Name _____

(write your name on every sheet)

HST 131/Neuro 200
Exam I, Sept 24, 2003

There are 25 questions. Point values for each are given. 100 points total.

E1) (3 pts) Circle all the correct statements:

a) Aside from its affect on Nernst potentials, the Na^+-K^+ ATPase can hyperpolarize a cell because it pumps more Na^+ out than K^+ in.
b) The time constant for equilibration of a voltage-gated ion channel to the new open probability after a voltage step is most rapid near the half-activation potential.
c) The GHK equations assume that inward flow through a channel does not affect outward flow.**
d) If the leak current of a cell only goes through K^+ channels open at rest, blocking half these K^+ channels will not alter the cell's resting potential.**
e) The reversal potential of a K^+-selective channel is in part determined by its conductance.

E2) (2 pts) What was the technical breakthrough that Hodgkin and Huxley used to study voltage-gated channels?

a) Keeping voltage fixed while measuring current **
b) Keeping current fixed while measuring voltage
c) The giant squid axon, because it only has sodium channels
d) Inside-out patch clamping

E3) (3 pts) The m, n and h parameters that Hodgkin and Huxley used were really just variables in a mathematical formalism that can describe sodium and potassium currents. Nevertheless, imagining them as physical gates is a useful way to think about channels, and is not so far from modern views based on molecular structure. With this caveat, which of the following are true?

a) Three m gates have to open before a channel can conduct. **
b) Four n gates have to close before a channel can close.
c) h gates are opened by hyperpolarization. **
d) n gates generally open and close faster than m gates
e) Increasing temperature makes channels open faster because of the RT/zF term in the Nernst potential equation
f) For potassium channels that do inactivated (where open probability might be described as n4h) the amino terminus of the protein acts like an h gate. **

E5) (2 pts) Which of the following help set up the gradient found in mammalian intracellular and extracellular ion concentrations? Circle all that apply.

a) The Na/K ATPase pump extrudes 3 Na ions and brings in two K ions.
b) K leak channels open at rest allow K fluxes to equilibrate the concentrations until Erest~-70mV.
c) Cl leak channels, which only allow Cl to flow in one direction.
d) The Ca-ATPase pump, which pumps one Ca into the cell for each ATP hydrolyzed.
e) The equivalent circuit Na battery, which balances the outward Na flux through the Na channels due to the chemical gradient with an electrical gradient only felt by Na ions.

E7) (4 pts) Label the properties of axons (A), dendrites (D), both (A&D) or neither (leave blank).
___ Originates from a specialized segment from the cell body
___ Unmyelinated
___ Contains ER or ribosomes
___ Cylindrical in shape
___ Does not branch
___ Can contain presynaptic release sites
___ Contains voltage-gated ion channels

E8) (4 pts) Recently researchers have used viruses injected into leg muscles of mice to deliver genetic material to the cell bodies of motor neurons. Judging from your knowledge of axonal transport, what is the most likely motor that transports this virus?
_____ (dynein)

What neuronal cytoskeletal component would this motor travel on? _____
(microtubules)

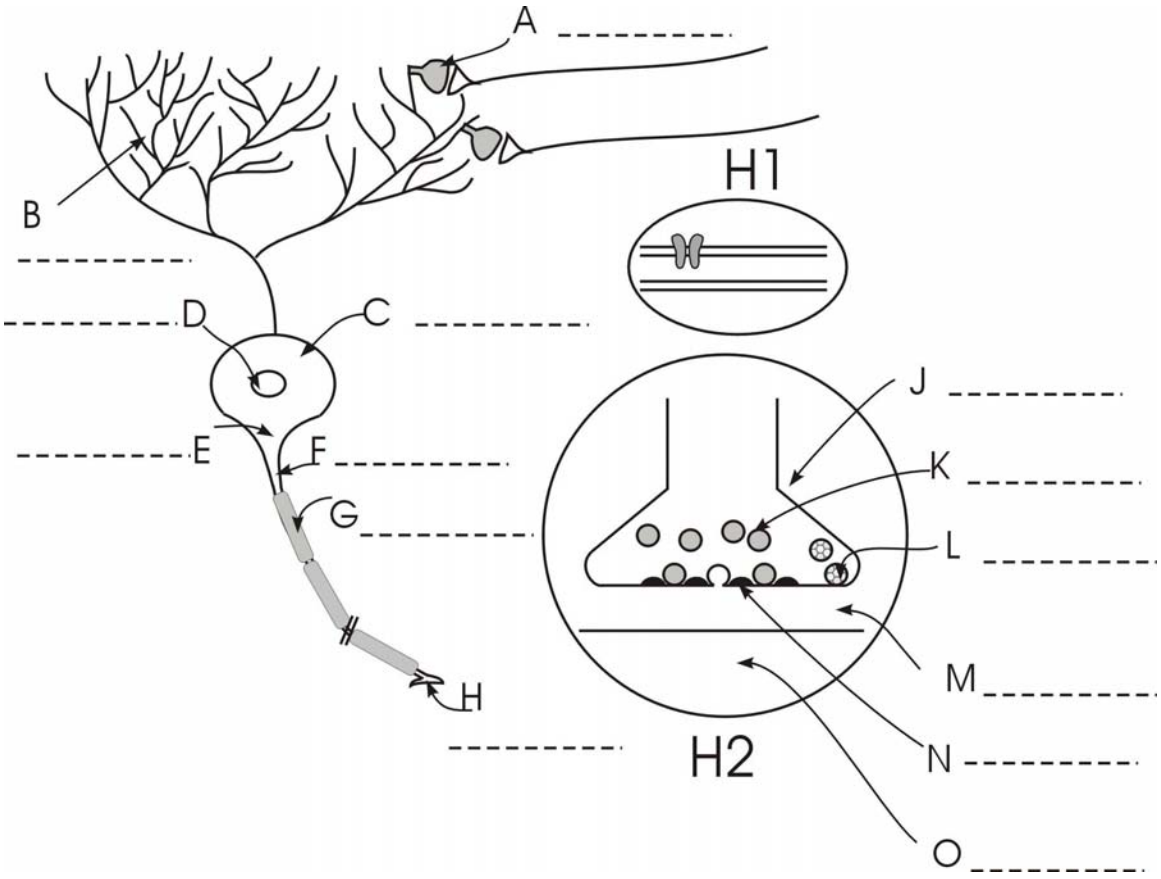
How long would this transport take, assuming a 10cm motor neuron? _____
(0.5 day at ~200mm/day)

Name two diseases that use this transport mechanism. _____

E9a) (8 pts) Label the structures from A to G. (see next page)

b) H1 is a schematic of an electrical synapse. Name the proteins that form the channel found in these synapses. Draw their spatial distribution in the synapse. (The diagram has already been started for you.)

c) H2 is a schematic of a chemical synapse. Label the structures from J-O. In the space below, give one example of a receptor channel found in the CNS, and one in the PNS, and draw their distribution in the synapse.



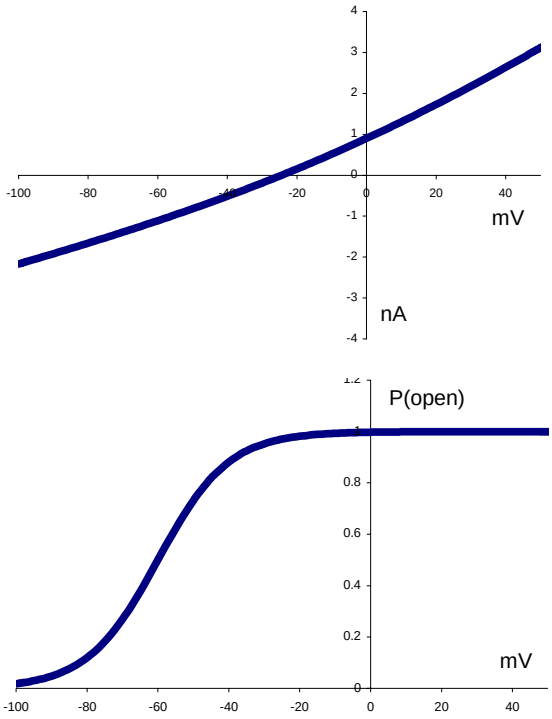
E10) (2 pts) For typical mammalian ion concentrations, list the reversal potentials of the following channels in order from most negative to most positive by their enumeration. (e.g. 1.=2.<3.<4.<5. etc.)

1. Voltage-gated potassium channel
2. Voltage-gated sodium channel
3. Voltage-gated calcium channel
4. AChR channel
5. Connexon (Gap Junction) Channel
6. NMDA receptor channel
7. GABA receptor channel

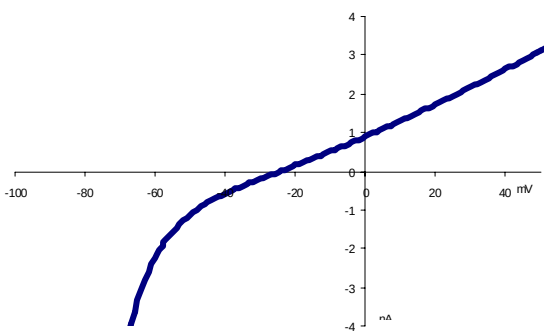
1<7<4=5=6<2<3

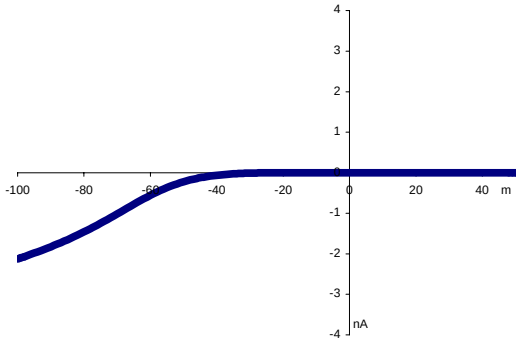
Jim's Questions

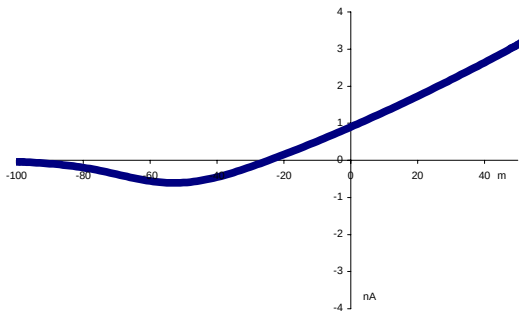
J1) (3 pts) You are studying the chloride conductance by two-electrode voltage clamp in Xenopus oocytes. Based on your chloride concentrations and previous studies, you predict the following open channel IV and P(open) curves:

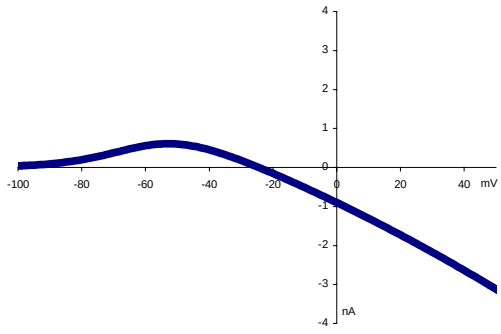


Choose the correct steady-state IV that you predict based upon the above curves:









J2) (2 pts) In order to design a computer model for a newly discovered type of neuron, you need to determine the intracellular sodium concentration. After isolating the sodium current by pharmacologically blocking all other currents, you voltage-clamp the neuron and record
–10nA of current at 0mV and –22nA of current at –60mV. Using your bath concentration of sodium (150mM), calculate the internal sodium concentration.

a) 101mM
b) 20.9mM**
c) 13.6mM
d) 5.31mM

J3) (2 pts) You are recording from a remarkably spherical mast cell. Following stimulation, you realize that due to so much exocytosis, the diameter of the cell has doubled! (d->2d). Based upon your original calculation that the membrane's time constant is 8ms, predict what the new time constant will be.

a) 2ms
b) 4ms
c) 16ms
d) 32ms**

Lecture 5: Action Potentials
J4) (2 pts) Briefly (<20 words each), describe the salient features of the following:

Absolute refractory period:

Relative refractory period:

J5 a) (2 pts) For each of the following, state whether the threshold voltage would be hyperpolarized, depolarized, or remain the same.

-You block 25% of the cell's sodium channels with a small amount of TTX.
-You apply a drug that shifts the V_{mid} for opening of potassium channels to a voltage which is 50mV more depolarized.

b) For each of the following state whether the half-width of the action potential will increase, decrease, or remain the same.

-You slow potassium channel opening by a factor of 4.
-A mutation causes sodium channels to inactivate with a time constant 3 times faster than normal.

J6) (1 pt) By increasing the membrane _____ and decreasing the membrane _____, myelin acts to increase the conduction velocity of an action potential down an axon.

Epilepsy:

J7) (5 pts) An "aura" of altered consciousness is primarily associated with which type of seizure?

A) Simple Partial
B) Complex Partial
C) Tonic-Clonic Generalized
D) Absence Generalized

a) What fraction of children diagnosed with epilepsy have "medically intractable epilepsy"?

A) 1/6
B) 1/4
C) 1/3
D) 1/2

b) List two treatment options for these patients.

Mac's questions

M1. (3 pts) For the following proteins of the core release machinery, state whether they are:
(a) localized to the synaptic vesicle or the plasma membrane/active zone, and
(b) how many coiled coils they contribute to the core complex

	Localization	# coiled coils
Synaptobrevin		
Syntaxin		
SNAP-25		

M2a) (4 pts) Evidence that the SNARES are essential for synaptic transmission is indicated by the action of tetanus and botulinum toxins on these proteins. Despite similar targets, tetanus toxins cause a rigid paralysis and botulinum toxins cause a flaccid paralysis. In one or two sentences, explain why.

b) Evidence that the SNARES are essential for synaptic transmission is indicated by the action of tetanus and botulinum toxins on these proteins. Briefly, provide a molecular mechanism for these toxins in disrupting synaptic transmission.

M5. (3 pts) What are three required conditions for the NMDA receptor to open and allow current to pass?

a. (Bind glutamate (agonist))

b. (Bind glycine (co-agonist))

c. (Cell must be depolarized to remove Mg+2 block)

M6. (3 pts) Name three ways to generate diversity of response within the ionotropic glutamate receptor channel family:

a. (RNA editing)

b. (Alternative splicing)

c. (Heteromultimers/different subunit construction)

M7. (2 pts) Which of the following are true of RNA editing in ionotropic glutamate receptors?

a. Receptor editing occurs in NMDA-R subunits and not AMPA-R subunits (F)
b. The frequency of RNA editing is developmentally regulated (T)
c. RNA editing confers Ca^{2+} permeability on channels containing the edited subunit (F)

M8. (2 pts) One example of splice variation in receptor composition is the FLIP/FLOP splice cassettes of AMPA channels. Which of the following are true:

a. Channels cannot contain subunits with both FLIP and FLOP (F)
b. FLOP is expressed early in development, while FLIP is expressed later (F)
c. Larger currents pass through FLIP than FLOP because these channels are less likely to desensitize (T)
d. The FLIP/FLOP splice cassette is in the extracellular domain of the protein (T)

M9. (1 pt) Which of the following are the major inhibitory neurotransmitter receptors of the central nervous system?
a. Glycine receptors
b. Endogenous opioid receptors
c. NMDA receptors
d. GABAa receptors
e. 5-HT3 receptors

M10. (2 pts) Which of the following statements about G-protein coupled receptors are true?

a. All of them contain 7 transmembrane domains (T)
b. Unlike many ionotropic receptors, they do not desensitize (F)
c. They are ADP- ribosylated by pertussis and cholera toxins, which render them constitutively active (F)
d. They can amplify a signal by activating numerous G-proteins (T)

M13. (2 pts) In a certain neuron, activation of mGluRs results in phosphorylation of K+ channels which are normally open at rest. This closes many K+ channels that are normally open at rest by shifting the open-probability curve.

a. Will this cause E_{rev} for K+ to be more positive, more negative, or no change?

b. Will this cause membrane resistance (Rm) to increase, decrease, or stay the same?

c. Suppose the synaptic terminal contains both AMPA receptors and mGluRs. What will the effect of mGluRs be on the EPSC magnitude in response to a single presynaptic action potential?

d. Suppose the synaptic terminal contains both AMPA receptors and mGluRs. What will the effect of mGluRs be on the EPSC magnitude following a train of pulses?

M14. (3 pts) Activation of the parasympathetic nervous system can cause the heart rate to slow by release of neurotransmitter onto cardiac cells. This long-lasting effect is mediated by a G-protein coupled receptor.

a. What neurotransmitter is used?

b. What pharmacological subtype of transmitter receptor transduces this signal?

c. What type of channel is affected in the cardiac cells that slows the heart rate?
Specifically, name:
The ion the permeates the channel:
Whether channel is more likely to be open/closed following the G-protein cascade:
The subtype/name of this channel:

K1) (2 pts) Hyperkalemic periodic paralysis: (circle all that are true)

a) caused by a mutation in a sodium channel that impairs its ability to inactivate
b) may cause myotonia due to depolarization of the muscle cell.
c) may cause flaccid paralysis due to hyperpolarization of the muscle cell.
d) may cause seizures or cardiac arrythmia because the affected channel is expressed in many tissues
e) may be the result of very few (< 5%) of the sodium channels having a mutation

Answers: A, B, E

K2) (2 pts) An axon synapses onto a dendrite and causes a depolarization of 20 mV. The length constant of the cell is 200 m and the time constant is 10 ms. What is the peak depolarization 300 m away from the site of the input?

Answer:

V = Vo*e^(-x/lamda)
V = 20*e^(-300/200)
V = 4.46 mV

K3) (3 pts) Which of the following statements about dendrites is/are true?
a. The solution for the length constant of the cell does not depend on membrane capacitance because it assumes the voltage is at steady state
b. An EPSP will typically spread farther from the soma into the dendrites than from a site on the distal dendrites toward the soma.
c. An inhibitory input will attenuate an excitatory input more if it arrives more distally relative to the excitatory input as opposed to arriving closer to the soma than the excitatory input.
d. An action potential generated in the axon hillock will typically travel only down the axon because leak channels in the soma prevent it from propagating back into the dendrites.
e. If several nearby synapses are activated at the same time they can generate a local action potential because dendrites are not always passive membranes.

Answer: A, B, E

K4) (2 pts) After many long hours of struggle, you are able to patch onto the cell body of a Bergmann glia which ensheaths the synapses of the climbing fiber onto the Purkinje cell. These glia have AMPA receptors, but you find that the depolarization caused by glutamate binding to these receptors is much less than the depolarization that the glutamate causes in the Purkinje cell. You imagine there are two reasons for this. What are they?

Answers: 1. Purkinje cell AMPA receptors are directly opposed to the climbing fiber release site. Therefore a much higher concentration of glutamate reaches these synaptic receptors than reaches the AMPA receptors on the nearby glia. Also, the input resistance of the glia is much lower than that of the neuron, so the current causes less depolarization.

K5) (3 pts) You are patching cells in a cerebellar slice and you begin to worry that you may accidentally patch onto a glial cell and mistake it for a neuron. But then you relax because you realize that if you were to patch a glial cell, there are three easy ways you could tell the difference between it and a neuron. What are they?

Answers: 1. Lower input resistance
2. Lower resting membrane potential
3. No action potentials in response to current injection

K6) (2 pts) Which of the following about glia are true?

a. Astrocytes must be in direct contact with cultured neurons for synapses to form.
b. Once synapses have formed, astrocytes can be removed from neuronal cultures and the synapses will remain intact.
c. Electrical activity of neurons is necessary for division of oligodendritic precursor cells.

d. Newly differentiated oligodendrocytes cannot survive long-term and will undergo apoptosis after several days if they do not come in contact with trophic factors, either secreted by astrocytes or on the surface of neurons.

Answer: C

Amy's Questions

A1. (2 pts) Which of the following proteins are located on the presynaptic plasma membrane and are thought to play an important role in vesicle fusion? (Circle all that apply).

a)synaptotagmin
b)n-Sec1(munc-18)
c)synaptobrevin
d)syntaxin
e)SNAP-25

Answer: d, e

A3. (3 pts) When a neuron is stimulated with 5 successive pulses at 100 Hz, the second EPSC of the postsynaptic neuron is larger than the first, but each subsequent EPSC is smaller than the first. Which of the following most likely explain these phenomena? (Circle all that apply).

a)the facillitation of the second EPSC results from build up of residual calcium near the release machinery in the presynaptic terminal
b)the facillitation of the second EPSC results from more neurotransmitter being pumped into synaptic vesicles in response to increased activity in the nerve terminal
c)the facillitation of the second EPSC results from many more vesicles being transported to the active zone
d)the depression of the subsequent responses results from the desensitization of the release machinery to calcium
e)the depression of subsequent responses results from depletion of vesicles at the active zone
f)none of the above

Answer: a, e

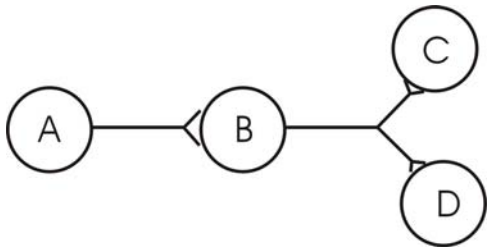
A4. (3 pts) You have isolated two neurons in a dish. You stimulate one neuron that releases glutamate and record currents from its postsynaptic target. Which of the following manipulations would decrease the magnitude of the response? (Circle all that apply)

a)blocking neurotransmitter reuptake
b)insertion of new more glutamate receptors in the postsynaptic membrane

c)activating a metabotropic receptor that closes a class of potassium channels in the postsynaptic membrane
d)activating a metabotropic receptor that closes a class of sodium channels in the postsynaptic membrane
e)applying benzodiazepine, which enhances GABA transmission
f)none of the above

Answer: d

A5. (2 pts) You stimulate neuron A, and neuron B fires an action potential. Neuron B is connected to Neuron C and Neuron D. Neuron C is excited by stimulation of Neuron A, which Neuron D is depressed. What are the most likely explanations? (Circle all that apply)



a)Neuron B releases glutamate from its nerve terminals that connect to Neuron C, while it releases GABA from nerve terminals that connect to Neuron D
b)Neuron B releases glutamate. Neuron C expresses AMPA receptors, while Neuron D expresses metabotropic receptors that act to decrease excitability
c)Neuron B releases glutamate. Neuron C expresses AMPA receptors, while Neuron D expresses NMDA receptors
d)Neuron B releases GABA. Neuron B is connected to Neuron C through gap junctions, while Neuron D expresses ionotropic GABA receptors
e)none of the above

Answer: b, d

A6. (3 pts) You stimulate Neuron X, which releases neurotransmitter onto Neuron Y. You measure an EPSC in Neuron Y that decays with a time constant of 1 msec. This time constant for currant decay through ionotropic receptors:

a)depends on the capacitance of the membrane
b)depends on the duration the neurotransmitter remains in the synaptic cleft
c)depends on the desensitization rate of the neurotransmitter receptors
d)a and b
e)a and c
f)b and c
g)all of the above
h)none of the above
Answer: f

A7. (2 pts) You are treating a depressed patient with a drug that blocks norepinephrine reuptake. Which of the following factors would best correlate with the clinical effect

(alleviation of depression)? Circle all that apply.

a)increased levels of neurotransmitter
b)increased number of beta-norepinephrine receptors
c)increased levels of second messengers such as cAMP and PKA
d)increased levels of transcriptional regulators such as CREB
e)increased levels of glucocorticoids

Answer: c,d

A8. (3 pts) You are treating a patient with schizophrenia. Which of the following drugs would you expect to alleviate your patient's symptoms? Circle all that apply.

a)a drug that increases dopamine release
b)a drug that blocks dopamine reuptake
c)a drug that activates D2 dopamine receptors
d)a drug that blocks D2 dopamine receptors
e)a drug that activates 5HT-2 serotonin receptors
f)a drug that blocks 5HT-2 serotonin receptors

Answer: d,e