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 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	j	a. dopamine D2 receptors
___morphine	i	b. Na+/dopamine cotransporters
___caffeine	f	c. 5HT transporters
___LSD	d	d.serotonin receptors
___tetrahydrocannabinol	k	e. $GABA_A$ receptors
___cocaine	b	f. adenosine receptors
___reserpine	g	g. vesicular H+/dopamine antiporters
___amphetamines	g,h,a	h. monoamine oxidase
___chlorpromazine	a	i. μ-opiate receptors
___barbiturates	e	j. nACh receptors
___benzodiazepines	e	k. CB1 receptors
___imipramine	c	l. NMDA receptors

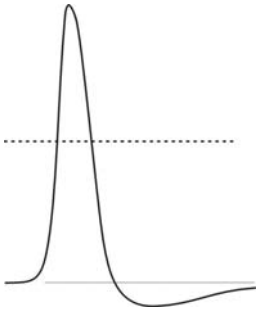
3. (6 pt) For each of the following choose the correct receptor(s). Your choices are
1 = AMPA receptor 2 = NMDA receptor 3 = metabotropic glutamate receptor

a.	mediates the fastest excitatory transmission	____1
b.	has seven transmembrane domains	____3
c.	is blocked by extracellular Mg^{+2}	____2
d.	is activated by glutamate	____1,2,3
e.	associates with G-proteins	____3
f.	variability in function caused by RNA editing	____1

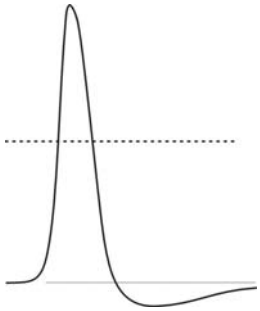
4. (4 pt) Sketch the action potential after the manipulations described below. A control trace is already sketched in each panel. The ionic conditions are given below

[K+]in = 140 mM [K+]out = 4 mM
[Na+]in = 10 mM [Na+]out = 140 mM

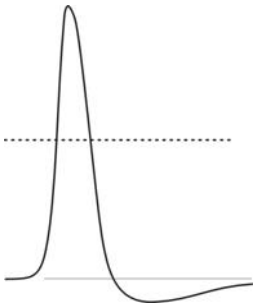
A. The sodium channels have a mutation which slows inactivation.



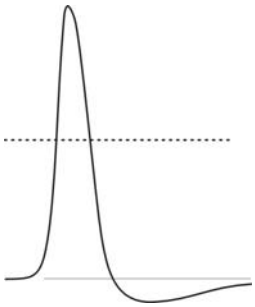
B. Enough TTX is added to block about half of the sodium channels.



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



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



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

a. Cholera toxin and pertussis toxin inhibit neurotransmission by cleaving proteins of the SNARE complex.

b. Synaptobrevin is the Ca^{2+} sensor triggered by Ca^{2+} influx through voltage-gated calcium channels.

c. At a typical presynaptic terminal in the CNS, the readily releasable pool of vesicles numbers only 100-200.

d. Ca^{2+} accumulation during multiple presynaptic action potentials causes facilitation of transmitter release.

e. Presynaptic G-protein coupled receptors can inhibit transmitter release both by inhibiting voltage-gated Ca^{2+} channels and by activating potassium channels.

Neuroanatomy ----------

6. (5 pt) Which of the following structures are CONTRALATERAL from the most relevant area of cerebral cortex?
   a. Medial lemniscus
   b. Lateral lemniscus
   c. Red nucleus
   d. Dentate nucleus
   e. Dentate gyrus

7. (5 pt) Which one of the following structures does not belong in this group?
   f. Nucleus cuneatus
   g. Nucleus of the spinal tract of V
   h. Mesencephalic nucleus of V
   i. Dorsal cochlear nucleus
   j. 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?
   k. Oculomotor nucleus, trochlear nucleus, facial nucleus
   l. Primary visual cortex, primary auditory cortex, primary motor cortex for the arm
   m. Dentate nucleus, septal nucleus, putamen
   n. Nucleus gracilus, hypoglossal nucleus, mamillary body
   o. 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)?
   p. Upper motor neurons & lower motor neurons
   q. Trochlear nucleus and Edinger-Westphal nucleus
   r. Anterior horn cells and nucleus of Clarke's column
   s. Substantia nigra, pars compacta and raphe nuclei
   t. Substantia nigra, pars reticulata and ciliary ganglion neurons

10. (5 pt) Which of the following statements is the most accurate?
   u. Circadian rhythms depend on hypothalamic synthesis of melatonin
   v. The posterior limb of the internal capsule separates thalamus from hypothalamus
   w. The medial longitudinal fasciculus carries information from the hypothalamus to the brainstem
   x. The stria terminalis is a bidirectional connection between the hypothalamus and the amygdala
   y. 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
direction of acceleration (or gravity)
cochlear inner hair cell
auditory frequency
spiral ganglion neuron
auditory frequency (and intensity)
lateral superior olive neuron
loudness difference between the two ears
medial superior olive neuron
arrival time difference between the two ears
primary auditory cortex neuron
frequencies and duration of sound;

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			x	x
responds best to inputs from one eye only	x	x	x	x
receptive field is ON-center/OFF-surround	x	x	x	
responds best to oriented stimuli (bar at an angle)			x	x

14. (6 pt) Indicate all the following that are true about the cerebellum:

a. Across the different functional areas of the cerebellum, the cortical structure is remarkably similar.

b. Phylogenetically speaking, the fastigial nucleus is the oldest part of the cerebellum.

c. The spinocerebellum consists of the vermis and intermediate zones, plus their deep output nuclei.

d. The interposed nuclei affect distal motor control on the same side of the body.

e. Most of the input to the most lateral parts of the cerebellar hemispheres comes directly from the cerebral cortex.

f. 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?

Pharm treatments should center on dopamine levels
L-Dopa, MAOIs, or DopaR agonists acting to relieve the loss of dopaminergic transmission.

Surgical treatments I see as being either deep brain stimulation or a pallidotomy to relieve the overactivity of the basal ganglia's indirect pathway.

Development and Cognitive Disorders----------

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

__5___ a. Egg cytoplasm

__1___ b. Animal pole

__2___ c. Vegetal pole

__7___ d. Entry of sperm

__6___ e. Dorsal lip of the blastopore

__3___ f. Blastula

1) Location of sperm entry
2) Will become endoderm
3) Is a hollow sphere of cells
4) Contains the three germ layers in the right position
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.

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.

Growth cones release ACh spontaneously and in response to electrical stimulation before they contact myotubes.

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

Cultured myotubes cluster postsynaptic receptors in the absence of motor neurons.

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

Tello: after nerve lesion motor fiber clusters are maintained and new nerves growing onto the fiber synapse on these old clusters.

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

Anderson and Cohen: although cultured myotubes cluster postsynaptic receptors autonomously, co-cultured motor neurons contact the myotubes at sites without clusters and new clusters form at the site of neuronal contact.

22. (5 pt) Indicate which of the following statements about myelination are true:
a. A Schwann cell forms only a single internode.
b. An oligodendrocyte is able to form internodes on multiple different axons.
c. Schwann cells are located in the central nervous system; oligodendrocytes are in the peripheral nervous system.
d. Oligodendrocytes originate from peripheral blood monocytes which migrate into the CNS.
e. Oligodendrocytes secrete factors which are able to cluster axonal nodal proteins (Na+ channels, K+ channels, etc.) in cultured axons.

23. (5 pt) Indicate whether each statement is a feature of apoptosis (A), necrosis (N):

__N___ Mitochondrial breakdown is observed.

__A___ Chromatin pattern in nucleus is disturbed.

__N___ Following swelling, membrane breaks down.

__A___ Can be regulated by neurotrophins.

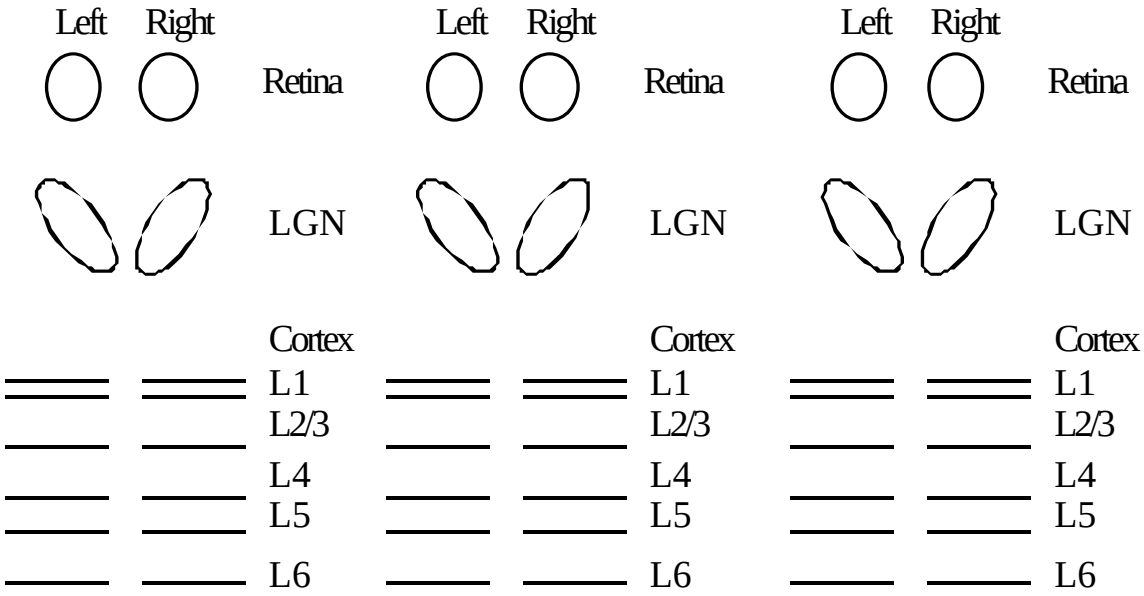
__A___ Cells condense.

24. (4 pt) Circle all true statements:
a. Apoptosis is a natural process that is regulated by a balance between pro-survival Bcl-2 like proteins and pro-apoptotic Bax like proteins.
b. Axons compete for limiting amounts of neurotrophins produced by target cells.
c. The neurotrophic hypothesis states that axons fail to regenerate because of the absence of neurotrophins in the central nervous system.
d. NGF and BDNF both induce dephosphorylation of Trk receptors.

25. (5 pt) Indicate which of the following is/are true of neuronal stem cells.
a. 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.
b. To be classifed as a stem cell, a cell must have unlimited capacity for self-renewal.
c. Neuronal stem cells are not as well studied as hematopoetic stem cells because of the lack of a true reconstitution assay.
d. Stem cells can be classified as totipotent or multipotent.
e. 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.



Points for:

1) correct crossing of ganglion axons (nasal crosses, temporal does not)
2) LGN projects to layer IV of cortex.
3) LGN layer segregation in newborn
4) cortical arbor overlap in newborn*
5) LGN layer segregation in 3 year old
6) cortical arbor segregation in 3 year old
7) LGN layer shrinkage of left, expansion of right in MD
8) cortical arbor shrinkage of left, expansion of right in MD.

27. (6 pt) Circle all true statements.

a. The cellular swelling which occurs during ischemia is due to Na+ and Cl-.
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

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 Aβ, the major component of plaques.

c. Deposition of Aβ 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

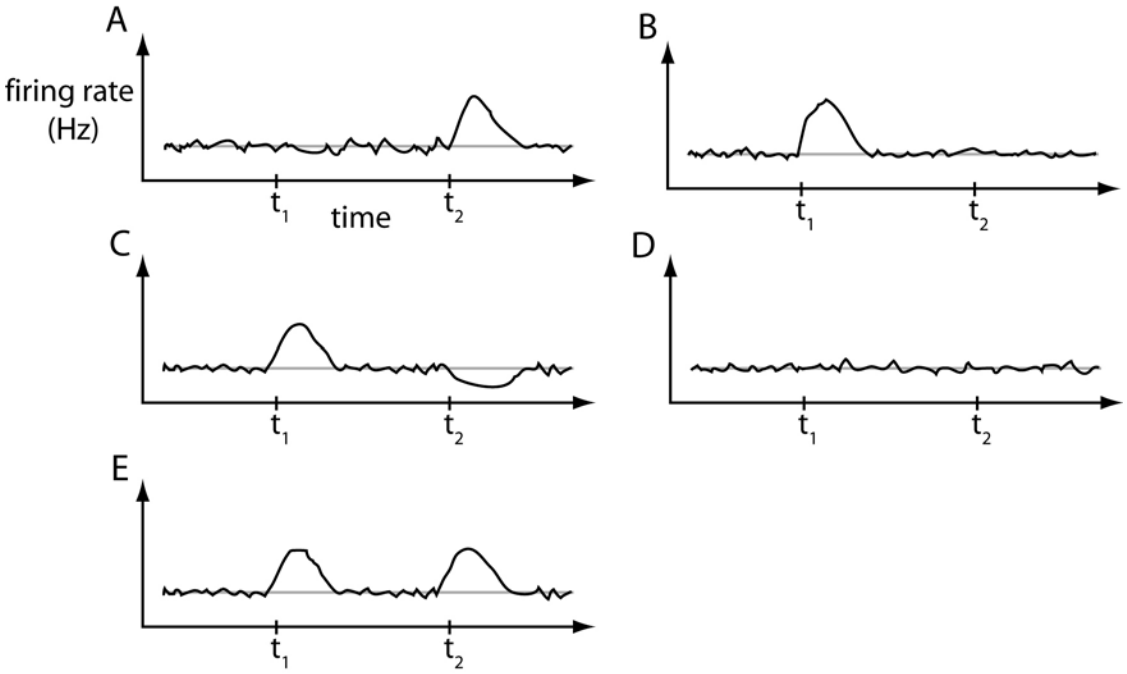
Memories can be distorted by misattribution, suggestibility or BIAS

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

SEMANTIC encoding of information is the most effective way to remember

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

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