1. [20 points] Choose the most correct statement AND briefly explain why each of the remaining statements are not correct.

    A. Cardiac muscle cells do not have a t-tubular system.
    B. The diameter of cardiac muscle cells is significantly smaller than the diameter of skeletal muscle cells.
    C. With regard to the source(s) of Ca^{2+} for contraction, cardiac muscle is more like skeletal muscle than like smooth muscle.
    D. Cardiac muscle receives its innervation from the somatic nervous system.

    A. Cardiac muscle cells do not have a t-tubular system.

This is not correct: cardiac muscle cells have a t-tubular system. The T tubules are positioned at the Z lines.

    B. The diameter of cardiac muscle cells is significantly smaller than the diameter of skeletal muscle cells.

        This statement is correct as written.

    C. With regard to the source(s) of Ca^{2+} for contraction, cardiac muscle is more like skeletal muscle than like smooth muscle.

It is not correct. With regard to the source(s) of Ca^{2+} for contraction, cardiac muscle is more like smooth muscle than like skeletal muscle. Calcium for skeletal muscle is entirely intracellular (from SR) whereas it is both intracellular (from SR) and extracellular

for cardiac or smooth muscle.

	Cardiac	Skeletal	Smooth
Ions for AP	Na^+, K^+, Ca^{2+}	Na^+, K^+	Na^+, K^+
Ca^{2+} for contraction	intracellular and extracellular	intracellular	intracellular and extracellular
Ca^{2+} removal	SR and extrusion	SR	SR and extrusion
Ca^{2+} transient	variable	constant	variable
Variation of force	Ca^{2+} transient, stretch	recruitment, tetany	Ca^{2+} transient

D. Cardiac muscle receives its innervation from the somatic nervous system.

This is not correct. The cardiac muscle is innervated by the automatic nervous system. Skeletal muscle receives its innervation from the somatic nervous system (video 3 – slide 2)

2. [20 points] Explain why each of the following statements is **incorrect** ...
   A. Excitation/contraction coupling in cardiac muscle is similar to excitation/contraction coupling in skeletal muscle.
   B. The t-tubular system in cardiac muscle plays a significant role in removing Ca^{2+} from the myofilament space.
   C. Inositol triphosphate (IP_3) is the trigger for release of Ca^{2+} from myosin light chains in cardiac muscle.
   D. Removal of Ca^{2+} from troponin in cardiac muscle requires the activation of myosin light chain phosphatase.

A. Excitation/contraction coupling in cardiac muscle is similar to excitation/contraction coupling in skeletal muscle.

The excitation/contraction coupling in cardiac muscle is different to the one in skeletal muscle. Excitation/contraction coupling in cardiac muscle is electrochemical (involving Ca^{2+}-induced Ca^{2+}-release of calcium), in skeletal muscle it is electromechanical (involving direct interactions between the DHPR in the T tubule and the RYR in the sarcoplasmic reticulum).

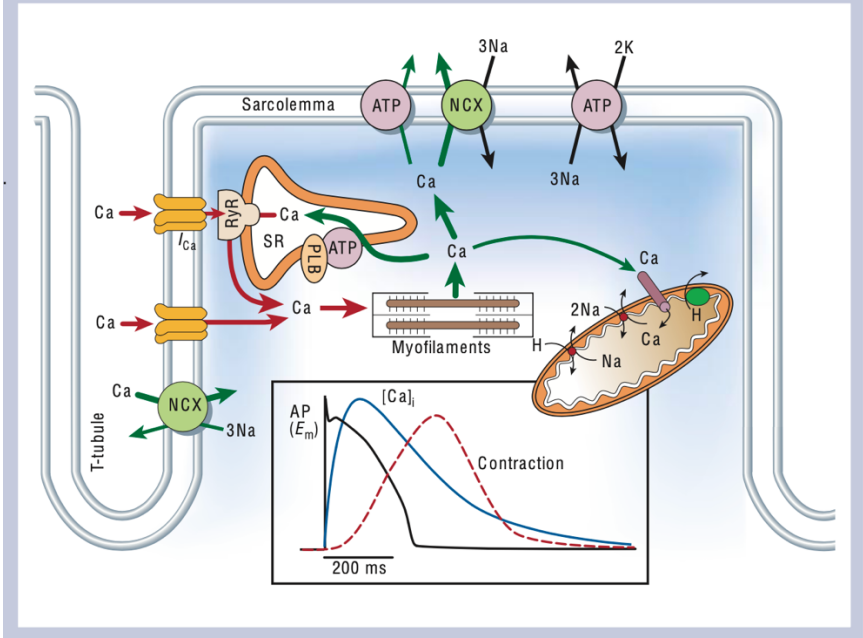

Fig. 1: Excitation-contraction coupling in the cardiac in the heart requires Ca^{++} influx through voltage-gated L-type calcium channels in the sarcolemma and T tubules (Bers DM: Nature 415:198-205, 2002, and B&L[15] fig 13.2).

B. The t-tubular system in cardiac muscle plays a significant role in removing Ca^{2+} from the myofilament space.

In cardiac muscle, the t-tubular does not play any role in removing calcium from the myofilament space. However, the sarcoplasmic reticulum plays a significant role in removing Ca^{2+} from the myofilament space. $3Na^{+}$-$1Ca^{++}$ antiporter (NCX) also extrudes calcium from the cytosol (SR removes about 70% of the calcium from the myofilament space and NCX 28%).

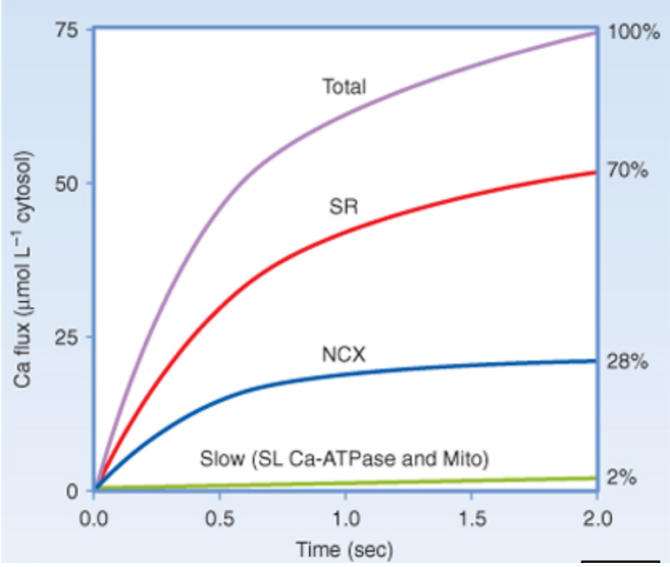

Fig. 2: Ca^{++} sequestration by the SR accounting for the majority of reduction (≈70%) in cytosolic Ca^{++} with some calcium being extruded by the $3Na^{+}$-$1Ca^{++}$ antiporter (≈28%) (Module 5 - Video 2 slide).

C. Inositol triphosphate (IP_3) is the trigger for release of Ca^{2+} from myosin light chains in cardiac muscle.

In smooth muscle *and not in cardiac muscle*, IP_3 is the second messenger binding to a receptor on the membrane of smooth muscle sarcoplasmic reticulum (SR), which *triggers* a bolus release of Ca^{2+} from the SR, *and not from the myosin light chains*, into the cytosol

(The initial trigger is the binding of a stimulus to a sarcolemma G-protein-linked receptor which allows the conversion of PIP2 into the second messenger IP3 which opens InsP3-gated Ca^{2+} channels in the SR).

D. Removal of Ca^{2+} from troponin in cardiac muscle requires the activation of myosin light chain phosphatase.

Removal of Ca^{2+} from troponin in cardiac muscle requires a reaccumulation of Ca^{2+} by the sarcoplasmic reticulum through the SR Ca^{2+}-ATPase pump and to a smaller extent extrusion from the muscle by the sodium-calcium exchanger (NCX). It is not related to the activation of myosin light chain phosphatase (see figure 1 and 2).

(In smooth muscle, the myosin light chain phosphatase binds to myosin, removes the phosphate group, then the myosin reverts to its original conformation, in which it cannot interact with the actin so the muscle relaxes).