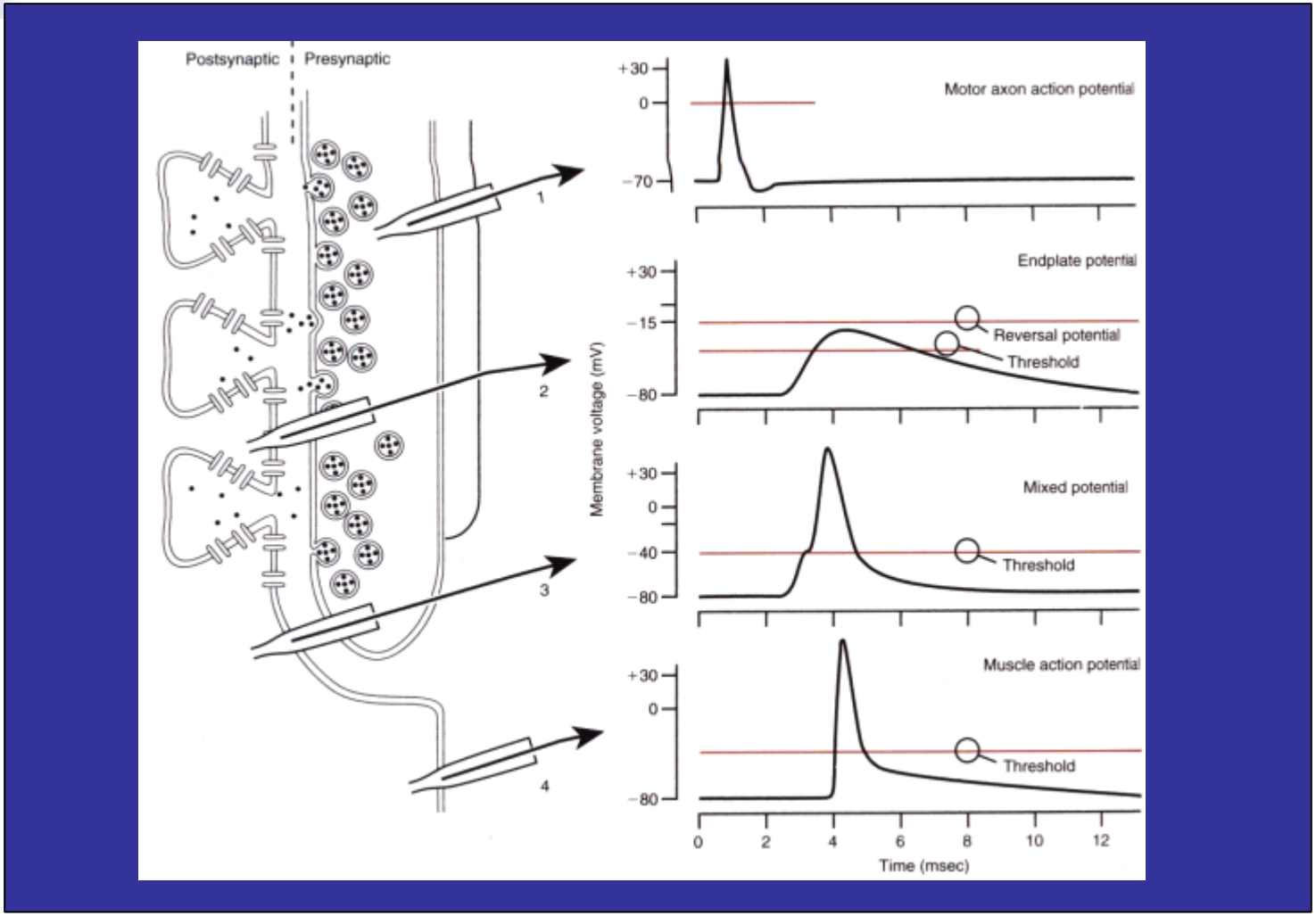
# Processes of neuromuscular transmission




- **End-plate potential (EPP): depolarization of motor end plate of skeletal-muscle fiber in response to acetylcholine; initiates action potential in muscle plasma membrane.**

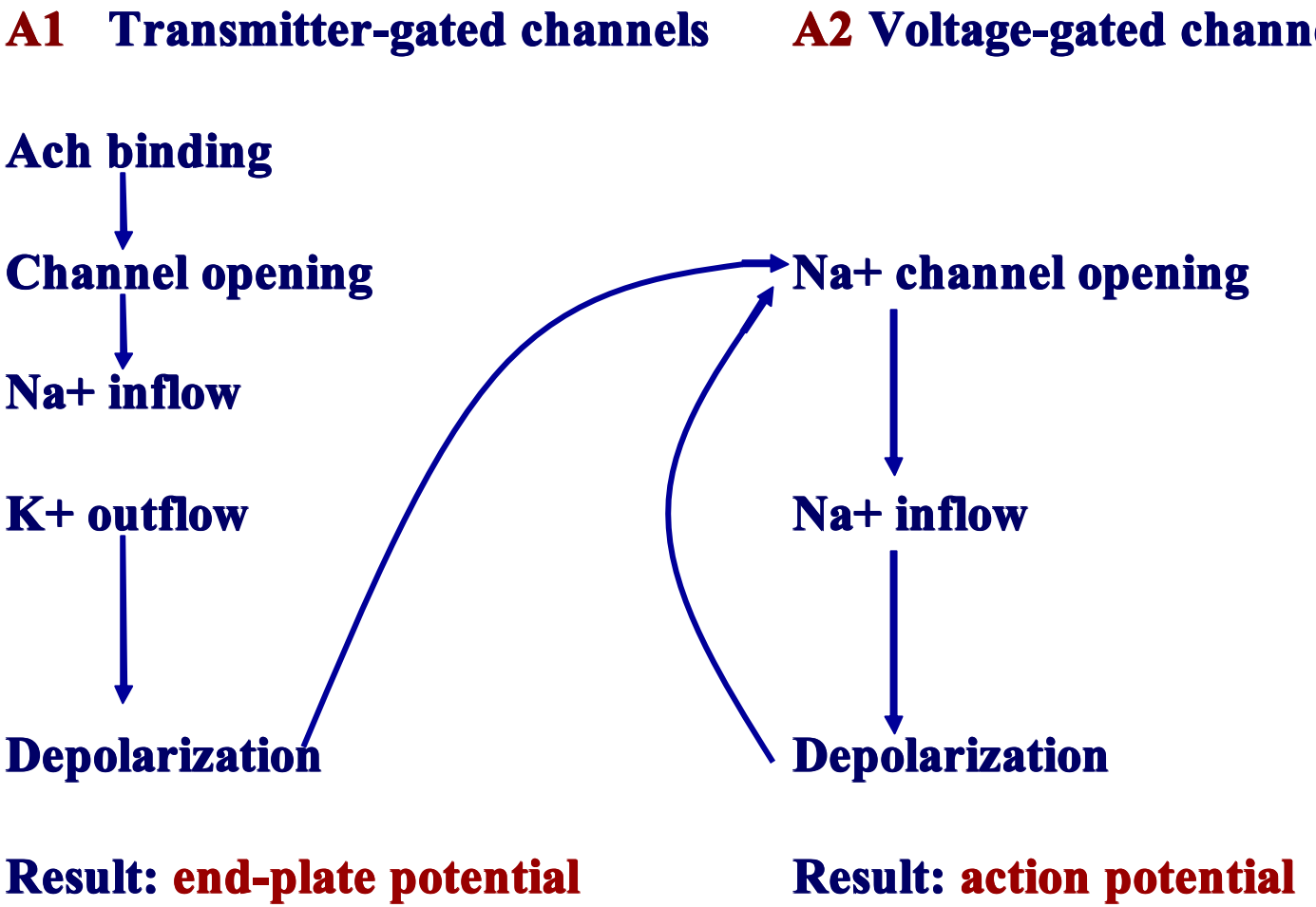
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Processes of neuromuscular transmission



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Processes of neuromuscular transmission

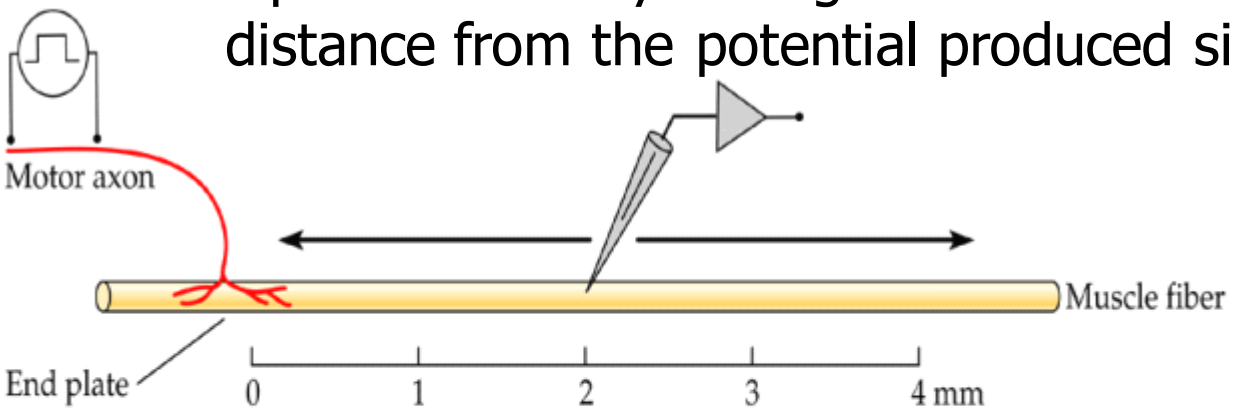


由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

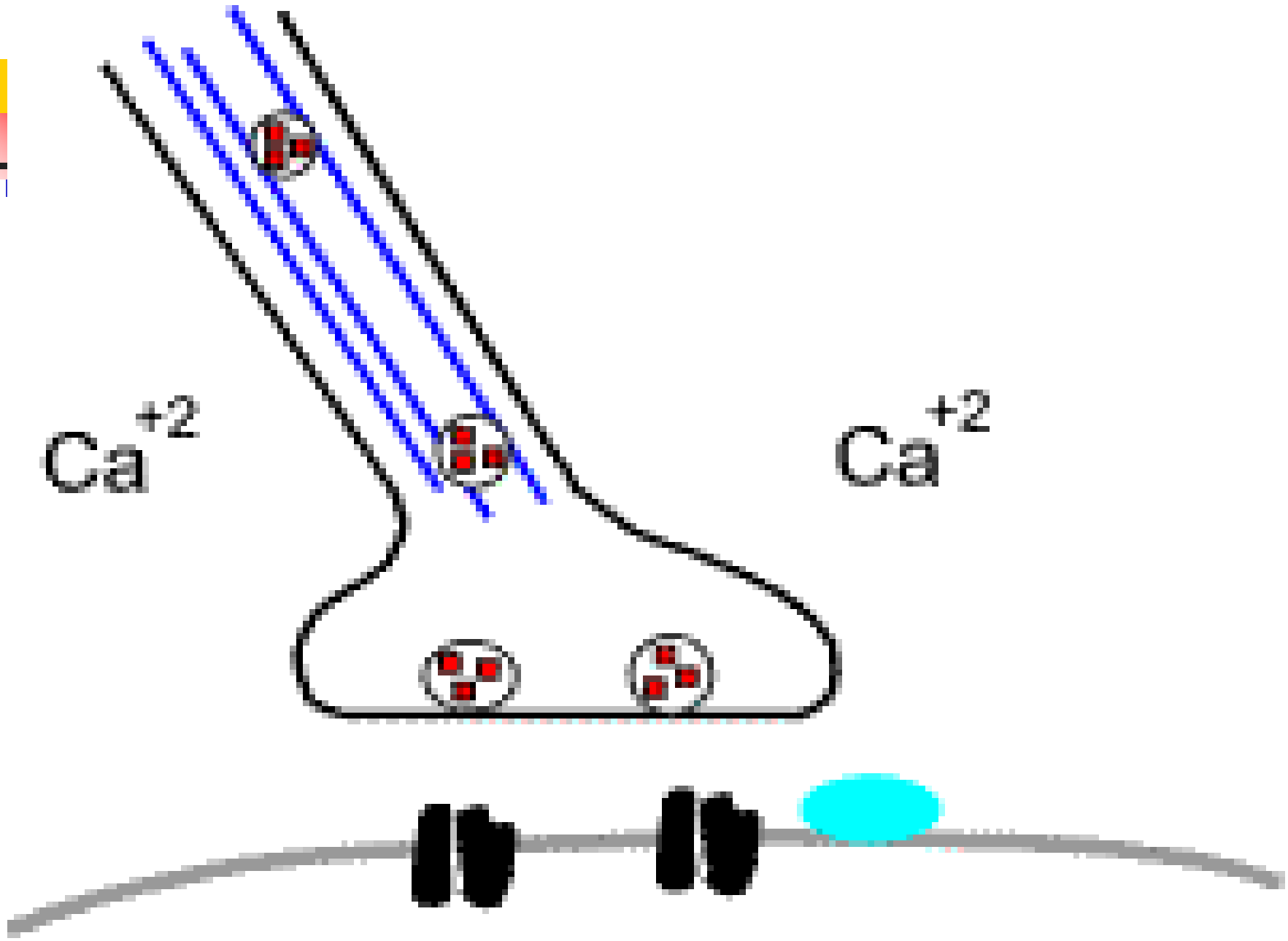
# Characteristics of end-plate potential

- **Electrotonic propagation**

The potential decays along a axon according to the distance from the potential produced site.

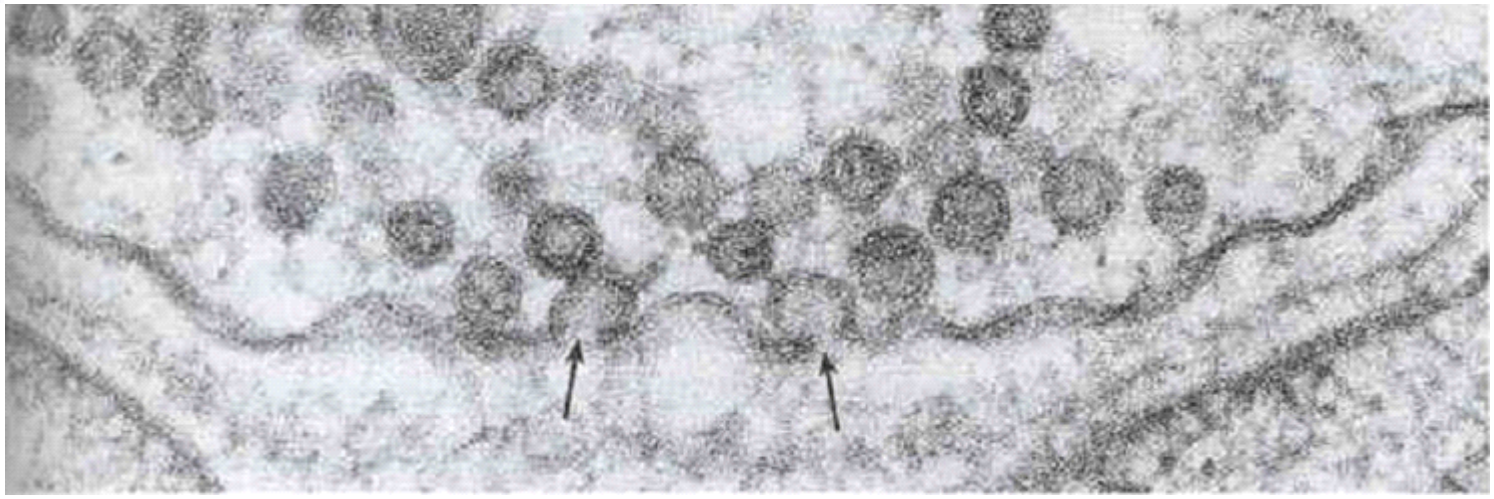


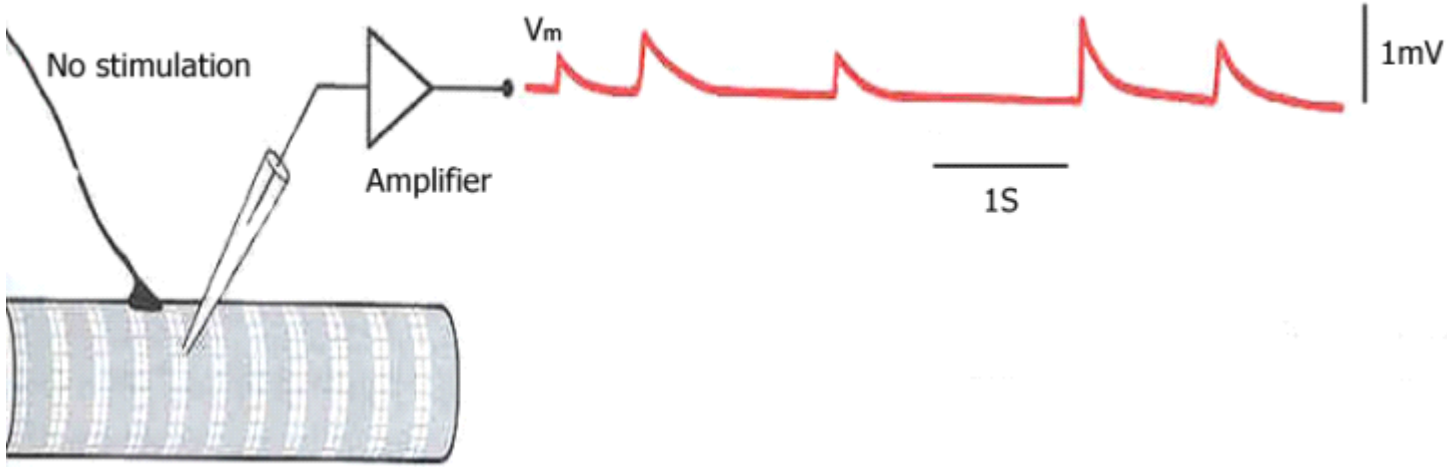
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Miniature end-plate potential





由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估.

# Disruption of neuromuscular transmission

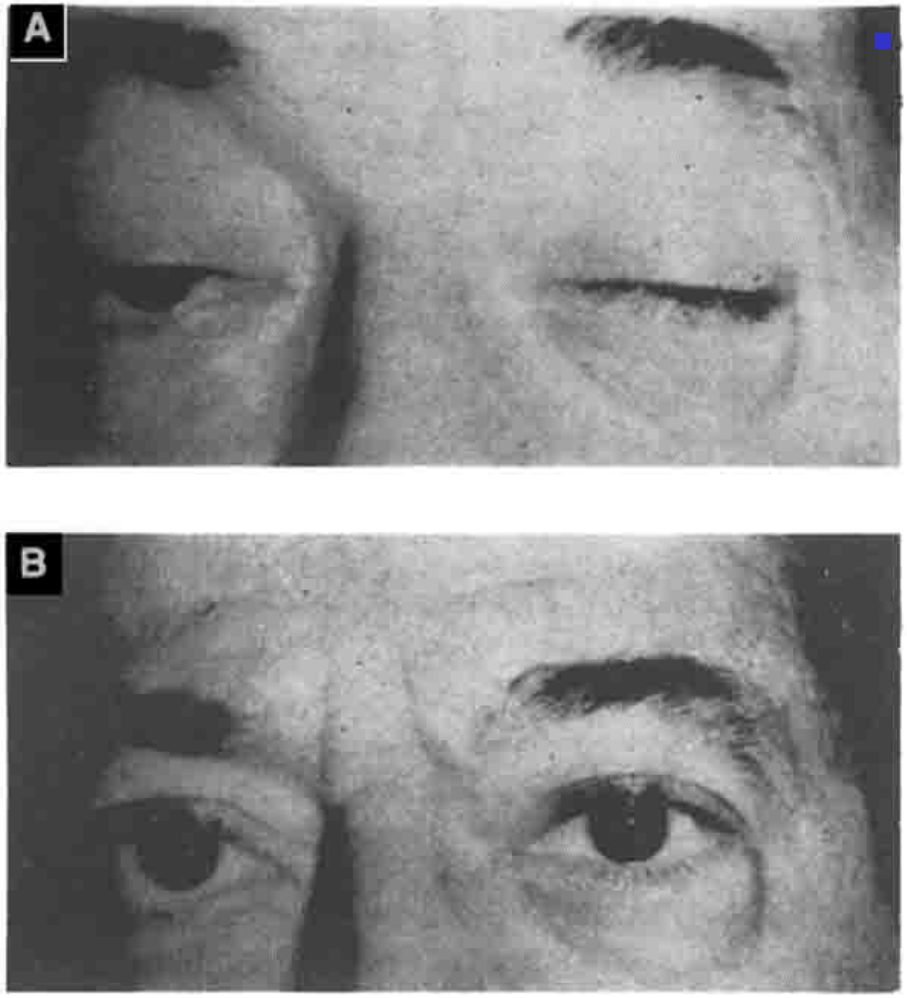
- **Activity of ACh receptor: tubocurarine**
- **Acetylcholinesterase (AChE) inhibitor: pyridostigmine**
- **Release of ACh: botulinum toxin**

➢Tubocurarine binds strongly to N type Ach receptors, but does not open the ion channels and is not destroyed by acetylcholinesterase.

➢Botulinum toxin is an enzyme that breaks down a protein required for the binding and fusion of ACh vesicles with the plasma membrane of the axon terminal.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Myasthenia Gravis(MG)



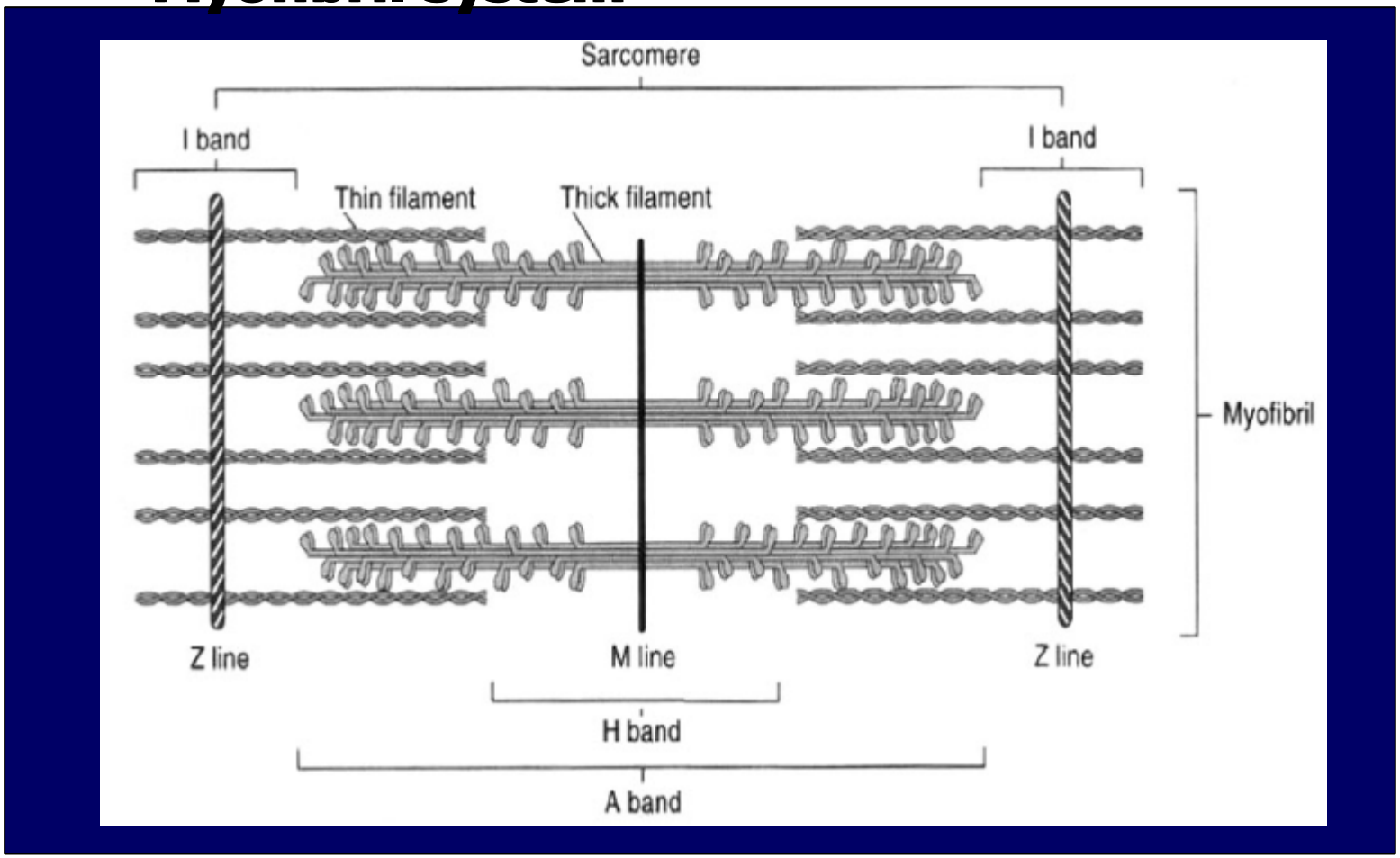

Wendy Chu: a 23-yr-old photographer for a local newspaper.Over the last 8 months, she experienced 'strange' symptoms: severe eyestrain reading for longer than 15 min, tired when she chewed, brushed, extreme fatigue on the job. Physician initiated a trial of pyridostigmine, an acetylcholinesterase inhibitor, immediately felt better, antibody test was positive,confirming the diagnosis of MG.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Anatomy of striated muscle

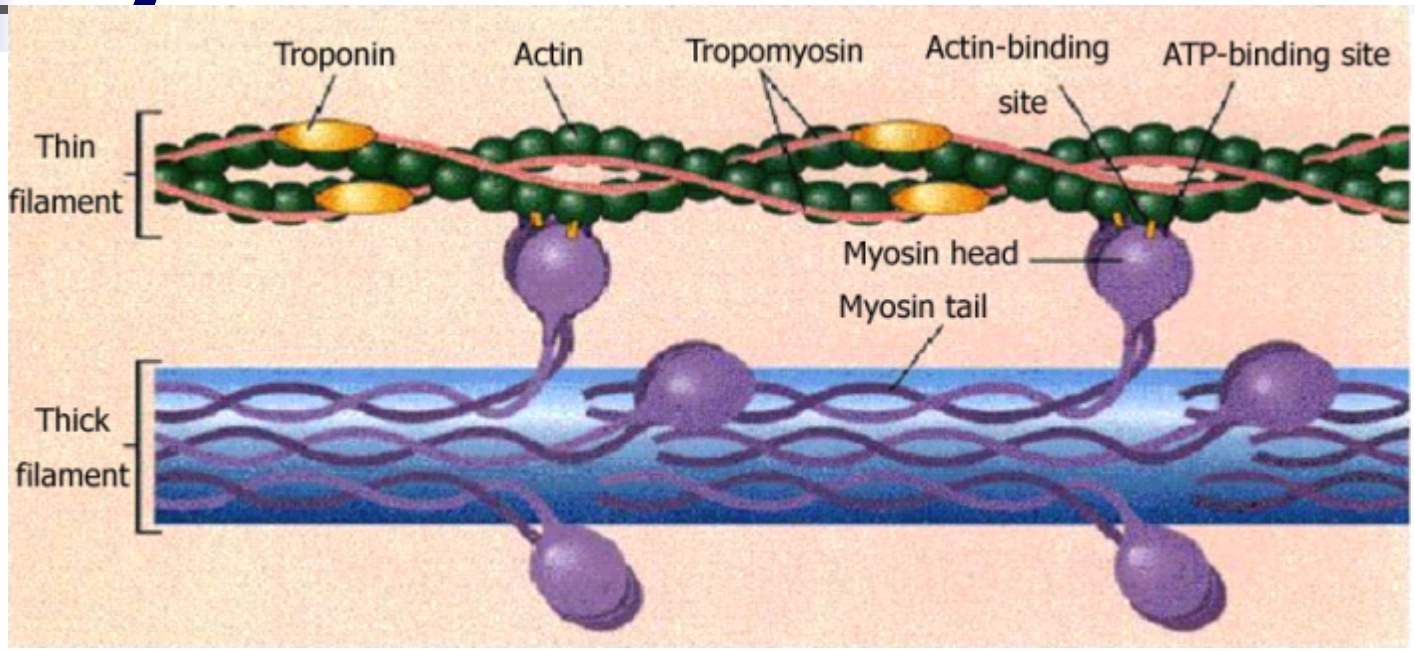
## Myofibril and sarcomere

- **Myofibril system**



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

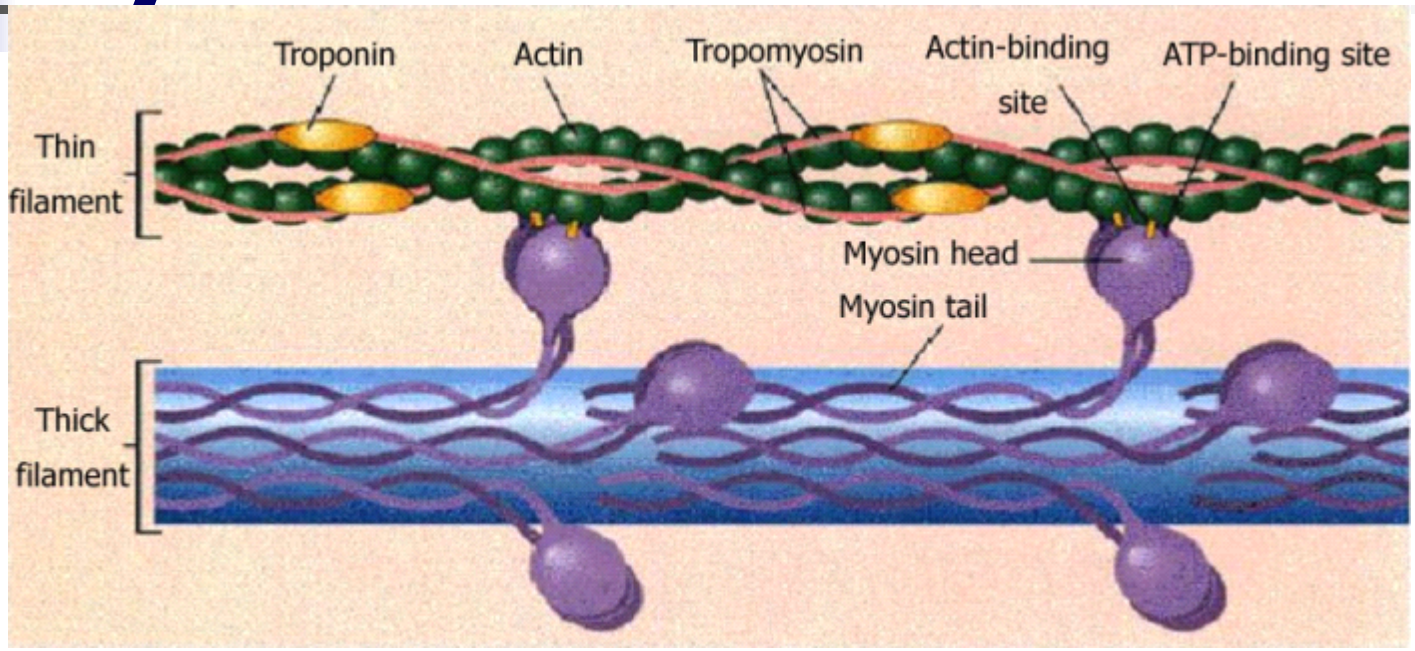
# Molecular components of myofilament




- The thick filaments are composed almost entirely of the contractile protein myosin.
- The thin filaments contain the contractile protein actin, as well as the other two proteins, troponin and tropomyosin.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

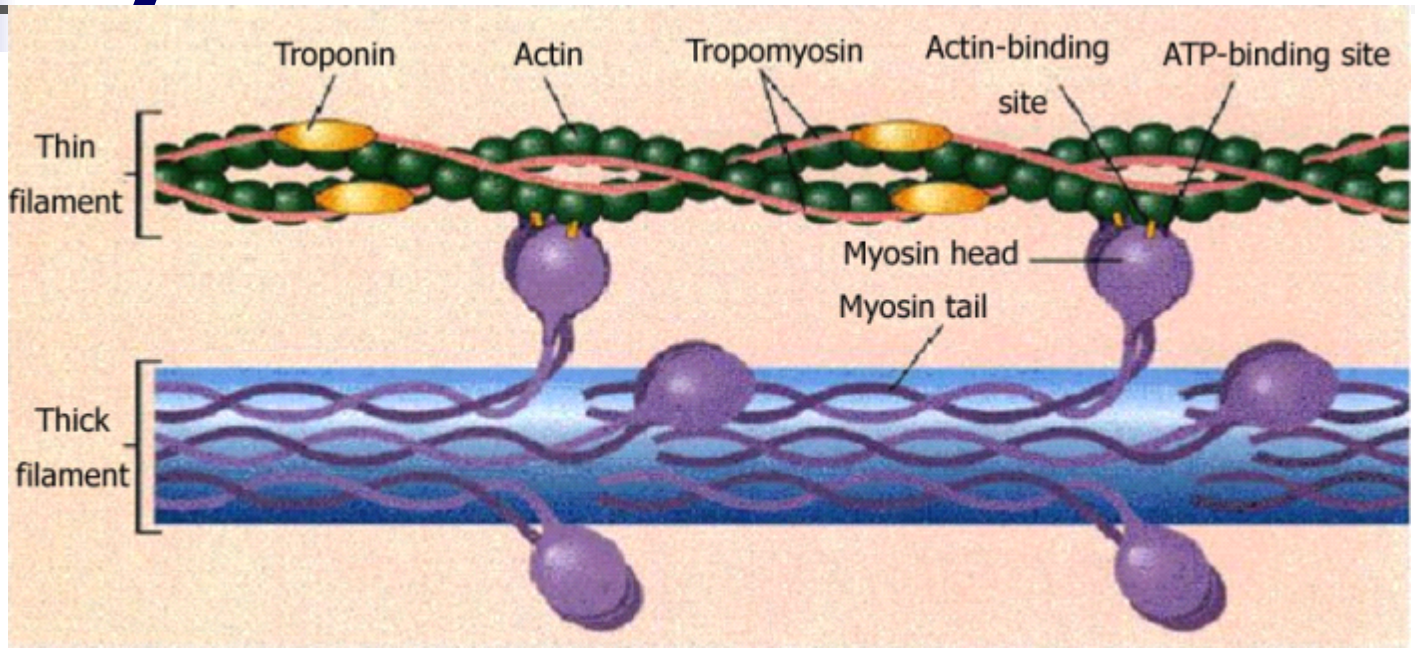
# Molecular components of myofilament




- Tropomyosin is a rod-shaped molecule with a length equal to that of seven actin molecules. These tropomyosin molecules partially cover the myosin-binding site on each actin molecule, thereby preventing the cross-bridge from making contact with actin.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

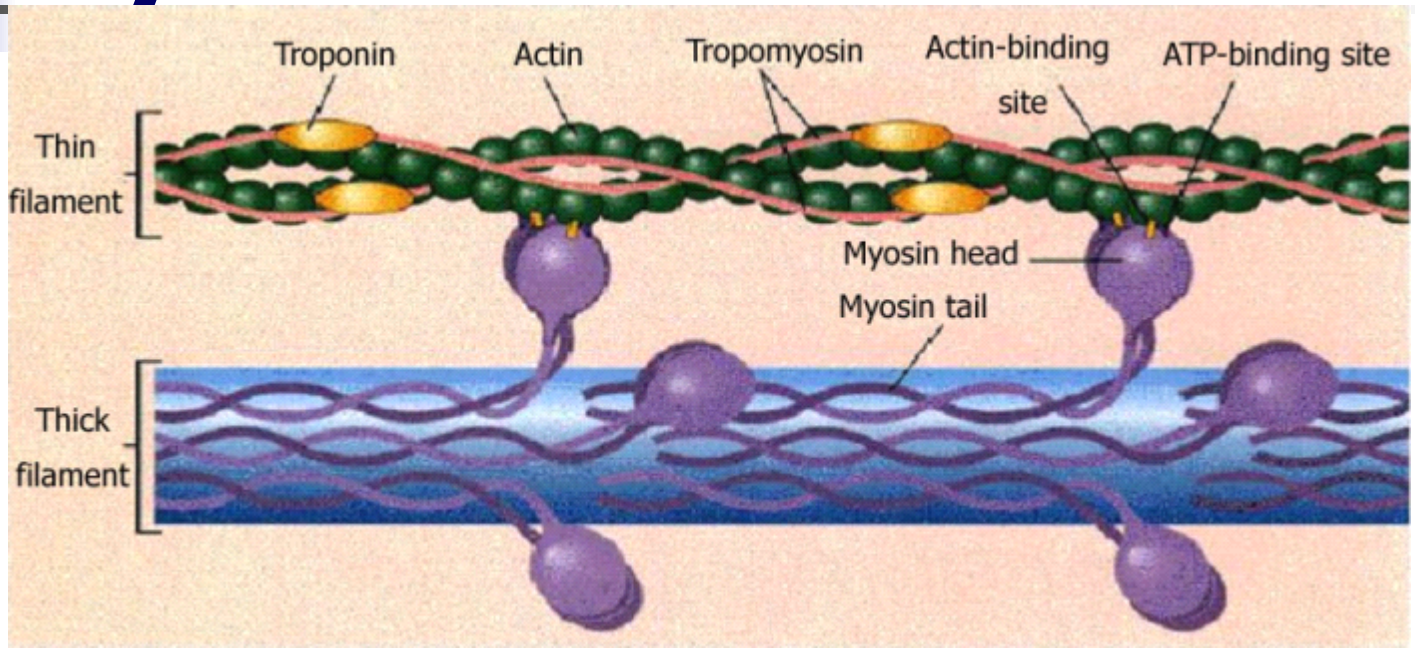
# Molecular components of myofilament




- Troponin is a smaller, globular protein that is bound to both tropomyosin and actin. One molecule of troponin binds to each molecule of tropomyosin and regulates the access to myosin-binding sites on the seven actin molecules in contact with tropomyosin.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Molecular components of myofilament

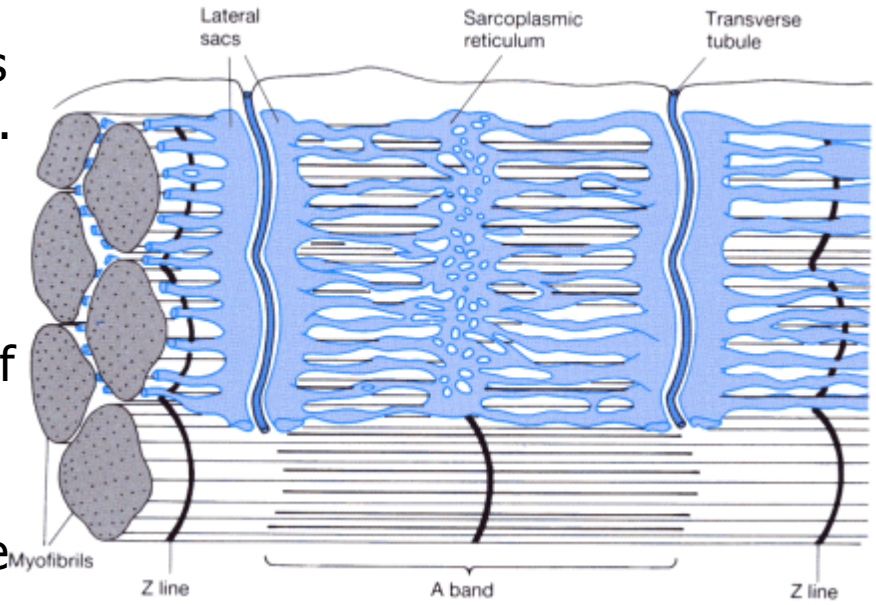



➢When calcium binds to specific binding sites on troponin, the binding produces a change in the shape of troponin. This change drags tropomyosin away from the myosin binding site on each actin molecule.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Transverse tubule-sarcoplasmic reticulum system

- Transverse tubule (T-tubule) crosses the muscle fiber at the level of Z line.
- The membrane of T tubule is able to propagate action potential. Once an action potential is initiated, it is rapidly conducted over the surface of the fiber and into its interior by way of the T-tubules.
- The sarcoplasmic reticulum in muscle is homologous to the endoplasmic reticulum found in most cells. It is composed of two major parts:
- (1)Long longitudinal tubules
- (2)Terminal cisternae: large chambers of the end of longitudinal tubules.




**T tubule: L-type $Ca^{2+}$ channel**

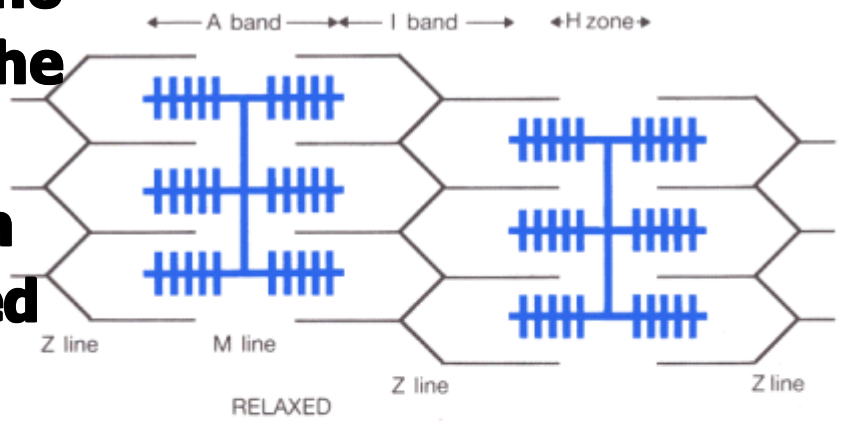
**LSR: $Ca^{2+}$ pump**

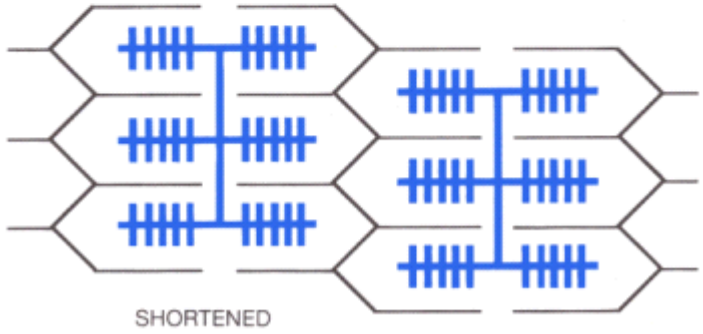
**JSR: $Ca^{2+}$ release channel (ryanodine receptor,RYR)**

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Mechanism of striated muscle contraction

- During the contraction, there is no change in the lengths of either the thick or thin filaments.
- Each myosin attached to an actin forces the thin filaments attached to successive Z lines toward the center of the sarcomere.
- **Myofilament sliding theory**: process of muscle contraction in which shortening occurs by thick and thin filaments sliding past each other.



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估.

# Steps of cross-bridge cycle

- Actin binding
- Movement of cross-bridge
- Dissociation of cross-bridge from actin
- ATP hydrolysis

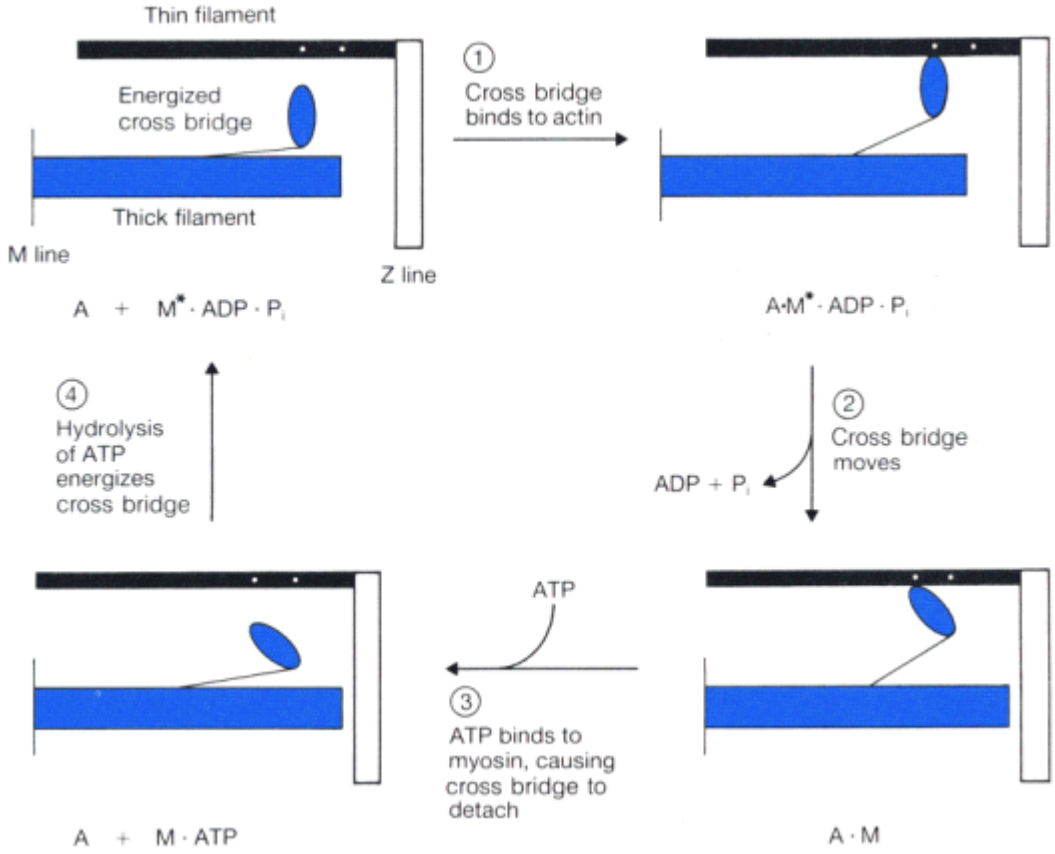
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Process of muscle contraction

## Cross-bridge cycling

### Step 1 Actin binding

- In a resting muscle fiber, no binding between myosin and actin. However, the cross-bridges are in an energized state produced by the splitting of ATP. The hydrolysis products ADP are still bound to myosin.
- Cross-bridge cycling is initiated by calcium entry into the cytoplasma. The cycle begins with the binding of an energized myosin cross bridge to a thin filament actin molecule.



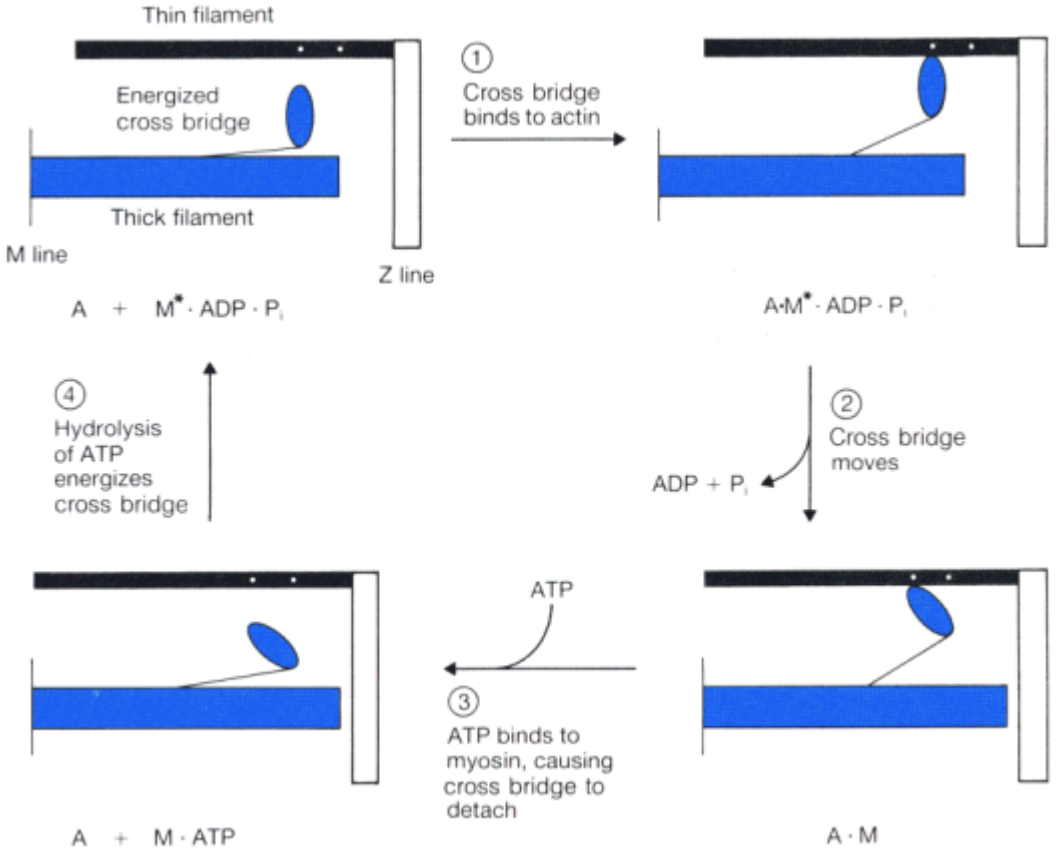
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Process of muscle contraction

## Cross-bridge cycling

### Step 2 Movement of cross-bridge

The binding of energized myosin to actin triggers the movement of the bound cross-bridge and the release of Pi and ADP.



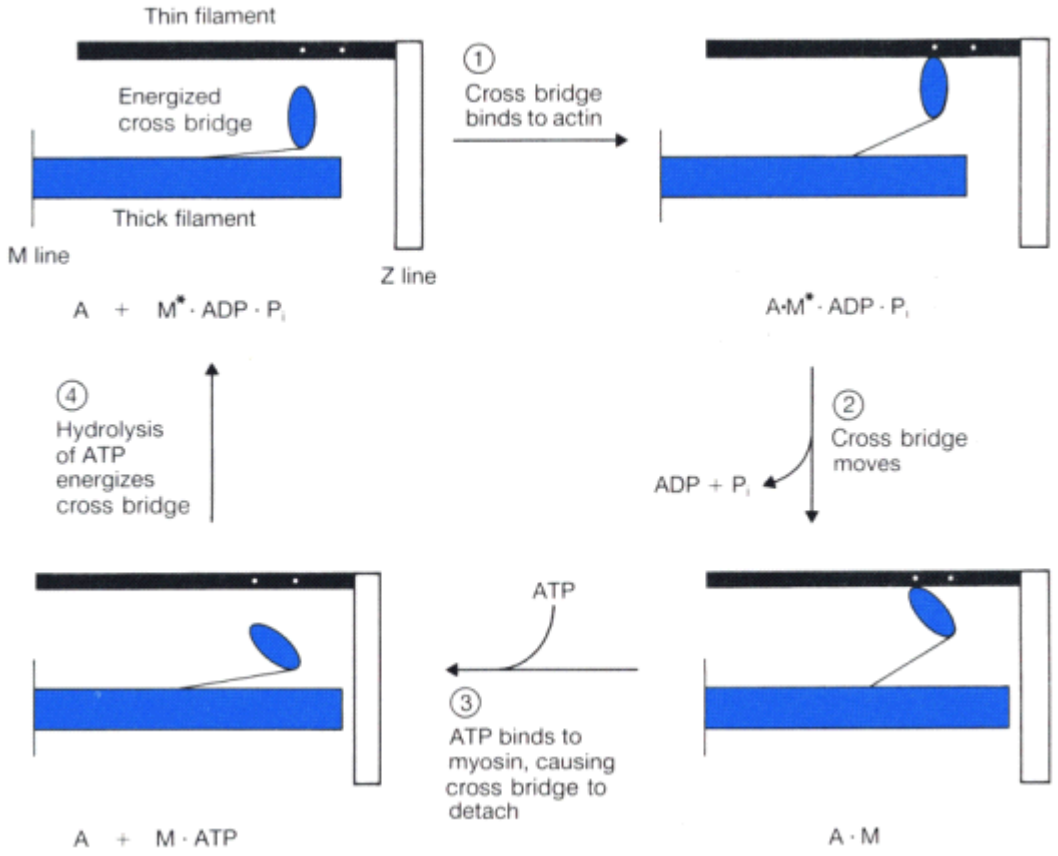
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Process of muscle contraction

## Cross-bridge cycling

### Step 3 Dissociation of cross-bridge from actin

The binding of a new molecule of ATP to myosin breaks the link between actin and myosin. The binding of ATP at one site on myosin decreases myosin's affinity for actin bound at another site.



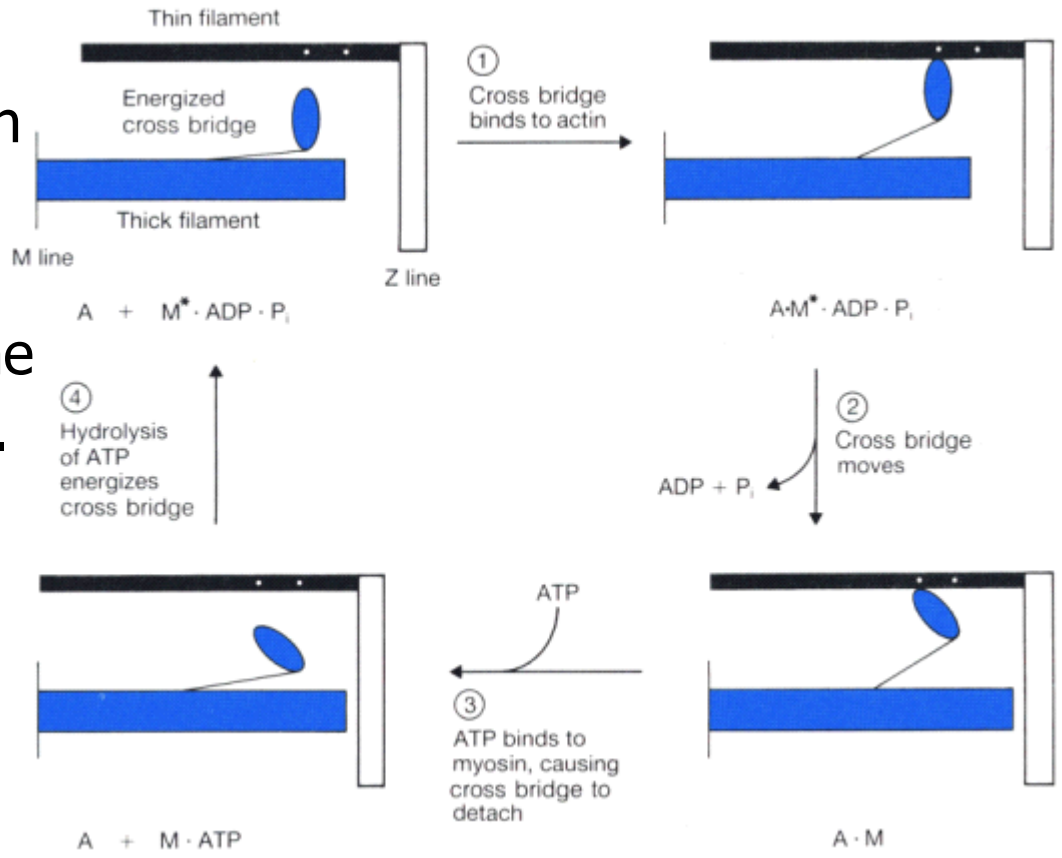
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Process of muscle contraction

## Cross-bridge cycling

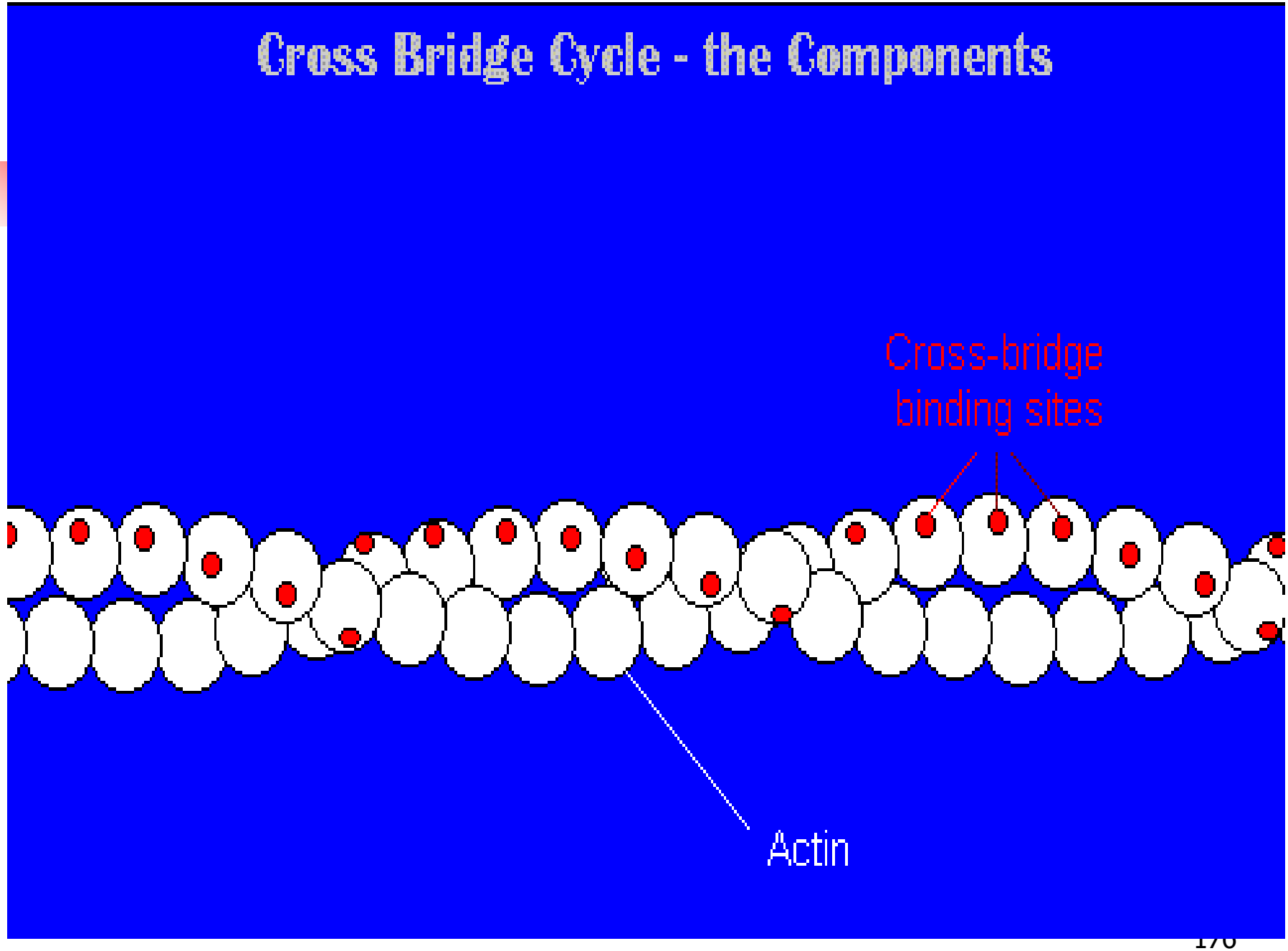
### Step4 ATP hydrolysis

- Following the dissociation of actin and myosin, the ATP bound to myosin is split, thereby reforming the energized state of myosin.
- If calcium is still present at this time, the cross-bridge can reattach to a new actin in thin filament and the cross-bridge cycle repeats.



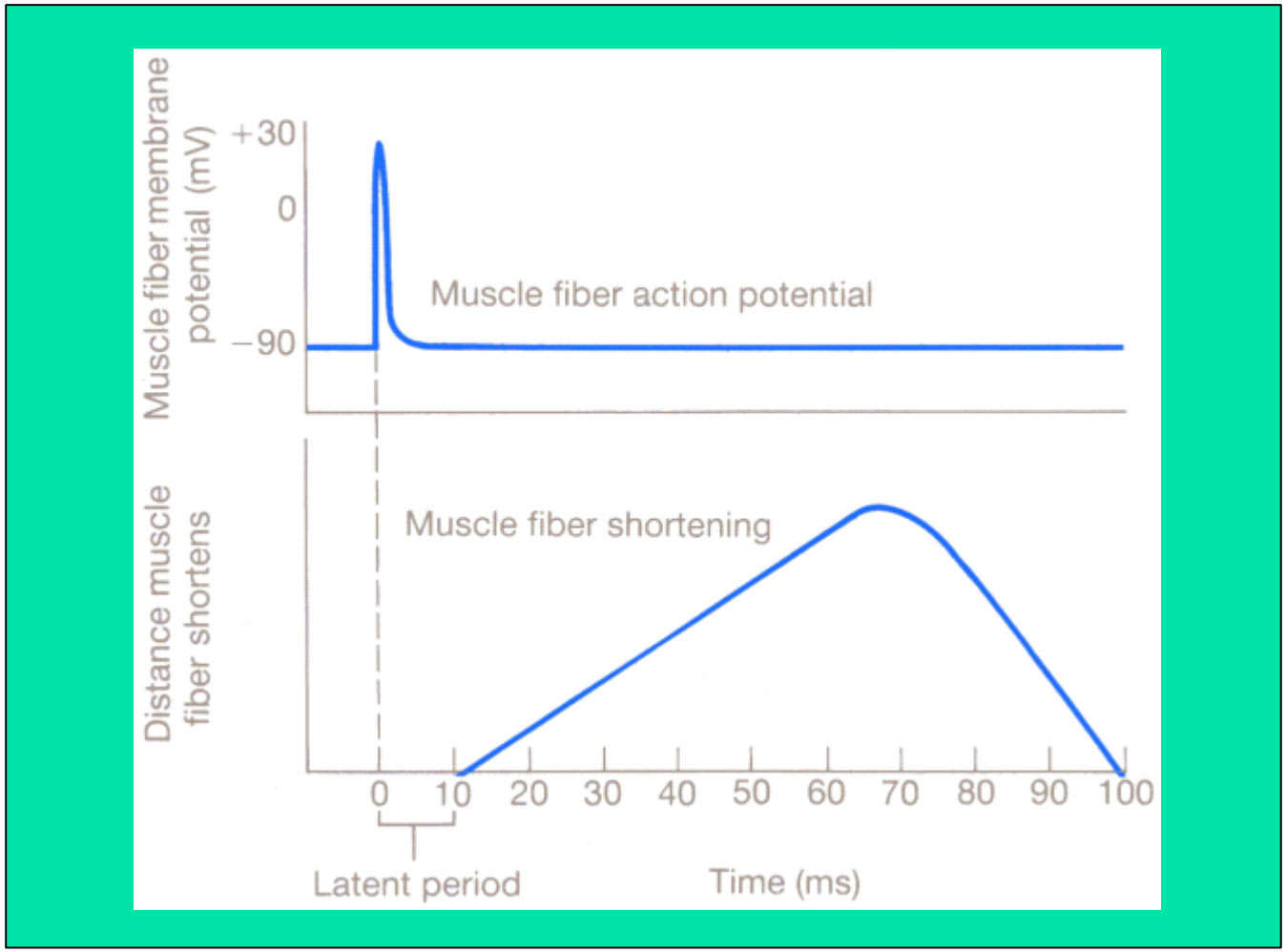
由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Cross Bridge Cycle - the Components



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Time relationships between action potential and the resulting shortening and relaxation of the muscle fiber



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估.

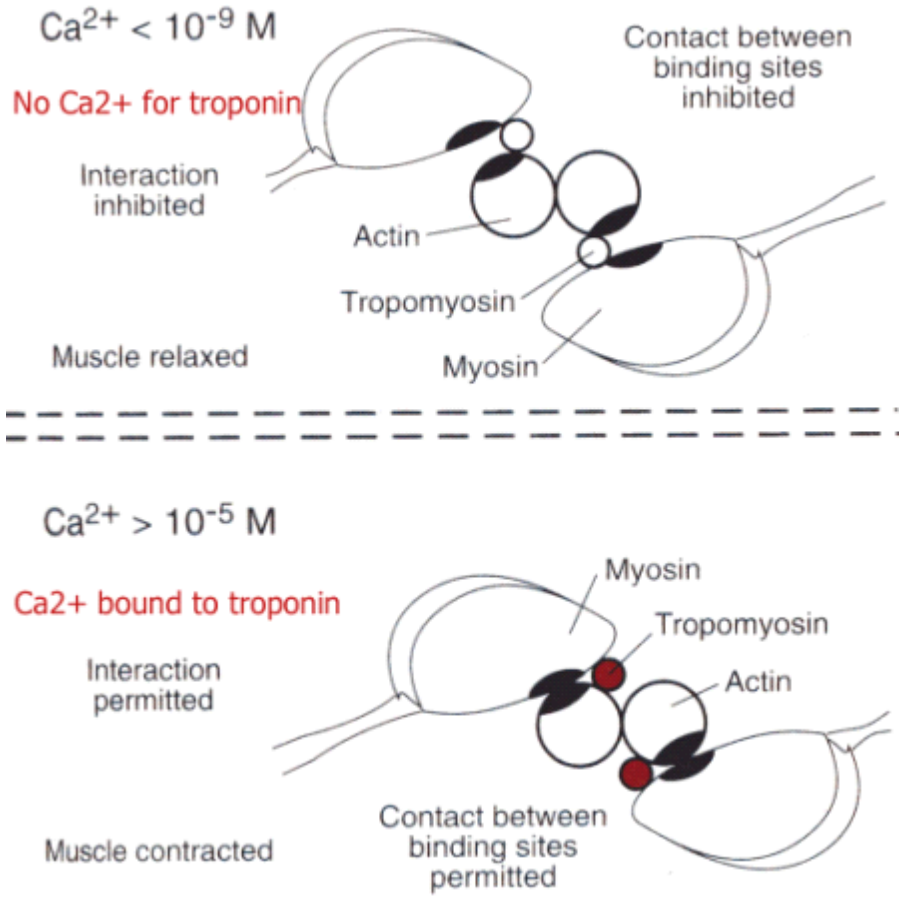
# Excitation-contraction coupling

- **Excitation-contraction coupling**: mechanism in muscle fibers linking plasma-membrane depolarization with cross-bridge force generation.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Excitation-contraction coupling

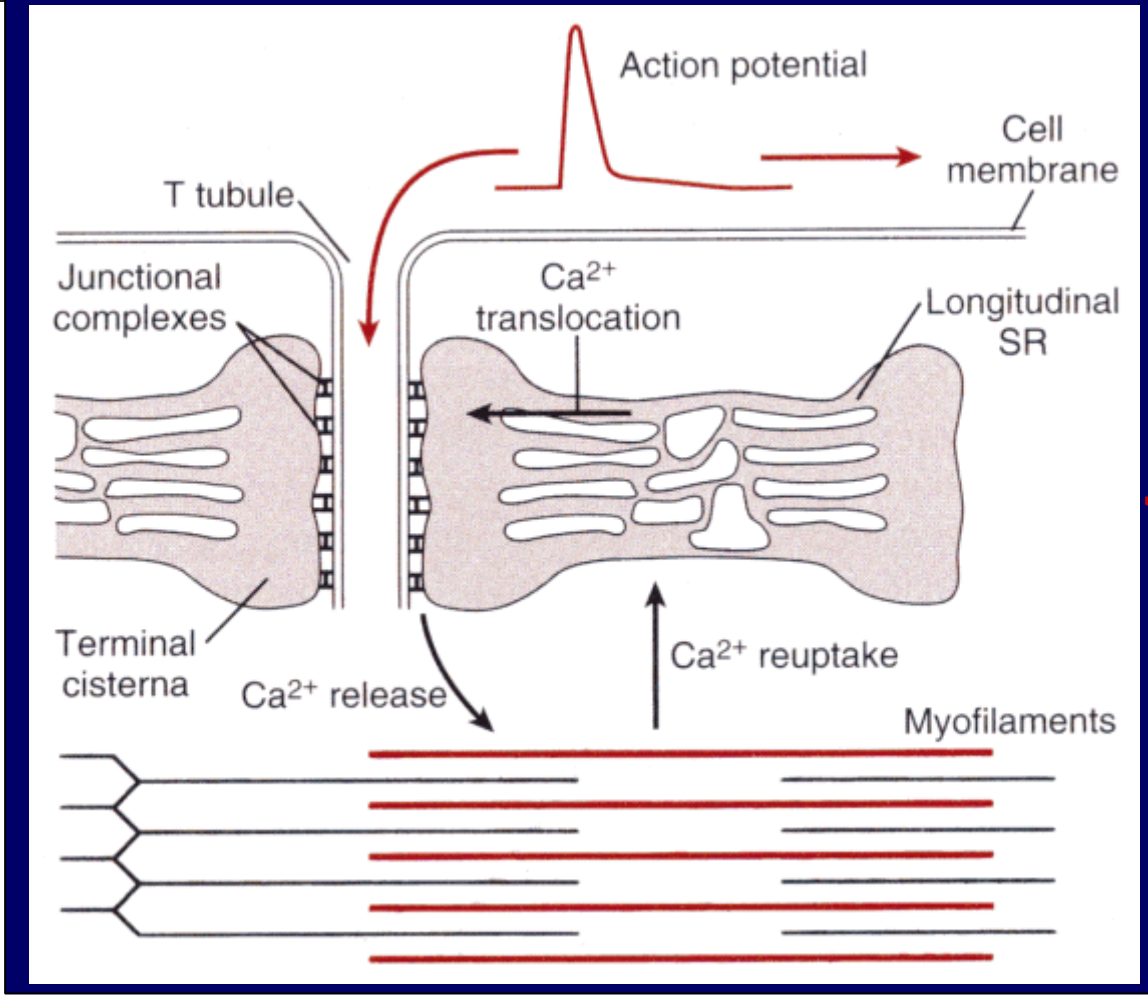
**Intracellular $Ca^{2+}$ is the key of excitation-contraction coupling**




- In a resting muscle fiber, the concentration of free calcium in the cytosol surrounding the thick and thin filaments is very low. At this moment, very few calcium binding sites on troponin are occupied.
- Following an action potential, there is a rapid increase in cytosolic calcium concentration. Calcium binds to troponin, removing the blocking of tropomyosin and allowing cross-bridge to bind to actin.

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Excitation-contraction coupling

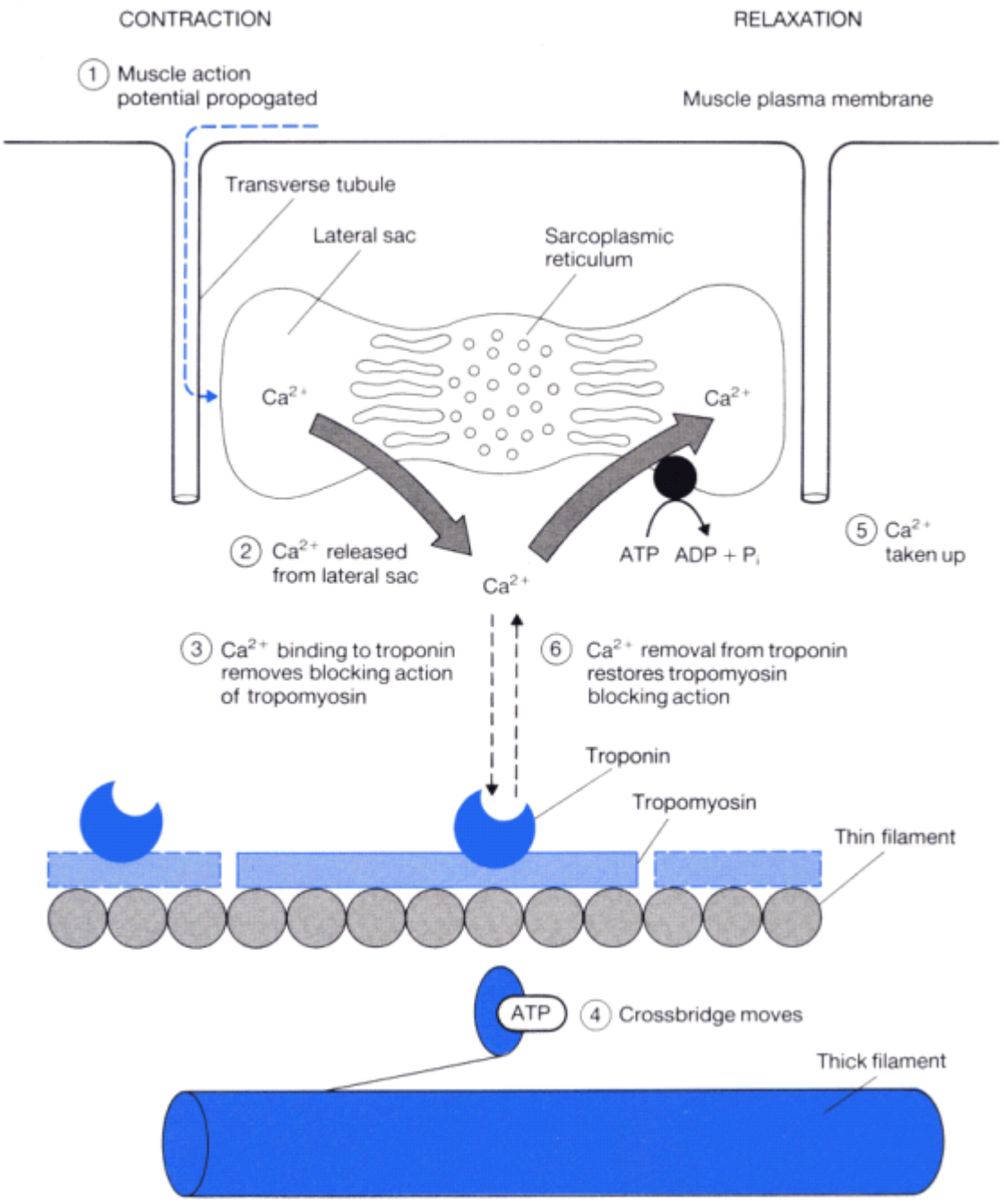



**T tubule**: voltage-sensitive calcium channel (dihydropyridin receptor, DHP)

**JSR**: $Ca^{2+}$ release channel (ryanodine receptor,RYR)

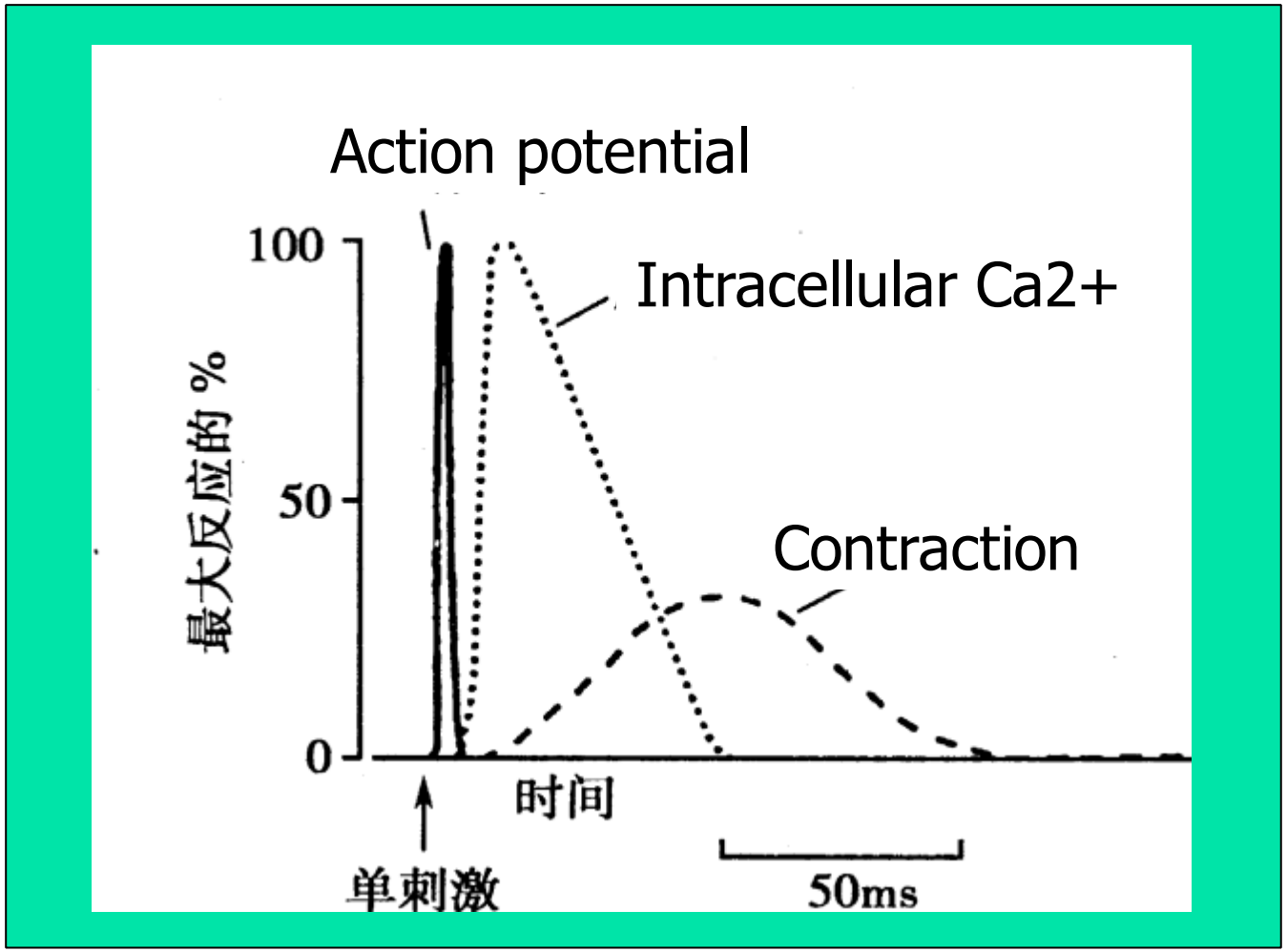
**LSR**: $Ca^{2+}$ pump

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

# Time relationships between action potential, intracellular [$Ca^{2+}$] and twitch tension



由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。

由 Foxit PDF Editor 编辑
版权所有 (c) by Foxit Software Company, 2003 - 2009
仅用于评估。