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SBE2 2012: Exam 1 Solutions

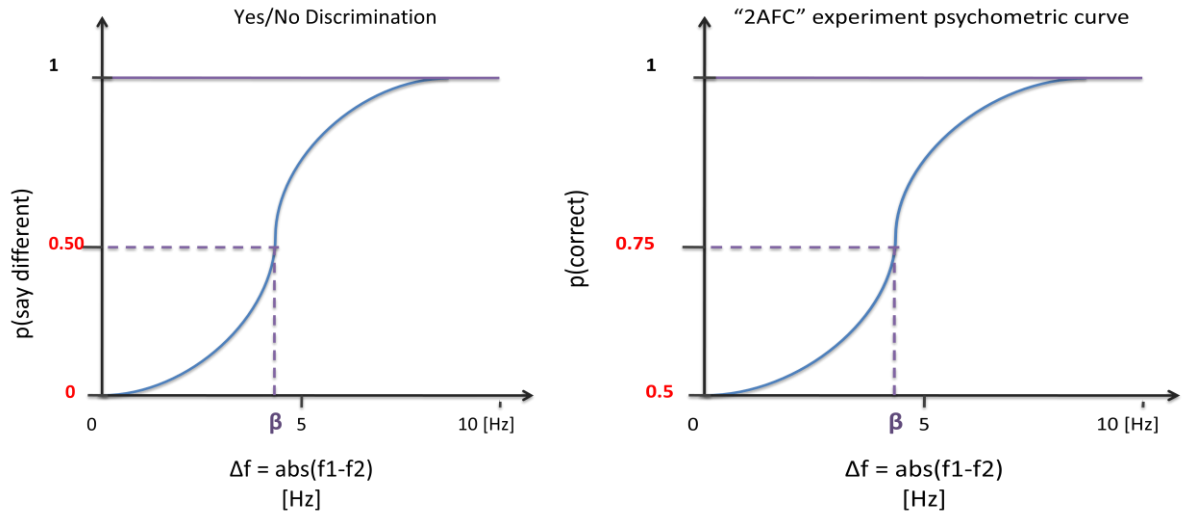
Dr. Wang's Questions [18 pts total]

Problem 1 [18 pts]

In a psychophysics experiment, a subject performs a behavioral task to determine the frequency discrimination threshold, as follows:

In each trial, two brief sounds are played in succession to the subject from a loudspeaker, Sound-1 (S1) and Sound-2 (S2). The subject's task is to tell whether S1 and S2 are the same or different. S1 and S2 are tones of frequencies f1 and f2, respectively, and have the same duration and intensity (i.e., they only differ in frequency). The frequencies of each S1-S2 pair are randomly drawn from the following list: {100, 101, 102, .., 110} Hz. For example, a S1-S2 pair could have frequencies of {100 Hz and 101 Hz}, {103 Hz and 110 Hz}, {105 Hz and 105 Hz}, etc. There are N trials such that all frequency combinations, including identical frequency pairs, are tested multiple times. Sketch a psychometric function of the above-mentioned behavioral task. Label x-axis and y-axis. Explain how you would determine the frequency discrimination threshold from this psychometric function.

Two possible correct answers to describe how one would determine b (the discrimination threshold):



Note: For the x-axis any monotonically increasing distance metric is acceptable, such as the absolute value of the difference between the frequencies of the two sounds.

In both cases the discrimination threshold, β, is the x-axis value for which the sigmoidal psychometric curve is exactly halfway between its minimum and its maximum (the transition point).

The meaning of the y-axis could be either the fraction of trials in which the subject perceived the two sounds at having different frequencies, or the fraction of trials in which the subject was correct when giving an answer "same" or "different". The minimum in the second case of the 2AFC is not 0 but 0.5, because when the subject cannot tell if the sounds are "same" or "different", they are guessing, and they have 50% chance of being right. The se two different solutions are possible because the Same/Different task is a special case of 2AFC – most other 2AFC tasks will only work when plotted the second way.

Name: _____

Dr. Young's Questions [40 pts total]

Problem 2 [15 pts]

You are the first neurophysiologist to study calcium channels, so all you know about channel electrophysiology is the Hodgkin-Huxley (HH) analysis. You are recording intracellularly in a neuron in some region of cortex. Consistent with HH, you use voltage-clamp to hold the membrane at -60 mV and then depolarize from that potential and measure currents in a voltage-clamp analysis.

Part a) You will not see currents from all the calcium channels with this method. Explain why and describe the characteristics of the channels you will not see. It will be sufficient to draw m_∞ and h_∞ functions for these channels.

T-type Ca channels are inactivated at -60 mV. You should draw m-infinity and h-infinity functions like those shown in lecture 3 that show *m* activating at about -65 mV and *h* completely inactivated at about -70 mV. The exact voltages are not critical, as long as the channel is completely inactivated ($h_\infty = 0$) at -65 mV.

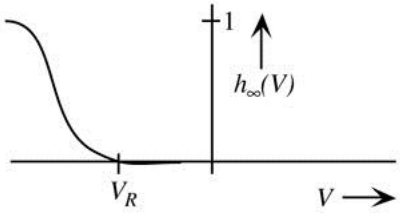
Part b) Describe a voltage-clamp protocol that you could use to study the currents missed in part a).

The voltage clamp should step to a low voltage, say -80 to -100 mV and hold that potential for long enough to remove the inactivation, then step to various depolarized potentials for the usual voltage clamp analysis.

Problem 3 [15 points]

A so-called H channel has the Hodgkin-Huxley model sketched below.

$$g_h = G_h\, h(t,V) \qquad \text{where} \qquad \frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)}$$



The variables in the equation have their usual meanings and, in the plot of h_∞ versus V. V_R is the nominal resting potential.

Part a) When is the channel activated? That is, what membrane potential events must occur in the cell to activate the channel?

(1) Hyperpolarize the membrane from rest

(2) Depolarize the membrane from rest

(3) Increase the intracellular calcium

(4) Hyperpolarize the membrane followed by depolarization

The answer is (1), hyperpolarize to de-inactivate the channel.

Part b) The channel allows Na^+ and K^+ to permeate with equal conductance. What is its effect on membrane potential when it is activated?

Name: _____

(1) Hyperpolarize the membrane

(2) Depolarize the membrane

(3) Decrease the membrane conductance and block action potentials

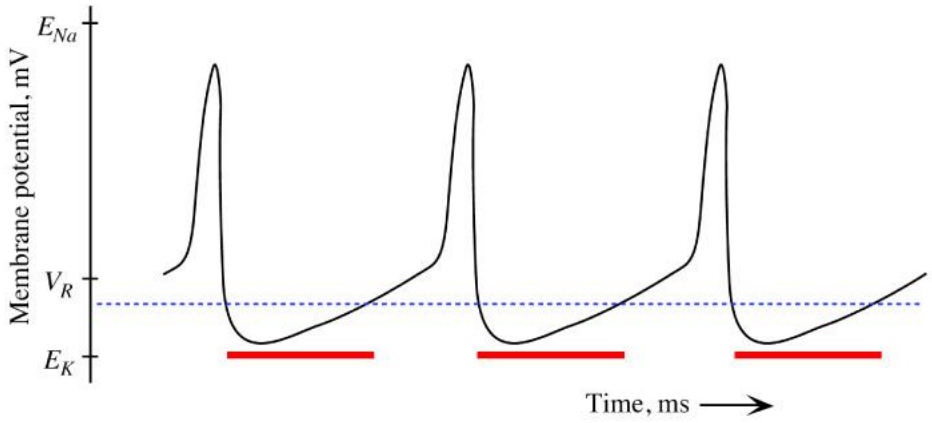
(4) No effect because the K^+ and Na^+ effects cancel.

The answer is (2) - depolarize, because the reversal potential of the synapse is halfway between E_{Na} and E_K.

$$E_{syn} = \frac{g_K E_K + g_{Na} E_{Na}}{g_K + g_{Na}} = \frac{E_K + E_{Na}}{2}$$

Part c) Suppose the cell is a pacemaker, giving the membrane potential trajectory sketched below. Mark the approximate time range(s) over which the H channel would be activated. In fact the H channel is responsible for the pacemaker activity in many cells.

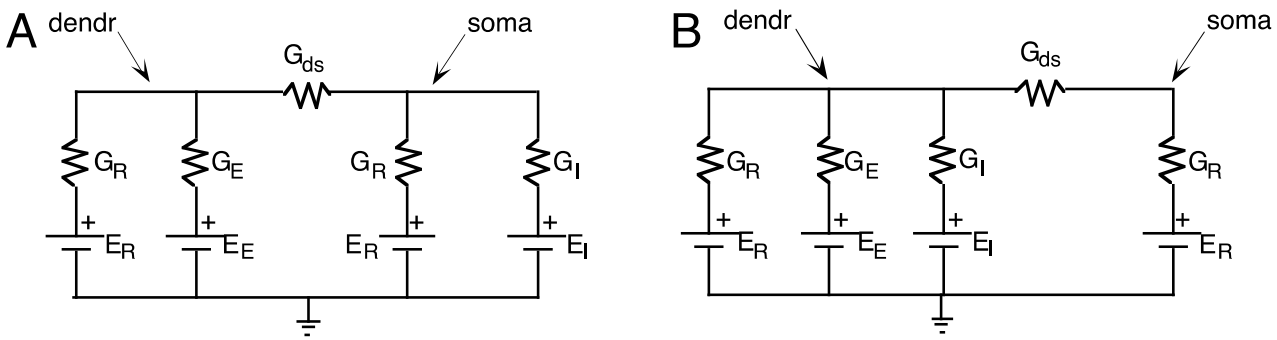
The activation region should be something like the red lines below. The dashed blue line is at the approximate threshold of the inactivation gate, just below V_R as in the problem statement. They can put the activation anywhere at or slightly below V_R.



Problem 4 [10 pts]

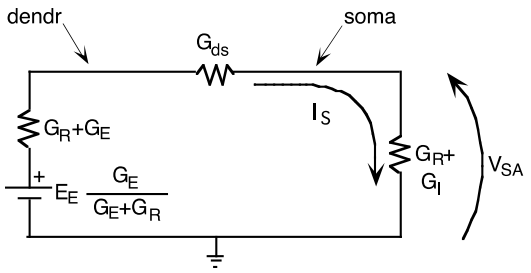
Consider the two cable models below, which are simplified models of a neuron with a cell body (*soma*) and one dendrite (*dendr*). In *B*, there is an excitatory (G_E) and an inhibitory (G_I) synapse in the dendritic compartment and in ***A* the inhibitory synapse is in the cell body**. All the other membrane conductances are gathered into G_R and E_R, assumed passive. To simplify the algebra, the membrane capacitances are not shown, so only steady-state DC potentials are relevant.

Name: _____



Part a) Write equations for the potential in the soma for these two cases. This is a bit messy, so to simplify the calculation, assume that E_R=E_I=0. That is, express membrane potentials relative to the resting potential and assume that the inhibition is pure shunting, with no IPSP. Because the problem is linear, you can also assume that E_R=0, so the only battery that remains is E_E. (Hint: Use Equivalent Circuits)

The point of this problem is to compare the effect of an inhibitory input in the soma versus one in the same dendritic compartment as an excitatory input.



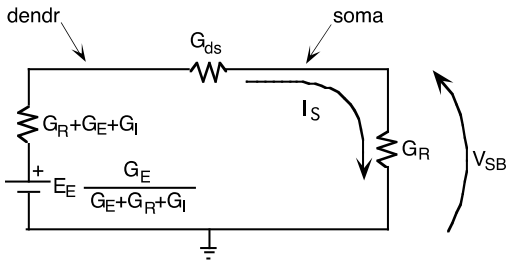
This is basically a problem in circuit theory.

The circuit in A is equivalent to the circuit at right, after the various assumptions in the problem statement are applied. All the batteries have been set to zero except E_E, the excitatory synapse potential, and the circuit elements in the soma and dendritic compartments have been replaced by Thévenin equivalents. I_S is the current into the soma from the dendrite.

The potential across the somatic membrane is V_{SA} given by:

$$V_{SA} = I_S\left(\frac{1}{G_R+G_I}\right) = \frac{E_E\dfrac{G_E}{G_E+G_R}}{\dfrac{1}{G_R+G_E}+\dfrac{1}{G_{DS}}+\dfrac{1}{G_R+G_I}}\left(\frac{1}{G_R+G_I}\right) = \frac{E_E\dfrac{G_E}{G_E+G_R}}{\dfrac{G_R+G_I}{G_R+G_E}+\dfrac{G_R+G_I}{G_{DS}}+1}$$

The first part of the equation above is Ohm's law for the conductance G_R+G_I of the soma; the second part computes I_S from the battery potential and the three series resistances. Proceeding in the same way, the circuit of B can be drawn as at right and the potential V_{SB} is given by:



$$V_{SB} = I_S\frac{1}{G_R} = \frac{E_E\dfrac{G_E}{G_E+G_R+G_I}}{\dfrac{1}{G_R+G_E+G_I}+\dfrac{1}{G_{DS}}+\dfrac{1}{G_R}}\frac{1}{G_R} = \frac{E_E\dfrac{G_E}{G_E+G_R+G_I}}{\dfrac{G_R}{G_R+G_E+G_I}+\dfrac{G_R}{G_{DS}}+1} \qquad (2$$

Name: _____

Part b) Verify that substantial inhibition is seen in both cases by comparing the potential in the soma with the inhibitory conductance turned on versus off (i.e. set to 0). To do this, assume that $G_E = G_R = G_{DS}$ and that $G_I = 10\ G_R$. Which inhibition is more potent?

With the values of the conductances given in the problem statement, the potentials from the Eqns 1 and 2 are given by:

$$V_{SA} = \frac{E_E \dfrac{1}{1+1}}{\dfrac{1+10}{1+1} + \dfrac{1+10}{1} + 1} = \frac{E_E}{35} \quad \text{and} \quad V_{SB} = \frac{E_E \dfrac{1}{1+1+10}}{\dfrac{1}{1+1+10} + \dfrac{1}{1} + 1} = \frac{E_E}{25} \tag{3}$$

In the absence of inhibition ($G_I \approx 0$) the somatic potential takes the value below in both cases:

$$V_S = \frac{E_E \dfrac{G_E}{G_E + G_R}}{\dfrac{G_R}{G_E + G_R} + \dfrac{G_R}{G_{DS}} + 1} = \frac{E_E \dfrac{1}{1+1}}{\dfrac{1}{1+1} + \dfrac{1}{1} + 1} = \frac{E_E}{5} \tag{4}$$

So the inhibitory synapse reduces the EPSP in the soma by a factor of 5-7 fold, with case *A*, inhibition in the soma, more effective.

Dr. Kirkwood's Questions [14 pts total]

Problem 5 [6 pts]

Input specificity and associativity are important properties that make LTP an attractive learning mechanism.

Part a) Explain what input specificity and associativity are.

Input specificity means that only conditioned synapses will express LTP, whereas non-conditioned inputs remain unaltered. This property allows a large storage capacity as each synapse can be modified in and independent manner.

Associativity means that a weak tetanus that normally does not enhance synaptic responses can results in LTP if paired with a strong tetanus in other inputs. This is basically a cellular model of Pavlovian learning.

Part b) How do the properties of NMDA receptors account for input specificity and associativity?

Input specificity: NMDAR will be activated only the stimulated inputs
Associativity: NMDAR activation requires glutamate binding and postsynaptic depolarization to remove the magnesium block. Activating the weak input provides the glutamate; the strong input provides the postsynaptic depolarization.

Name: _____

LTP is specific because it is induced by intracellular calcium concentration, and we learned from Dr. Young's lectures that calcium is almost completely restricted to the spine it enters. So in order to get LTP at a given synapse, you need to allow calcium to enter the NMDA receptors at that same synapse. Now, remember that in order to get calcium to enter NMDA receptors we need both 1) glutamate (from the presynaptic cell) and 2) Depolarization of the post-synaptic cell. #1 is another way to get specificity (since glutamate won't diffuse between two different synapses.) #2, however, is not specific, since as we also learned from Dr. Young, spines are electrically transparent, so you can depolarize the post-synaptic terminal really easily with backpropagating action potentials, which could be triggered by any sufficiently strong synapse(s).

So if a synapse A is strong, and synapses B and C are weak, and if A and B happen to activate simultaneously and repeatedly, whereas there is no correlation between A and C, you will get LTP at synapse B (demonstrating associativity between A and B) but NOT at synapse C (demonstrating specificity to B).

Problem 6 [4 pts]

What is spike timing dependent plasticity (STPD), how does it differ from LTP and LTD induced with tetanic stimulation or pairing? What is the role of the backpropagating action potential in STPD?

- In STDP the timing between pre and postsynaptic action potentials determines plasticity. Pre then post → LTP, post then pre → LTD.
- In LTP/D induced with titanic stimulation, plasticity is determined by the level of postsynaptic activity. In STDP plasticity is determined by the correlation between pre and postsynaptic activity. Note that timing effects do not appear in tetanic stimulation because there, presynaptic activation always precedes post-synaptic.
- The backpropagating AP serves to boost the NMDA activation.

Problem 7 [4 pts]

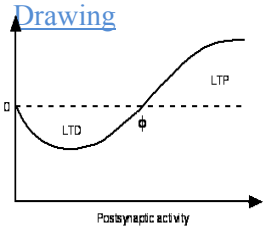
Define the synaptic scaling and sliding threshold mechanisms of metaplasticity.

Sliding threshold. There are 2 ways of explaining it: with a formula, with words or with a drawing:

Said with words :

- The polarity of plasticity is determined by the difference between postsynaptic activity and the modification threshold (ϕ).
- The magnitude of plasticity is determined primarily by the presynaptic activity

Drawing



Name: _____

The value of ϕ is not fixed, but it changes according to the activity of the postsynaptic cell. It increases with high activity, which promotes LTD over LTD; it decreases with reduced activity, which promotes LTP over LTD .

Synaptic scaling
When activity is chronically reduced, the magnitude of unitary synaptic response is increased. Conversely, when activity is increased, unitary synaptic responses are decreased. These changes in strength affect equally all synapses in a cell, thus preserving the relative weight of the synapses.

Dr. Hsiao's Questions [14 pts total]

Problem 8 [6 pts]

Describe how the perceptions of a) spatial form and b) cold are represented and processed in the peripheral afferent fibers.

There are two acceptable ways of answering this, with whichever route would have yielded the most points being the one graded by.

Route 1)

a)

1) ANY: Mechanoreceptors (Meissner, Merkel, Ruffini, Pacinian / SAI,SAII,RAI,PC), proprioceptors (GTO, muscle spindles, joint).
2) Aα fibers (proprioceptors), or Aβ fibers(mechanoreceptors).
3) Dorsal-column-medial-lamniscus pathway

b)

1) bare nerve endings
2) Aδ or C fibers (according to lecture; only Aδ)
3) Spinothalamic pathway (or ascends in anteriolateral quadrant)

Route 2)

a)

firing rate carries information regarding stimulus properties. An increase in firing rate corresponds to increased stimulation.

b)

firing rate, but not linearly decreasing with temperature. There are two unique temperatures which correspond to the same firing rate, so the properties of the spike trains must be considered as well. Rapid cooling elicits a significantly greater response than gradual cooling.

Problem 9 [8 pts]

How do we know that area 3b and area 1 are two separate areas of cortex? Include both anatomical, physiological, and behavioral evidence in your answer.

1) Staining (e.g. how Brodman distinguished them in the first place)
2) Somatotopic reversal at the border between fields

Name: _____

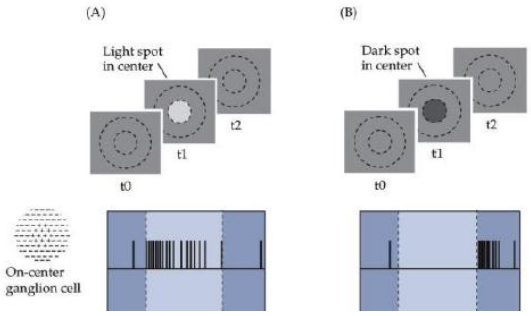
3) Monkey cortical ablation experiments: 3b (all tactile function impaired, takes very long time to learn) 1 (texture, takes long time to learn)
4) Differential activation in different tasks
5) Parallel projections from thalamus to both areas
6) Different output pathways

Dr. Connor's Questions [14 pts total]

Problem 10 [2 pts]

Draw the receptive field of an on-center retinal ganglion cell, and indicate what part is responsive to light onset (and inhibited by light offset) and what part is responsive to light offset (and inhibited by light onset).

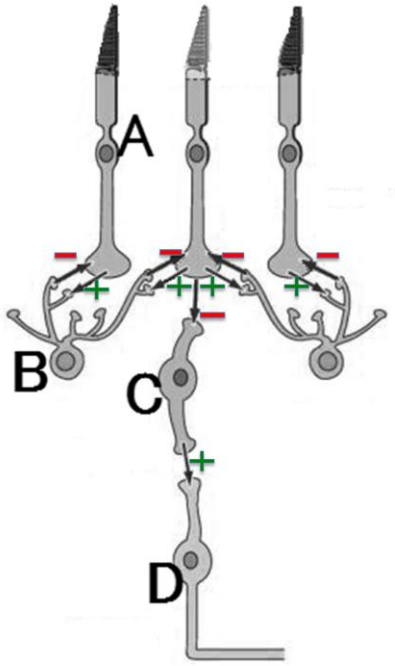
Draw 2 concentric circles; inner disk is responsive to light onset and inhibited by light offset, surround is responsive to light offset and inhibited by light onset.



Problem 11 [6 pts]

a) Label cell types A, B, C, and D on the following diagram.
b) If the retinal ganglion cell shown in the figure is **on-center**, label each arrow with a plus sign "+" if it's excitatory, or a minus sign "-" if it's inhibitory

Name: _____



NEUROSCIENCE, Fourth Edition

a)
Central photoreceptor (cone cell) (A)
Horizontal cell (B)
Bipolar cell (C)
Retinal ganglion cell (D).

b)
Glu release from photoreceptor terminals has a depolarizing (excitatory) effect on horizontal cells, while GABA released from horizontal cells has a hyperpolarizing (inhibitory) effect on receptor terminals.

The bipolar cell is normally inhibited (hyperpolarized) by transmitter from the central photreceptor, so when it is activated (depolarized), it causes it to release transmitter at its synapse onto the retinal ganglion cell. The retinal ganglion cell is thus activated (depolarized) and generates action potentials.

Problem 12 [3 pts]

How does the center-surround structure of retinal ganglion cells optimize representation of the visual image?

The cell does not respond to regions of constant brightness (i.e. all bright or all dark, because of the balance between center and surround). It only responds strongly to contrast edges (when the center and only part of the surround are stimulated). Contrast edges contain important visual information (while regions of constant brightness contain little information, so contrast sensitivity compresses the visual signal but retains the important information).

Problem 13 [3 pts]

List two ways in which parts-based, configural coding in the ventral visual pathway optimizes neural representation of objects.

There are 4 possible answers, only 2 are requested:

- compressed representation (in terms of a small number of parts, instead of a large number of pixels)
- more stable representation (because parts stay the same even when position, size, or orientation changes)
- a parts-based code can represent a very large number of objects (because of the combinatorial explosion of part combinations)

Name: _____

- parts-based coding provides structural information about objects (which is useful for understanding and interacting with objects)