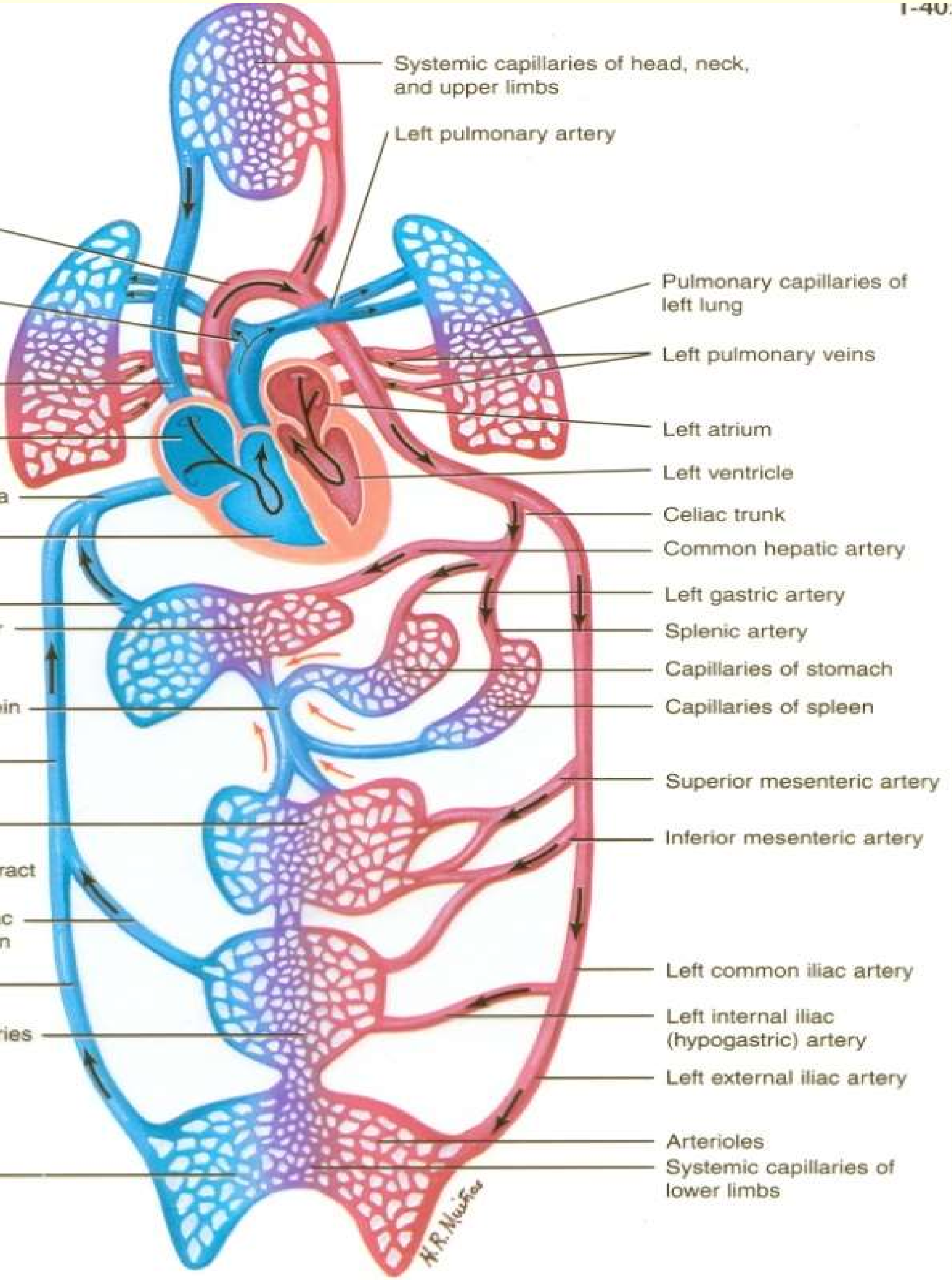
Cardiac Muscle Physiology

Faisal Mohammed, MD, PhD

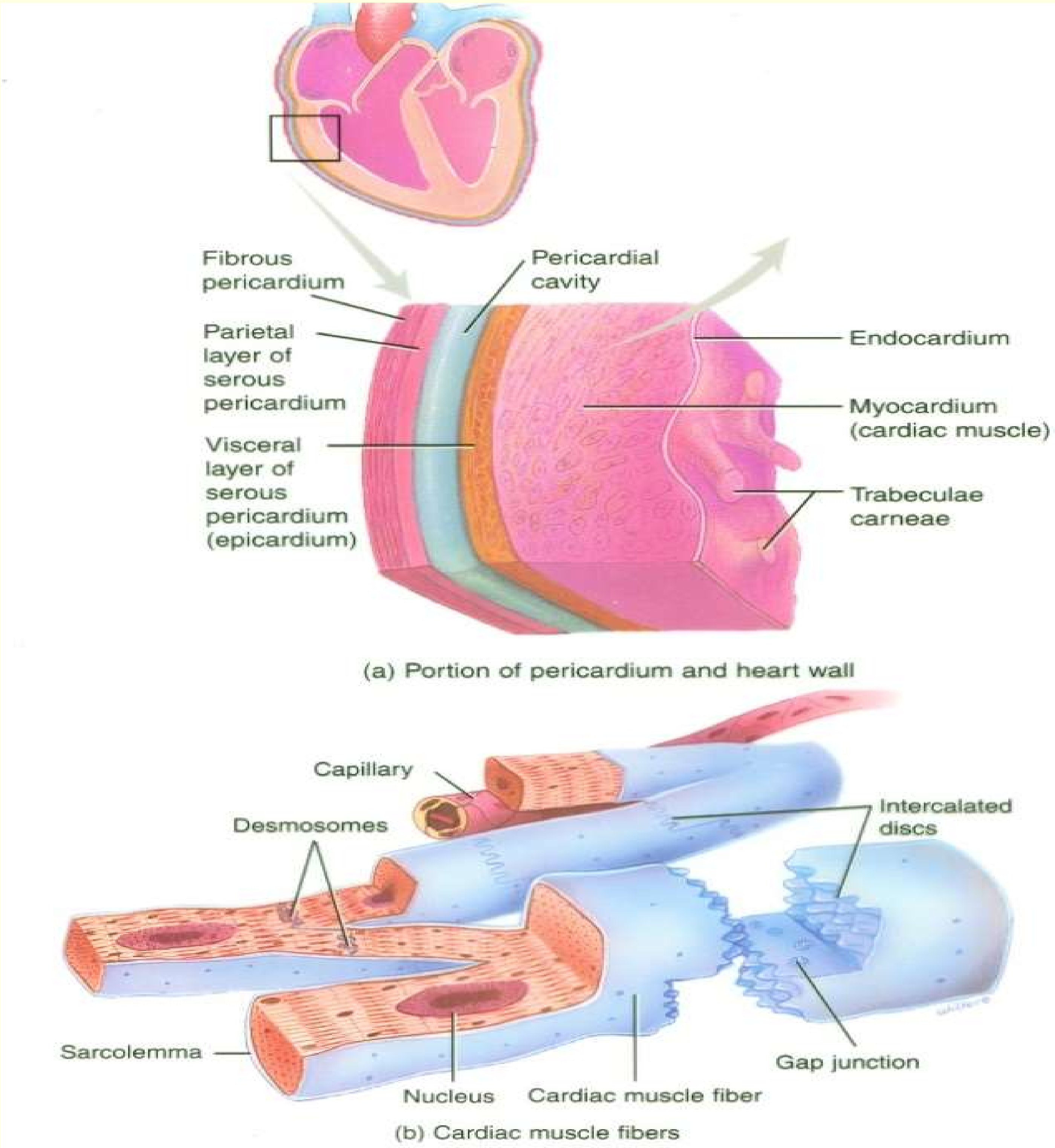
Objectives:

By The end of this lecture students should be able to:

- Distinguish the cardiac muscle cell microstructure
- Describe cardiac muscle action potential
- Point out the functional importance of the action potential
- Follow the cardiac muscle mechanism of contraction
- Delineate cardiac muscle energy sources
- Outline the intracellular calcium homeostasis
- Explain the relationship between muscle length and tension of cardiac muscle (Frank-Starling law of the heart)



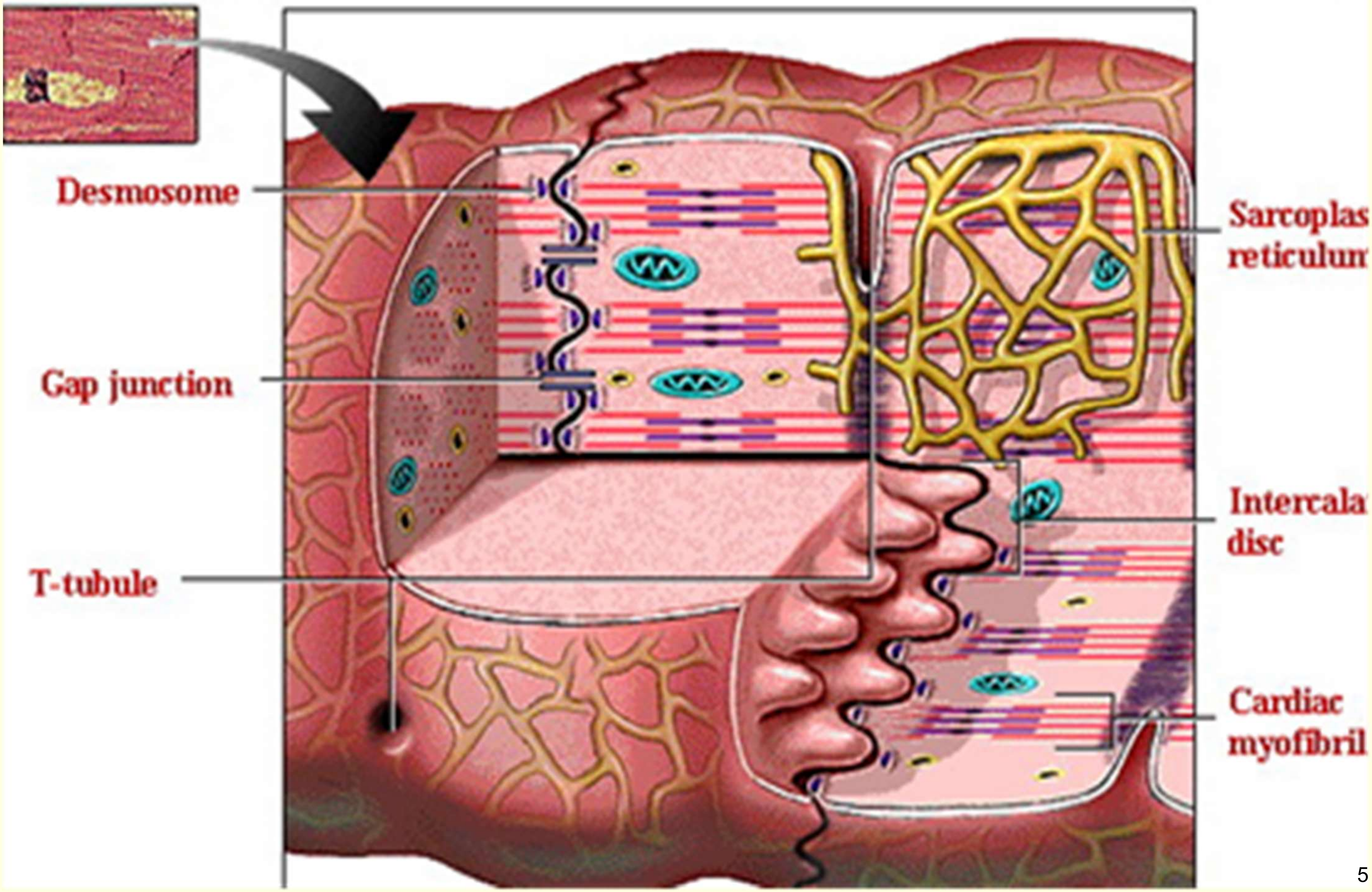
General plan of circulation

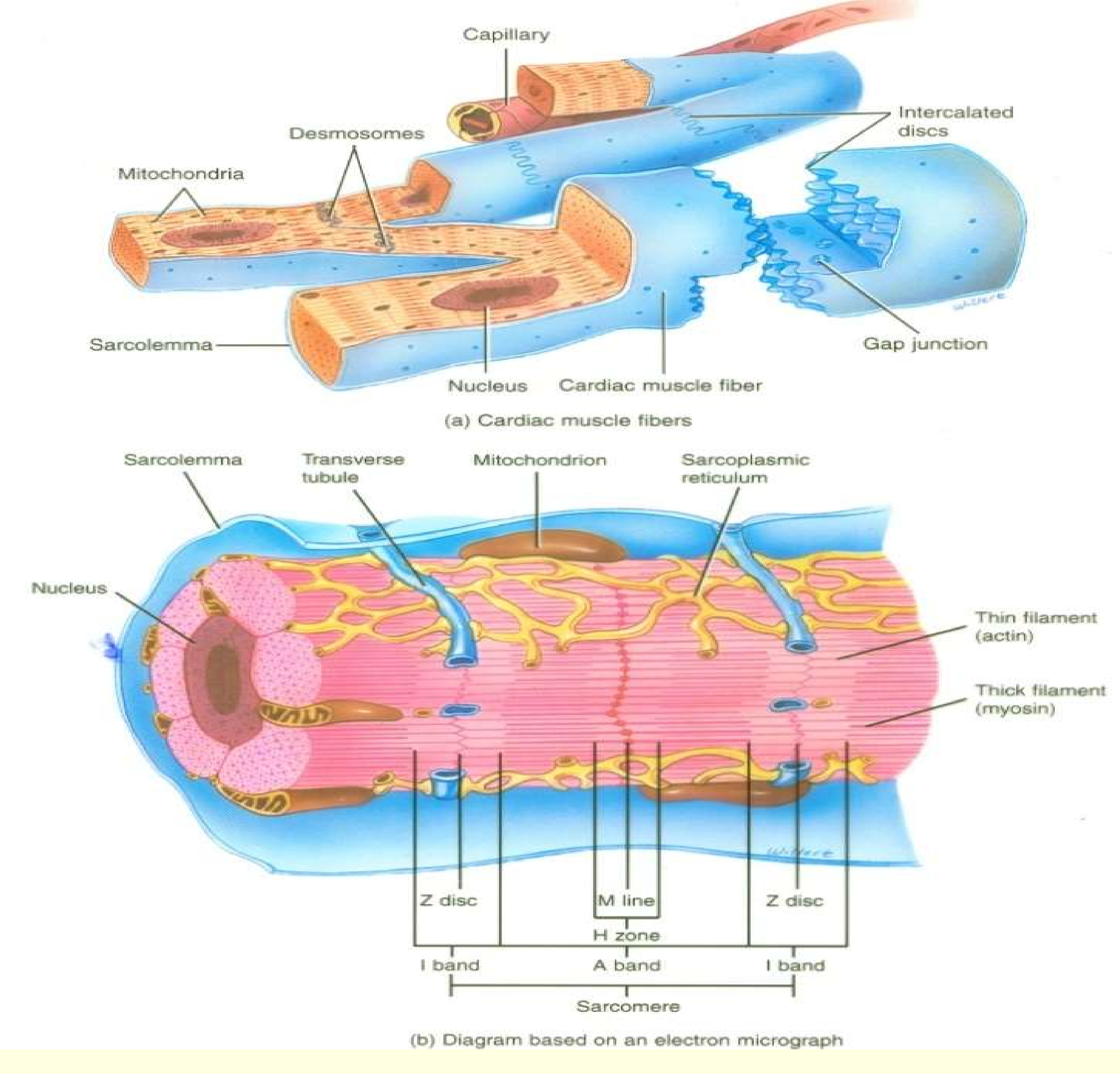


(a) Portion of pericardium and heart wall

(b) Cardiac muscle fibers

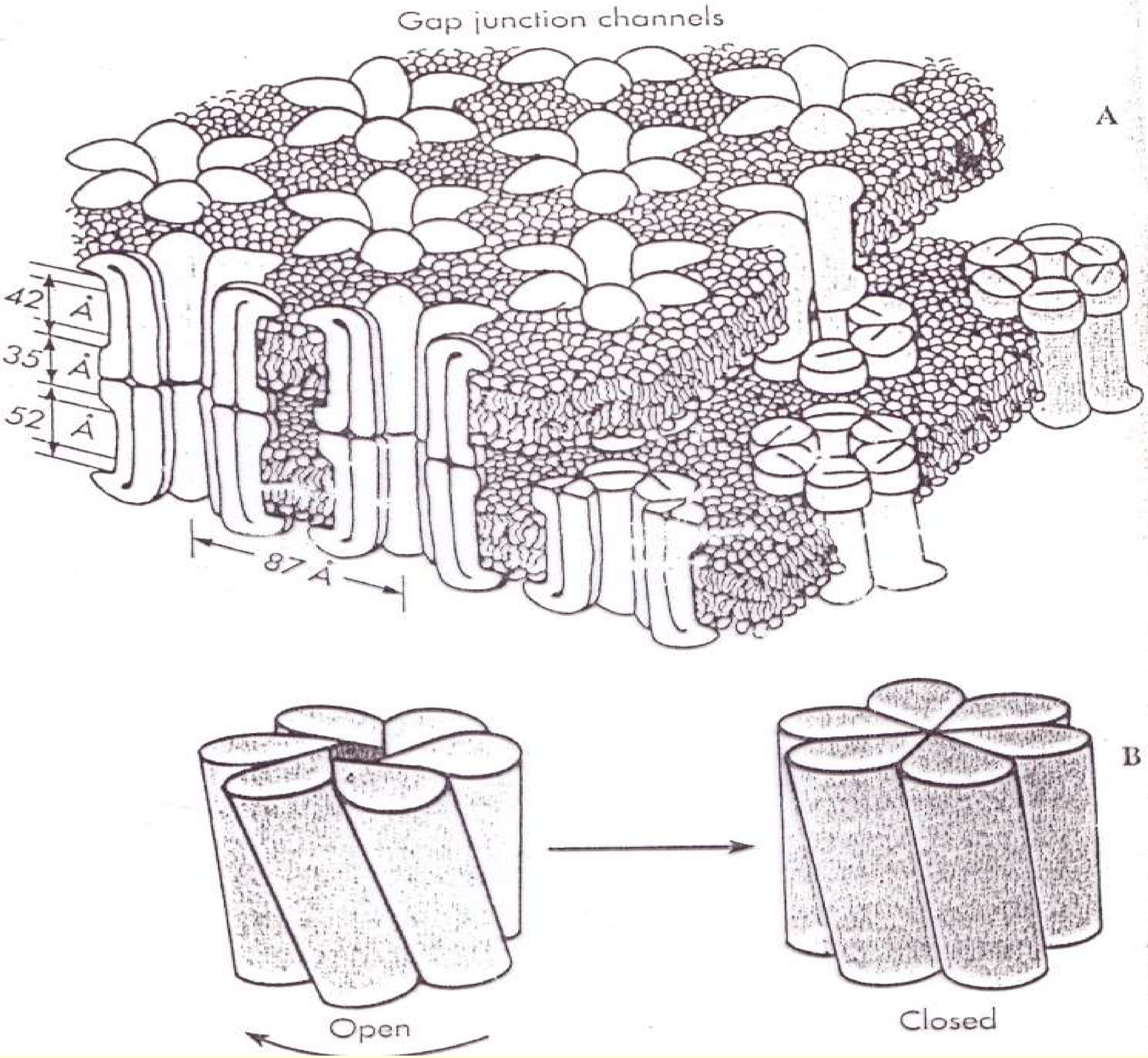
MAGNIFIED VIEW OF CARDIAC MUSCLE CELLS





(a) Cardiac muscle fibers

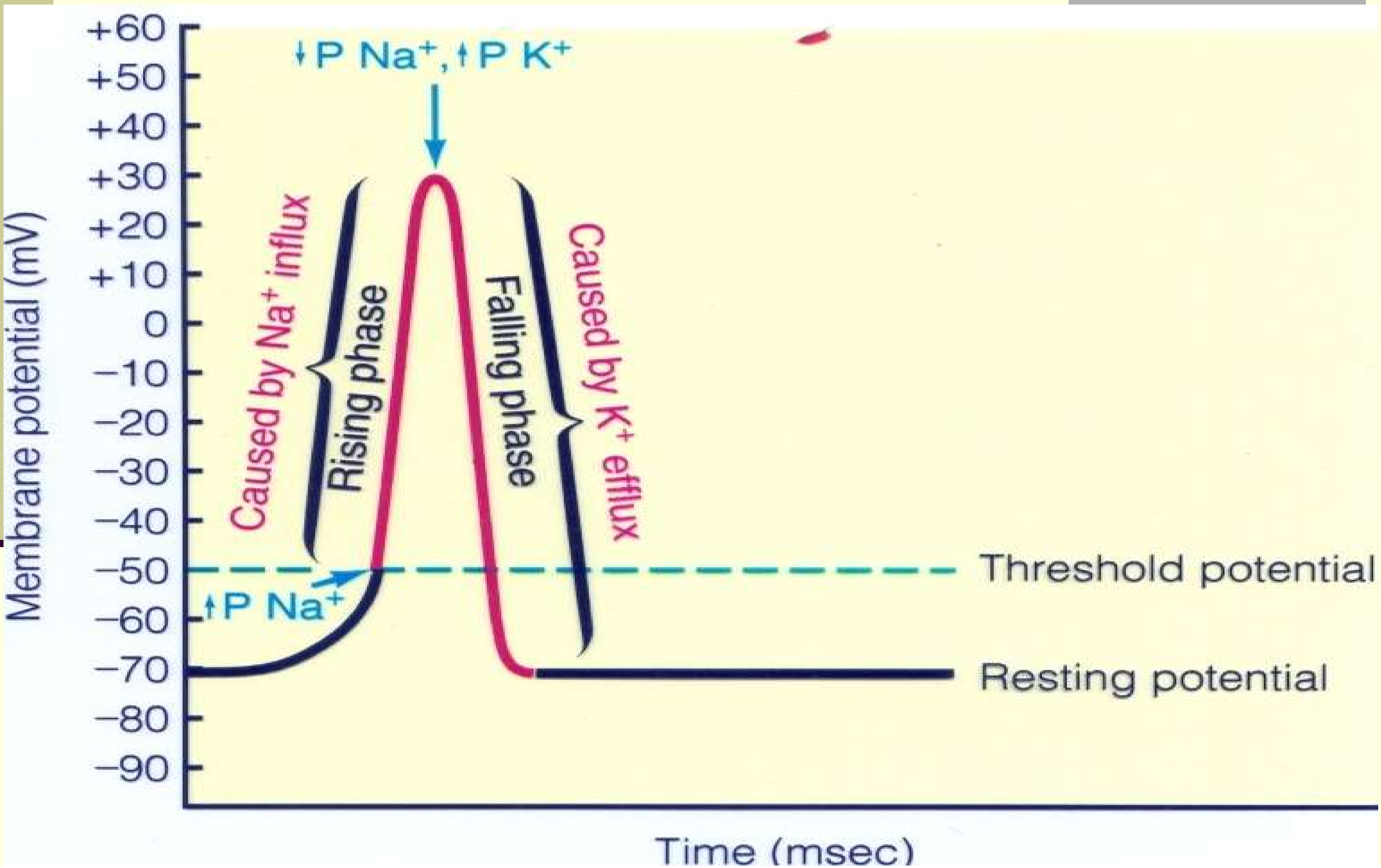
(b) Diagram based on an electron micrograph

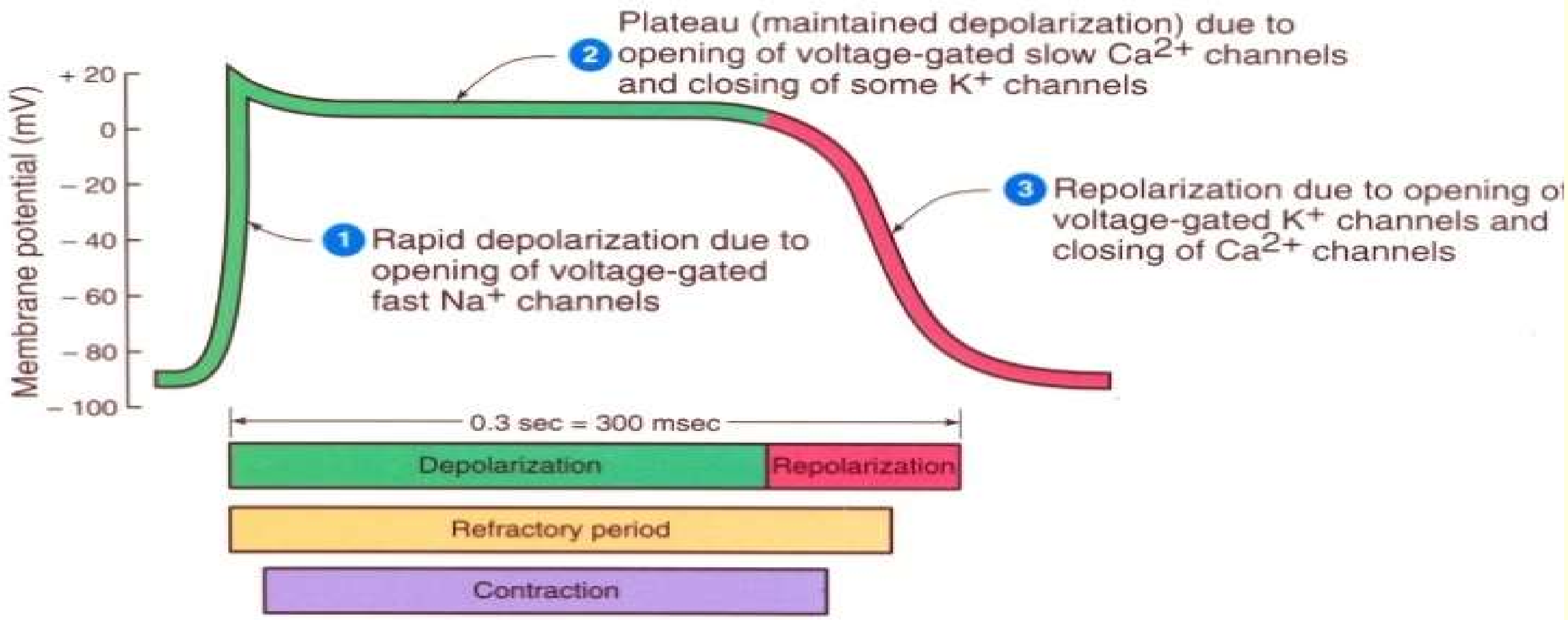

Gap junction channels
A
42 Å
35 Å
52 Å
87 Å
B
Open
Closed

Cardiac Muscle Vs Skeletal Muscle

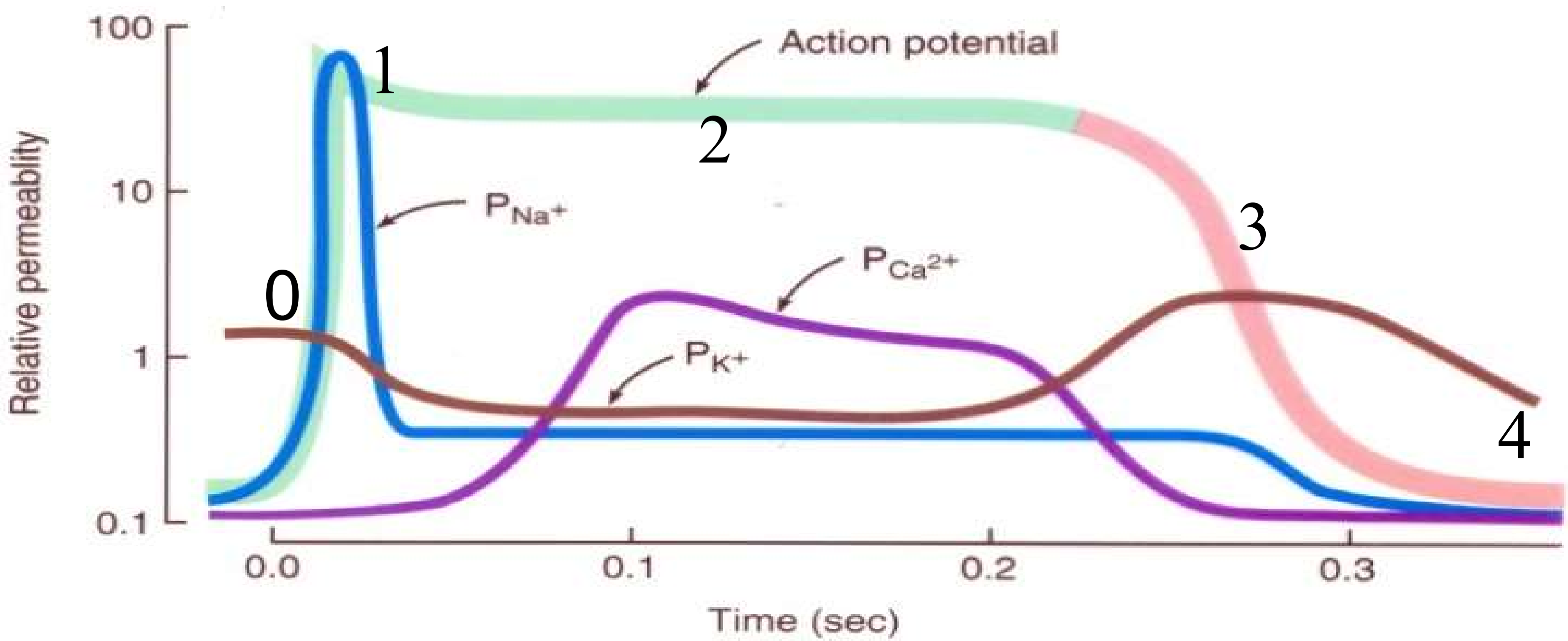
- Syncytium structure
- Gap Junction (electrical coupling) low resistance area
- Poorly developed Sarcoplasmic reticulum (SR)
- Transverse (T)Tubule on Z-line (i.e.One T-tubule per sarcomere)
- Rich in mitochondria
- Low in nuclei

Permeability Changes and Ionic Fluxes During an Action Potential (skeletal Muscle)



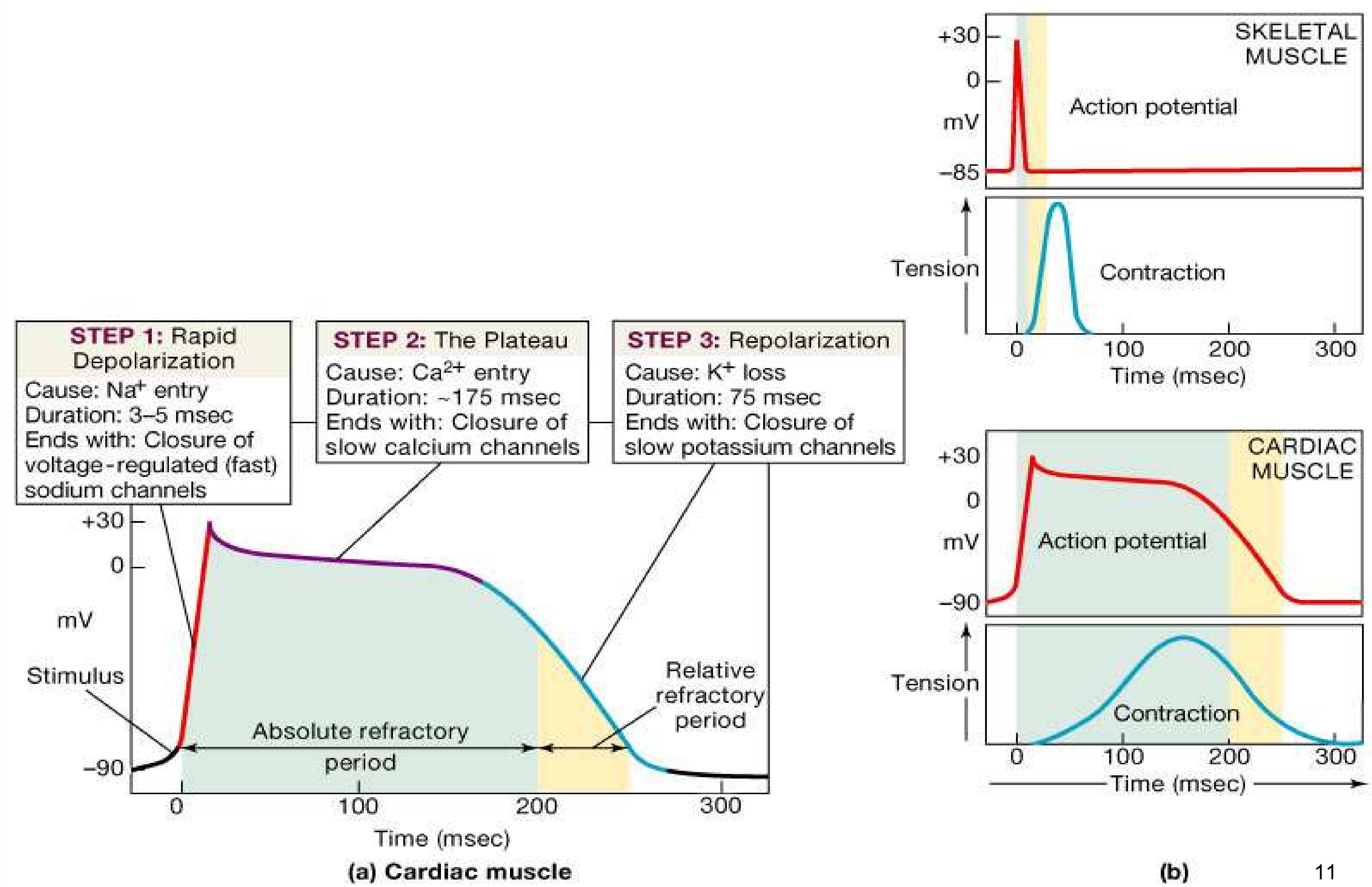


(a) Action potential, refractory period, and contraction

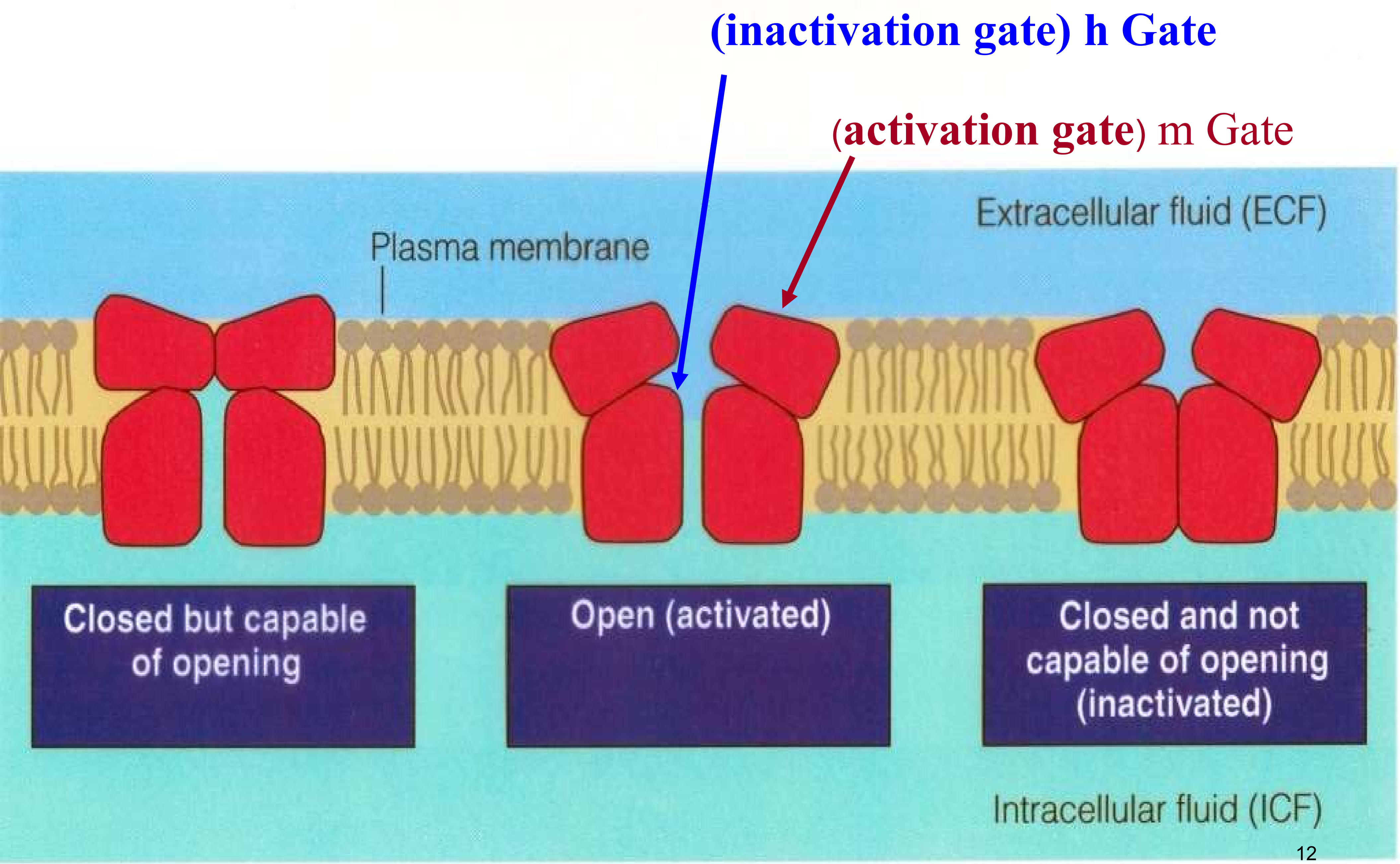


(b) Membrane permeability (P) changes

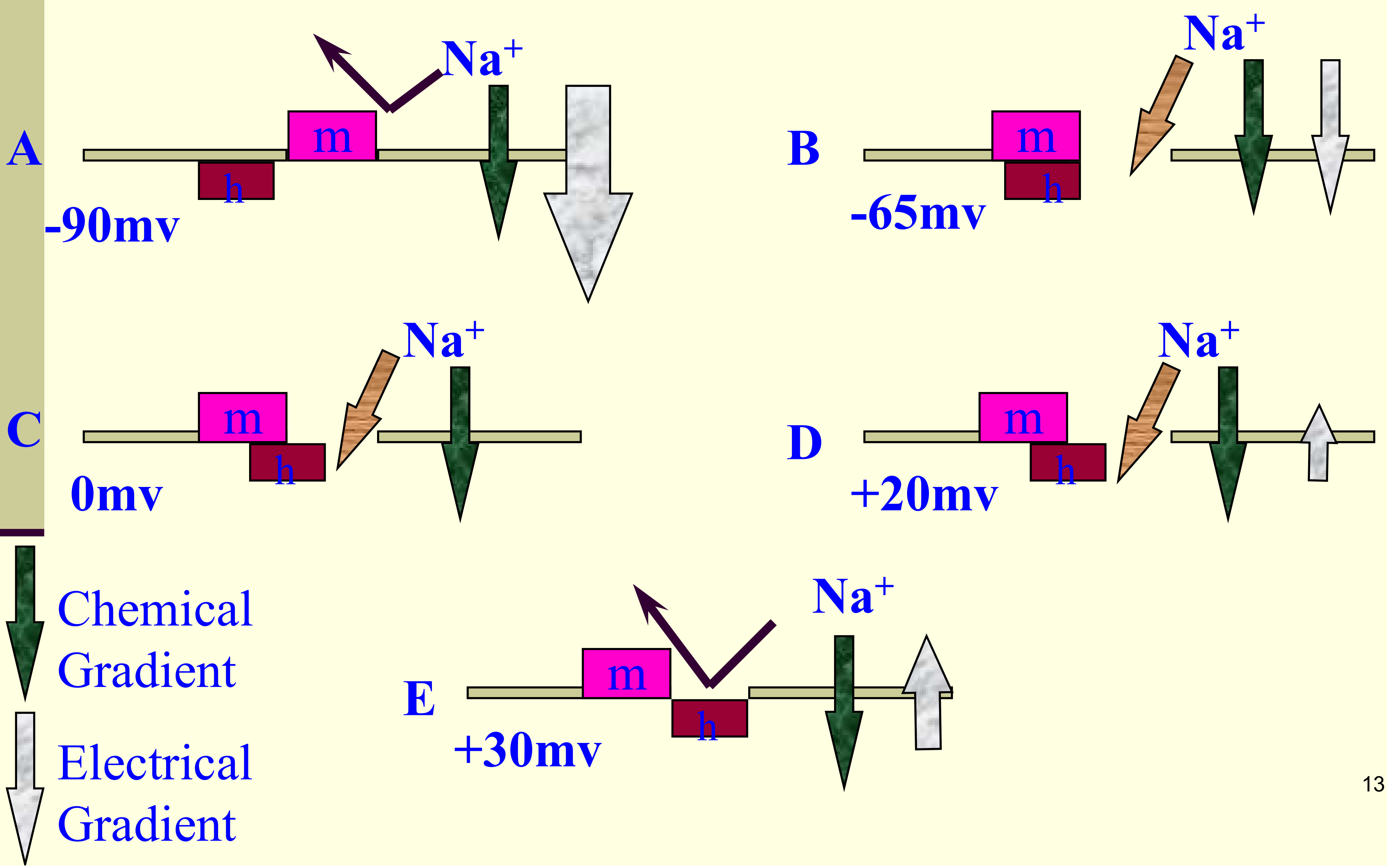
The Action Potential in Skeletal and Cardiac Muscle

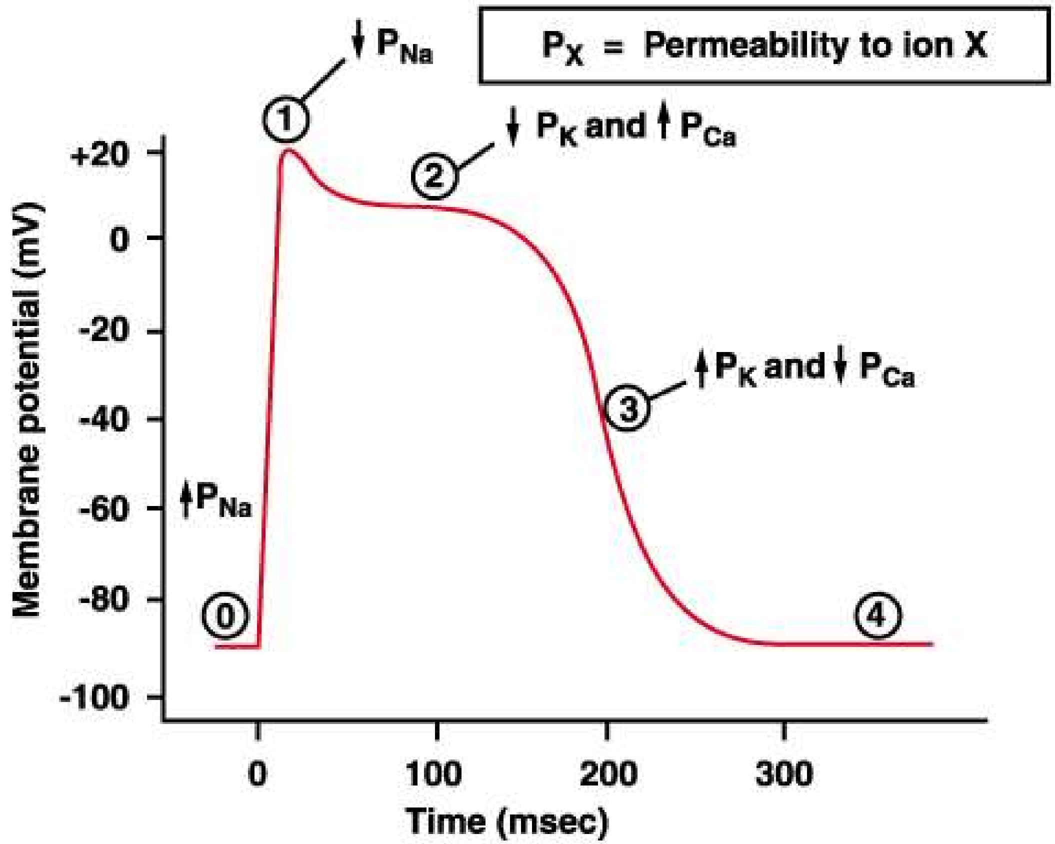


Conformations of a Voltage-Gated Na^+ Channel

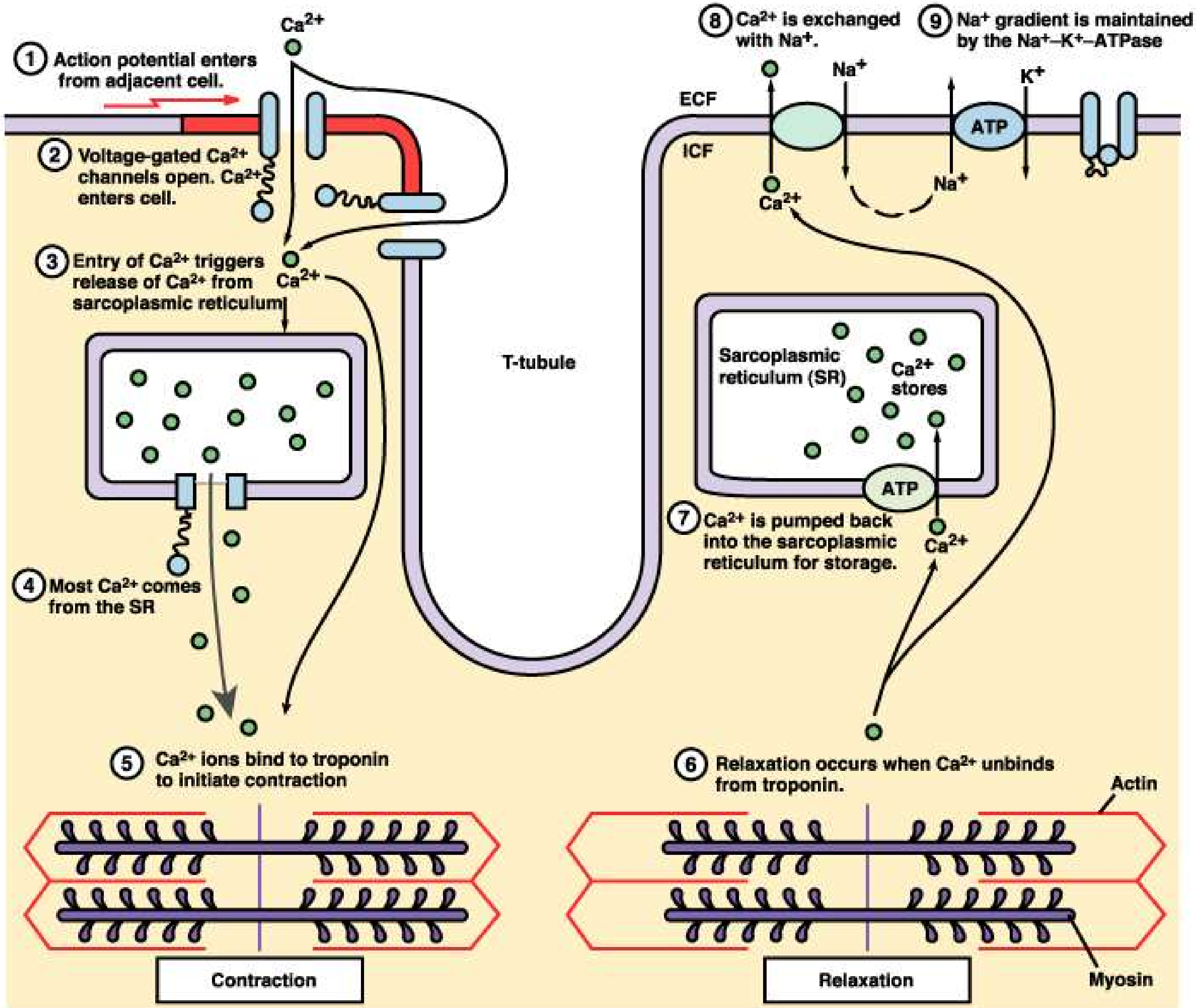


PHASE 0 OF THE FAST FIBER ACTION POTENTIAL



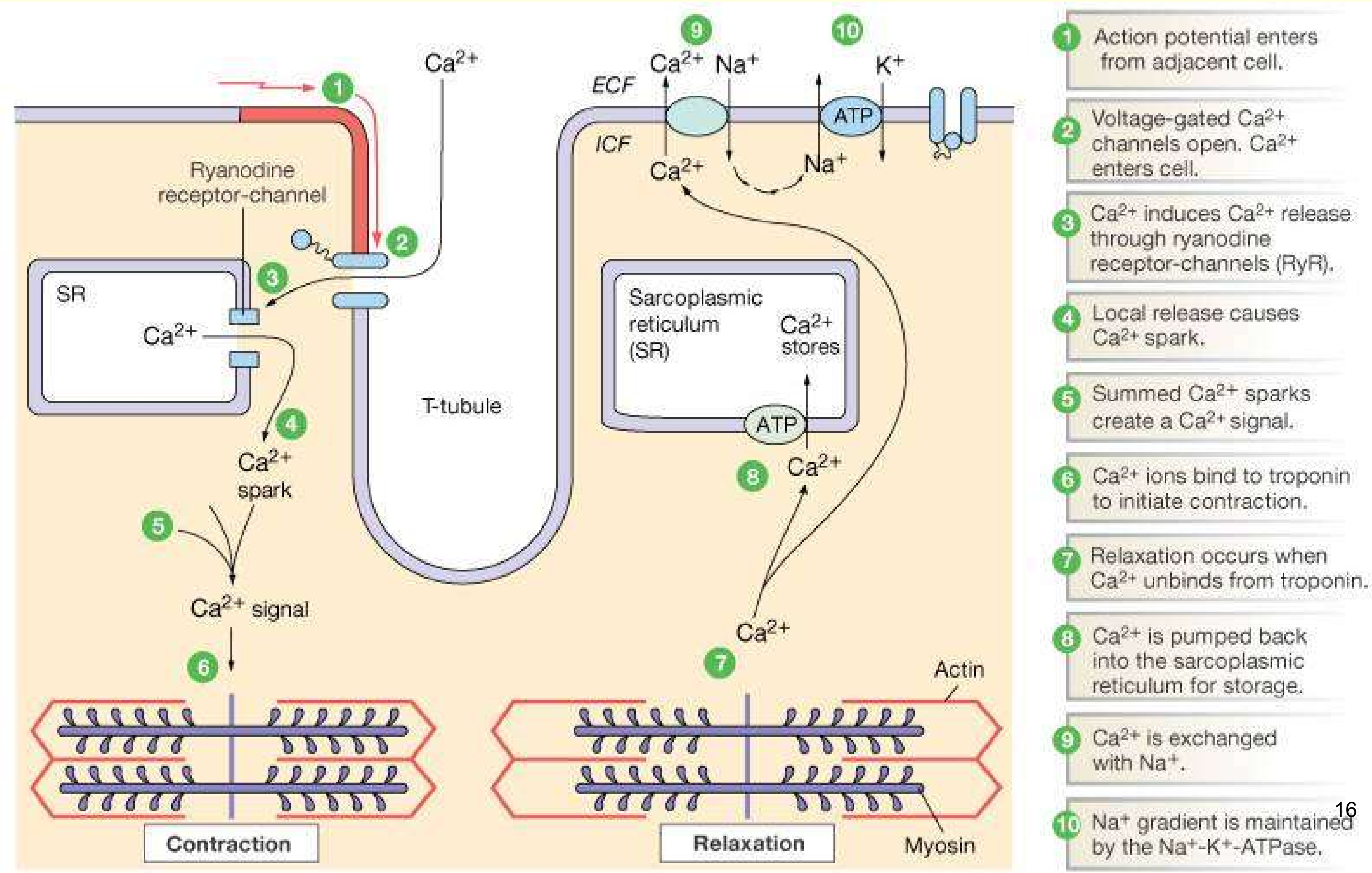


Phase	Membrane channels
0	Na^+ channels open
1	Na^+ channels close
2	Ca^{2+} channels open; fast K^+ channels close
3	Ca^{2+} channels close; slow K^+ channels open
4	Resting potential

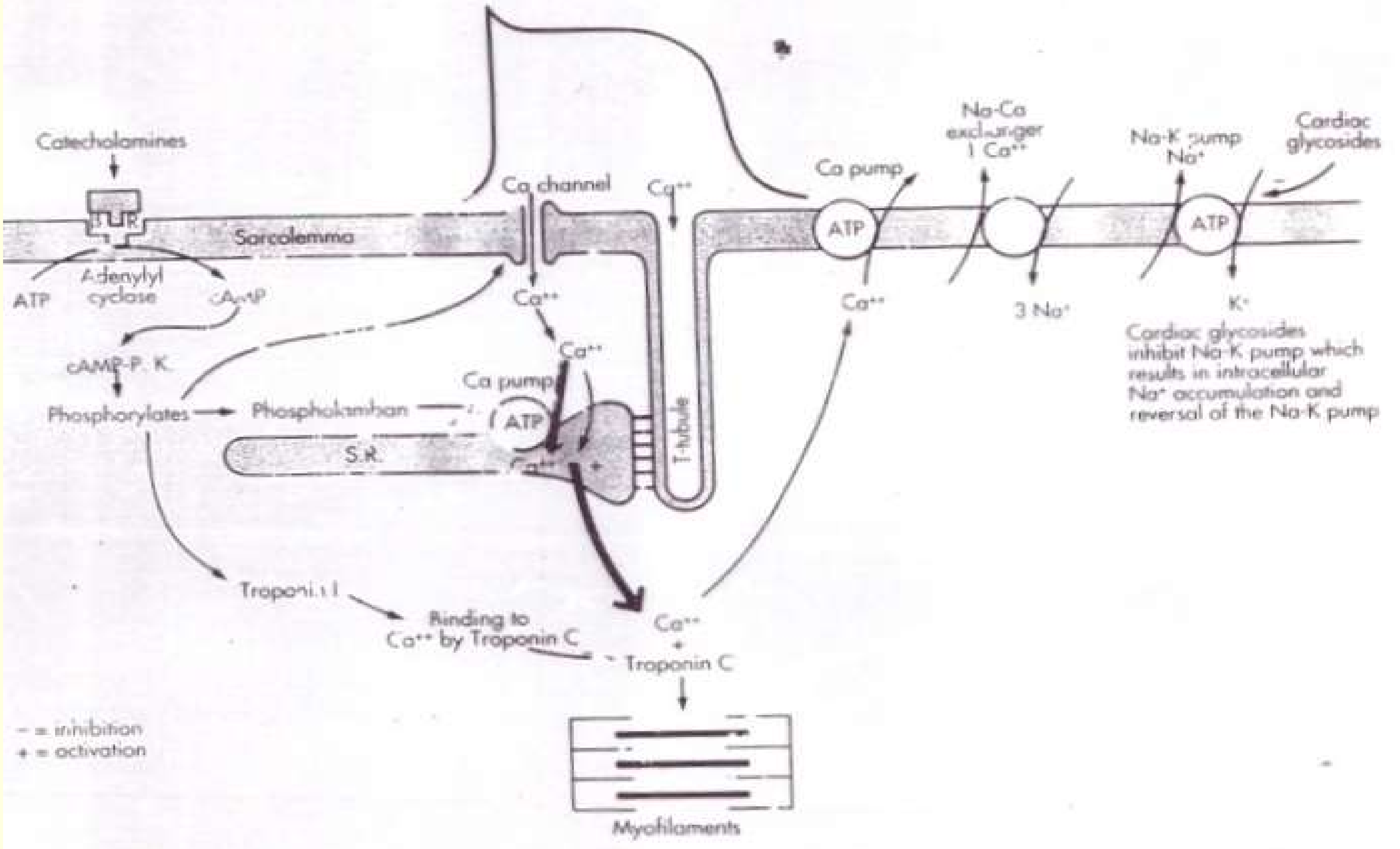


Ca2+
1 Action potential enters from adjacent cell.
2 Voltage-gated Ca2+ channels open. Ca2+ enters cell.
3 Entry of Ca2+ triggers release of Ca2+ from sarcoplasmic reticulum
Ca2+
4 Most Ca2+ comes from the SR
5 Ca2+ ions bind to troponin to initiate contraction
T-tubule
ECF
ICF
8 Ca2+ is exchanged with Na+.
9 Na+ gradient is maintained by the Na+–K+–ATPase
Na+
K+
ATP
Na+
Ca2+
Sarcoplasmic reticulum (SR)
Ca2+ stores
ATP
7 Ca2+ is pumped back into the sarcoplasmic reticulum for storage.
Ca2+
6 Relaxation occurs when Ca2+ unbinds from troponin.
Actin
Myosin
Contraction
Relaxation

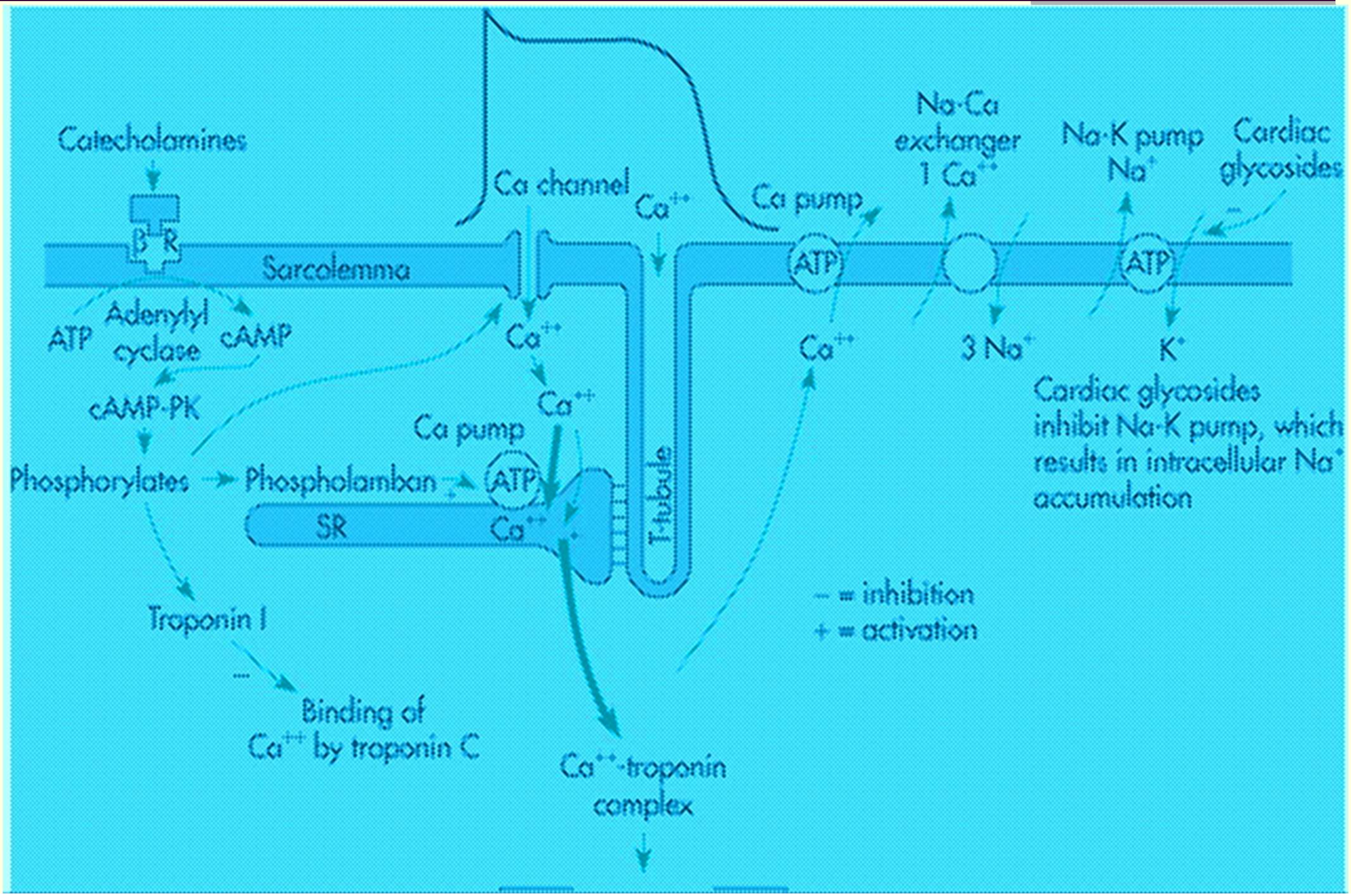
Mechanism of Cardiac Muscle Excitation, Contraction & Relaxation

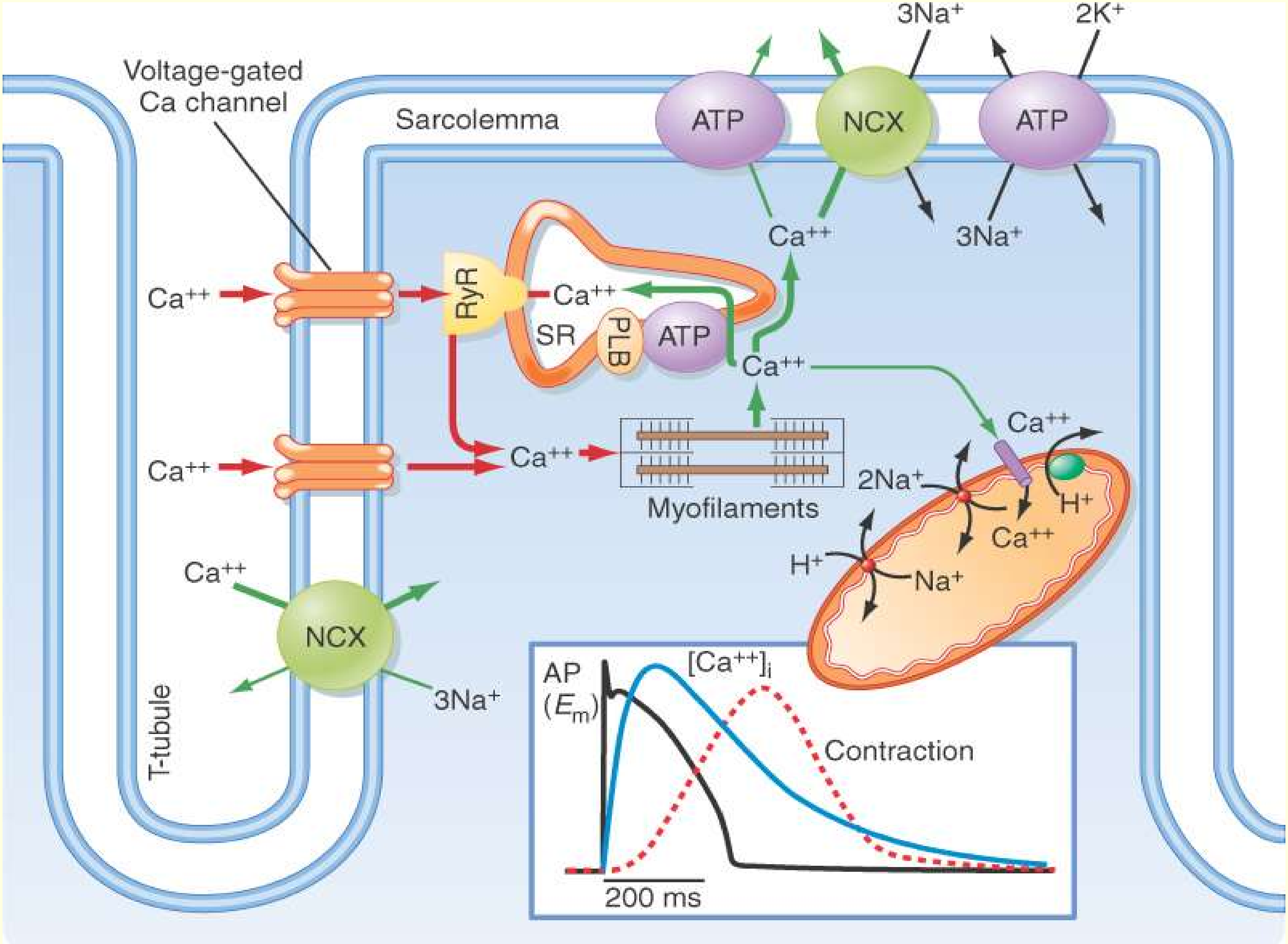


Intracellular Calcium Homeostasis…1



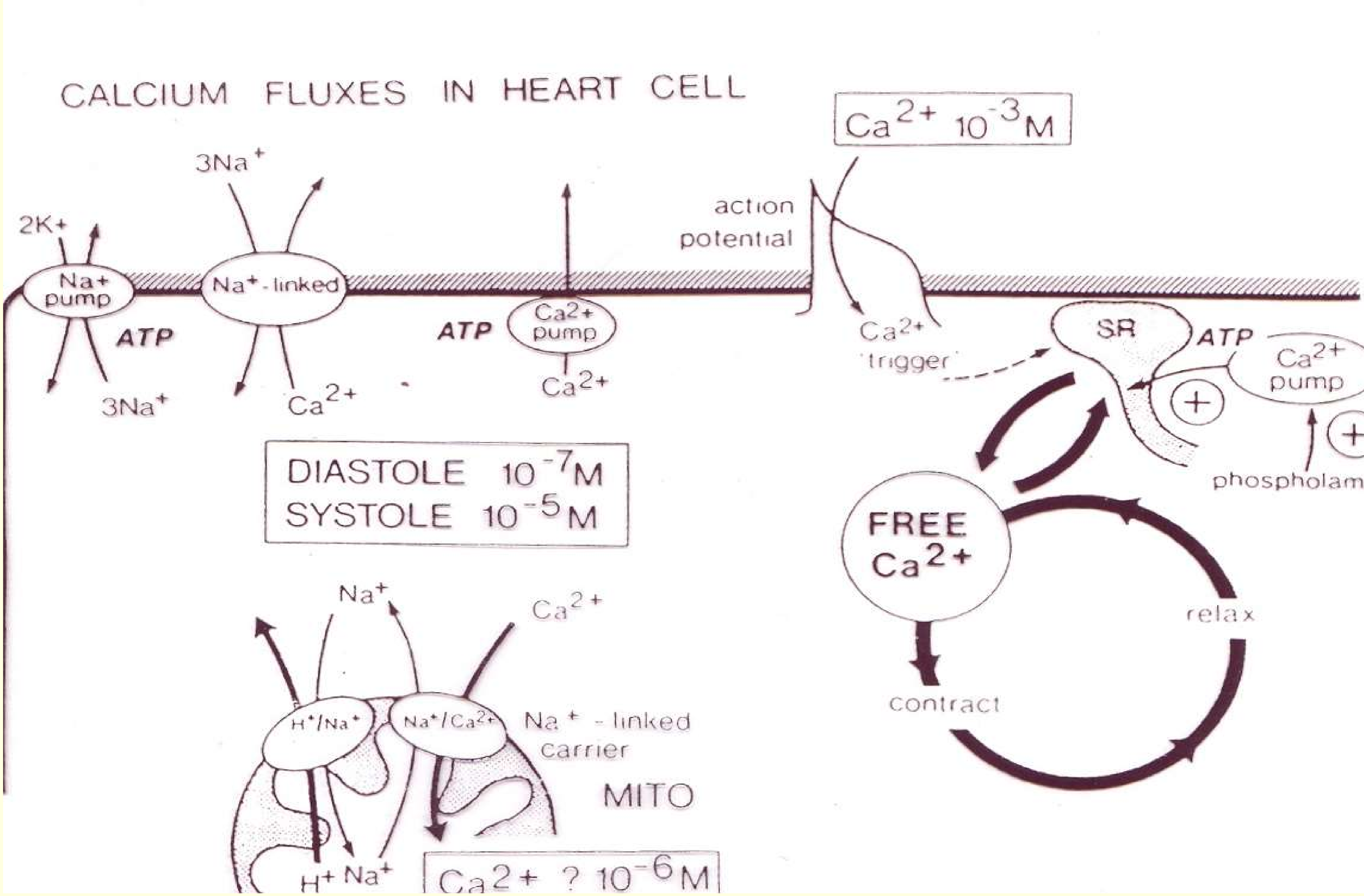
Intracellular Calcium Homeostasis…1



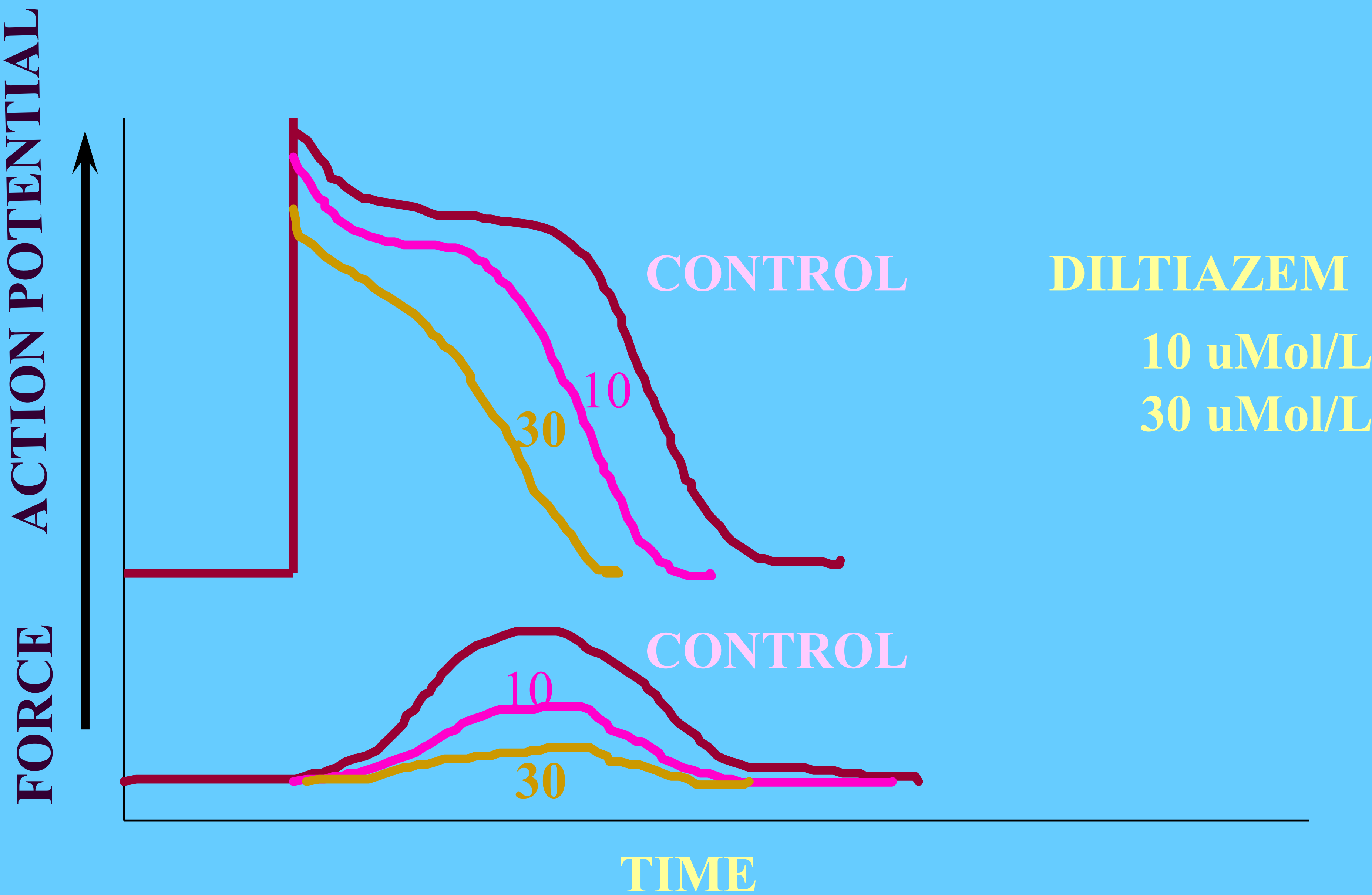


(Redrawn from Bers DM: Nature 415:198-205, 2002.)

Intracellular Calcium Homeostasis…2

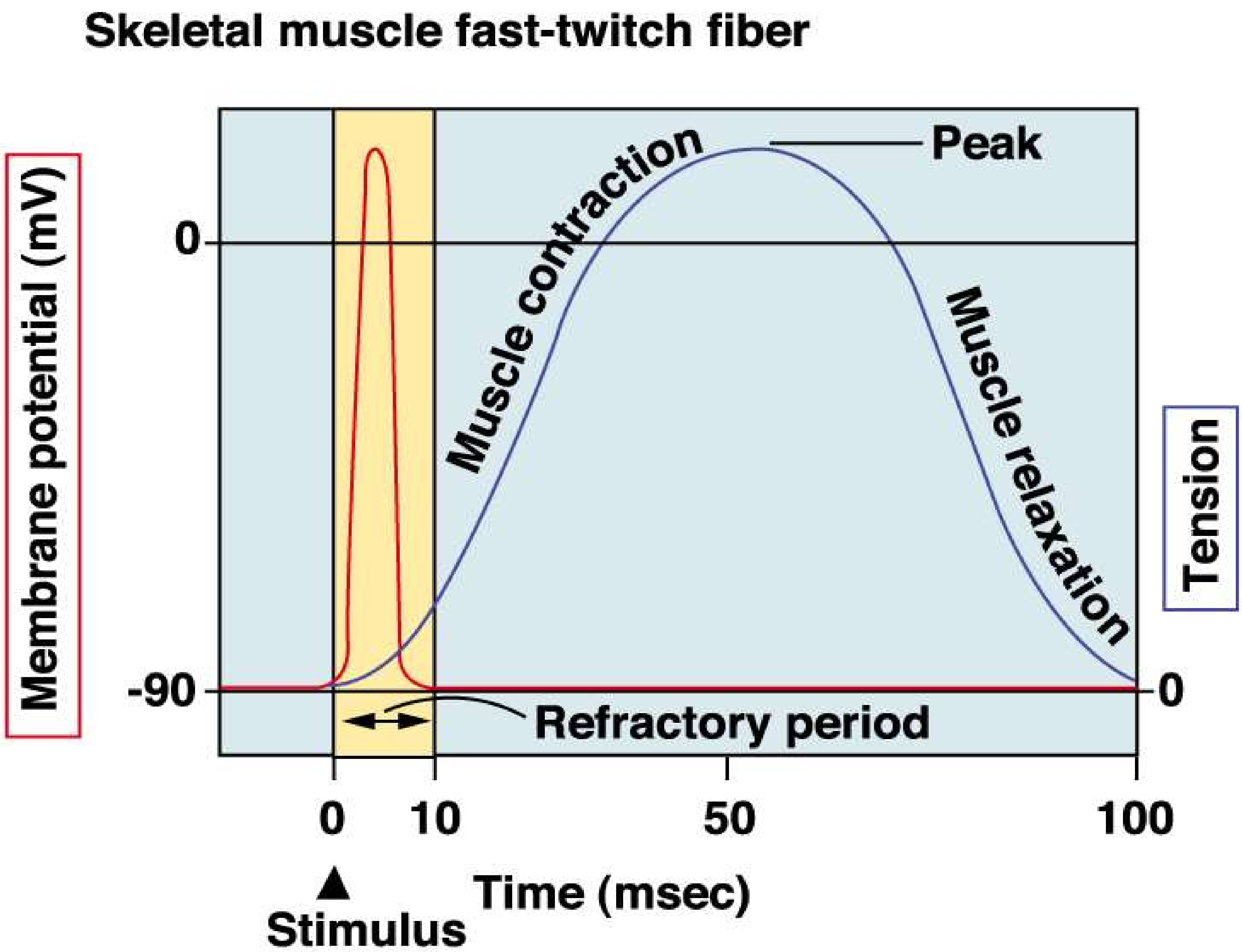


EFFECTS OF Ca++ CHANNEL BLOCKERS AND THE CARDIAC CELL ACTION POTENTIAL



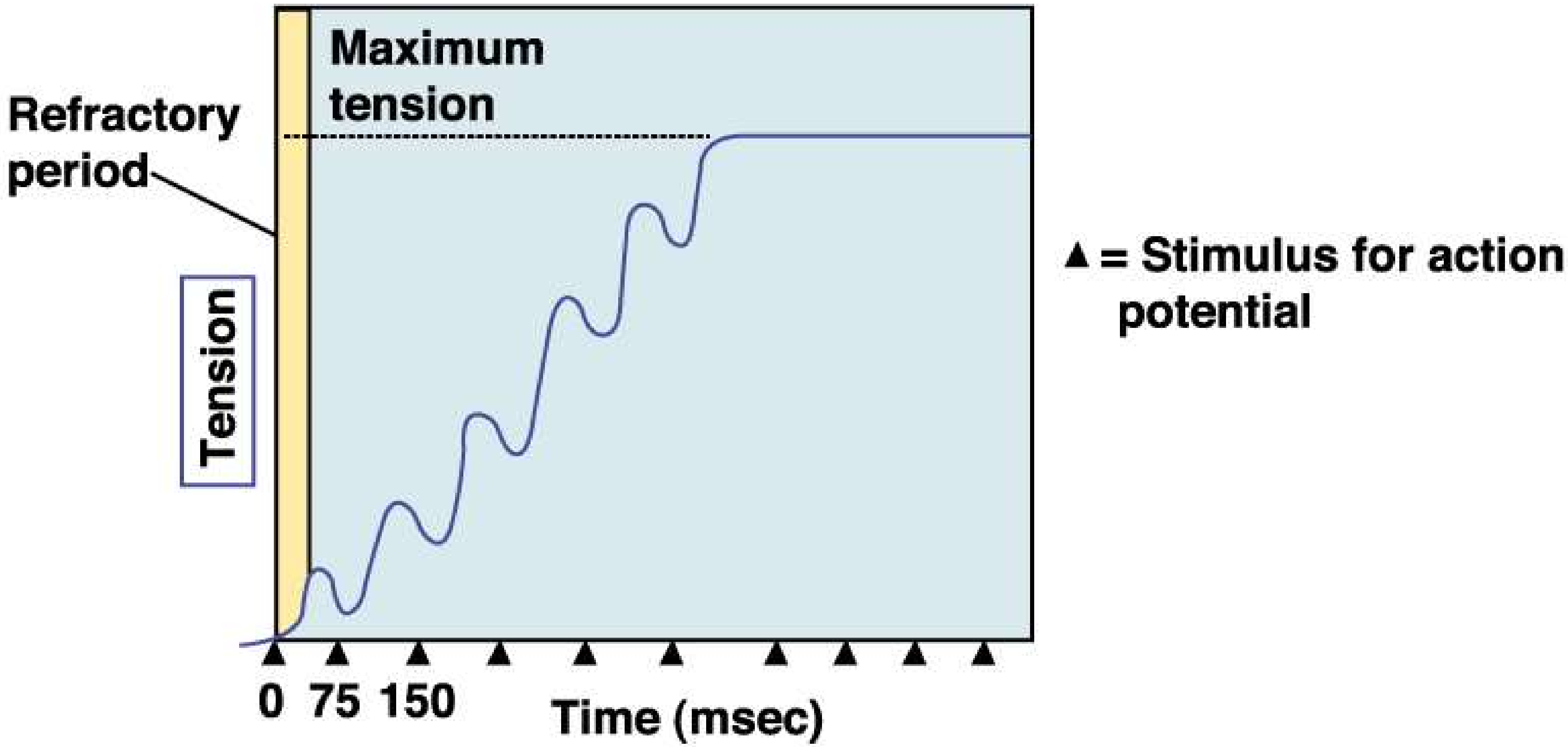
Cardiac Muscle action potential Vs. Skeletal Muscle

- Phase 0 –Depolarization phase (Na^+ influx)
- Phase 1 partial repolarization (Not in skeletal)
- Phase 2 Plateau (depolarization not in skeletal) slow calcium channels
- Phase 3 fast repolarization phase (K^+ efflux
- Phase 4 resting membrane potential

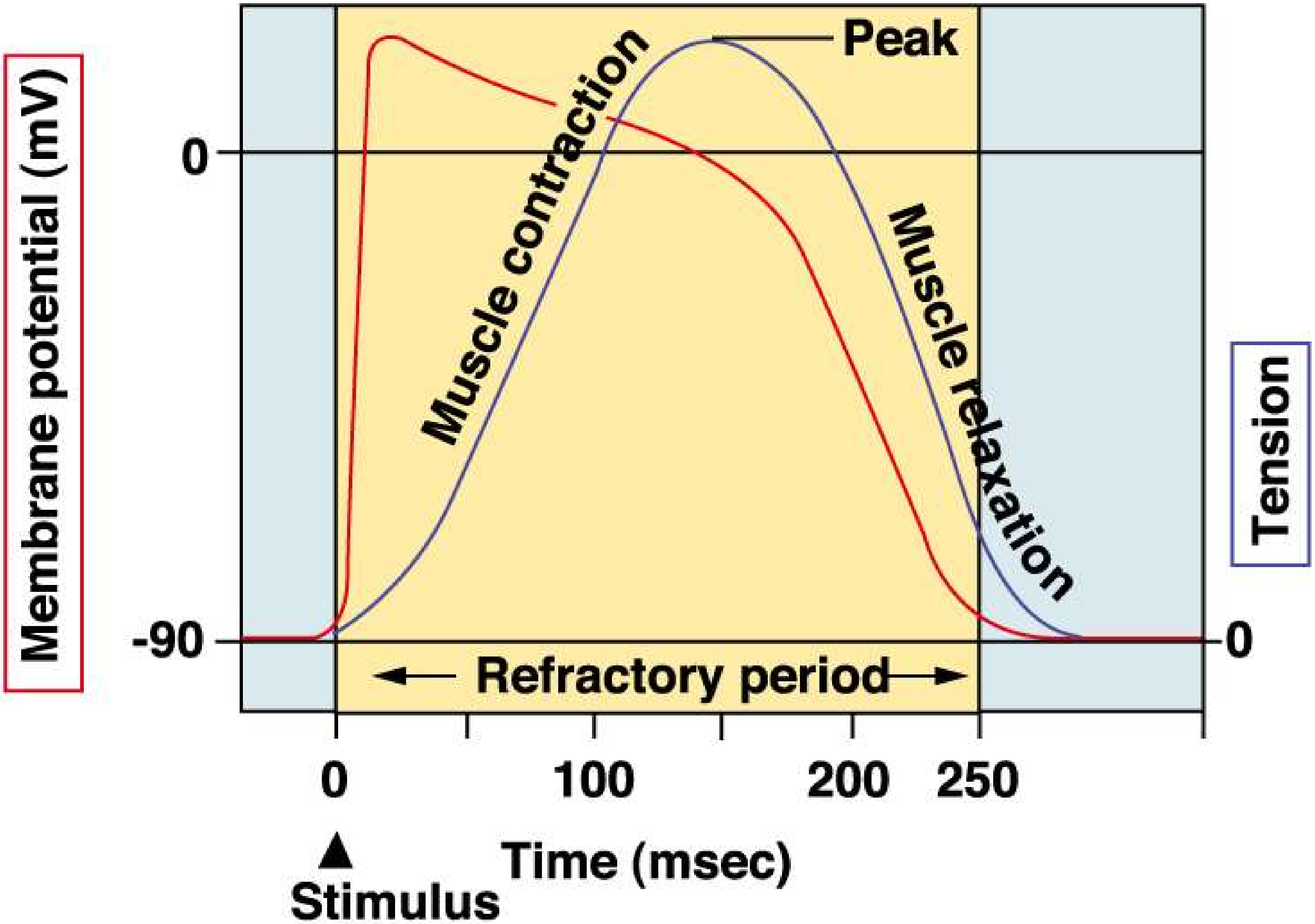


Skeletal muscle fast-twitch fiber
Membrane potential (mV)
0
-90
Muscle contraction
Peak
Muscle relaxation
Tension
0
Refractory period
0
10
50
100
Stimulus
Time (msec)

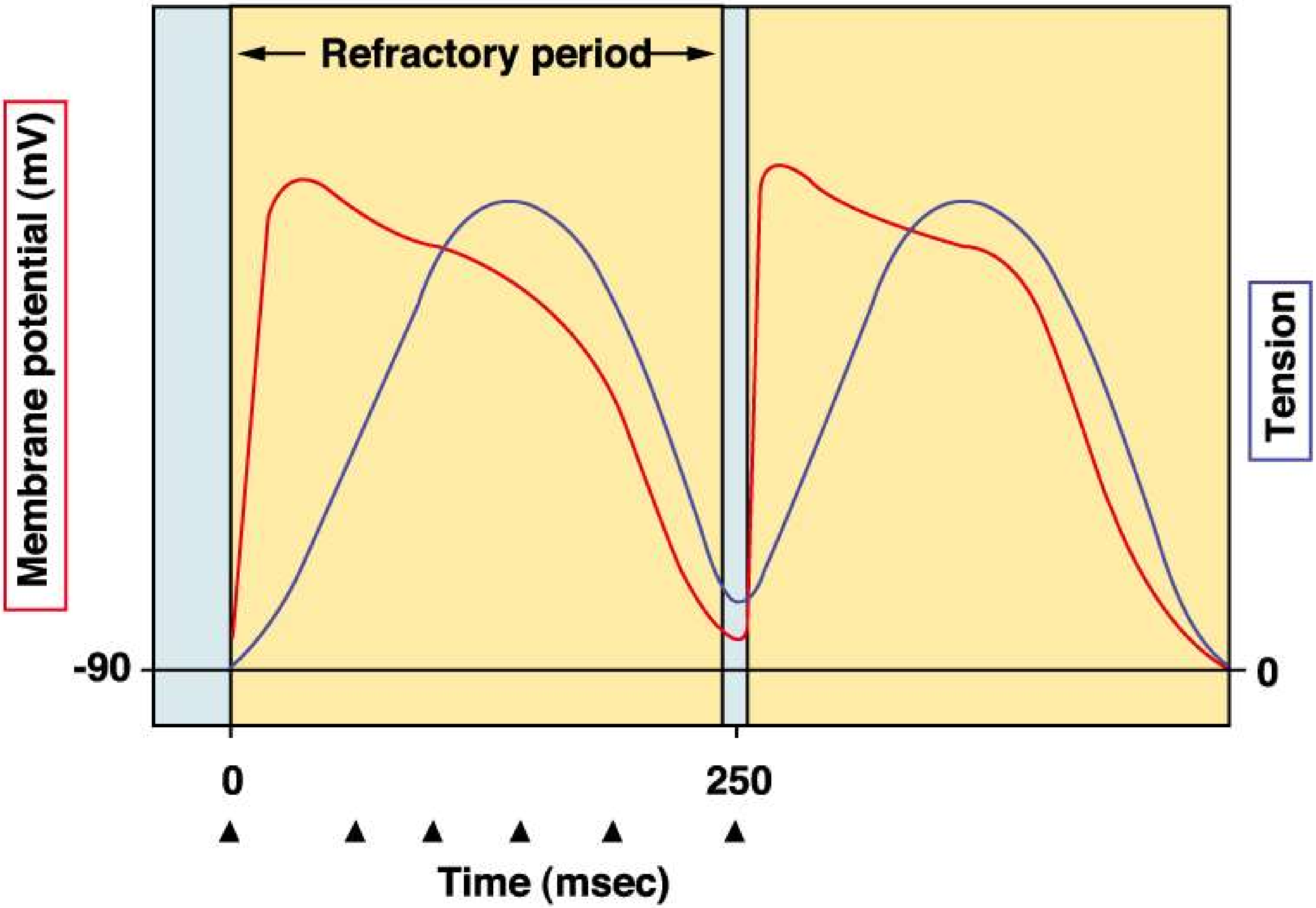
Tetanus in a skeletal muscle.
Action potentials not shown.

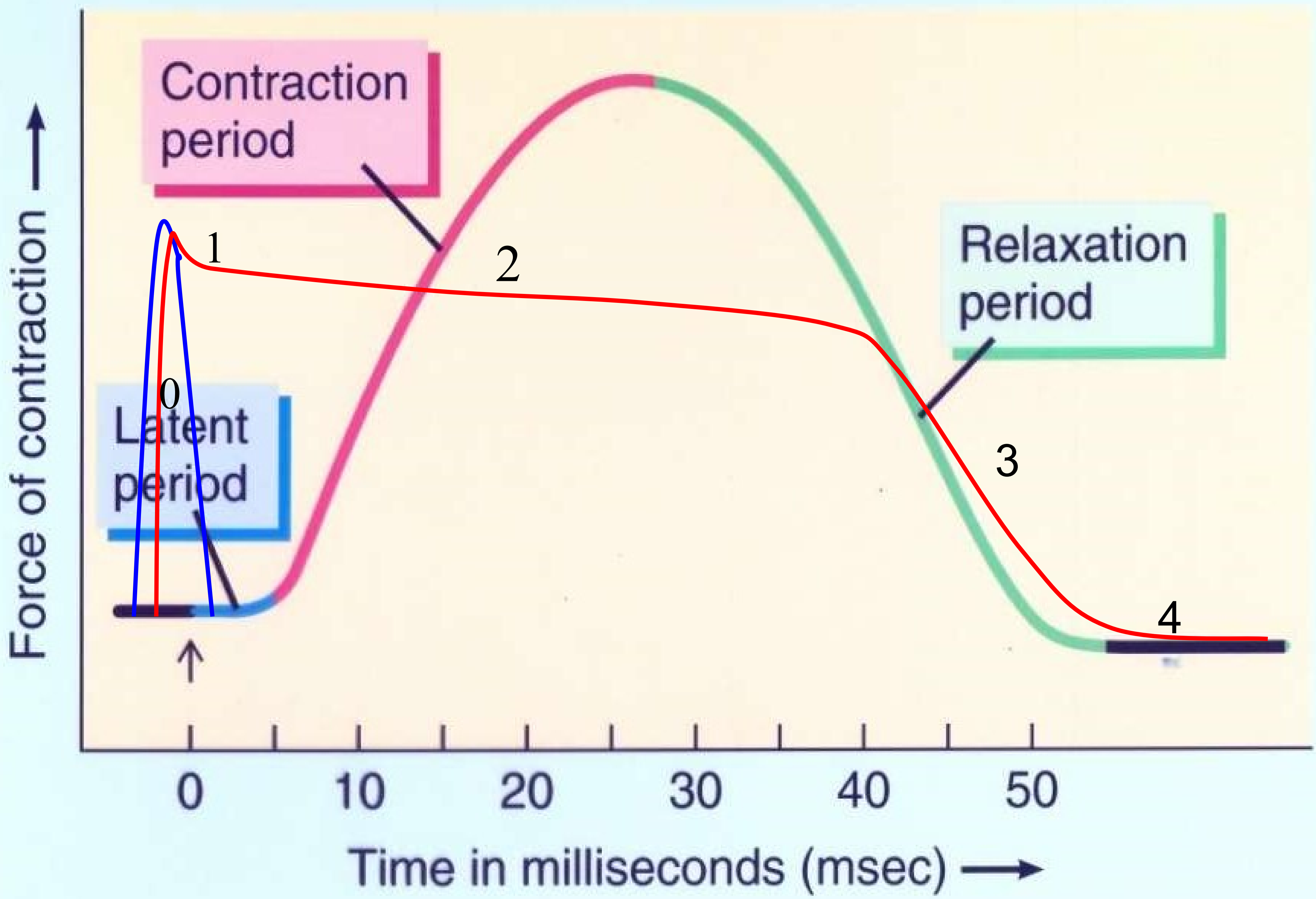


Cardiac muscle fiber



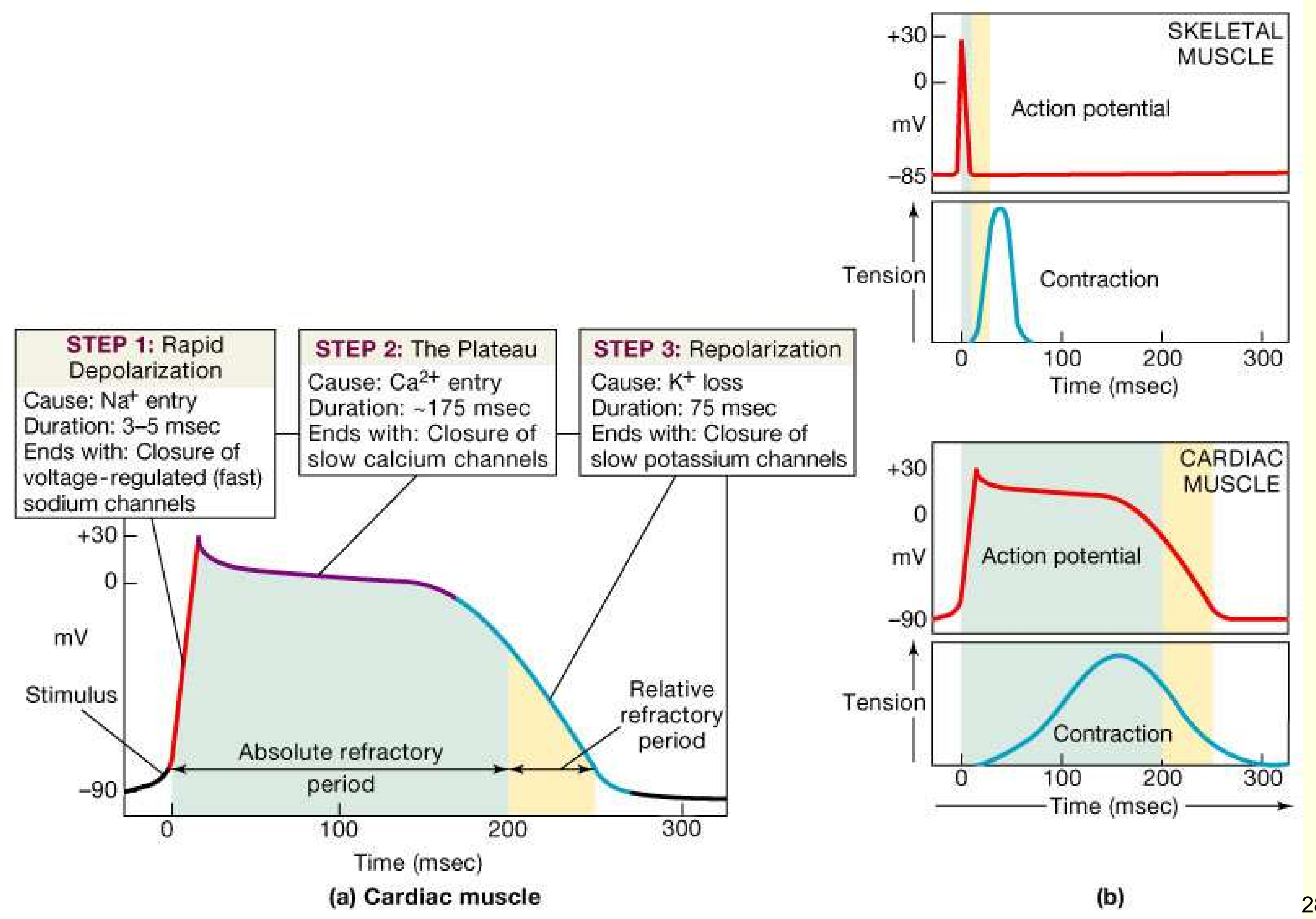
Long refractory period in a cardiac muscle prevents tetanus.

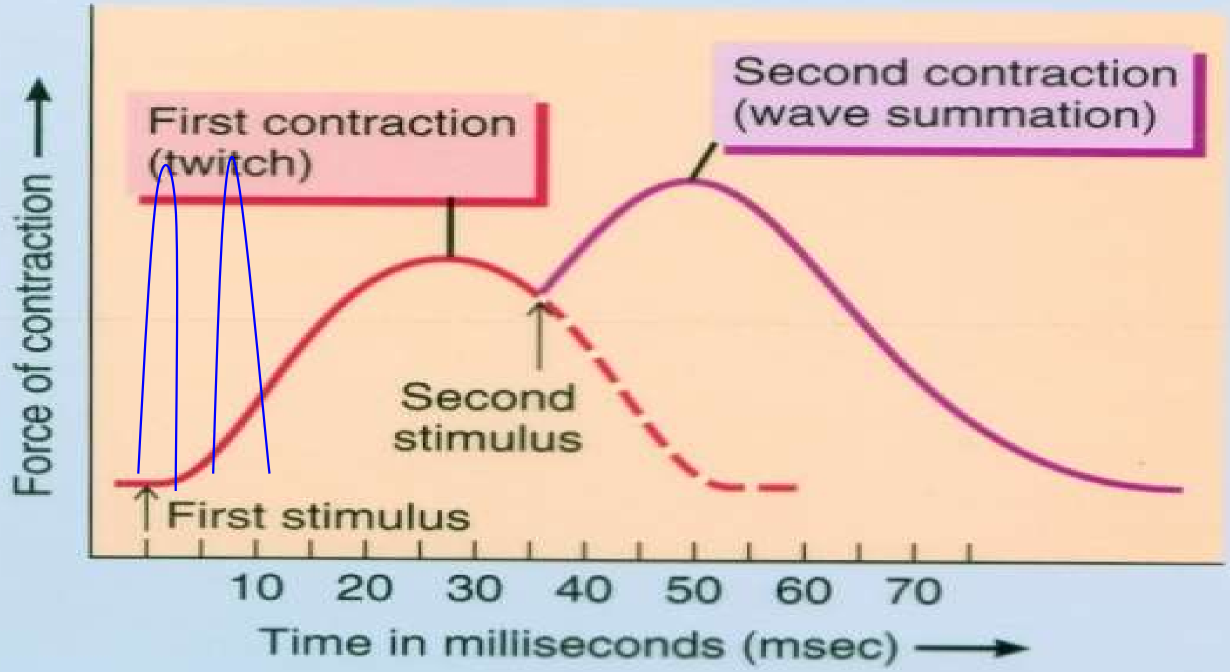




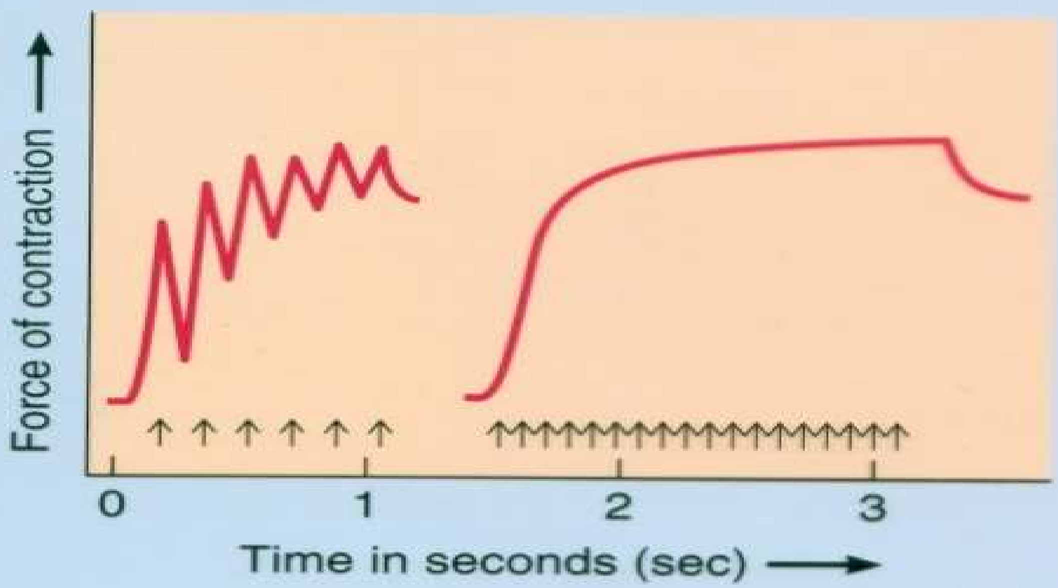
Contraction period
Relaxation period
Latent period
Force of contraction
Time in milliseconds (msec)
0
10
20
30
40
50
0
1
2
3
4

The Action Potential in Skeletal and Cardiac Muscle



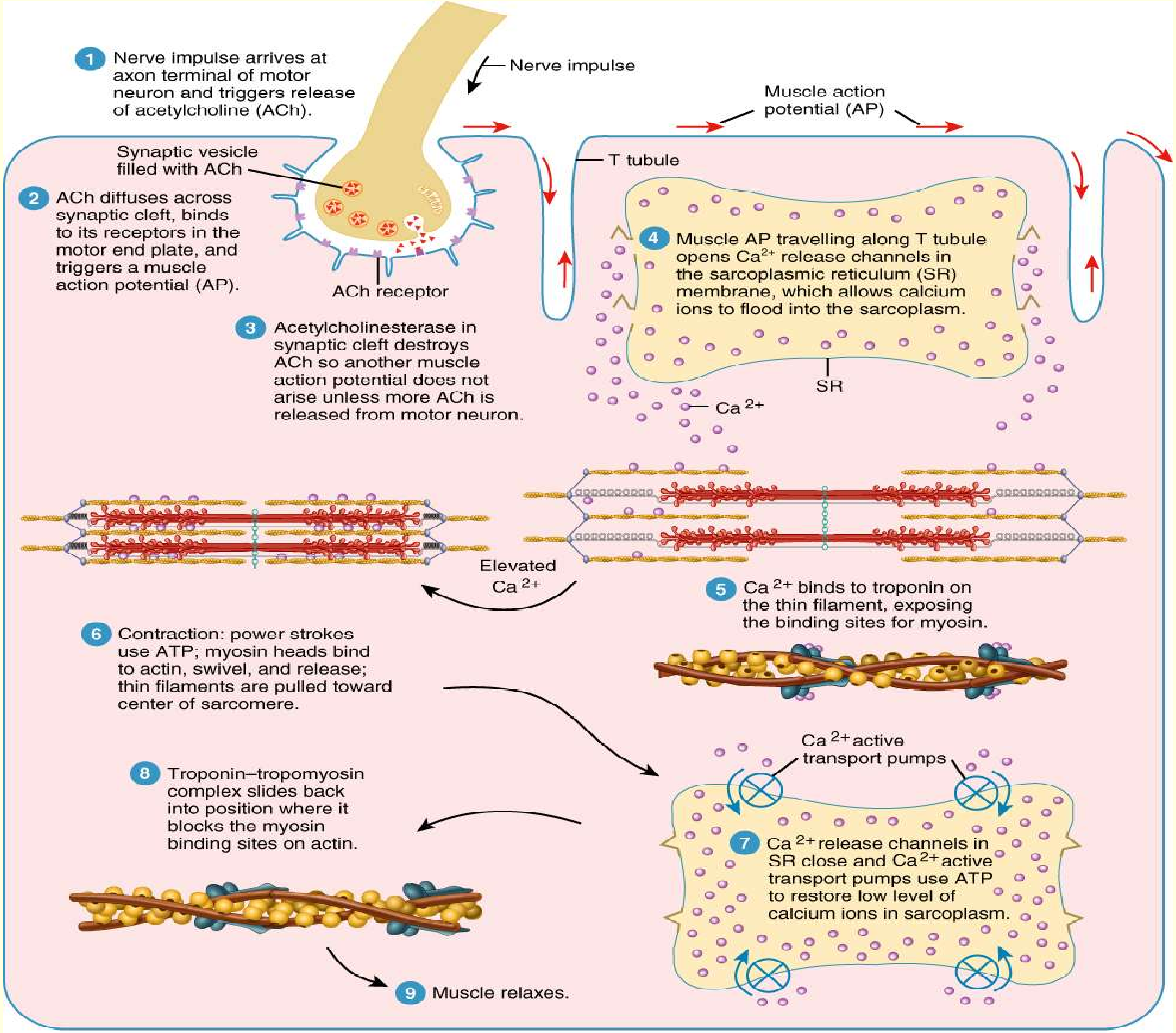


(a) Wave summation



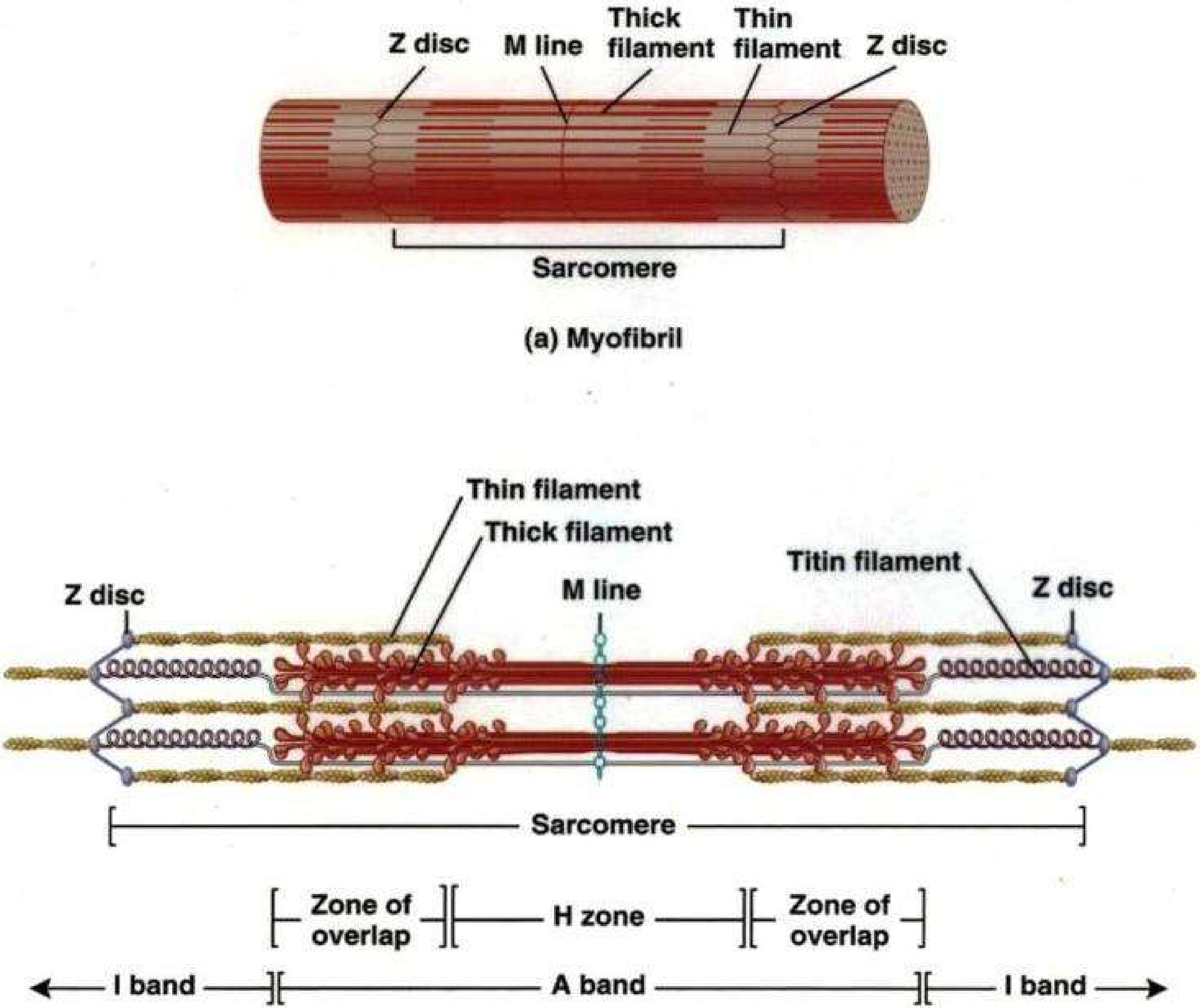
(b) Incomplete tetanus

(c) Complete tetanus



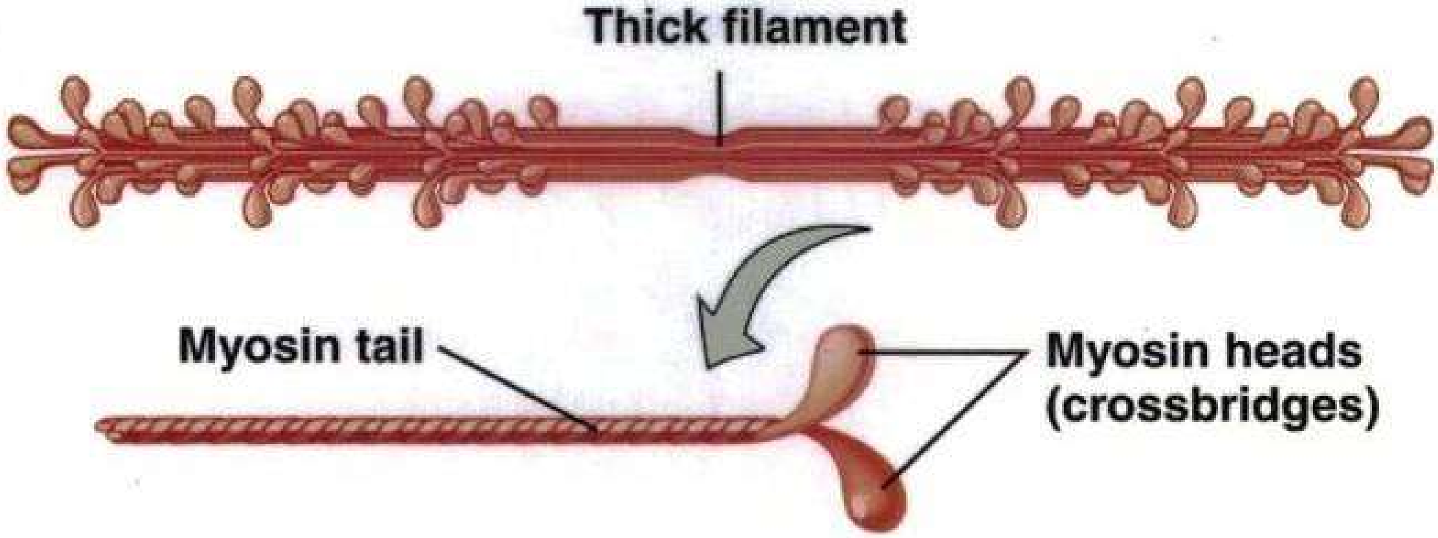
1 Nerve impulse arrives at axon terminal of motor neuron and triggers release of acetylcholine (ACh).
Nerve impulse
Muscle action potential (AP)
Synaptic vesicle filled with ACh
2 ACh diffuses across synaptic cleft, binds to its receptors in the motor end plate, and triggers a muscle action potential (AP).
ACh receptor
T tubule
4 Muscle AP travelling along T tubule opens Ca2+ release channels in the sarcoplasmic reticulum (SR) membrane, which allows calcium ions to flood into the sarcoplasm.
3 Acetylcholinesterase in synaptic cleft destroys ACh so another muscle action potential does not arise unless more ACh is released from motor neuron.
SR
Ca 2+
Elevated Ca 2+
5 Ca 2+ binds to troponin on the thin filament, exposing the binding sites for myosin.
6 Contraction: power strokes use ATP; myosin heads bind to actin, swivel, and release; thin filaments are pulled toward center of sarcomere.
Ca 2+ active transport pumps
8 Troponin–tropomyosin complex slides back into position where it blocks the myosin binding sites on actin.
7 Ca 2+ release channels in SR close and Ca 2+ active transport pumps use ATP to restore low level of calcium ions in sarcoplasm.
9 Muscle relaxes.

10.12

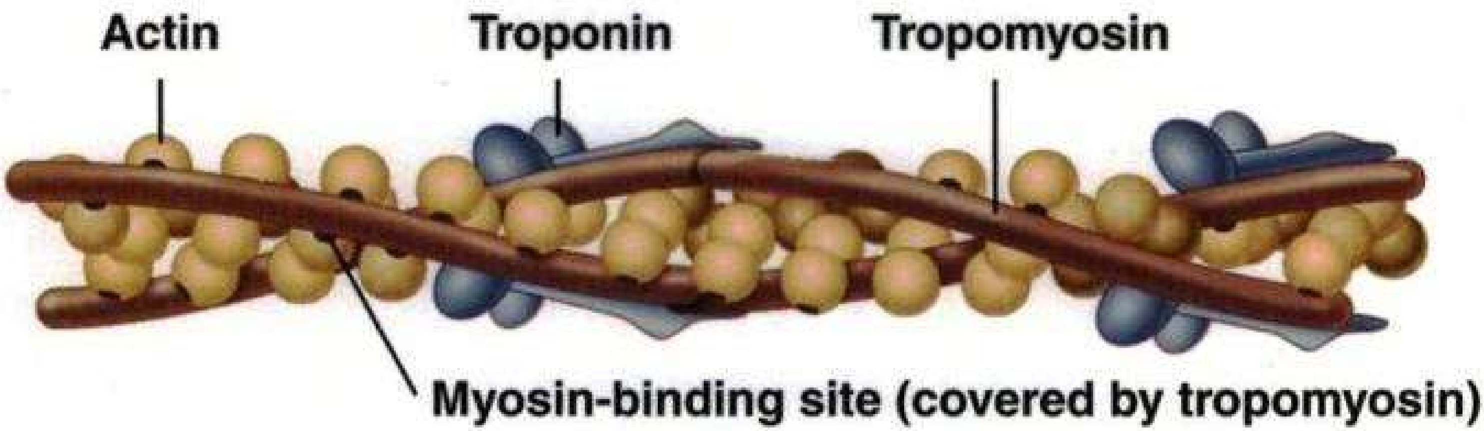


(a) Myofibril

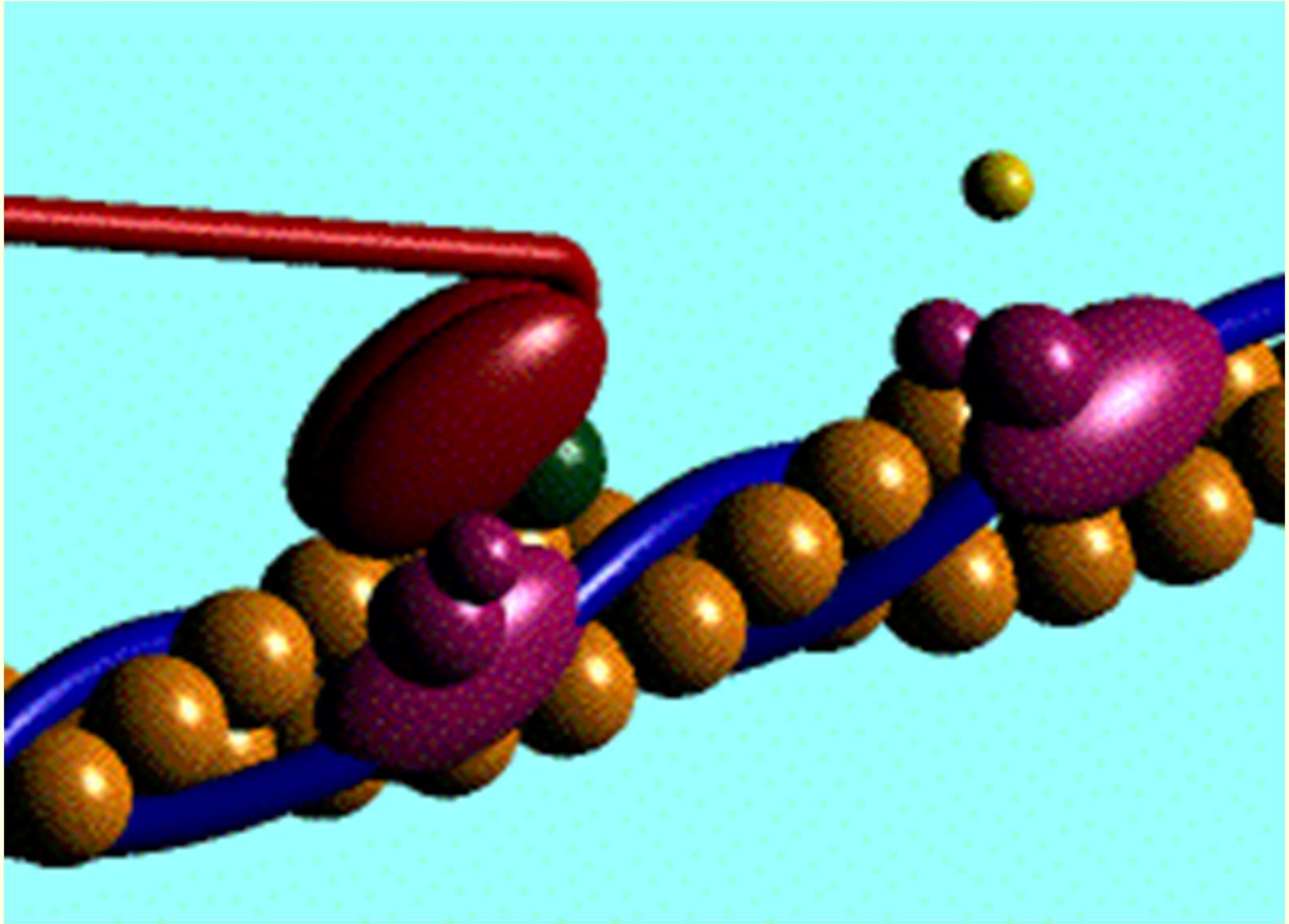
(b) Filaments

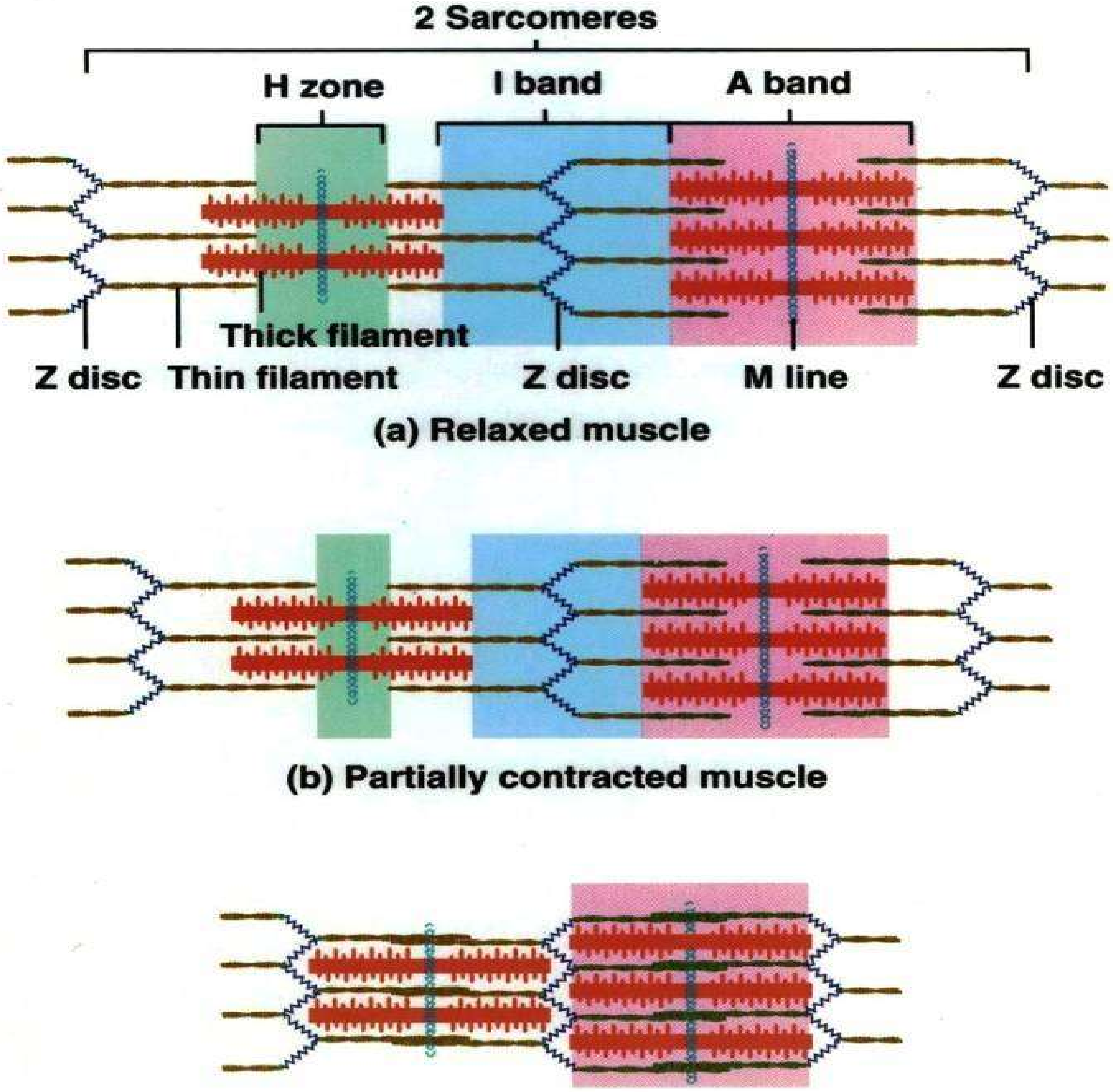


(a) One thick filament (above) and a myosin molecule (below)



(b) Portion of a thin filament

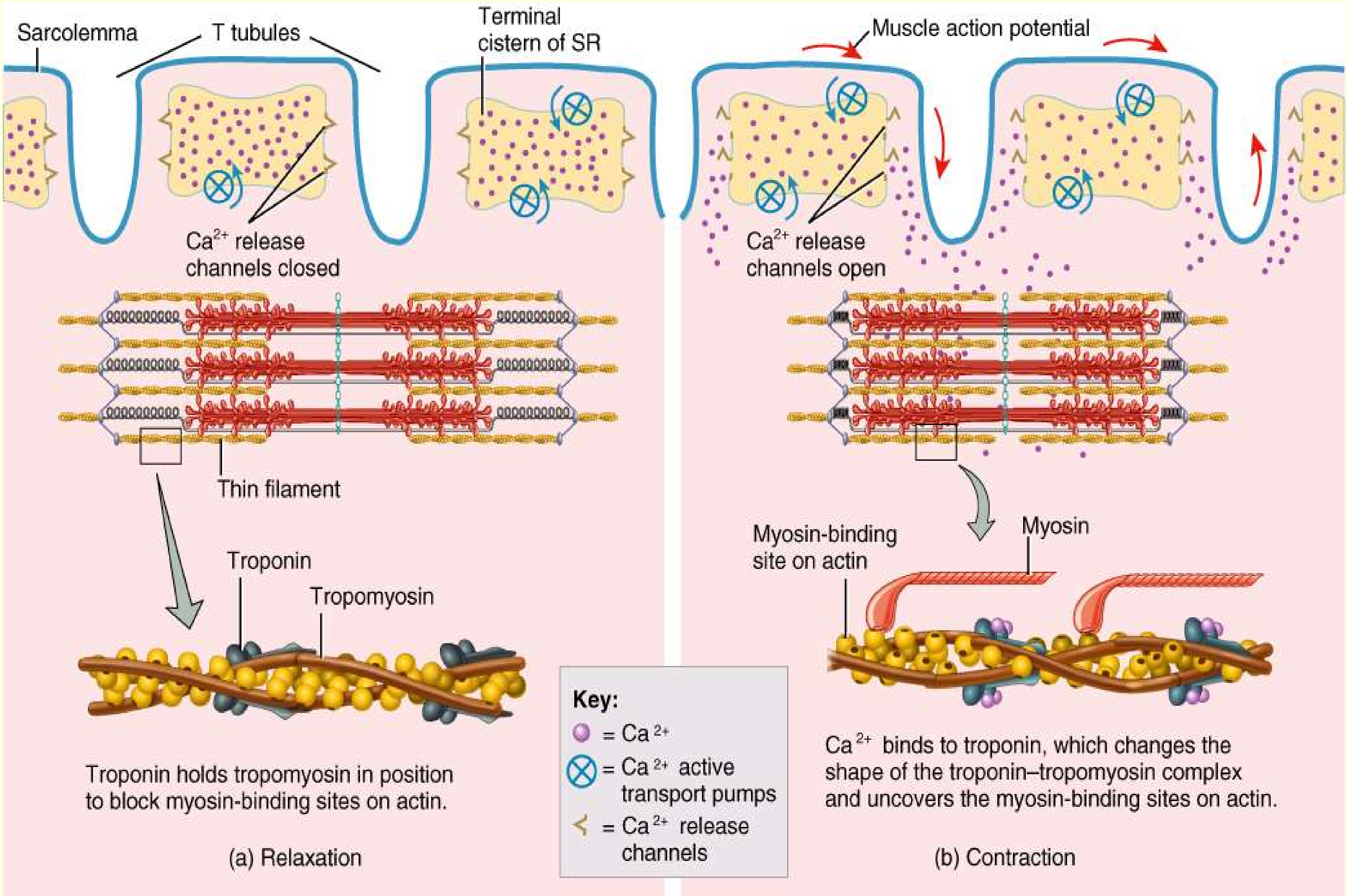




(a) Relaxed muscle

(b) Partially contracted muscle

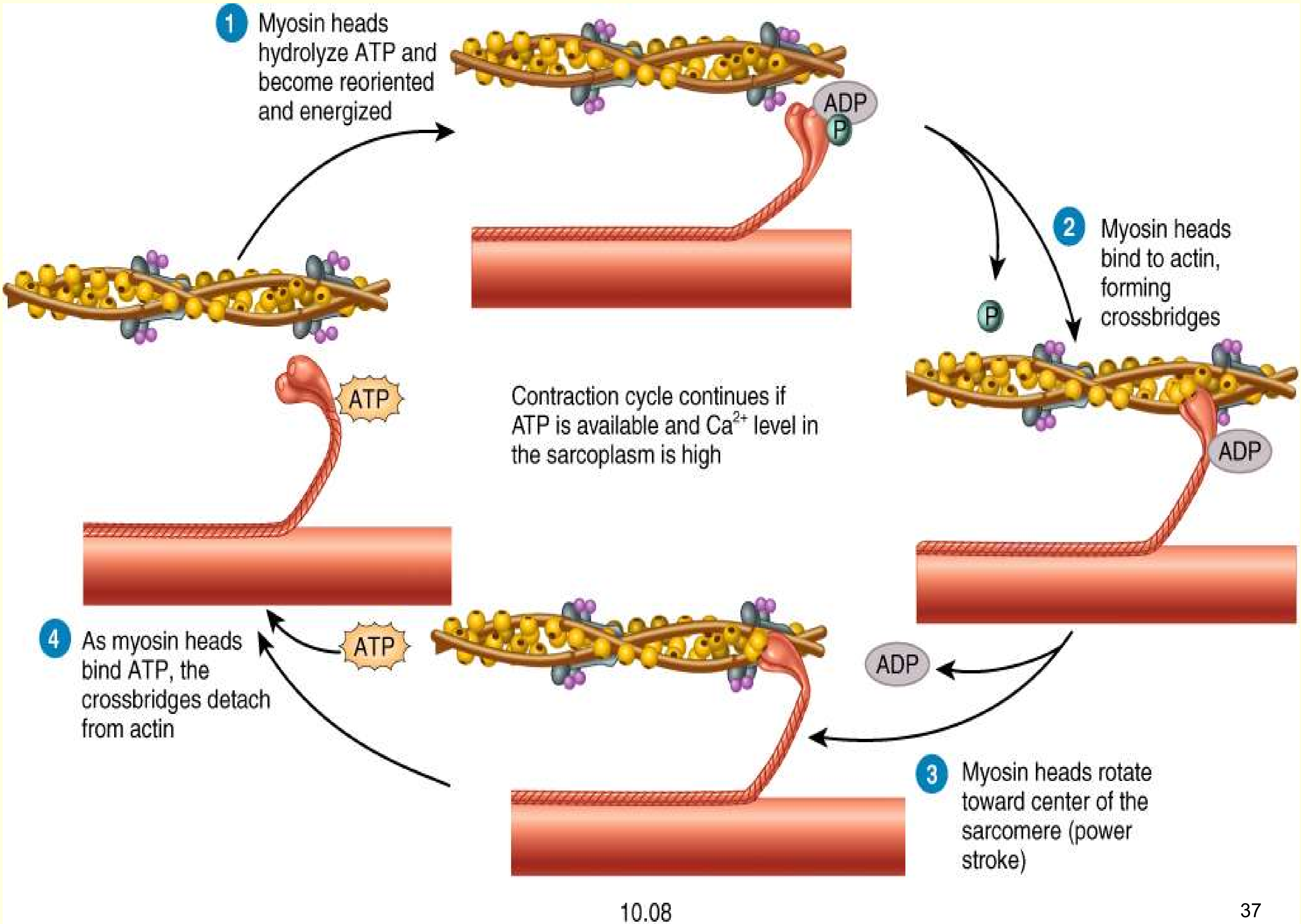
(c) Maximally contracted muscle

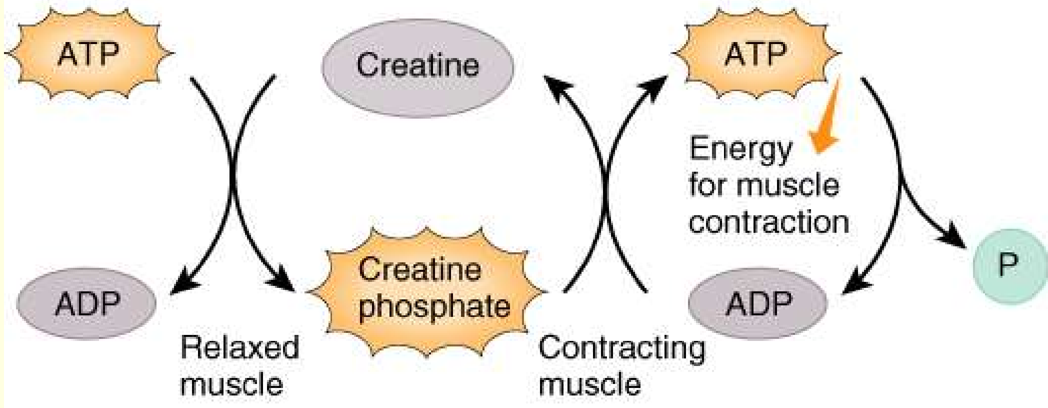

Sarcolemma
T tubules
Terminal cistern of SR
Muscle action potential
Ca^{2+} release channels closed
Ca^{2+} release channels open
Thin filament
Troponin
Tropomyosin
Myosin-binding site on actin
Myosin
Troponin holds tropomyosin in position to block myosin-binding sites on actin.
Ca^{2+} binds to troponin, which changes the shape of the troponin–tropomyosin complex and uncovers the myosin-binding sites on actin.
(a) Relaxation
(b) Contraction
Key:
= Ca^{2+}
= Ca^{2+} active transport pumps
= Ca^{2+} release channels

10.09

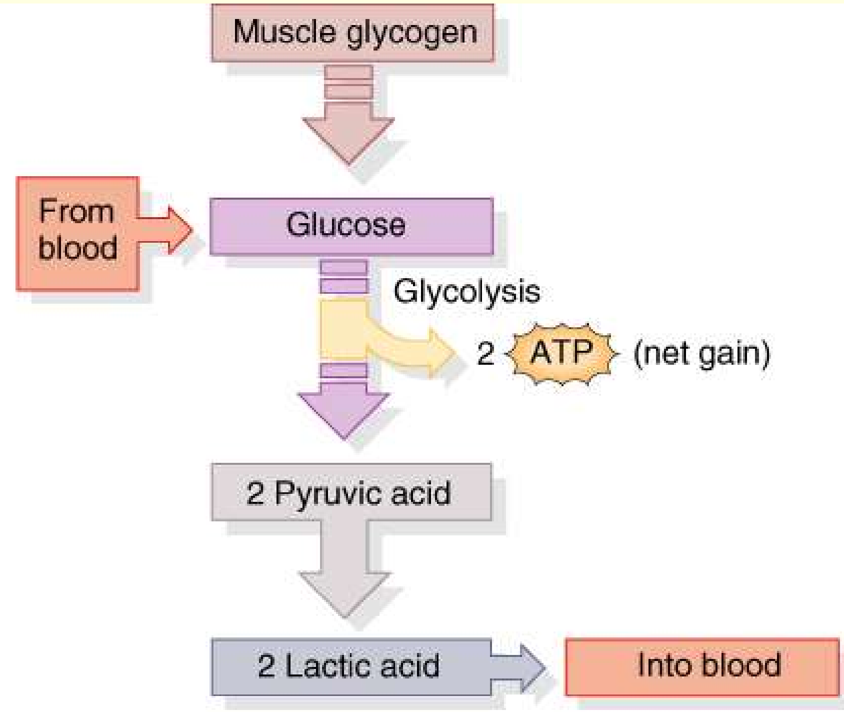
Cardiac Muscle contraction Vs. Skeletal Muscle

- Sliding filament hypothesis
- No tetany (Long refractory period because of plateau)
- Fatty acids main source of energy unlike skeletal muscle (Anaerobic and Aerobic)
- Attachment and detachment cycle and ATP dependence is the same

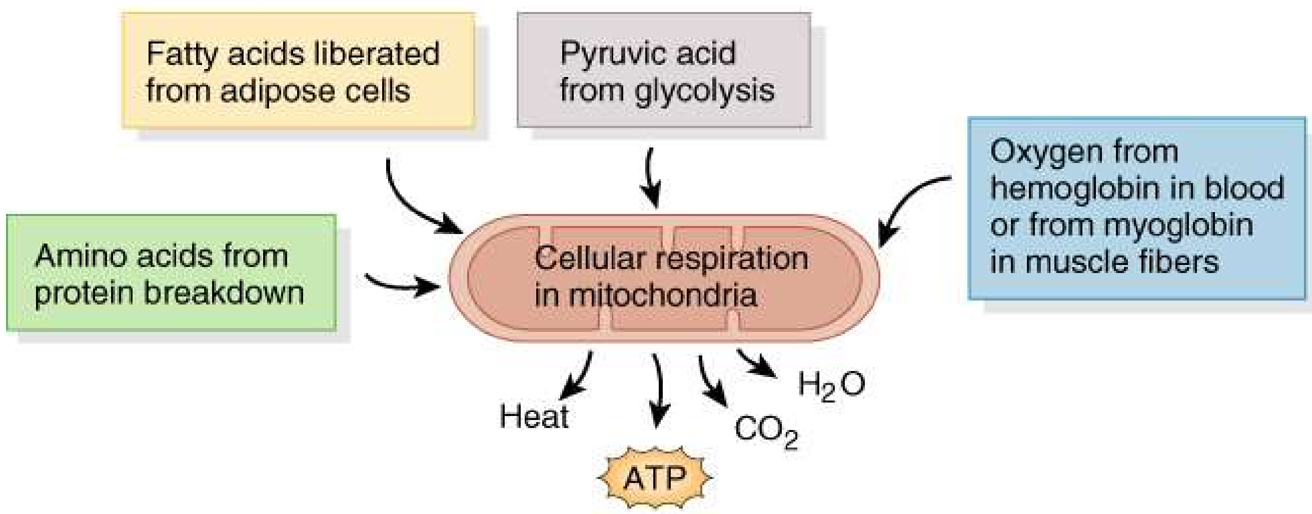

1 Myosin heads hydrolyze ATP and become reoriented and energized
ADP
P
2 Myosin heads bind to actin, forming crossbridges
P
ADP
ATP
Contraction cycle continues if ATP is available and Ca2+ level in the sarcoplasm is high
ADP
3 Myosin heads rotate toward center of the sarcomere (power stroke)
ATP
4 As myosin heads bind ATP, the crossbridges detach from actin
10.08



(a) ATP from creatine phosphate



(b) ATP from anaerobic respiration

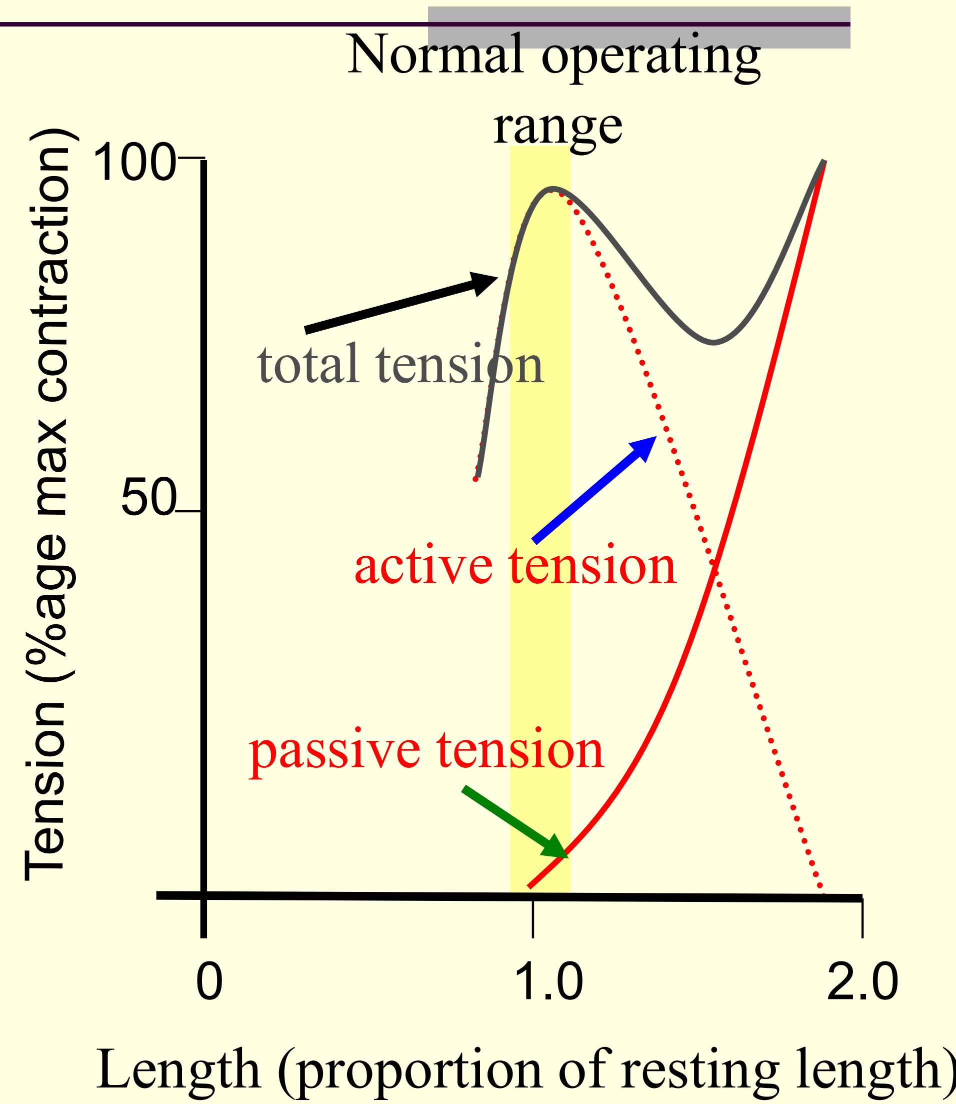


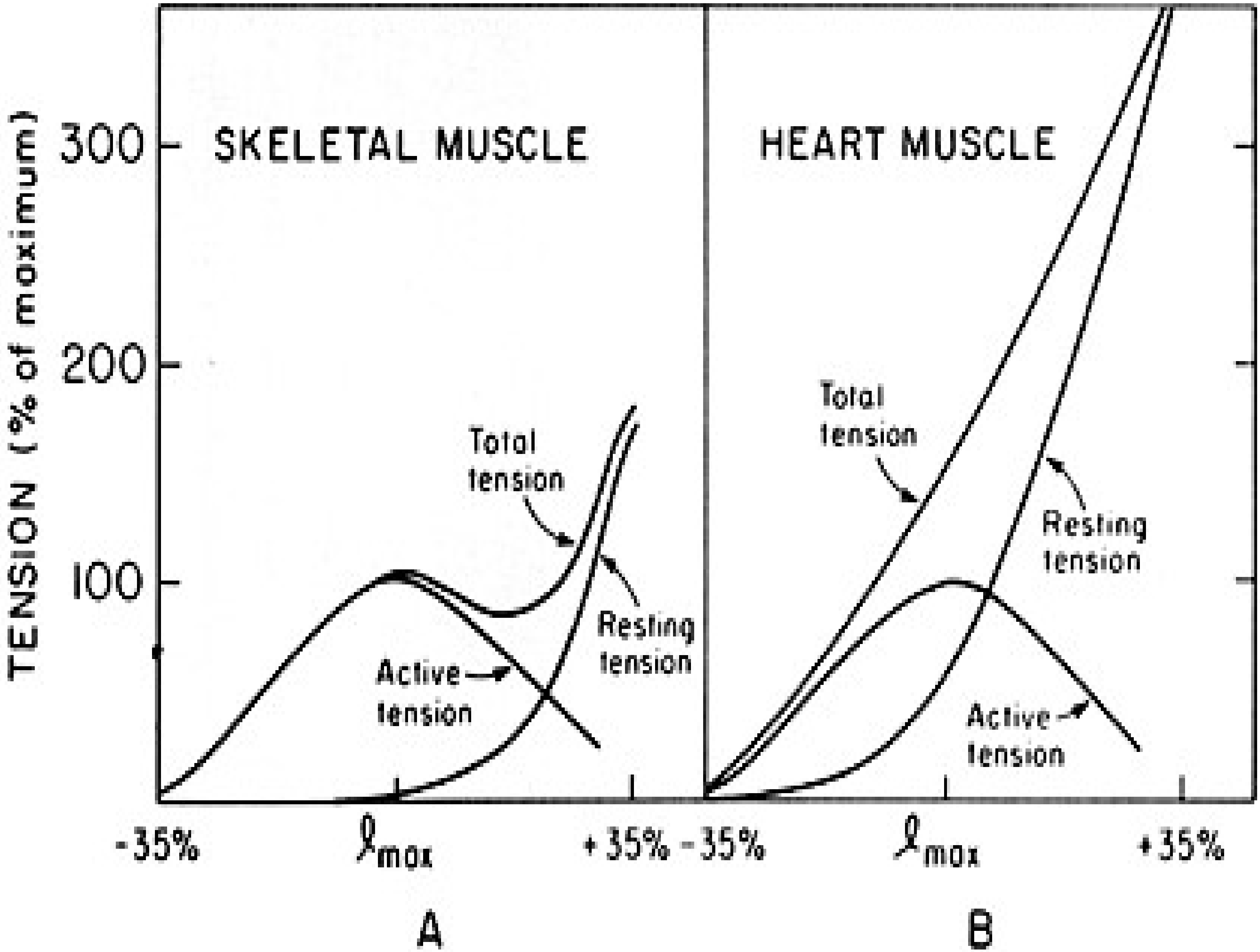
(c) ATP from aerobic cellular respiration

10.13

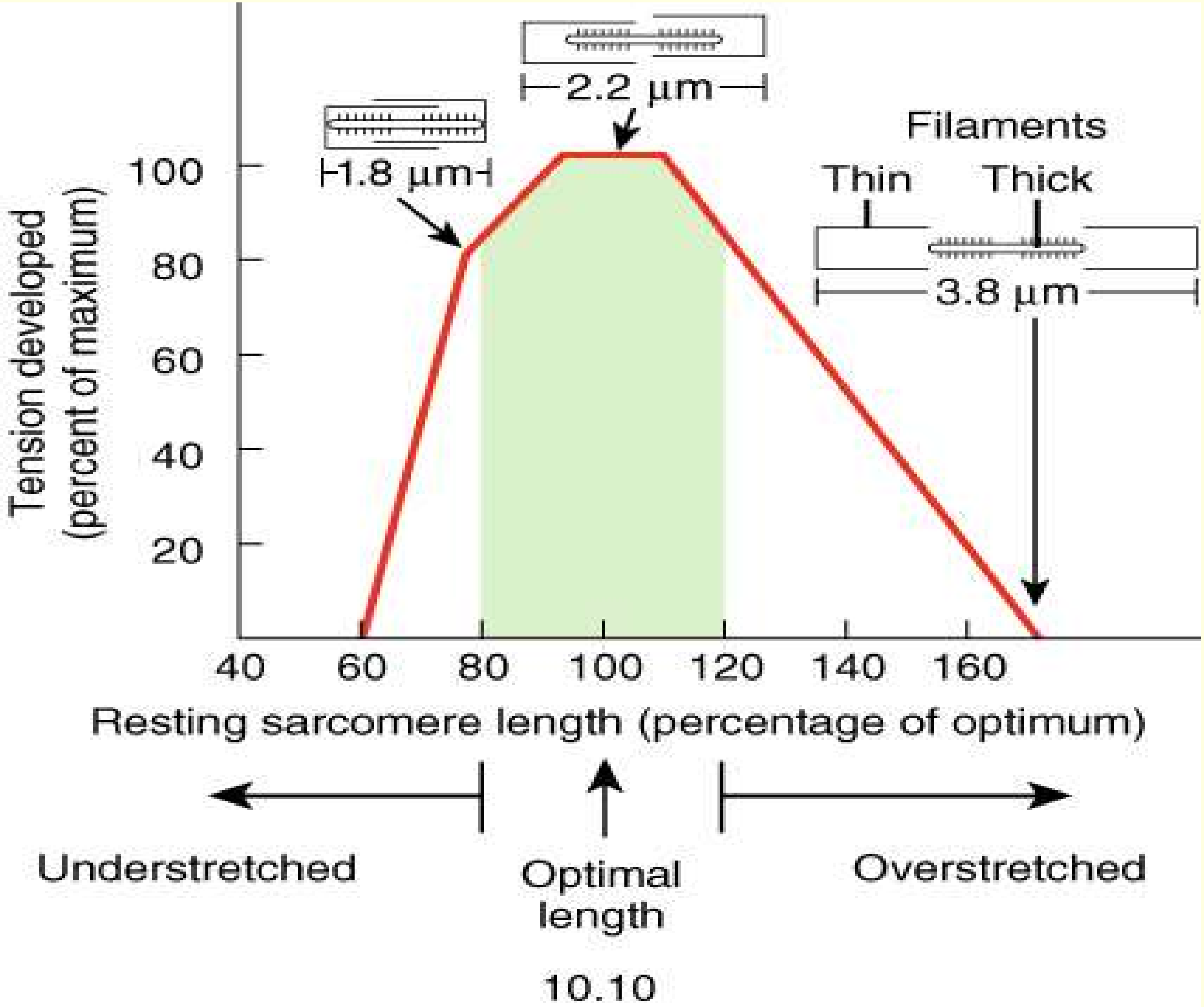
Length-Tension Relation for Skeletal Muscle

- Active tension cannot be measured directly
- What can be measured?
  - (1) passive tension - *tension required to extend a resting muscle*
  - (2) total tension - *active tension and passive combined*
- Active is calculated from 1 & 2
- (AT = TT – PT)
- Note that active tension falls away linearly with increasing length



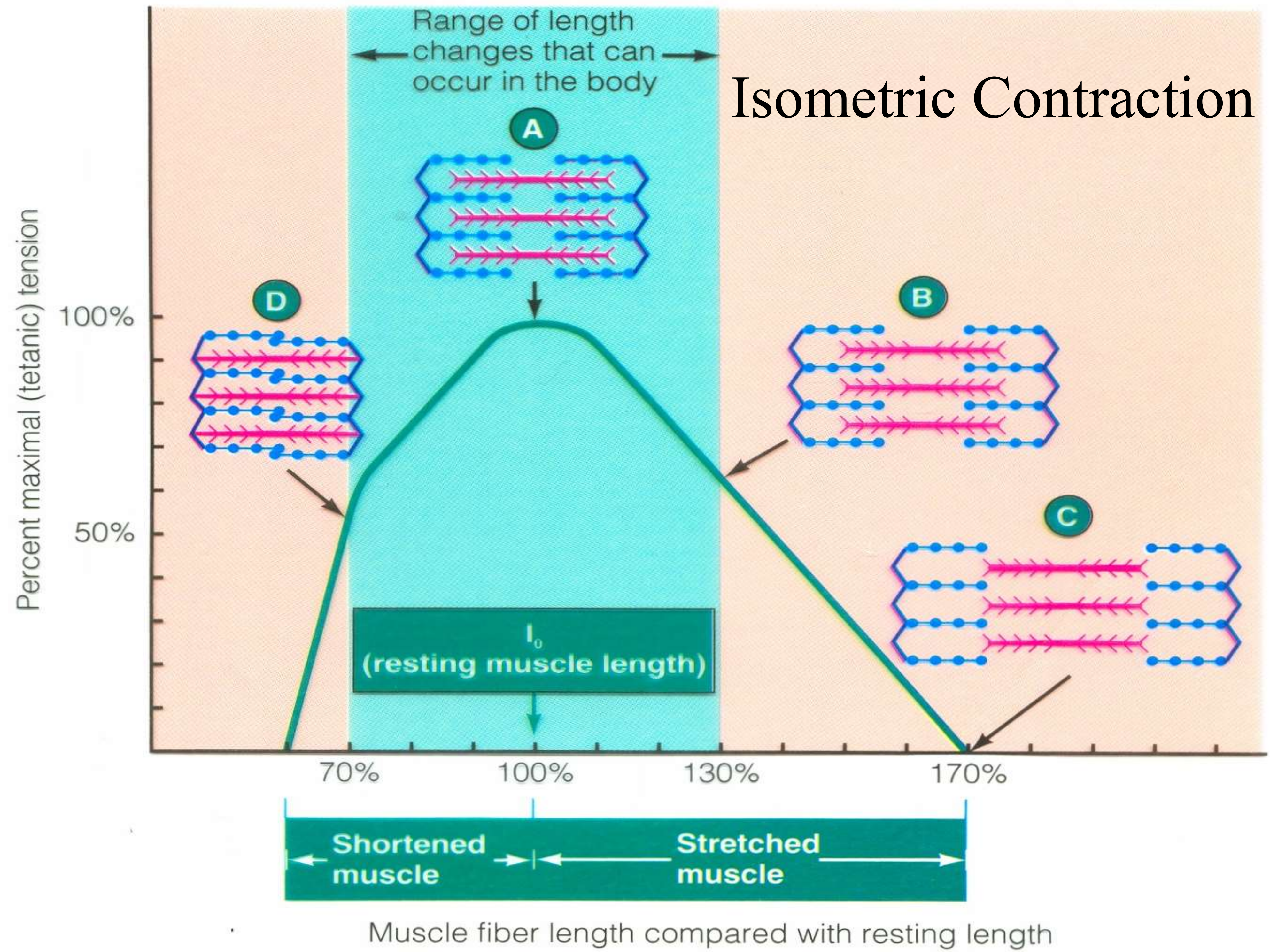


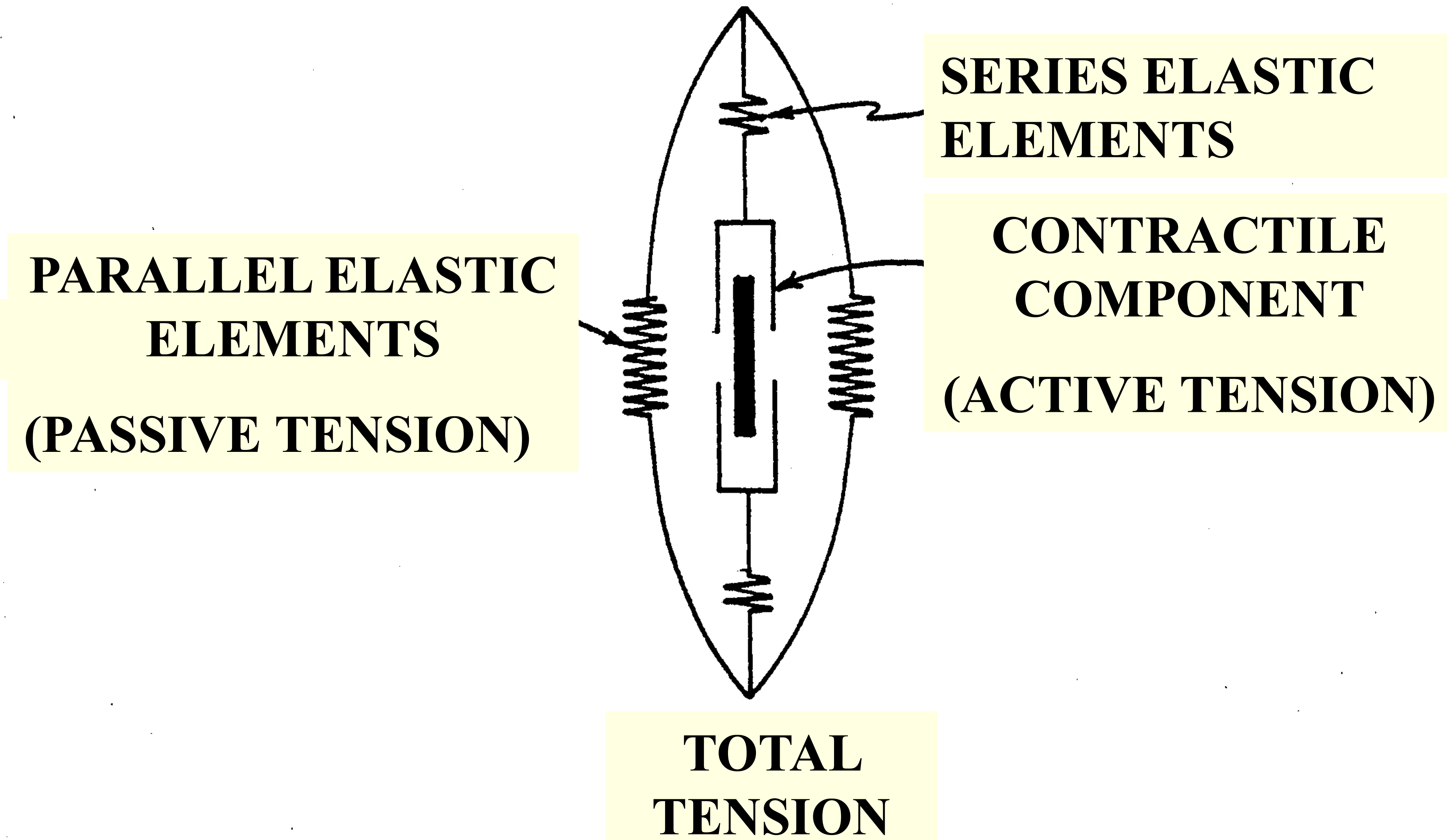
TENSION (% of maximum)
300
200
100
SKELETAL MUSCLE
HEART MUSCLE
Total tension
Resting tension
Active tension
Total tension
Resting tension
Active tension
-35%
l_{max}
+35%
-35%
l_{max}
+35%
A
B



2.2 µm
1.8 µm
Filaments
Thin
Thick
3.8 µm
Tension developed (percent of maximum)
100
80
60
40
20
40
60
80
100
120
140
160
Resting sarcomere length (percentage of optimum)
Understretched
Optimal length
Overstretched
10.10

Isometric Contraction

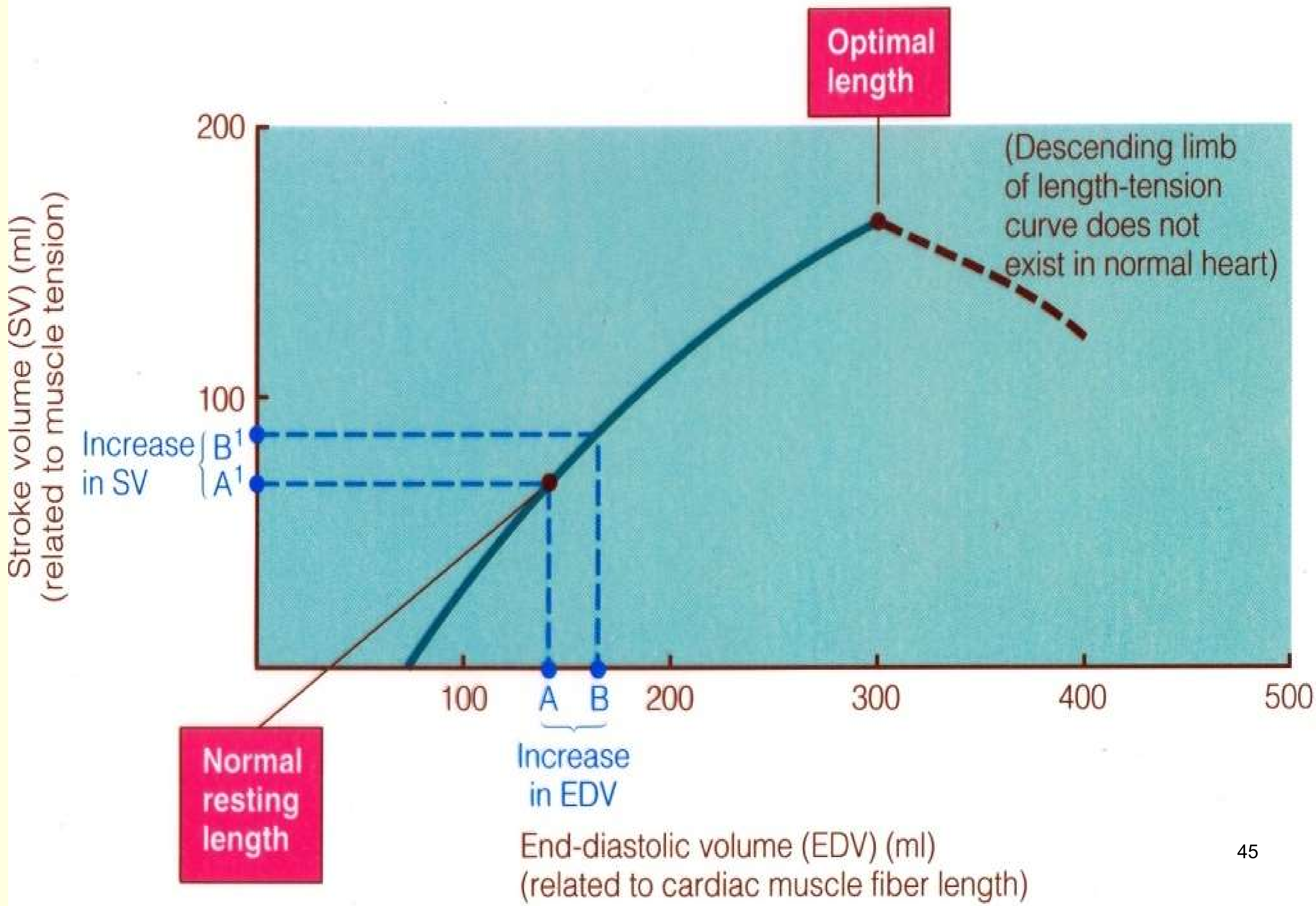



SERIES ELASTIC ELEMENTS
CONTRACTILE COMPONENT
(ACTIVE TENSION)
PARALLEL ELASTIC ELEMENTS
(PASSIVE TENSION)
TOTAL TENSION

Cardiac Muscle length-tension relationship

- Cardiac muscle works at much less than its maximum length in contrast to skeletal
- Total, Active and Passive length-tension relationship differ
- Frank-Starling law of the heart

Intrinsic Control of Stroke Volume (Frank-Starling Curve)



Thank You