General Instructions: READ THIS PAGE BEFORE YOU BEGIN THE EXAM.

1. Write your name on every page. (5 points off for EACH unnamed page.)

2. For your own benefit, write your answers LEGIBLY in the space allotted. If we cannot read your handwriting, we cannot give you credit for your answer.

3. Do NOT write on the BACK of any page unless you get a TA’s permission FIRST.

4. About writing answers:
   - All questions can be answered briefly.
   - Answer the question that is asked specifically, precisely, and accurately.
   - For full credit, show your calculations.
   - Problems that ask for an answer and for a reason, more credit will be given for a correct reason.
   - If you are asked for one reason, be sure you write down only the best one.

5. About grading:
   - We give credit for correct and relevant answers. We ignore true, but irrelevant statements.
   - We deduct points for statements that are both incorrect and irrelevant. (We don’t just ignore irrelevant answers because we need to let you know that you have some wrong ideas.)

6. Use a pen to write your answers, but do NOT use RED INK and DO NOT USE WHITE-OUT of any kind. (You cannot request a regrade if you use pencil.)

POTENTIALLY USEFUL EQUATIONS:

\[ E_{\text{ion}} = \frac{6L}{z} \log \frac{[X]_{\text{out}}}{[X]_{\text{in}}} \quad V = IR \quad w_T = nRT \int_{i}^{2} \frac{dV}{V} \]

\[ I_X = G_X (V_m - E_X) \quad R_{\text{total}} = \Sigma R_{\text{individual}} \]

\[ R = \frac{8\eta l}{\pi r^4} \quad E = mc^2 \]

\[ \frac{1}{R_{\text{total}}} = \Sigma \frac{1}{R_{\text{individual}}} \quad V_m = \frac{G_{\text{Na}}}{\Sigma G} E_{\text{Na}} + \frac{G_{\text{K}}}{\Sigma G} E_{\text{K}} + \frac{G_{\text{Cl}}}{\Sigma G} E_{\text{Cl}} \]

TOTAL \ 

WAIVER: By signing this waiver I give permission that this exam can be left for me to pick up in the hall 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                                                             Date
1. (18 points total) There is a strong relationship between insulin and blood glucose: if the concentration of glucose in the blood increases, the beta cells in the pancreas release insulin into the blood, which acts on all cells in the body to take up glucose from the blood, lowering the blood glucose level.

A. (9 points) Draw this relationship as a feedback loop. (To get you started, one box is provided.)

B. (3 points) Is the loop positive feedback or negative feedback? Briefly explain.

Short answer: It’s negative feedback, because there is one negative sign in the loop.

Long answer: Start at one box and follow the responses around the loop: an increase in blood glucose increases insulin release, which increases the cellular uptake of glucose, thereby decreasing the blood glucose. The feedback, therefore, is opposite to the starting signal, so it is negative feedback.

Eating affects this loop in two ways: (1) as soon as eating starts, taste receptors in the mouth activate neurons in the hypothalamus that excite neurons in the vagus nucleus which have axons in the vagus nerve that cause the pancreatic beta cells to release insulin; (2) in 20-30 minutes, the eaten food increases the amount of glucose in the blood.

C. (6 points) Add either of these effects of eating to the feedback loop you have drawn. Has this addition changed the nature of the feedback (positive vs. negative)? Briefly explain.

The effects of eating are perturbations, without any feedback, so they do not change the fact that this is a negative feedback system.

2. (5 points) Botulinum toxin is a protein produced by a bacterium, *Clostridium botulinum*, that is considered the most powerful neurotoxin ever discovered. Known by its commercial name (BOTOX), it is also used as a cosmetic as well as for a variety of medical treatments (e.g., it causes muscles to relax, thereby eliminating “frown lines” and wrinkles from aging faces, and it reduces tension in head and neck muscles that cause some migraine headaches). The toxin enters the presynaptic terminals of the NMJ and keeps synaptic vesicles from binding to the presynaptic membrane, an effect that lasts many months. Explain how this mechanism can lead to the toxin’s ability to relax muscles.

If the synaptic vesicles can’t bind to the membrane (i.e., they can’t be docked), they cannot be released. No release of vesicles means no synaptic transmission, and the muscles cannot contract if there is no synaptic transmission, so the muscles stay relaxed.
3. (15 points total) An SIO marine biologist discovered a strange-looking worm in a hydrothermal vent in mid-Pacific Ocean. In investigating the worm’s nervous system, she found that a group of neurons had the following concentrations of Na⁺, K⁺, and Cl⁻ (in mM) inside and outside their cell membrane:

<table>
<thead>
<tr>
<th></th>
<th>Inside</th>
<th>Outside</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>15</td>
<td>150</td>
</tr>
<tr>
<td>K⁺</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>12</td>
<td>120</td>
</tr>
</tbody>
</table>

Surprisingly, she found the membranes of these neurons to be permeable only to Na⁺ at rest. All other ionic properties of these neurons were similar to those in frog muscles. Based on these observations:

A. (5 points) What would be the resting potentials of these neurons? Show your calculations.

\[ E_{\text{Na}} = +61 \log \left( \frac{150}{15} \right) = +61 \log 10 = +61 \text{ mV} \]

(This is an unusual worm—it has neurons with positive resting potentials!)

B. (5 points) These neurons receive synaptic input that opens a channel that has a Na⁺ conductance three times as large as the K⁺ conductance. What is the reversal potential for this PSP? Show your calculations.

\[ V_{\text{syn}} = E_{\text{Na}} \left( G_{\text{Na}} / \Sigma G \right) + E_{\text{K}} \left( G_{\text{K}} / \Sigma G \right) = 61 \left( \frac{3}{4} \right) + (-61) \left( \frac{1}{4} \right) = 45.75 - 15.25 = 30.5 \]

In words: the reversal potential is 3/4 of the way from \( E_{\text{K}} \) to \( E_{\text{Na}} \).

C. (5) What would be the threshold voltage for producing an action potential in these neurons? Briefly explain. If you do not have enough information to answer this question, say what you need.

These neurons cannot produce action potentials, because all the voltage-gated Na⁺ channels are inactivated.

...unless the neuron got strong hyperpolarizing input (normally considered to be “inhibitory”) that would re-activate all the inactivation gates; the cell would then fire an action potential as it went back to its +61 mV resting potential.

4. (10 points total) There is a major bloom of “red tide” along the La Jolla shore right now. If you go swimming in these waters, keep your mouth shut! Red tide is caused by a particular species of unicellular dinoflagellates, Karenia brevis, that produce a complex molecule called brevetoxin that is poisonous to fish, birds, and people. Experiments on crayfish and squid giant axons found that brevetoxin had two effects on voltage-gated Na⁺ channels: (1) it lowers the spike threshold so much that Na⁺ channels start opening at resting potential; and (2) it partially blocks Na⁺ channel inactivation.

A. (5 points) Explain how these effects would affect the activity of any animal that swallows these dinoflagellates.

Because of (1), it would cause neurons and muscles to fire some action potentials without a stimulus, causing muscle spasm; because of (2), it would make the action potentials last longer (which partially offsets the increased excitability).

B. (5 points) Other species of dinoflagellates produces another toxin called saxitoxin, which also binds to the voltage-gated Na⁺ channels but it completely blocks them. Saxitoxin is significantly more toxic than brevetoxin. Briefly explain why.

No action potentials would be generated, so there would be complete paralysis of muscles; the cause of death would probably be lack of breathing.
5. (10 points total) You stimulate the axon of a motor neuron to initiate two action potentials at the same time, one at the soma and the other near the axon terminal in the muscle. The two action potentials conduct along the axon and meet somewhere in the middle.

A. (5 points) If you were recording intracellularly at the site of the meeting, would the amplitude of the collided action potentials be larger, smaller, or the same size as the individual action potentials? Briefly explain.

It would probably be somewhat larger, since the two action potentials might, together, open more Na$^+$ channels than either one alone, but it could never be more positive than $E_{Na}$. [Full credit was given for saying "same size" if you said that each action potential opened as many Na channels as possible.]

B. (5 points) Would one, or both, or neither of the action potentials be conducted past the meeting site? Briefly explain.

Neither. Both of them would run into membrane in its absolute refractory period, and would stop conducting.

6. (15 points total) Below is a diagram of a reflex arc.

A. (2 points) What is the name of the reflex that this pathway produces?

The flexion (or withdrawal) reflex

B. (10 points) Name the labeled elements (be as specific as possible):

a. spinal nerve (can't tell which one)

b. ventral root

c. dorsal root ganglion

d. ventral horn

e. anterolateral tract

C. (3 points) If you stimulated electrically at the location indicated by the lightning bolt, how would the reflex differ from the normal reflex? Briefly explain.

Both the motor and the sensory axons would be activated at the same time. Stimulating the motor axon would cause a muscle contraction; stimulating the sensory cells would cause a second (later) contraction, through the reflex pathway, as well as a sensation of pain, which is part of the flexion reflex.
7. (5 points) Myasthenia gravis is an auto-immune disease in which the immune system destroys ACh receptors on postsynaptic membranes. A standard treatment for this disease (in addition to immunosuppressants) is cholinesterase inhibitors. Explain why this is an effective treatment.

As myasthenia gravis progresses, more and more of the ACh receptors are lost. Inhibiting the AChase prolongs the action of the ACh in the synaptic cleft, so that each receptor is activated for a much longer time, thereby making the remaining receptors more effective in activating the postsynaptic cell.

8. (10 points total) After a car crash, you come to the scene as an EMT. The driver of one of the cars complains of pain in his right hand (it looks broken) but when you touch it gently, he says he cannot feel your hand on his, but he does feel your hand on his right shoulder.

A. (5 points) What part of the nervous system—both the structure and the location—is likely to be damaged? Briefly explain.

Because he can feel pain in his hand but cannot feel touch, his anterolateral tract is likely to be OK but his right dorsal column is probably damaged. Because he feels light touch to his shoulder, the damage must be between the cervical segments responsible for the hand and the shoulder.

B. (5 points) He also cannot feel that his right foot is touching hot metal. Can this problem be explained by the problem with his hand and shoulder? Briefly explain.

No. Pain is carried in the anterolateral tract, which is intact in the cervical area. Not being able to feel pain in his right foot means that there must be damage to the left anterolateral tract somewhere between the sacral and cervical spinal cord.
9. (12 points total) For the following three groups of statements, 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 the statement is false.

A. Acute motor axonal polyneuropathy (AMAN), an unusual disease first reported in Chinese children, and Guillain-Barre syndrome (GBS) are two diseases of peripheral axons that cause paralysis (inability to move) in humans.
   a. Both AMAN and GBS show a decrease in conduction velocity in peripheral nerves.
   b. In addition to the paralysis, patients with AMAN can feel a pin prick but GBS patients cannot, showing that GBS damages both sensory and motor axons but AMAN damages only motor axons.
   c. Autopsy reports show that GBS patients have damage to the peripheral myelin, whereas AMAN patients have normal peripheral myelin.
   d. In AMAN, the size of the summed action potentials measured from the outside of a peripheral nerve is smaller, indicating a loss of axons.
   (b,c,d; p. 289-90 in the 5th edition of Silverthorn)

B. Synaptic transmission at the NMJ differs from transmitter release at an autonomic synapse:
   a. the NMJ releases ACh at the tips of axon terminals, whereas autonomic axons release transmitter at a number of swellings (“varicosities) along the ends of the axons.
   b. ACh released at the NMJ activates excitatory ionotropic receptors whereas Epi released at all autonomic synapses activates inhibitory metabotropic receptors.
   c. ACh is broken down into its components that are recycled in the presynaptic terminal, whereas Epi is recycled in sympathetic presynaptic structures without being broken down.
   d. ACh is released onto nicotinic ACh receptors at the NMJ, whereas NorEpi is released onto alpha receptors at sympathetic synapses, and onto beta receptors at parasympathetic synapses.
   (a,c; pp. 392-3 in the 5th edition of Silverthorn)

C. Gamma motor neurons:
   a. are small motor neurons that innervate extrafusal muscle fibers.
   b. have no influence on the stretch reflex.
   c. keep the muscle stretch receptors active, no matter what the resting muscle length is.
   d. are activated along with the alpha motor neurons (which innervate tension-generating muscle fibers) during a voluntary contraction of a muscle, a process called alpha-gamma coactivation.
   (c,d; pp. 451-3 in the 5th edition of Silverthorn)