Cardiovascular Physiology

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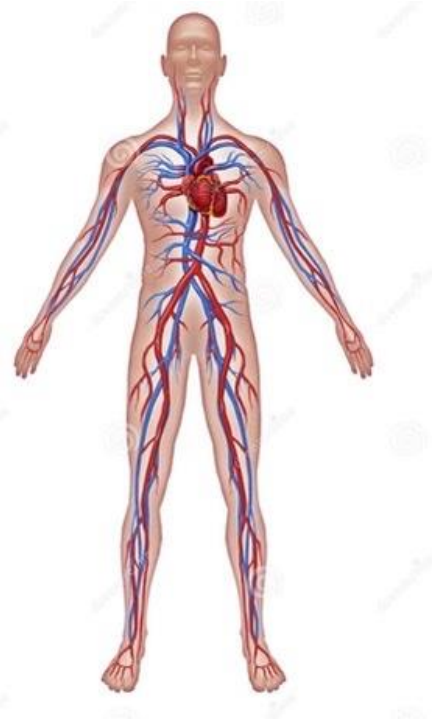

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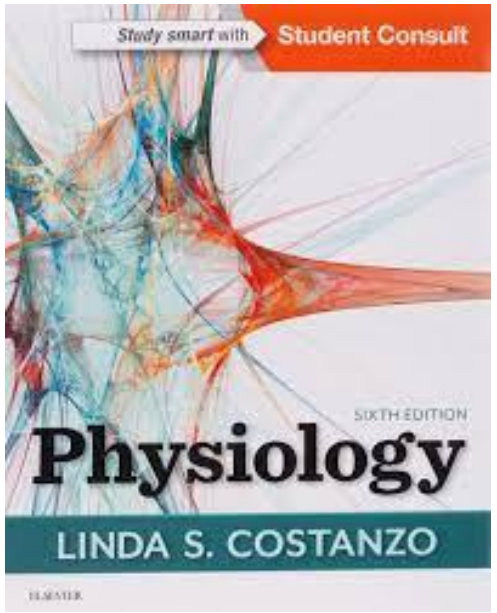
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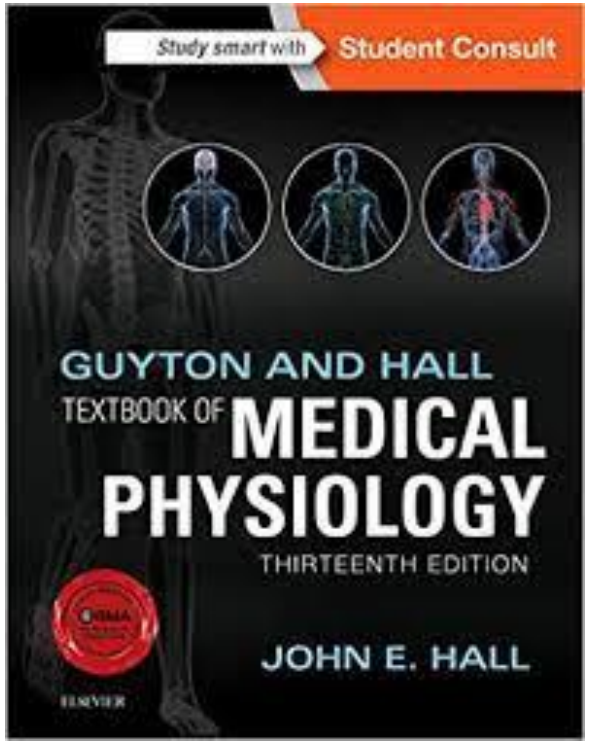
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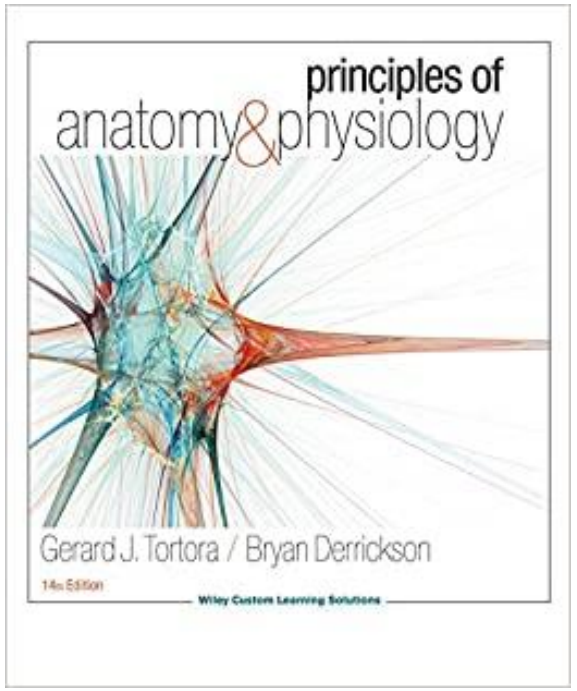
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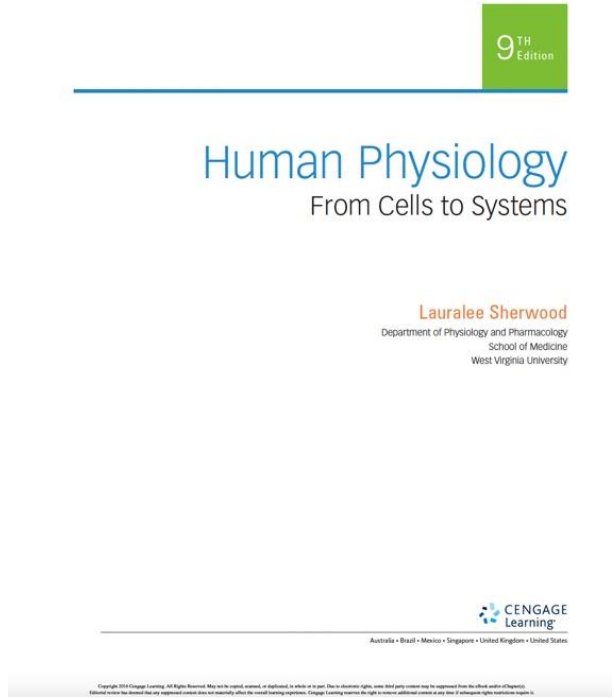
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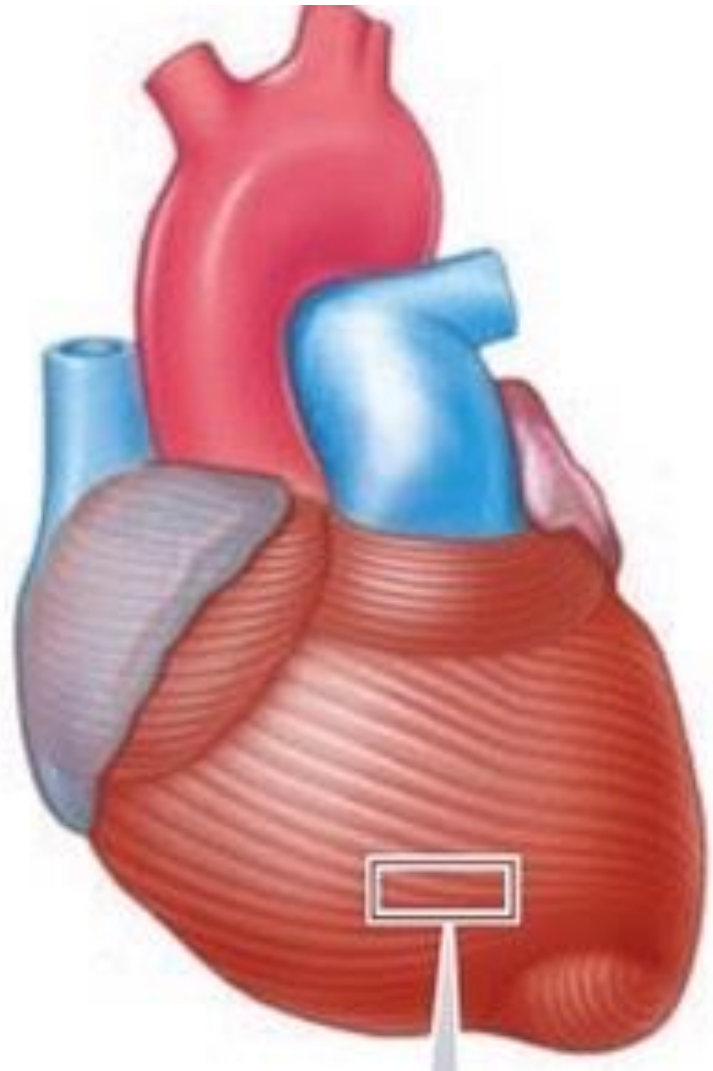
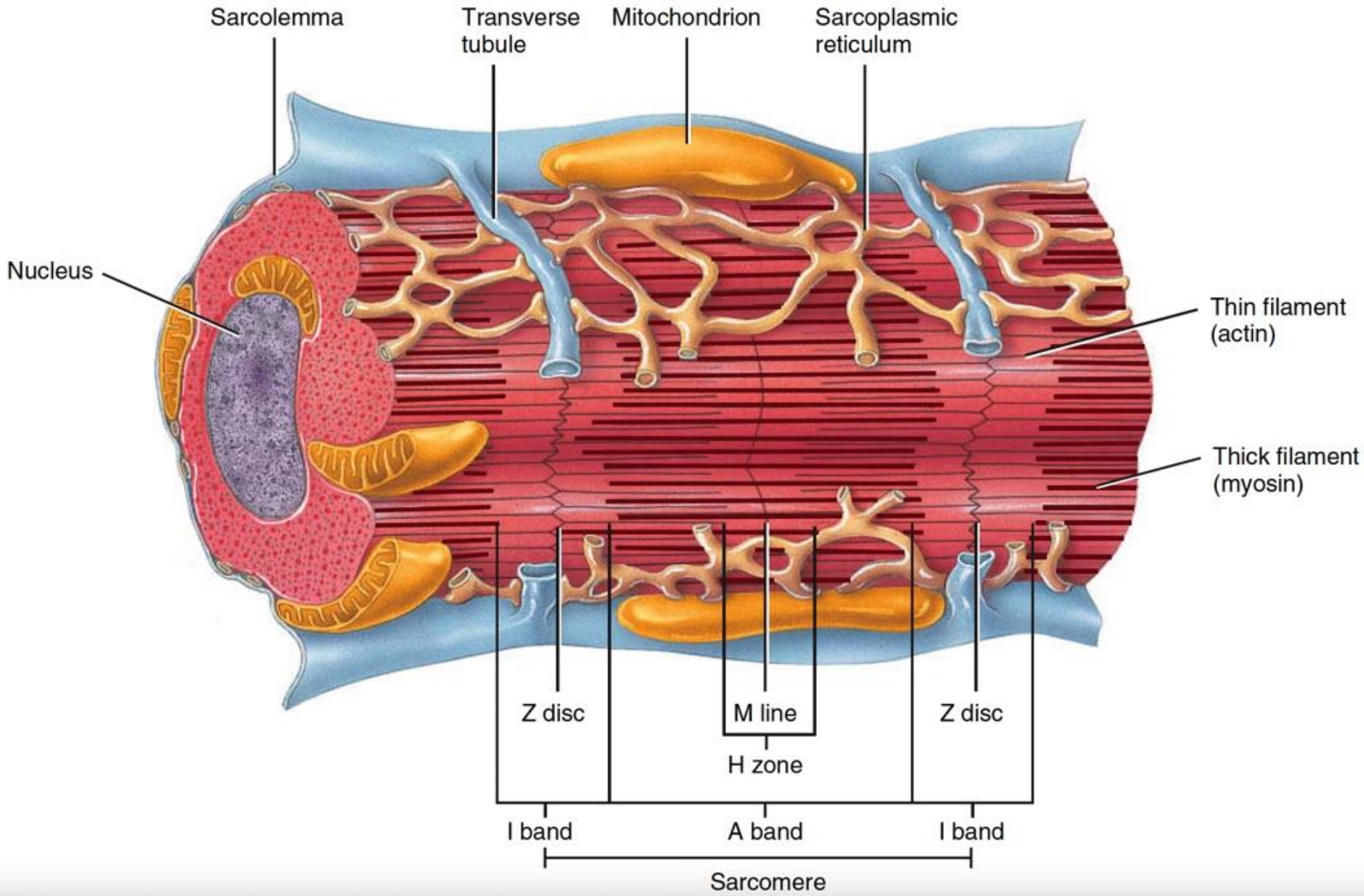
Cardiac muscle




Sarcolemma
Transverse tubule
Mitochondrion
Sarcoplasmic reticulum
Nucleus
Thin filament (actin)
Thick filament (myosin)
Z disc
M line
Z disc
H zone
I band
A band
I band
Sarcomere

T-tubules

- The transverse tubules of cardiac muscle are wider but less abundant than those of skeletal muscle; the one transverse tubule per sarcomere is located at the Z disc.

SR

- The sarcoplasmic reticulum of cardiac muscle fibers is less well developed than the SR of skeletal muscle fibers.
- As a result, cardiac muscle has a smaller intracellular reserve of Ca+.

Mitochondria

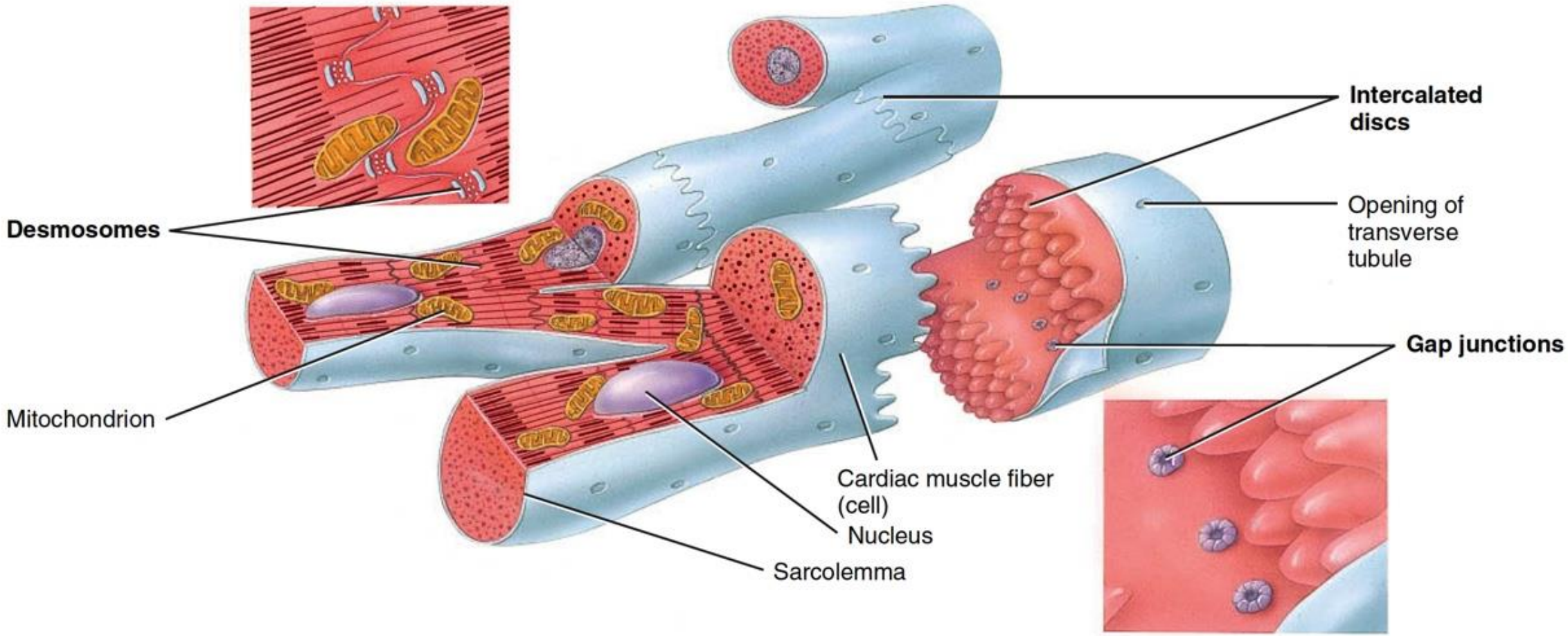
- Mitochondria are larger and more numerous in cardiac muscle fibers than in skeletal muscle fibers.

ATP Production

- In contrast to skeletal muscle, cardiac muscle produces little of the ATP it needs by anaerobic cellular respiration.
- Instead, it relies almost exclusively on aerobic cellular respiration in its numerous mitochondria.
- The needed oxygen diffuses from blood in the coronary circulation and is released from myoglobin inside cardiac muscle fibers.

ATP Production

- Cardiac muscle fibers use several fuels to power mitochondrial ATP production.
- In a person at rest, the heart's ATP comes mainly from oxidation of fatty acids (60%) and glucose (35%), with smaller contributions from lactic acid, amino acids, and ketone bodies.
- During exercise, the heart's use of lactic acid, produced by actively contracting skeletal muscles, rises.
- Like skeletal muscle, cardiac muscle also produces some ATP from creatine phosphate.



(a) Cardiac muscle fibers

Intercalated disc

- The discs contain desmosomes and gap junctions.
- Desmosomes are specialized adhesive protein complexes that localize to intercellular junctions and are responsible for maintaining the mechanical integrity of tissues.
- At each intercalated disc, the cell membranes fuse with one another to form permeable communicating junctions (gap junctions) that allow rapid diffusion of ions.

Syncytium

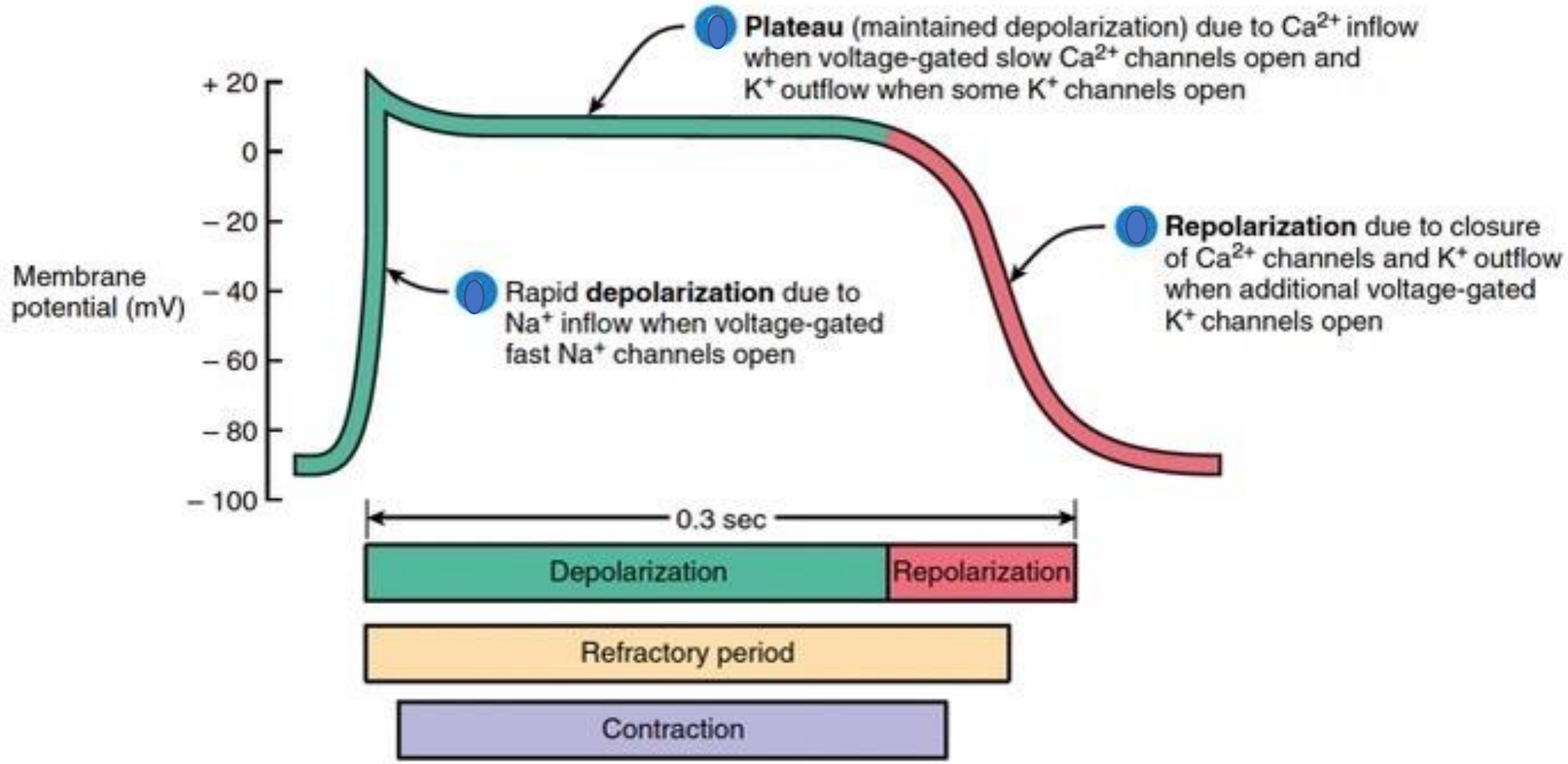
- The heart actually is composed of two syncytia; the atrial syncytium and the ventricular syncytium.
- The atria are separated from the ventricles by fibrous tissue that surrounds the A-V valvular openings between the atria and ventricles.
- Normally, potentials are not conducted from the atrial syncytium into the ventricular syncytium directly through this fibrous tissue. Instead, they are only conducted by the A-V bundle.

Syncytium

- This division of the muscle of the heart into two functional syncytia allows the atria to contract a short time ahead of ventricular contraction, which is important for the effectiveness of heart pumping.

- No gap junctions between atria and ventricles.

Action potential



Duration of contraction

- Cardiac muscle begins to contract a few milliseconds after the action potential begins and continues to contract until a few milliseconds after the action potential ends.

- Therefore, the duration of contraction of cardiac muscle is mainly a function of the duration of the action potential, including the plateau.

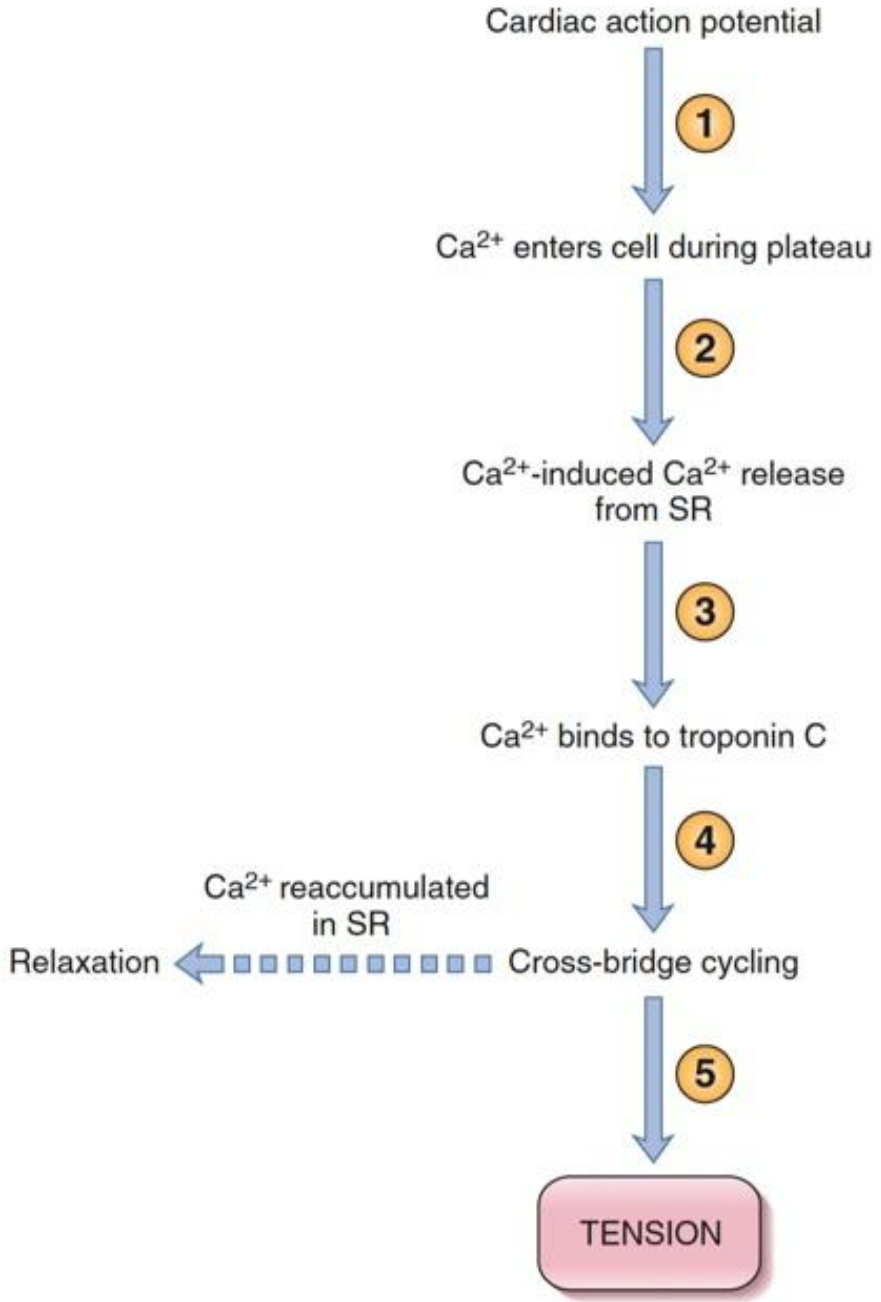
Refractory period

- The period during which a normal cardiac impulse cannot re-excite an already excited area of cardiac muscle.
- The normal refractory period of the ventricle is 0.25 to 0.30 second, which is about the duration of the prolonged plateau action potential.
- There is an additional relative refractory period of about 0.05 second during which the muscle is more difficult to excite than normal but can be excited by a very strong excitatory signal (early premature contraction).
- The refractory period of atrial muscle is much shorter; about 0.15 second.

Excitation-contraction coupling

- In addition to the calcium ions that are released into the sarcoplasm from the sarcoplasmic reticulum, calcium ions also diffuse into the sarcoplasm from the T tubules at the time of the action potential, which opens voltage-dependent calcium channels in the membrane of the T tubule.

- Calcium entering the cell then activates calcium release channels (ryanodine receptor channels) in the SR membrane, triggering the release of calcium into the sarcoplasm.


Cardiac action potential
1
Ca^{2+} enters cell during plateau
2
Ca^{2+}-induced Ca^{2+} release from SR
3
Ca^{2+} binds to troponin C
4
Ca^{2+} reaccumulated in SR
Relaxation
Cross-bridge cycling
5
TENSION

Calcium

- Without the Ca+ from ECF, the strength of cardiac muscle contraction would be reduced considerably because the SR of cardiac muscle is less well developed than that of skeletal muscle and does not store enough calcium to provide full contraction.

Calcium

- The T tubules of cardiac muscle have a diameter five times as great as that of the skeletal muscle tubules.

- Also, inside the T tubules is a large quantity of mucopolysaccharides that are electronegatively charged and bind an abundant store of calcium ions, keeping them available for diffusion to the interior of the cardiac muscle fiber when a T tubule action potential appears.

Relaxation

- At the end of the plateau of the cardiac action potential, the influx of calcium ions to the interior of the muscle fiber is suddenly cut off, and calcium ions in the sarcoplasm are rapidly pumped back out of the muscle fibers into the sarcoplasmic reticulum and T tubule–extracellular fluid space.

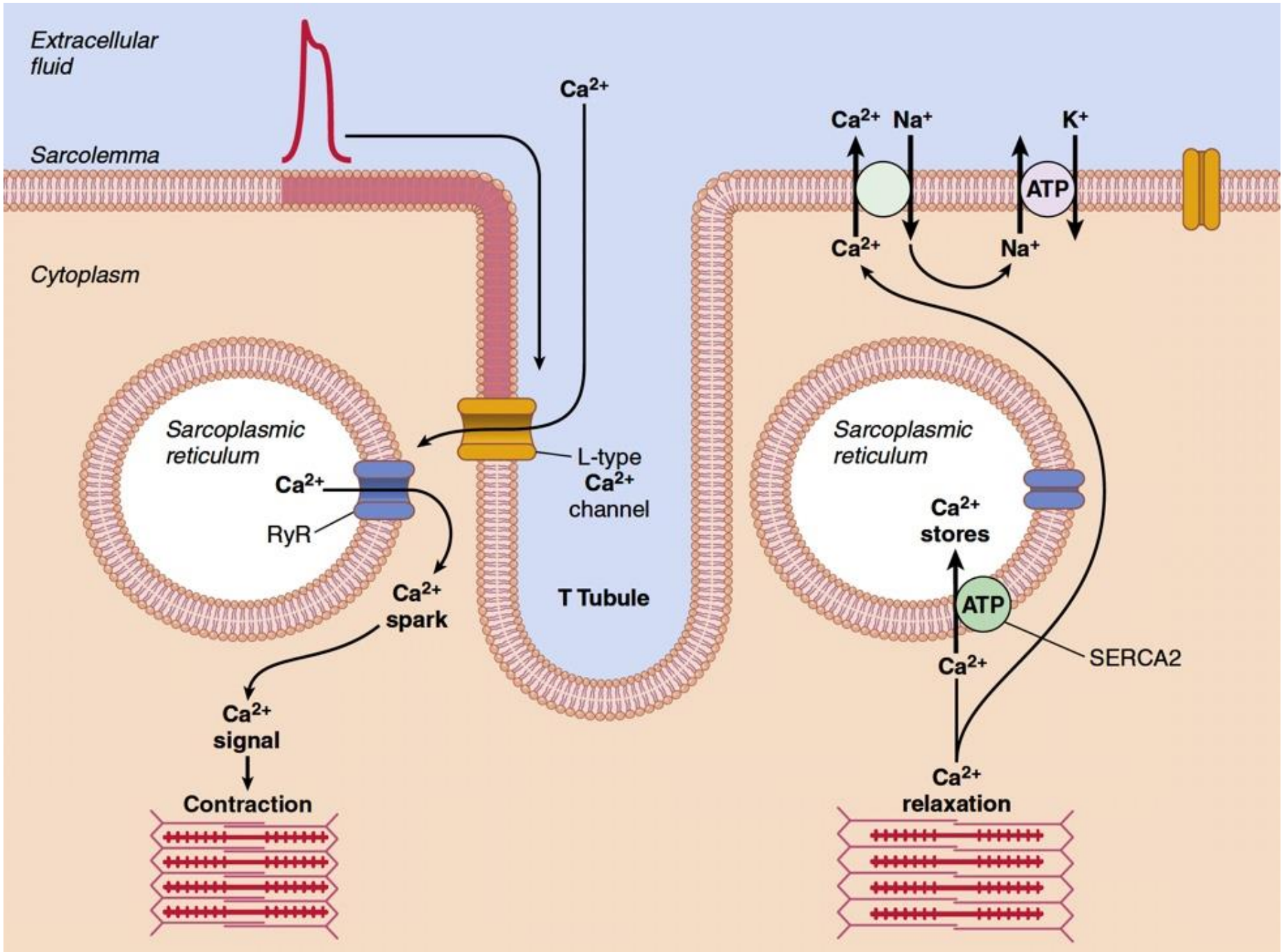
Relaxation

- Transport of calcium back into SR is achieved with the help of a calcium pump (SERCA2).
- Calcium ions are also removed from the cell by a Na-Ca exchanger.
- Na that enters the cell during this exchange is then transported out of the cell by Na-K ATPase pump.
- As a result, the contraction ceases until a new action potential comes along.

Relaxation

- these sarcolemmal transporters pump Ca+ out of the cell against its electrochemical gradient, with the Ca+ ATPase using ATP directly and the Ca2+-Na+ exchanger using energy from the inward Na+ gradient.

- As a result of these transport processes, the intracellular Ca+ concentration falls to resting levels, Ca+ dissociates from troponin C, actin-myosin interaction is blocked, and relaxation occurs.


Extracellular fluid
Sarcolemma
Cytoplasm
Ca2+
Ca2+ Na+
K+
ATP
Ca2+
Na+
Sarcoplasmic reticulum
Ca2+
RyR
L-type Ca2+ channel
T Tubule
Ca2+ spark
Ca2+ signal
Contraction
Sarcoplasmic reticulum
Ca2+ stores
ATP
SERCA2
Ca2+
Ca2+ relaxation

Contractility

- Contractility, or inotropism, is the intrinsic ability of myocardial cells to develop force at a given muscle cell length.

- Agents that produce an increase in contractility have positive inotropic effects.
- Positive inotropic agents increase both the rate of tension development and the peak tension.

- Agents that produce a decrease in contractility have negative inotropic effects.
- Negative inotropic agents decrease both the rate of tension development and the peak tension.

Contractility

- Contractility correlates directly with the intracellular Ca+ concentration, which in turn depends on the amount of Ca+ released from sarcoplasmic reticulum stores during excitation-contraction coupling.

- The amount of Ca+ released from the SR depends on two factors:
- The size of the inward Ca+ current during the plateau of the myocardial action potential.
- The amount of Ca+ previously stored in the SR for release.

- Therefore the larger the inward Ca+ current and the larger the intracellular stores, the greater the increase in intracellular Ca+ concentration and the greater the contractility.

Contractility

- The magnitude of the tension developed by myocardial cells is proportional to the intracellular Ca^{2+} concentration.

- Therefore, hormones, neurotransmitters, and drugs that alter the inward Ca^{2+} current during the action potential plateau or that alter SR Ca^{2+} stores would be expected to change the amount of tension produced by myocardial cells.

Thank you