READ THIS PAGE BEFORE YOU BEGIN THE EXAM.

1. Write your name on every page. (5 points off for EACH unnamed page.)
2. Do NOT write on the BACK of any page unless you get a TA’s permission FIRST.
3. About writing answers:
   - All questions can be answered briefly.
   - For full credit, discuss mechanisms.
   - In problems asking for an answer and a reason, more credit is given for a correct reason.
4. Use a pen or pencil to write your answers, but do NOT use RED INK and DO NOT USE WHITE-OUT of any kind. However, if you use pencil, you cannot request a regrade.

POTENTIALLY USEFUL EQUATIONS:

\[
\begin{align*}
F &= A\eta^2\frac{AV}{\Delta X} \\
R &= \frac{8 \eta l}{\pi r^4} \\
Q &= \frac{(P_2-P_1) \pi r^4}{8 \eta l} \\
V &= IR \\
P &= QR \\
A &= \pi r^2 \\
J &= -PS(C_{out}-C_{in}) \\
J &= k[(P_{cap}+\pi_{int})-(P_{int}+\pi_{cap})] \\
\pi &= \alpha RT(C_o-C_i) \\
v &= \frac{Q}{A} \\
E_x &= \frac{RT}{ZF} \ln \frac{[X^+]_{out}}{[X^+]_{in}} \\
\frac{1}{R_{Total}} &= \Sigma \frac{1}{R_i}
\end{align*}
\]

SCORE:

Page 2 ________
Page 3 ________
Page 4 ________
Page 5 ________
Page 6 ________
Page 7 ________
TOTAL _________

WAIVER: By signing this waiver I give permission that this exam can be left for me to pick up in the hall across from the elevator on the third floor of Pacific Hall. I realize that this procedure may expose my grade to public scrutiny and my exam to theft. If I do not sign this waiver, I understand I will be able to get my graded exam back only as described in on the course Web site.

__________________________
Signature

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PID
1. (11 points total) Use GnRH and ADH as examples to distinguish a releasing factor from a hormone. In particular:
   A. (4 points) Discuss two major ways that a hormone differs from a releasing factor.

   B. (4 points) Discuss two major ways that a hormone is similar to a releasing factor.

C. (3 points) There are many kinds of tumors, both cancerous and noncancerous, that can grow in or near the pituitary. Some of these tumors cause excessive production of hormones, whereas others restrict normal function in part of the pituitary. Name three places where a tumor might be located if your body stops producing ADH and oxytocin, but all other hormonal systems are normal.

2. (12 points total) The compound thapsigargin is extracted from Thapsia garganica, a plant commonly called the “deadly carrot”. Thapsigargin is an inhibitor of the Ca^{2+}-ATPase of the sarcoplasmic reticulum of both skeletal and cardiac muscle. It is a deadly poison.

   A. (4 points) Predict the effects of thapsigargin on the first skeletal muscle twitch. Briefly explain.

   B. (4 points) Predict the effects of thapsigargin on the 100\textsuperscript{th} skeletal muscle twitch. Briefly explain.

   C. (4 points) Fendiline is an L-type calcium channel blocker. Could Fendiline be used to treat thapsigargin poisoning? Briefly explain, citing any differences between the effects of the two drugs on heart and skeletal muscles.
3. (15 points total) A scientist at UCSD studied the mechanism of muscle contraction. She isolated a muscle fiber and did a variety of experiments, each time causing the muscle to twitch by electrically stimulating it to produce a single action potential. For each experiment, plot Tension vs. Time.

A. (3 points) A single normal muscle twitch.

![Graph](Tension vs. Time for normal twitch)

B. (3 points) Administered a DHP receptor inhibitor. Explain any differences from the normal twitch.

![Graph](Tension vs. Time for DHP inhibitor)

C. (3 points) Administered a DHP receptor inhibitor while the muscle fiber is bathed in calcium. Explain any differences from the effect of the DHP inhibitor alone.

![Graph](Tension vs. Time for DHP inhibitor with calcium)

D. (3 points) Administered a Ca\(^{++}\)-ATPase inhibitor. Explain any differences from the normal twitch.

![Graph](Tension vs. Time for Ca\(^{++}\)-ATPase inhibitor)

E. (3 points) Removed the majority of the sarcoplasmic reticulum from the muscle fiber. Explain any differences from the normal twitch.

![Graph](Tension vs. Time for sarcoplasmic reticulum removal)
4. (8 points total) As a graduate student, you discover a drug (which you call “Gapnix”) that selectively blocks the gap junctions between smooth muscle cells. What effect would Gapnix have on:

A. (4 points) Your ability to focus your vision? Briefly explain.

B. (4 points) Your ability to pass food through your small intestine? Briefly explain.

5. (12 points total) A cardiac disease called SQTS was first described in 2004. SQTS results from a mutation in the voltage-gated K⁺ channels in ventricular muscle fibers. This mutation causes voltage-gated K⁺ channels to activate faster and have a larger conductance than normal.

A. (3 points) On the recording of the ventricular muscle action potential shown below, draw a dashed line showing how an action potential would be different in the muscle fibers with the mutated K⁺ channels.

B. (3 points) On the line below the action potentials, draw a solid line to show what the ECG would look like from a person with the normal ventricular action potentials. Label the ECG components.

C. (3 points) On the same ECG recording, draw a dashed line that shows what the ECG would look like in a person with SQTS. Explain any differences compared to the normal ECG.

D. (3 points) People die from SQTS because it can result in ventricular fibrillation. Explain how the abnormalities you have shown above could lead to ventricular fibrillation.
6. (12 points total) “Valvular insufficiency” is a condition of a heart valve: it cannot close completely during the cardiac cycle (i.e., it remains partially open during the time it would normally be shut). If the aortic valve is in this condition (called “Aortic insufficiency”):

A. (4 points) it produces a back-flow (also called “regurgitation”) of blood from the aorta to the ventricle during diastole. Briefly explain why.

B. (2 points) would there be a change in one or both of the heart sounds? If there is any change, briefly explain why.

C. (3 points) is the stroke volume abnormal? Briefly explain.

D. (3 points) If this condition persists for many months, does it cause a change in the ECG compared to normal? If so, explain what changes; if nothing changes, explain why not.
7. (10 points total) The active component of the length-tension relationship for a muscle tells a great deal about its function.
   A. (4 points) Describe how an active length-tension curve is generated.

   B. (4 points) Compare the active length-tension curves of skeletal and cardiac muscle fibers.

   C. (2 points) How would an active length-tension curve for smooth muscle in your intestinal tract differ from a length/tension curve for one of your skeletal muscles?

8. (8 points total) Ivabradine is a selective blocker of If channels. Ivabradine is marketed as Procoralan to treat heart pain (this pain is called angina pectoris). Angina can have a number of different causes, such as lack of blood to the coronary vessels, a clot in a pulmonary artery, tachycardia, narrowing of the aortic valve (technical term: aortic stenosis), or inflammation of tissue around the heart or lungs

   A. From your knowledge of If channels, how would Procoralan affect:
      (a) (3 points) heart rate? Briefly explain.
      (b) (3 points) strength of cardiac muscle contraction? Briefly explain.

   B. (2 points) Based upon your answer to part A, what kind of problem that causes angina could be treated effectively with Procoralan? Briefly explain.
9. (12 points total) For the following three groups of statements (A, B, and C), circle every letter that makes a TRUE statement. Note that any number of statements may be true—including none of them—so that if you do not circle a letter you are indicating that you believe that the statement is false. (You lose a point for every incorrect answer circled and for every correct answer not circled.)

A. Chemical communication is complex:
   a. hormones are chemicals secreted by a cell or group of cells into the blood for transport to a distant target, where they exert their physiological effects on distant targets.
   b. pheromones have been called “ectohormones” because they are chemicals produced by an animal within its body that acts on the outside of the animal’s body to produce its physiological effect.
   c. some substances that fit the definition for being a hormone are also used within the CNS as a neurotransmitter.
   d. many cytokines are not considered to be hormones because they have effects only locally, without being secreted into the circulatory system.

B. Muscle disorders can have a variety of causes:
   a. in some types of muscular dystrophy, contractile fibers break down.
   b. an absence of enzymes may limit the availability of energy from the breakdown of glycogen.
   c. toxins produced by infectious diseases can disrupt the release of ACh at the NMJ.
   d. prolonged inactivity (as when a limb is immobilized in a cast) can lead to atrophy which, if prolonged, can be permanent.

C. Smooth muscle differs from skeletal muscle:
   a. skeletal muscle can operate over a greater range of lengths.
   b. contractions in smooth muscles may be initiated by chemical signals without an action potential in the cells membrane.
   c. smooth muscle cells lack specialized postsynaptic regions.
   d. smooth muscle cells have less actin and myosin than striated muscle cells.