Solutions to Homework Assignment - Module 3

1. [20 points] Choose the statement about the mammalian skeletal muscle neuromuscular junction that is the most correct. Briefly explain why the remaining choices are not correct.

   A. Binding of acetylcholine (ACh) to receptors on the muscle cell membrane causes a decrease in membrane sodium conductance (g_{Na}).
   This statement is not correct. Binding of acetylcholine (ACh) to receptors on the muscle cell membrane causes an **increase (not a decrease)** in membrane sodium conductance (g_{Na}).

   B. When an action potential reaches the motor nerve terminal bouton (swelling; this is the end of the motor nerve axon branch) the change in nerve membrane potential allows the entry of chloride ion (Cl^-) into the terminal bouton, which in turn allows the release of acetylcholine (ACh) from the nerve terminal bouton.
   This statement is not correct. When an action potential reaches the motor nerve terminal bouton (swelling; this is the end of the motor nerve axon branch) the change in nerve membrane potential allows the **entry of calcium (Ca^{2+}) ion, not chloride ion (Cl^-) into** the terminal bouton, which in turn allows the release of acetylcholine (ACh) from the nerve terminal bouton.

   C. A drug that binds to acetylcholine (ACh) receptors on the muscle membrane but whose binding does not affect muscle membrane ion permeability can uncouple excitation-contraction coupling.
   This statement is correct as written.

   D. Increased entry of Ca^{2+} into the muscle cell following binding of acetylcholine (ACh) to ACh receptors on the muscle membrane initiates a muscle membrane action potential.
   This statement is not correct. Increased entry of **Na^+ (not Ca^{2+})** into the muscle cell following binding of acetylcholine (ACh) to ACh receptors on the muscle membrane initiates a muscle membrane action potential.

2. [20 points] Choose the statement about mammalian skeletal muscle that is the most correct. Briefly explain why the remaining choices are not correct.

   A. Binding of Ca^{2+} to tropomyosin allows the S-1 heads of crossbridges to attach to their binding sites on the actin thin filament.
   This statement is not correct. Binding of Ca^{2+} to **TnC (troponin C), not tropomyosin,** allows the S-1 heads of crossbridges to attach to their binding sites on the actin thin filament.

Rev 0, 8/17/17 - from Spring 2016, converted to Pages
Rev 1, 9/14/17 - replace Q2 with correct Q & formatting changes
Rev 2, 9/27/17 - re-write in form “this is wrong because”
Rev 4, 2/21/18 - correct error in (rewrite) response 5D
Rev 4, 2/23/18 - correct error in response 2A
Rev 5, 8/2/18 - update to 601; minor wording changes, no real content changes

B. In response to an action potential in the T-tubular system Ca^{2+} is actively pumped out of the lateral cisternae (sacs) of the sarcoplasmic reticulum into the myofilament space.
This statement is not correct. In response to an action potential in the T-tubular system Ca^{2+} **passively diffuses down its concentration gradient (it is not actively pumped)** out of the lateral cisternae (sacs) of the sarcoplasmic reticulum into the myofilament space.

C. The action potential in the T-tubular system is coupled to the membrane of the sarcoplasmic reticulum by gap junctions between the two membrane systems.
This statement is not correct. The action potential in the T-tubular system is coupled to the membrane of the sarcoplasmic reticulum by **the DHPR in the membrane of the T-tubule and the RyR associated with the SR membrane, not** by gap junctions between the two membrane systems.

D. Relaxation requires that Ca^{2+} be removed from the myofilament space by an active, ATP-powered pump in the membrane of the sarcoplasmic reticulum.
This statement is correct as written.

3. [20 points] Assume the existence of a drug whose only effect is to prolong the time course of the binding of Ca^{2+} to troponin-C (TnC) in skeletal muscle by a factor of about 3. In comparison to an untreated muscle, a muscle treated with this drug will … (chose the most correct response). Briefly explain why the remaining choices are not correct.

A. Have an increased rate of rise of force in an isometric twitch.
This statement is not correct, because the rate of rise of force in an isometric twitch is limited by the rate at which crossbridges cycle, which is in turn a function of the muscle's myosin ATPase rate (there are other factors that affect the rate of rise of force, but the myosin ATPase rate is usually the limiting factor).

B. Require a lower stimulus repetition rate to achieve a fused tetanus.
This statement is correct as written.

C. Have a larger velocity of unloaded shortening (V_o).
This statement is not correct, because the velocity of unloaded shortening (V_0) is limited by the rate at which crossbridges cycle, which is in turn a function of the muscle's myosin ATPase rate.

D. Relax more quickly.
This statement is not correct, since relaxation requires that crossbridges, once detached, cannot reattach. If the time that Ca^{2+} is bound to TnC is

prolonged the crossbridges can remain attached longer, thereby prolonging the twitch time course. Thus, relaxation is delayed.

4. [20 points] With reference to mammalian skeletal muscle, choose the equation that best describes the detachment of the "used" crossbridge from the thin filament following the power stroke. Briefly explain/describe the steps in the crossbridge cycle represented by the remaining choices.

A. $A + M{\bullet}ATP \rightarrow A + M^*{\bullet}ADP{\bullet}P_i$
This equation describes the hydrolysis of ATP (on the myosin S-1 head) to form energized myosin S-1; actin and myosin are not attached - step 4.

B. $A + M^*{\bullet}ADP{\bullet}P_i \rightarrow A{\bullet}M^*{\bullet}ADP{\bullet}P_i$
This equation describes the attachment of an energized myosin (M*) cross bridge to actin - step 1.

C. $A{\bullet}M^*{\bullet}ADP{\bullet}P_i \rightarrow A{\bullet}M + ADP + P_i$
This equation describes the power stroke, in which the energy in M* is converted to mechanical energy in the form of force and/or movement.

D. $A{\bullet}M + ATP \rightarrow A + M{\bullet}ATP$
This equation best describes the detachment of the "used" crossbridge from the thin filament following the power stroke.

5. [20 points] Choose the statement which best describes a role of ATP in skeletal muscle ***relaxation***. Briefly explain why the remaining choices are not correct.

A. ATP binds to myosin S-2, which allows bound crossbridges to release from the thin filament.
This statement is not correct because in order for bound crossbridges to release from the thin filament ATP binds to **myosin S-1, not to myosin S-2.**

B. Chemical energy from the hydrolysis of ATP is transformed into mechanical energy when bound crossbridges rotate from the 90° to the 45° configuration.
This statement does not describe a role of ATP in skeletal muscle ***relaxation;*** rather, **it describes the power stroke (contraction).**

C. Chemical energy from the hydrolysis of ATP is needed to power the pumps in the SR that take up Ca^{2+}.
This statement best describes a role of ATP in skeletal muscle relaxation.

D. ATP binds to TnI, allowing tropomyosin to rotate into the groove of the actin helix, thus blocking attachment of crossbridges to the thin filament.

This statement contains two errors. First, the regulation of contraction in skeletal muscle does not involve the binding of ATP to TnI (ATP does not bind to TnI during any part of the the skeletal muscle contraction/ relaxation cycle). Note that it is the binding (unbinding) of Ca^{2+} to TnC that allows tropomyosin to rotate into (out of) the actin-actin groove. Second, it is the rotation of tropomyosin out of (not into) the actin-actin groove that blocks attachment of S-1 to actin.

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