

Name \_\_\_\_\_

(write your name on every sheet)

HST 131/Neuro 200  
Exam IV, Dec 17, 2004

**There are 31 questions.**  
**Point values for each are given.**  
**175 points total.**

*Electrophysiology*-----

1. (7 pt) Long-term potentiation at the CA3-to-CA1 synapse in the hippocampus has these characteristics (circle all that apply):

- a. requires extracellular  $\text{Ca}^{2+}$
- b. requires postsynaptic depolarization
- c. involves activation of protein kinase A
- d. involves insertion of new AMPA receptors in the presynaptic membrane
- e. is blocked by botulinum toxin in the postsynaptic cytoplasm
- f. shares essentially the same mechanism at all synapses that use glutamate receptors
- g. is mediated by binding of anandamide at CB1 receptors

2. (12 pt) A great many psychoactive drugs affect proteins associated with synaptic transmission. Match the drug or class of drugs with its target(s).

- |                          |   |
|--------------------------|---|
| ___ nicotine             | a. dopamine D2 receptors                        |
| ___ morphine             | b. $\text{Na}^+$ /dopamine cotransporters       |
| ___ caffeine             | c. 5HT transporters                             |
| ___ LSD                  | d. serotonin receptors                          |
| ___ tetrahydrocannabinol | e. $\text{GABA}_A$ receptors                    |
| ___ cocaine              | f. adenosine receptors                          |
| ___ reserpine            | g. vesicular $\text{H}^+$ /dopamine antiporters |
| ___ amphetamines         | h. monoamine oxidase                            |
| ___ chlorpromazine       | i. $\mu$ -opiate receptors                      |
| ___ barbiturates         | j. nACh receptors                               |
| ___ benzodiazepines      | k. CB1 receptors                                |
| ___ imipramine           | l. NMDA receptors                               |

3. (6 pt) For each of the following choose the correct receptor(s). Your choices are  
 1 = AMPA receptor    2 = NMDA receptor    3 = metabotropic glutamate receptor

- a. mediates the fastest excitatory transmission \_\_\_\_\_
- b. has seven transmembrane domains \_\_\_\_\_
- c. is blocked by extracellular  $\text{Mg}^{+2}$  \_\_\_\_\_
- d. is activated by glutamate \_\_\_\_\_
- e. associates with G-proteins \_\_\_\_\_
- f. variability in function caused by RNA editing \_\_\_\_\_

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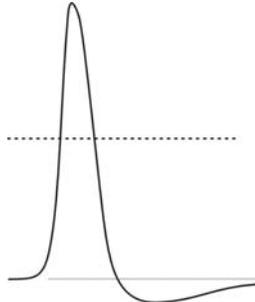
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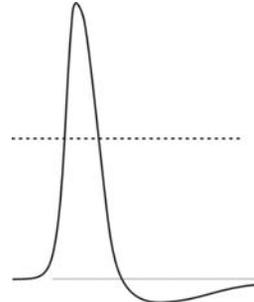
4. (4 pt) Sketch the action potential after the manipulations described below. A control trace is already sketched in each panel. The ionic conditions are given below

$[K^+]_{in} = 140 \text{ mM}$        $[K^+]_{out} = 4 \text{ mM}$   
 $[Na^+]_{in} = 10 \text{ mM}$        $[Na^+]_{out} = 140 \text{ mM}$

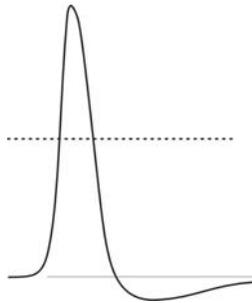
A. The sodium channels have a mutation which slows inactivation.



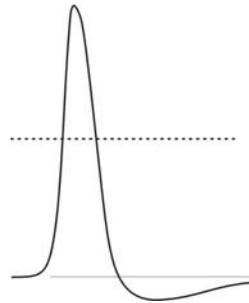
B. Enough TTX is added to block about half of the sodium channels.



C. The extracellular potassium concentration is increased to 6 mM.



D. The extracellular sodium concentration is increased to 150 mM.



5. (5 pt) Which of these are true of vesicle release?

- Cholera toxin and pertussis toxin inhibit neurotransmission by cleaving proteins of the SNARE complex.
- Synaptobrevin is the  $Ca^{2+}$  sensor triggered by  $Ca^{2+}$  influx through voltage-gated calcium channels.
- At a typical presynaptic terminal in the CNS, the readily releasable pool of vesicles numbers only 100-200.
- $Ca^{2+}$  accumulation during multiple presynaptic action potentials causes facilitation of transmitter release.
- Presynaptic G-protein coupled receptors can inhibit transmitter release both by inhibiting voltage-gated  $Ca^{2+}$  channels and by activating potassium channels.

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Neuroanatomy -----

6. (5 pt) Which of the following structures are CONTRALATERAL from the most relevant area of cerebral cortex?
- Medial lemniscus
  - Lateral lemniscus
  - Red nucleus
  - Dentate nucleus
  - Dentate gyrus
7. (5 pt) Which one of the following structures does not belong in this group?
- Nucleus cuneatus
  - Nucleus of the spinal tract of V
  - Mesencephalic nucleus of V
  - Dorsal cochlear nucleus
  - Olfactory bulb
8. (5 pt) You are examining a brain that has been cut in the sagittal plane. Which of the following combinations of structures are you most likely to see on a single slice?
- Oculomotor nucleus, trochlear nucleus, facial nucleus
  - Primary visual cortex, primary auditory cortex, primary motor cortex for the arm
  - Dentate nucleus, septal nucleus, putamen
  - Nucleus gracilis, hypoglossal nucleus, mamillary body
  - Anterior nucleus of the thalamus, inferior colliculus, middle cerebellar peduncle
9. (5 pt) Which of the following combinations of structures would be identified by staining for choline acetyl transferase (ChAT)?
- Upper motor neurons & lower motor neurons
  - Trochlear nucleus and Edinger-Westphal nucleus
  - Anterior horn cells and nucleus of Clarke's column
  - Substantia nigra, pars compacta and raphe nuclei
  - Substantia nigra, pars reticulata and ciliary ganglion neurons
10. (5 pt) Which of the following statements is the most accurate?
- Circadian rhythms depend on hypothalamic synthesis of melatonin
  - The posterior limb of the internal capsule separates thalamus from hypothalamus
  - The medial longitudinal fasciculus carries information from the hypothalamus to the brainstem
  - The stria terminalis is a bidirectional connection between the hypothalamus and the amygdala
  - Activity in the most anteromedial hypothalamus is associated with stress responses

*Sensory and Motor Systems* -----

11. (6 pt) The receptive field of a photoreceptor can be defined in terms of color and position of an object in space. For these various cells in the ascending auditory pathway, describe *in a few words* what characteristics define their receptive fields:

- saccular hair cell
- cochlear inner hair cell
- spiral ganglion neuron
- lateral superior olive neuron
- medial superior olive neuron
- primary auditory cortex neuron

12. (5 pt) Circle all the following that are true about the retina.

- a. On average, more rods than cones converge onto a single bipolar cell.
- b. The photoreceptors are nurtured by blood vessels that enter the eye via the optic nerve.
- c. ON-bipolar cells increase their rate of firing action potentials in response to light.
- d. The glutamatergic synapses between photoreceptors and OFF-bipolar cells are excitatory.
- e. Horizontal cells mediate surround inhibition by synapsing onto surrounding ganglion cells.

13. (4 pt) When making extracellular recordings from single cells in the cat visual system, in the style of Hubel and Wiesel, you will find cells with different properties depending on where your electrode is in the brain. Check all the boxes appropriate to indicate which cell types could have the properties listed on the left.

	Parvocellular LGN cell	Magnocellular LGN cell	Simple cortical cell	Complex cortical cell
Reponds best to input from both eyes				
responds best to inputs from one eye only				
receptive field is ON-center/OFF-surround				
responds best to oriented stimuli (bar at an angle)				

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14. (6 pt) Indicate all the following that are true about the cerebellum:
- Across the different functional areas of the cerebellum, the cortical structure is remarkably similar.
  - Phylogenetically speaking, the fastigial nucleus is the oldest part of the cerebellum.
  - The spinocerebellum consists of the vermis and intermediate zones, plus their deep output nuclei.
  - The interposed nuclei affect distal motor control on the same side of the body.
  - Most of the input to the most lateral parts of the cerebellar hemispheres comes directly from the cerebral cortex.
  - The leading theory on how the cerebellum operates is that complex spikes provide an "error signal" used to modify parallel fiber input through long-term depression of the parallel fiber-Purkinje cell synapse.
15. (4 pt) Describe one pharmacological treatment and one surgical treatment for Parkinsonism. What are they and how are they thought to work?

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*Development and Cognitive Disorders*-----

16. (6 pt) Match the following (refers to *Xenopus* development):

- |  |  |
|--|--|
| _____ a. Egg cytoplasm                   |  |
| _____ b. Animal pole                     | 1) Location of sperm entry                                 |
| _____ c. Vegetal pole                    | 2) Will become endoderm                                    |
| _____ d. Entry of sperm                  | 3) Is a hollow sphere of cells                             |
| _____ e. Dorsal lip of<br>the blastopore | 4) Contains the three germ layers in the<br>right position |
| _____ f. Blastula                        | 5) Has an uneven distribution of particles                 |
|  | 6) Induces the formation of the neural tube                |
|  | 7) Generates the dorsal-ventral axis                       |
|  | 8) Generates the anterior-posterior axis                   |

17. (4 pt) Which are true statements about the development of the cerebral cortex:

- a. Cell division processes control brain size
- b. Neurons arise close to their final destination in the brain so that they only have to migrate short distances.
- c. The deepest cortical layers are formed later in development than shallow layers
- d. Neurons can only migrate up to 100 times their body length due to the high metabolic cost of the process

18. (5 pt) Circle any mechanism used to change how an axon responds to cues in its environment

- a. Increase in cAMP levels
- b. Decrease in cGMP levels
- c. Target induced changes in gene expression
- d. Local protein synthesis.
- e. Changes in the composition of receptors in the growth cone.

19. (5 pt) Circle all true statements:

- a. Axons navigate distances as long as a meter to find their final targets.
- b. Slit signaling regulates whether netrin is attractive or repulsive.
- c. Semaphorins are secreted repellents for a subset of neurons in the DRG.
- d. Axon guidance molecules use small GTPases which regulate the distribution of microtubules in the growth cone.
- e. Retinotopic maps form in part because retinal ganglion cells find low levels of Ephrin attractive but high levels of Ephrin are repulsive.

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20. (4 pt) Circle all true statements:

- a. CNS axons fail to regenerate because axon guidance cues are not present in the adult nervous system.
- b. The Nogo receptor binds MAG and Omgp, which are present in CNS myelin.
- c. All axons grow at the same basic rate.
- d. Oligodendrocytes produce inhibitory factors such as Nogo66, which can induce growth cone collapse in vitro.

21. (8 pt) In class, we discussed various models for the development of the neuromuscular junction (NMJ), and discovered that no simple model seems to explain all of the experiments. Please list one experimental observation which is INCONSISTENT with each of the following hypotheses.

(1) The motor neuron requires signals from the myotube to form its synaptic machinery.

(2) The myotube requires signals from the motor neuron in order to cluster its synaptic components (e.g. AChRs).

(3) The motor neuron randomly contacts the myotube and then induces the myotube to cluster synaptic components (e.g. AChRs).

(4) The myotube generates postsynaptic clusters (e.g. AChRs) autonomously, and the motor neuron is stabilized when it encounters the postsynaptic density.

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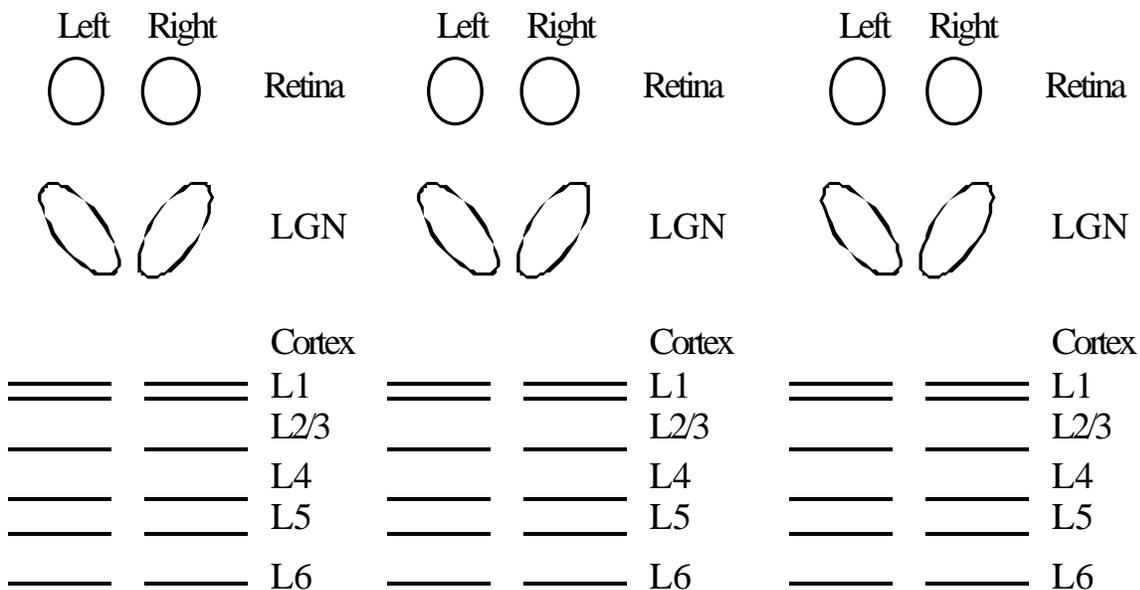
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22. (5 pt) Indicate which of the following statements about myelination are true:
- A Schwann cell forms only a single internode.
  - An oligodendrocyte is able to form internodes on multiple different axons.
  - Schwann cells are located in the central nervous system; oligodendrocytes are in the peripheral nervous system.
  - Oligodendrocytes originate from peripheral blood monocytes which migrate into the CNS.
  - Oligodendrocytes secrete factors which are able to cluster axonal nodal proteins (Na<sup>+</sup> channels, K<sup>+</sup> channels, etc.) in cultured axons.
23. (5 pt) Indicate whether each statement is a feature of apoptosis (A), necrosis (N):
- \_\_\_\_\_ Mitochondrial breakdown is observed.
- \_\_\_\_\_ Chromatin pattern in nucleus is disturbed.
- \_\_\_\_\_ Following swelling, membrane breaks down.
- \_\_\_\_\_ Can be regulated by neurotrophins.
- \_\_\_\_\_ Cells condense.
24. (4 pt) Circle all true statements:
- Apoptosis is a natural process that is regulated by a balance between pro-survival Bcl-2 like proteins and pro-apoptotic Bax like proteins.
  - Axons compete for limiting amounts of neurotrophins produced by target cells.
  - The neurotrophic hypothesis states that axons fail to regenerate because of the absence of neurotrophins in the central nervous system.
  - NGF and BDNF both induce dephosphorylation of Trk receptors.
25. (5 pt) Indicate which of the following is/are true of neuronal stem cells.
- Though *in vivo* neurogenesis is limited to the subventricular zone, *in vitro* studies have shown that there are neuronal precursors in many other brain regions.
  - To be classified as a stem cell, a cell must have unlimited capacity for self-renewal.
  - Neuronal stem cells are not as well studied as hematopoietic stem cells because of the lack of a true reconstitution assay.
  - Stem cells can be classified as totipotent or multipotent.
  - It is not yet possible to induce neurogenesis in regions of the adult brain where it does not normally occur.

26. (6 pt) Consider the pathway from temporal retina of the left eye and the nasal retina of the right eye through the LGN and to visual cortex. Using a solid line for the left eye projection and a dashed line for the right eye projection, draw a schematic picture of the retinogeniculate projection and thalamocortical projection (including the arbor) from **cats** of the following ages. Indicate the layer of cortex that LGN neurons project to:

- a) late prenatal (e50)
- b) 3 years old
- c) 3 years old, with the first 6 months with the left eye sutured shut.



27. (6 pt) Circle all true statements.
- a. The cellular swelling which occurs during ischemia is due to Na<sup>+</sup> and Cl<sup>-</sup>.
  - b. During ischemia, increases in intracellular calcium contribute to cell death
  - c. A decrease in reactive oxygen species is a sign of ischemia as the mitochondrial oxidative phosphorylation machinery slows down
  - d. Within 45 minutes of a stroke the ischemic damage is irreversible and so recovery of CNS function is not possible
  - e. A majority of strokes are due to intracerebral hemorrhage
  - f. "Lacunar" strokes are due to defects in small cerebral vessels

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28. (5 pt) Circle all true statements about Alzheimer's Disease:

- a. Plaques are present in the neuropil, while tangles occur inside the neuronal cell body.
- b. Cleavage by gamma secretase is essential for production of  $A\beta$ , the major component of plaques.
- c. Deposition of  $A\beta$  is a clear indicator of the changes in cognition associated with Alzheimer's Disease.
- d. APP is a transmembrane protein whose biochemical functions are unknown.
- e. The pathology of Alzheimer's Disease is usually preceded by obvious changes in cognition and behavior.

29. (4 pt) Mark whether each of these statements about memory is true or false. If the statement is false, rewrite the statement correctly.

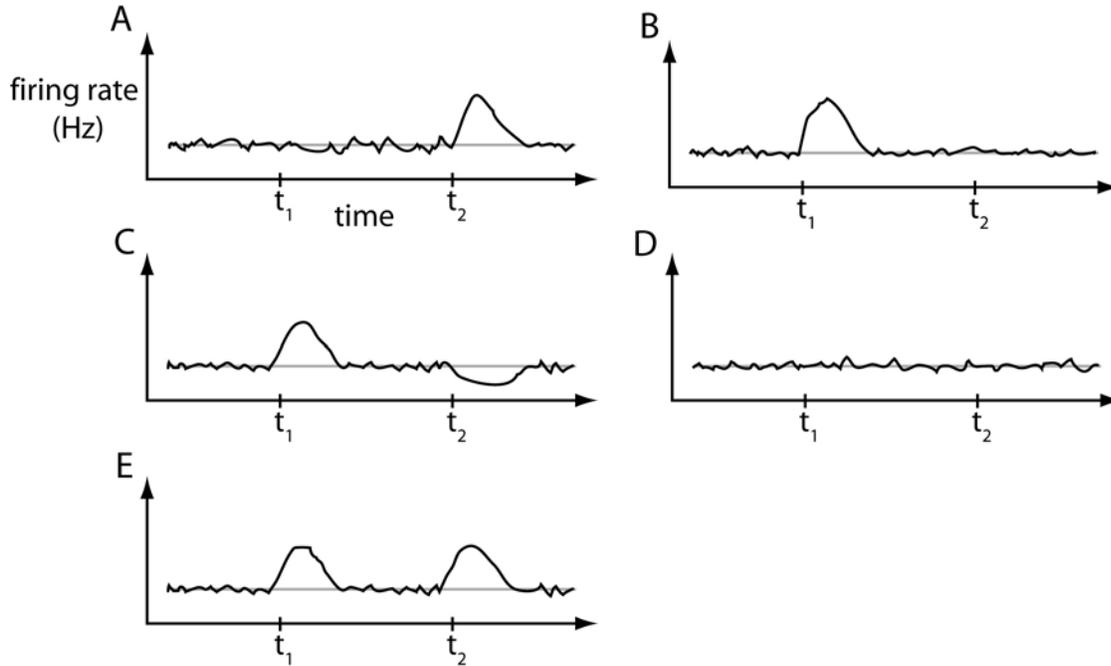
False memories activate neurons in the hippocampus: T F

Memories can be distorted by misattribution, suggestibility or lapses in attention: T F

Structural encoding of information is the most effective way to remember: T F

Implicit and explicit forms of memory are regulated by the hippocampus and basal ganglia respectively: T F

30. (6 pt) Depicted are a series of peri-stimulus time histograms (PSTHs) of the response of a dopaminergic neuron in the substantia nigra pars compacta. Match each of the following PSTHs with the description of the experimental situation that would give rise to it. As a reminder, a PSTH is a plot of the average firing rate of the neuron over time. Firing rate is plotted on the ordinate and time is on the abscissa. The baseline firing rate is shown as a grey line. In A, for example, the neuron exhibits a brief increase in its firing rate (a “burst”) after an event at time  $t_2$ .



	event at $t_1$	event at $t_2$
_____	no event	reward!
_____	no event	no reward
_____	random tone which gives no information about future probability of reward	reward!
_____	tone which predicts reward at $t_2$ , but animal has never heard the tone before	reward!
_____	tone which predicts reward at $t_2$ , and animal has learned the tone-reward pairing	reward!
_____	tone which predicts reward at $t_2$ , and animal has learned the tone-reward pairing	no reward

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31. (13 pt) From the wide range of topics covered in the fourth block, you have learned a lot about how certain neurological disorders can arise. Match each disease in the left column with a related statement about neurobiology in the right column. More than one statement may be appropriate, not all statements need to be used, and statements can be used more than once. Write the appropriate number(s) next to the disease in the first column.

a. Alcoholism	1. May be caused by abnormal dispersion of GABAergic neurons in the cortex
b. Cataracts	2. Has been conclusively shown to be a disease of the peripheral immune system
c. Post traumatic stress disorder	3. Affects both Gaba-R and NMDA-R
d. Abnormal eye movements	4. Caused by abnormal regulation of axon guidance signals
e. Hallucinogenic drugs	5. May be due to defects in oligodendrocytes
f. Schizophrenia	6. Caused by mutations in components of the cell death pathway
g. Loss of pain sensitivity	7. Depletes energy supplies and leads to accumulation of glutamate in the extracellular space
h. Multiple sclerosis	8. Occurs when convergent extension fails
i. Brain tumors	9. Caused by an abnormal form of BDNF that is not properly regulated by activity
j. Spina bifida	10. Activation of serotonergic neurons which project throughout the brain
k. Stroke	11. Reveal the presence of a critical period in development
l. ALS	12. Due to mutations in TrkA
m. Spinal cord injury	13. Is a disease of fear conditioning
	14. May be due to defects in Schwann cells
	15. May be treated with $\beta$ -adrenergic blockers in the future
	16. Is caused by loss of myelin in the peripheral nervous system
	17. Induces formation of a glial scar