BMED 3100: Systems Physiology
Test 2, February 6, 2009

KEY

Last Name

Honor Pledge

All students are required, when requested, to attach the following statement to any material turned in for a grade in any course at Georgia Institute of Technology:
On my honor, I pledge that I have neither given nor received inappropriate aid in the preparation of this assignment.

_____
Signature

_____
Name (Printed)

Be brief in your answers.
Write clearly.
Backs of pages will not be graded.

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Multiple Choice: Write the *best* answer on the line to the right. (2 pts each)

1. The following are all true of the Na^+/K^+-ATPase pump *except:* ____**C**____
   A. Proper functioning of the Na^+/K^+-ATPase pump uses most of the cellular ATP.
   B. The Na^+/K^+-ATPase pump is electrogenic.
   C. The Na^+/K^+-ATPase pump maintains low intracellular potassium concentration and high intracellular sodium.
   D. The Na^+/K^+-ATPase pump directly contributes very little to the resting membrane potential.
   E. At steady state resting potential the Na^+/K^+-ATPase pump balances out ion flux through channels.

2. A given neuron can ____**E**____
   A. be either a presynaptic neuron or a postsynaptic neuron.
   B. receive information from more than one other neuron.
   C. transmit information to more than one other neuron.
   D. simultaneously release more than one type of neurotransmitter.
   E. do all of these things.

3. Compartments A and B are separated by a membrane that is permeable to K^+ but not to Cl^-. At time zero, a solution of KCl is poured into compartment A and pure H_2O is poured into compartment B. At equilibrium, ____**E**____
   A. the concentration of K^+ in A will be lower than it was at time zero.
   B. diffusion of K^+ from A to B will be equal to the diffusion of K^+ from B to A.
   C. there will be a potential difference across the membrane, with side A negative relative to side B.
   D. the electrical and diffusion potentials for K^+ will be equal in magnitude and opposite in direction
   E. All of the choices are correct.

4. In a resting neuron, ____**C**____
   A. the plasma membrane is freely permeable to sodium ion.
   B. the concentration of sodium ion is greater inside the cell than outside.
   C. the permeability of the plasma membrane to potassium ion is about 50 times greater than its permeability to sodium ion.
   D. the plasma membrane is completely impermeable to sodium ion.
   E. None of the choices are true.

5. If the concentration of ATP were depleted in a typical nerve cell, the ____**B**____
   A. resting membrane potential would increase (become more negative).
   B. resting membrane potential would decrease (become less negative).
   C. concentration gradient for Na^+ would remain the same.
   D. resting membrane potential would eventually become positive, inside with respect to outside.
   E. None of the choices are correct.

6. The equilibrium potential of a given ion across a membrane is ___**E**_____

A. a function of the concentration of that ion on both sides of the membrane.
B. the potential at which there is no net movement of that ion across the membrane.
C. the potential difference across the membrane that creates an electric force favoring diffusion of the ion in one direction that is equal in magnitude and opposite in direction to the diffusion force provided by the concentration difference of the ion across the membrane.
D. A and B are both correct.
E. all of the choices are correct.

7. Which of the following statements regarding the phases of an action potential is correct? ___**E**_____

A. During the depolarizing phase, the permeability of the membrane to Na^+ is greater than its permeability at rest.
B. During the repolarizing phase, the permeability of the membrane to K^+ is greater than its permeability at rest.
C. The relative refractory period of the membrane coincides with the hyperpolarized and second repolarizing phases.
D. A and B are both correct.
E. All of the choices are correct.

8. Which of the following statements about the refractory period of a membrane is true? ____E_____

A. The absolute refractory period refers to the period of time during which another action potential cannot be initiated in that part of the membrane that has just undergone an action potential, no matter how great the strength of the stimulus.
B. The relative refractory period refers to the period of time during which another action potential can be initiated in that part of the membrane that has just undergone an action potential, if the stimulus is strong enough.
C. The refractory period prevents the action potential from spreading back over the part of the membrane that just underwent an action potential.
D. The refractory period places an upper limit on the frequency with which a nerve cell can conduct action potentials.
E. All of the choices are correct.

9. Which of the following statements regarding action potentials generated in a membrane is *not* true? ___**A**_____

A. Action potentials travel decrementally down the membrane.
B. An action potential generates a new action potential in an adjacent area of membrane.
C. An action potential generates a local current that depolarizes adjacent membrane to threshold potential.
D. The first action potential generated is the same size as the action potential ultimately generated at the end of the membrane.
E. An action potential generated by a threshold stimulus is the same size as one generated by a supra-threshold stimulus.

10. Which of the following statements concerning the properties of action Potentials is true? ____**A**____

A. The rate of propagation of an action potential down an axon is independent of stimulus strength.
B. Action potentials can be summed.
C. A supra-threshold stimulus is required to stimulate an action potential during the absolute refractory period.
D. Action potentials are conducted decrementally down the axon.
E. None of the choices are true.

11. Which of the following statements concerning the rate of action potential propagation is true? ____**D**____

A. It is faster in large-diameter axons than in small-diameter ones.
B. It is faster for a strong stimulus than for a weak one.
C. It is faster in myelinated nerve fibers than in nonmyelinated ones.
D. Both it is faster in large-diameter axons than in small-diameter ones and it is faster in myelinated nerve fibers than in nonmyelinated ones are true.
E. All of the choices are true.

12. Exocytosis of neurotransmitter into the synaptic cleft is triggered by an influx of _____ in response to the arrival of an action potential in the axon terminal. ____**C**____

A. K^+
B. Na^+
C. Ca^{2+}
D. ATP
E. Cl^-

13. An inhibitory postsynaptic potential ____**B**____

A. is produced by an increased permeability to both Na^+ and K^+.
B. is produced by an increased permeability to Cl^- and/or K^+.
C. is a small depolarization in a postsynaptic cell.
D. can be summed with other IPSPs to trigger an action potential in the postsynaptic cell.
E. Both is produced by an increased permeability to both Na^+ and K^+ and can be summed with other IPSPs to trigger an action potential in the postsynaptic cell are correct.

14. Temporal summation on a postsynaptic membrane ____**A**____

A. refers to the effect on the membrane of one (or more) synaptic event before the effects of a previous synaptic event have died away.
B. refers only to addition of EPSPs.
C. refers only to the effect of stimulating different synapses repeatedly.
D. inevitably leads to action potentials in the axon.
E. is described by none of these choices.

15. Neuron X makes inhibitory axon-axon synaptic contact with neuron Y at the synapse of Y and neuron Z. Stimulation of action potentials in X ____**B**____
   A. will inhibit propagation of action potentials in Y.
   B. inhibit release of neurotransmitter by Y.
   C. make the Y-Z synapse more effective (i.e. increase the size of the postsynaptic potential in Z).
   D. A and B are both correct.
   E. None of the choices are correct.

16. Alzheimer's disease is thought to involve primarily ____**C**____
   A. loss of neurons that secrete or respond to catecholamines.
   B. loss of adrenergic neurons.
   C. loss of cholinergic neurons.
   D. loss of neurons that secrete or respond to dopamine.
   E. the inevitable loss of brain function with aging.

17. Parkinson's disease is thought to involve primarily ____**D**____
   A. loss of neurons that secrete or respond to catecholamines.
   B. loss of adrenergic neurons.
   C. loss of cholinergic neurons.
   D. loss of neurons that secrete or respond to dopamine.
   E. the inevitable loss of brain function with aging.

18. One of the most abundant excitatory neurotransmitters in the CNS is ____**A**____
   A. glutamate.
   B. dopamine.
   C. norepinephrine.
   D. gamma amino butyric acid (GABA).
   E. endorphin.

19. The major known classes of neurotransmitters and/or neuromodulators include each of the following *except* ____**B**____
   A. amino acids.
   B. cyclic nucleotides.
   C. neuropeptides.
   D. ACh.
   E. biogenic amines.

20. Drug X interferes with the action of norepinephrine at synapses. Which of the following mechanisms would *not* explain the effects of X? ____**C**____
   A. X inhibits synthesis of norepinephrine at the axon terminal.
   B. X inhibits norepinephrine release from the terminal.
   C. X blocks reuptake of norepinephrine by the terminal.
   D. X is a norepinephrine antagonist.
   E. X stimulates the breakdown of norepinephrine.

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True or False / Fill-in (2 pts each)

The Na and K channels that open during an action potential are voltage-gated. ____**T**____

The action potential elicited by a supra-threshold stimulus is larger than one elicited by a threshold stimulus. ____**F**_____

The absolute refractory period of an excitable membrane refers to the period of time during which no stimulus, however strong, will elicit a second action potential in the membrane. ____**T**____

The junction between two neurons that are communicating with each other is called a **synapse** _____ . The most common type of such junction is one in which a chemical messenger called a **neurotransmitter** _____ is released by the __ __**synaptic vesicle (axon terminals OK)** ____ ~~cell~~, sending the message, called the **presynaptic** ___ neuron. The cell receiving the message, called the **postsynaptic** _____ neuron, has specific receptors for the messenger. These receptors are most commonly found on the **cell body/soma**___ and **dendrites**_____ of the nerve cells.

Action potentials are propagated_____ **faster** _____(faster/slower) in myelinated axons than in nonmyelinated ones. The method of action potential propagation in myelinated axons is called ___**saltatory conduction**_____. The cells that myelinate neurons in the CNS are the _____**oligodendrocytes** _____, and those that form myelin in the PNS are the ___ **Schwan cells**_____.

The most abundant cells in the CNS are _____**interneurons**_____

Define the following and give an example (4 pts eatch

1. Specificity: **The ability of a receptor to bind only one type (or a limited number of structurally related types) of chemical messengers. E.g., AchR only binds Ach.**
2. Second messenger: **Intracellular substance that serves as relay from plasma membrane receptor to intracellular biochemical pathway, where it alters some aspect of cell's function. E.g., calcium or cAMP or cGMP etc….**
3. Ionotropic receptor: **A membrane receptor linked to an ion channel / (or a membrane protein through which ionic current is controlled by the binding of extracellular signaling molecules. E.g., AchR - skeletal muscle, NMDA R, AMPA R**
4. Metabotropic receptor: **A membrane receptor linked to a G-protein / (or a membrane receptor that initiates formation of secondary messengers when bound. E.g., metabotropic glutamate receptor, norepinephrine receptor, any G-protein R OK**
5. Ligand: **Any molecule or ion that binds to a protein surface by noncovalent bonds. E.g., Ach, dopamine, norepinephrine,….any neurotransmitter, or an extracellular matrix protein, or any other known ligand.**
6. Kinase: **An enzyme that transfers a phosphate (usually from ATP) to another molecule / An enzyme that phosphorylates a protein /molecule. E.g., tyrosine kinase, JAK kinase, cAMP-dependent protein kinase, etc.**

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Myasthenia Gravis is a disease that affects skeletal muscle because of destruction of AchRs on the motor end plate.

A. What type / category of disease is MG likely to be? _**Autoimmune (immune OK)**__

B. What happens to the end plate potential (EPP)? **It is reduced**.

C. What treatment strategy would you propose? Why? **Any of the following: 1) immune suppression (reduce attack on AchR); 2) Acetylcholinesterase inhibitors (increase Ach); 3) Acetylcholine (increase Ach); 4) genetic engineering approached to synthesize AchR (increase available AchR); 5) create synthetic, more potent Ach analogue (increase response at remaining AchRs).**

Botulinus toxin causes paralysis. It binds to presynaptic sites at the motor end plate and prevents exocytotic release of transmitter. Predict the consequence (increase, decrease, no change) of blocking the release of acetylcholine at the neuromuscular junction on the following
Reasons on next page.

Parameter	**Prediction**
1. presynaptic resting potential	**No change**
2. presynaptic action potential amplitude	**No change**
3. presynaptic Ca^{2+} influx	**No change**
4. presynaptic transmitter release	**Decrease**
5. postsynaptic resting potential	**No change**
6. postsynaptic end plate potential	**Decrease**
7. postsynaptic action potential amplitude	**No AP or no change**

Below are normal values for the extracellular and intracellular concentrations of sodium and potassium ions (answer the following; do your work on the back and place answers below)

a) For the values in the below table, calculate the resting membrane potential for a normal mammalian cell? Assume other ions have a negligible contribution.
b) What is the resting membrane potential if the permeability to Na^+ doubles?
c) What is the resting membrane potential if the permeability to K^+ doubles?

Ion	**Extracellular concentration**	**Intracellular concentration**	**Relative permeability**
Na^+	**150 µM**	**15 µM**	**1**
K^+	**5 µM**	**150 µM**	**50**

a) $V_m = 60 \log \frac{(p_k[K_o] + p_{Na}[Na_o])}{(p_k[K_i] + p_{Na}[Na_i])}$ **= -76.4 mV**

b) V_m= - 68.2 mV when permeability to Na doubles

c) V_m= - 81.8 mV when permeability to K doubles

NOT REQUIRED – FOR YOUR INFORMATION

1. presynaptic resting potential: The size of the resting potential is determined by resting ion permeabilities and the intracellular and extracellular ion concentrations, principally those of K^+. A change in the presynaptic transmitter release only affects postsynaptic structures and functions. It has no effect on the resting potential of the presynaptic neuron.

2. presynaptic action potential amplitude: Action potential amplitude is determined by the E_{Na} and the number of voltage-dependent Na^+ channels that open during the regenerative phase of the action potential. Changes in the presynaptic transmitter release affect events that occur subsequently, but do not change presynaptic factors like the presynaptic action potential.

3. presynaptic Ca^{2+} influx: Calcium influx into the presynaptic terminals results from the opening of voltage-sensitive Ca^{2+} channels on the arrival of an action potential at the terminals. Neither the presynaptic AP nor the Ca^{2+} channels are altered by the toxin. Hence, presynaptic transmitter release plays no role in presynaptic Ca^{2+} influx.

4. presynaptic transmitter release: Fusion of transmitter-containing synaptic vesicles with the presynaptic membrane leads to release of transmitter into the synaptic clefts. This process depends on Ca^{2+} entry into the presynaptic terminals. Any condition that interferes with presynaptic action potential generation, Ca^{2+} entry into the presynaptic terminals, vesicle fusion, or transmitter synthesis would reduce the transmitter release. Botulinus toxin does this. It reacts with achoring proteins in the presynaptic terminals, prevents exocytosis, and reduces the ACh release into the synaptic cleft in the neuromuscular junction.

5. postsynaptic resting potential: None of the factors that determine resting membrane potential is affected by transmitter release. Hence, the postsynaptic resting potential, like the presynaptic resting potential, is unaffected by a reduction in transmitter release.

6. postsynaptic end plate potential: The end plate is a localized depolarization caused by the opening of nonspecific ligand-binding cation channels in the postsynaptic membrane. These channels are opened by the binding of ACh to specific membrane receptors. A reduction in transmitter release from the presynaptic terminals will reduce the number of receptor molecules that bind with transmitter, and this will decrease the number of cation channels that are opened. The inward current at the end plate will be reduced; and hence, the depolarization of the end plate will be smaller (a reduced end plate potential).

7. postsynaptic action potential amplitude: Action potentials are all-or-none phenomena. They either occur or they do not. If the end plate potential is large enough to depolarize the part of the sarcolemma that contains voltage-sensitive Na channels so that the channels open regeneratively (threshold), an action potential of normal size will result. If the end plate potential is too small to depolarize the sarcolemma to threshold, no action potential will occur.