Dr. Wang (35 points)

Question 1 (15 pts) [suggested time: 10 minutes]

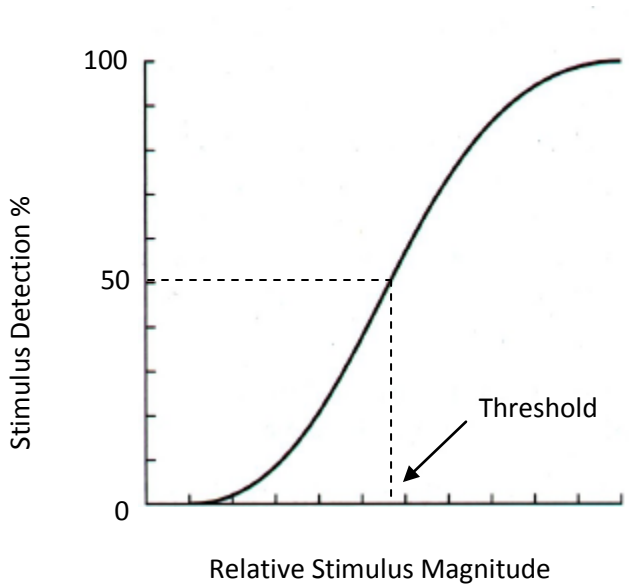
a) What is a "psychometric function"? What does it represent?

- In class definition:
  - A psychometric function provides the fundamental data for psychophysics, the scientific discipline that explores the connection between physical stimuli and subjective responses.
  - A psychometric function relates the subject's response to a physical stimulus and is used to quantitatively measure behaviors.
- The x-axis (abscissa) represents the physical parameter of a stimulus, and the y-axis (ordinate) plots the observers response as a percentage

3 points maximum, pulled potentially from:
- +1 mention psychophysics (or has description of such experiment, or mention "quantitative")
- +1 mention physical stimulus
- +1 for subject's response, probability
- +1 for threshold

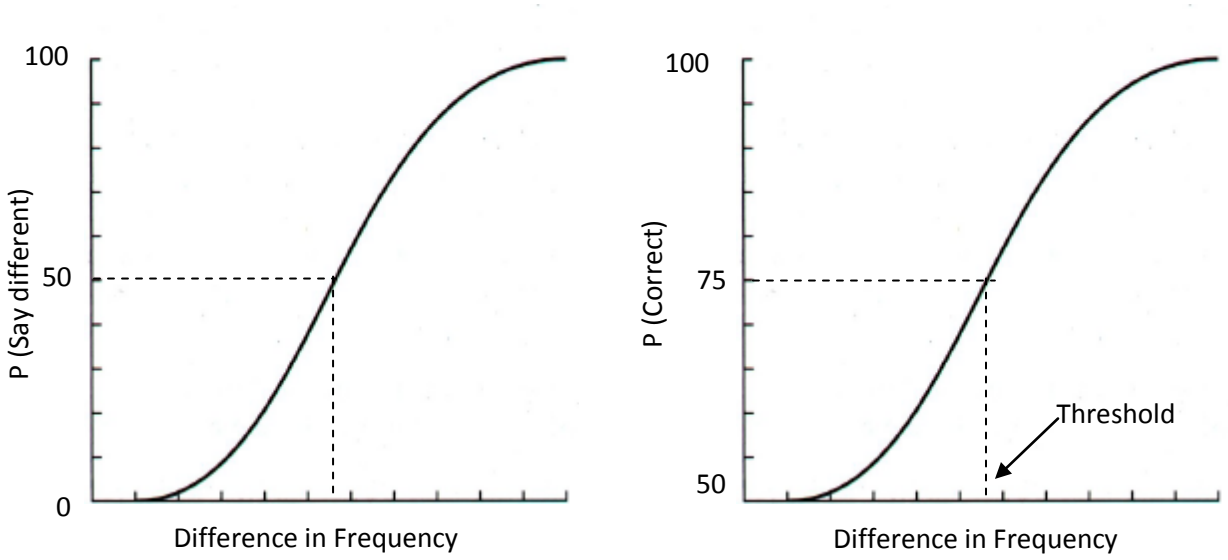
b) A subject is asked to perform the following tasks in psychophysics experiments. Sketch the psychometric function according to each task. Label x-axis and y-axis clearly. Explain how you would determine the detection threshold and frequency discrimination threshold from these psychometric functions, respectively.

Task-1: The subject places his/her finger on a mechanical vibrator and reports when he/she detects a vibration. The vibration stimuli are delivered at various magnitudes, from below detection threshold to above the threshold. (6 points)



- X-axis labeled clearly – Should be ‘stimulus magnitude’. ‘Vibration magnitude’, ‘vibration amplitude’, ‘vibration strength’ should all be acceptable. (1 point)
- Y-Axis labeled clearly. (2 points)
    - Y-axis should go from 0 to 100% or 0 to 1 (1 point)
    - Should say ‘stimulus detection’, or probability(detects vibration) or even probability(say yes), since the experimenter is asking if they sense vibration. (1 point)
- The curve should be monotonically increasing, from near 0% at lowest magnitude to near 100% to highest magnitude (1 points)
- Must include explanation that the detection threshold is stimulus magnitude at which the probability of detection is 50%. (2 points)

Task-2: The subject places his/her finger on a mechanical vibrator and reports whether two consecutive sinusoidal vibrations have the same or different frequencies.



- X-axis labeled clearly – Should be the same for either case. Should be ‘Frequency Difference”, “freq1 – freq2”, “abs(freq1-freq2) “etc. Here he clearly states that the frequencies between the two stimuli are the variable. (1 point)
- Y-Axis and curve (3 points, 1 for axis label, 1 for correct ymin and ymax, and 1 for correct corresponding slope)
    - Could decide to do either 2AFC or Yes/No
    - If y-axis goes from 0 -100%
        - P(say different) should correspond to a positive slope, because as small differences they will be less likely to say ‘different’.
        - P(say same) should correspond to a negative slope, because at small differences they will be very likely to say ‘same’

- If the y-axis goes from 50-100% axis should only be P(correct) because at large differences (down the x-axis) they should be correct most of the time.

- Detection threshold for Yes/No is the stimulus difference at which the P(say different) is 50%. Detection threshold for 2AFC will be the frequency difference at with P(correct) is 75%. (2 points)

Question 2 (20 pts) [suggested time: 10 minutes]

A sensory neuron is stimulated by a 50 Hz sinusidal stimulus (100 msec in duration, starting at time=100 msec). Below is a list of the time of occurrences (in msec) of spikes recorded from the neuron in response to 5 repetitions of the same stimulus. Recordings begin at time = 0 msec. and end at time = 200 msec.

Trial-1: [15 114 118 123 134 137 145 151 165 172 184]
Trial-2: [73 112 117 121 133 147 162 165 176 181 198]
Trial-3: [24 115 119 126 129 135 138 158 174 181 190]
Trial-4: [59 113 116 122 132 144 151 158 165 172 184]
Trial-5: [35 111 115 119 131 141 149 157 175 186 197]

a) Calculate mean firing rate (5 points)

answer: total number of spikes = 55 – overall (across 200 ms)
mean firing rate = # spikes / (# trials * duration)
= 55/(5*0.2)
= 55 spikes/s

Also acceptable:

answer: total number of spikes = 50 – in response to stimulus (after 100 ms)
mean firing rate = # spikes / (# trials * duration)
= 50/(5*0.1)
= 100 spikes/s

-2 if spikes number is not divided by # of trials
-2 if spikes number is not divided by duration
- 1 if 55 is not divided by 200 ms, and if 50 is not divided by 100 ms (confusing the 100ms/200ms window)
+1 if a correct equation is written but without numbers

b) Sketch and label the post-stimulus histogram (PSTH). Use binwidth of 10 msec, x-axis range [0, 200] msec. Is there "phase-locking" in the response of this neuron (please briefly explain your answer)?

Answer:

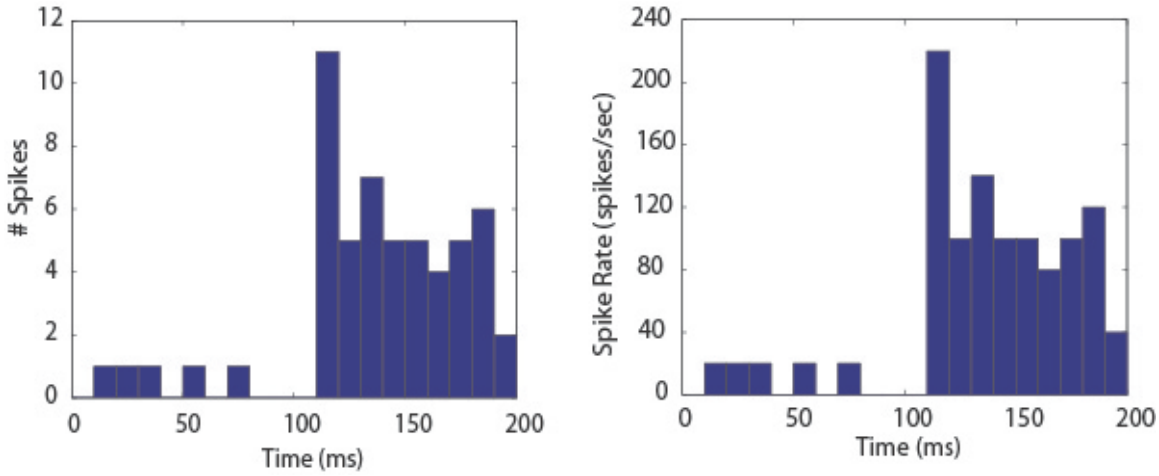
Time Interval (ms)	# Spikes						
0 – 10	0	51 – 60	1	101-110	0	151-160	5
11-20	1	61 – 70	0	111-120	11	161-170	4
21 – 30	1	71- 80	1	121-130	5	171-180	5
31 – 40	1	81 – 90	0	131-140	7	181-190	6 (5)
41 – 50	0	91 - 100	0	141-150	5	191-200	2 (3)

- X axis should be time
- For PSTH, the y-axis should be firing rate (spikes/sec)
    - For below, spike rate was calculated as

= (total number of spikes/ (5 trials * 10 ms window)) * (1000 ms/s)

To achieve spikes/sec

- It would also be acceptable to leave the calculate as spikes/ms
- Receive partial credit if y axis is # spikes



12 points total (subtract until reaching 0, using the way that generates the most points)
For spike number/rate calculations,
-0.5 for each incorrect value (6 maximum): only exception would be spike at 190. Depending on bin definition, last two bins can either be 6/2 or 5/3.
-1 for incorrect x-axis label
-1 for incorrect bin size
-1 for missing y-axis label
-2 if y-axis is # spikes (they only get to # of spikes)

-1 if y-axis is spikes/trial or spikes/bin width (incorrect spike rate calculation)
-1 if it's completely blank or having no bars.

- Phase locking: (3 points)
  The stimulus is not turned on until 100 ms, so we have some small baseline activity prior to this. At 100 ms, a 50 Hz stimulus is introduced. With a frequency of 50 Hz, the peak intensity of the stimulus should occur at every 20 ms. Since our bins are only 10 ms wide, we in theory could detect phase locking. We would expect to see higher activity aligned with the peak of the stimulus. So we should have periods of high activity, followed by periods of low activity, across the bins in 100ms-200 ms. However, it just looks like we have a burst of activity across all bins after 100 ms, so there does not appear to be phase-locking.

  - +1 for saying no phase locking
  - +1 for defining/explaining phase locking
  - +1 for knowing you can determining phase locking from the PSTH plot

Dr. Young (35 points total)

QUESTION 1: Cells generally contain several types of voltage- or ligand-gated (i.e. neurotransmitter activated) ion channels. One way to classify them is according to the ions that pass through the channel. Give one or more functions for the following ion channels in excitable cells. Mention the typical reversal potential for this channel and tell how the reversal potential affects the function of the channel. (12 pts)

Sodium: < excitability, to depolarize the membrane at the leading edge of the action potential. Ena is typically +40 mV or so (anything between +20 mV and +60 mV is OK). This means that when Gna increases, it pulls the membrane potential strongly in the depolarizing direction. >

Potassium: < repolarizing the membrane and holding it at or near the resting potential. Gk increases more slowly than Gna during the action potential and thus helps produce the down-slope of the action potential (along with Na inactivation). Ek is typically -90 mV [anything between -80 mV and -110 mV], so has a hyperpolarizing effect when activated. >

Chloride: < primarily found at inhibitory synapses in the postsynaptic receptor. Ecl is typically at or below the resting potential [-60 mV to -80mV]. The effect of Gcl activation (by a neurotransmitter) is to hyperpolarize the membrane by admitting negative charge to the cell or shunting the currents from excitatory inputs, for cases where Ecl is near rest. >

Calcium: < calcium has many roles in excitability. Eca is positive (they don't need to say anything more precise here), so Ca currents are inward (depolarizing) when Gca increases. Sometimes this produces action potentials, as in dendritic action potentials or the pedestal of a burst of action potentials. Dendritic action potentials are produced in the distal dendrites of neurons and help to communicate distal synaptic inputs to the soma. Ca currents increase the [Ca] in a domain near the channels. Increased [Ca] can produce neurotransmitter release, activate other channels (like the KCa channels that participate in repolarizing action potentials), or communicate a message of excitability that is important in plasticity. >

+12 total

+3 for each ion (1 for function (role in AP, role in synaptic input excitability/inhibition), 1 for reversal potential within given range, 1 for how reversal potential affects cell (hyperpolarizing/depolarizing))

QUESTION 2: Inhibitory synapses usually contain a chloride channel. However, sometimes synaptic activation can lead to inhibition or excitation through the gating of potassium channels by a metabotropic mechanism. Give a possible sequence of steps for such a mechanism. (4 pts)

< The metabotropic receptor does not contain an ion channel. Instead, it releases a second-messenger of some type, typically a G-protein. The 2nd messenger may bind to the potassium channel directly, opening it or closing it, or may activate a protein kinase which phosphorylates the potassium channel, again opening or closing it.>

+4 total
+2 for knowing a metabotropic receptor is not an ion channel (it releases a second messenger)
+2 for giving an example of second messenger opening or closing a channel for potassium (or mentioning an example of KCa channel).
(For each of the two, only +1 if the answer is partially correct)

QUESTION 3: Suppose a steady D.C. current I_0 is injected into a very long membrane cylinder (like an unmyelinated axon), long enough that it can be approximated as infinite in length. The current is injected at point x=0. After the system comes to steady-state (meaning no time variation in the membrane potential), the membrane potential is given by $V(x) = r_i \lambda I_0 e^{-x/\lambda}$, where r_i is the resistance/length of the cytoplasm and λ is the length constant of the cylinder, as defined in class. (9pts)

(a) What is the input conductance of the cylinder in steady state, i.e. the conductance as seen by the electrode through which the current is injected? This value is called G_∞ and is a useful parameter of the cylinder, whether it is infinite or not.

< $G_\infty = \frac{I_0}{V(0)} = \frac{I_0}{r_i \lambda I_0 e^{-0}} = \frac{1}{r_i \lambda}$ >

+3 for correct answer
Partial credit:
+1 for Io/V(0)
+2 for plugging in V(0) with x = 0

(b) How does G_∞ vary with the radius a of the membrane cylinder?

< Using the definitions of r_i and λ given in class and in the notes:

$$G_\infty = \frac{1}{r_i \lambda} = \frac{\pi a^2}{R_i} \sqrt{\frac{2R_i}{R_m a}} = \sqrt{\frac{2}{R_i R_m}} \pi a^{3/2} \quad >$$

+3 for correct final form
+1 for correct ri equivalence, given initial equation
+1 for correct lambda equivalence, given initial equation

For an answer with explanation only, no equations:
+3 if correctly stated that $G_{infinity}$ is proportional to $a^{3/2}$
+1 if stated that $G_{infinity}$ is proportional to some function of a

(c) Suppose a (finite) cylinder with conductance G_∞ branches into to two smaller cylinders. What should be the radii a_{branch} (assumed equal for the two branches) of the smaller cylinders so that the sum of the G_∞s of the branches is equal to the G_∞ of the main cylinder? Surprisingly dendritic trees seem to branch in this way.

< We want $G_\infty = 2G_{\infty\, branch}$, since conductances add in parallel. Because only the radius a varies in the definition of G_∞ this condition is met if $a^{3/2} = 2a_{branch}^{3/2}$. >

+3 total for correct answer
Partial credit:
+1 for explanation, correctly knowing $G_{infTotal} = 2G_{inf,branch}$
+1 for understanding $2G_{inf,branch}$ is proportional to $a_{branch}^{3/2}$
+2 if $a = 2a_{branch}$, even if not $a^{3/2}$

QUESTION 4: Consider synaptic democracy (SD), which means that synapses on neurons are adjusted to have roughly equal effect (e.g. EPSP size) in the soma. (10 pts)

(a) What is the problem? That is, why shouldn't synapses produce equal effects in the soma?

< cable properties of the dendrites mean that synaptic potentials should decay something like exponentially away from the source. >

+2 total
+1 must mention potential should decay
+1 for mentioning that this decay is due to cable properties

(b) Do NMDA receptors contribute to SD (yes/no)? If so how?

< NMDA receptors amplify EPSPs in very distal dendrites because the unmodified EPSPs there are large enough to relieve the Mg^{++} block of these receptors. >

+3 total
+2 for correctly saying 'yes'
+1 for correct explanation

(c) Same question for chloride channels.

< No. >

+2 total, must say 'no'

(d) Same question for calcium channels.

< Yes. Ca channels can produce Ca action potentials in the distal dendrites of larger cells, which amplify the effects of those synapses. >

+3 total
+2 for saying 'yes'
+1 for correct explanation

Dr. Kirkwood (15 points total)

1) Input specificity and associativity are cardinal properties that make LTP an attractive learning mechanism. (6 points total)

a) Explain what is input specificity and associativity. What is their potential benefit/function?

Input specificity means that only conditioned inputs will express LTP, 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 enhances synaptic responses can results in LTP if paired with a strong tetanus in other inputs. This is basically a cellular model of pavlovian learning

+2 for each
+1 for explanation
+1 for benefit/function

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

Input specificity: NMDAR will be activated only at the stimulated inputs, due to necessary glutamate binding

Associativity: NMDAR activation requires glutamate binding and postsynaptic depolarization. Activating the weak input provides the glutamate; the strong input provides the postsynaptic depolarization.

+2 total
+1 for specificity
+1 for associativity

2) Besides synaptic plasticity there is 'Metaplasticity. We discussed two of those mechanisms: the sliding threshold model (or BCM model) and synaptic scaling. Define them and point out their similarities. (9 points total)
In the sliding threshold model the activity threshold for LTP and LTD is not fixed and changes with the past activity of the cell (1 point). If the cell was very active the threshold for LTP increases, making LTD more likely (1 point). Conversely, if the cell was relatively inactive, the threshold for LTP decreases (1 point).

- Must state that the 'threshold' is for LTP vs LTD

In homeostatic scaling the strength of each synapse is increased or decreased according to the previous activity history (1 point). An increase in activity causes a global reduction in synaptic strength (1 point) whereas a decrease in activity increases the synaptic strength (1 point). These changes are global and multiplicative, meaning that all synapses in a cell are changed by the same factor

- For both, -1 if only a very descriptive figure is given. Must include an explanation. More points taken off if the student only includes a figure, and the figure is missing key components crucial for understanding the figure: LTD below threshold, LTP above threshold, boundary shift for low or high activity, axes labeled, etc.

Comparison: must include at least 3 below, or just the two bolded observations (3 point total)

Both models constitute negative feedback mechanisms that provide homeostatic stability to the cortical circuits

There is evidence for both of them as dark rearing affects LTP and synaptic strength in the predicted by those models

Both of them are global as they affect all synapses in a cell

None of those mechanisms should affect stored memories

Each of the model can account for the "funny" late increases in the inputs from both eyes observed after prolonged monocular deprivation

+9 total
+3 for each correct definition
+3 for comparison

Dr. Hsaio (15 points total)

1) Describe what is meant by the term specificity. Give two specific examples of specificity in the somatosensory system and describe how the afferent inputs achieve specificity. One example should be a large diameter fiber and the other should be a small diameter fiber. (9 points)

Specificity means that different receptors and afferents code different "specific" perceptions because they are selectively sensitive to different aspects of the stimulus. In addition, the afferents ascend in different pathways, depending on whether they are mechanoreptors/proprioceptors or nociceptors/thermoreceptors. These afferents also projects to different cortical areas. Lastly, an ordered somatotopy is present throughout, from the spinal cord, to the thalamus and cortex, which separates stimuli from different parts of the body.

Large diameter example possibilities:

(these ascend in dorsal column-medial lemniscal pathway, synapse in different areas of the thalamus- core for cutaneous and deep for proprio, project to different cortical areas)
Abeta/Meissner/RA1- codes skin motion, slip and grip control, flutter (low freq. vibration)
Abeta/Merkel/SA1- codes spatial form, texture, fine discrimination/touch
Abeta/Ruffini/SA2- codes skin stretch, hand shape
Abeta/Pacinian/PC/RA2- codes vibration (high freq.), tool use
Abeta/Joint afferents- code extreme joint angles
Aalpha/Golgi tendon organs- code muscle force
Spindle afferents- code muscle length/velocity, joint angle (primary- Aalpha, secondary- Abeta)

(these ascend in spinothalamic tract)
Adelta thermoreceptor- cold
Adelta nociceptor- pricking/sharp pain
Note: while Adelta fibers are technically large diameter, will accept as small diameter if the larger diameter example is either Aalpha or Abeta

Small diameter example possibilities: (ascend in spinothalamic tract)
C thermoreceptor- warm
C nociceptor- burning pain
C- itch

+3 for specificity explanation (need to mention at least two aspects of the specificity, 1.5 for each)

+1 for incomplete definition of specificity as responding to different inputs (including responding to different types of energy)
+3 max for each example (+1 for listing an example, +1 for each example of how it achieves specificity- codes for what, ascends in what tract, synapses in what area of thalamus, synapses in what area of cortex)

2) Why were areas 3a and 3b originally considered to be a single cortical area but are now considered to be different areas? In you answer include anatomical, and functions differences that suggest that these two areas are different. (6 points)

Originally considered to be one cortical area due to Brodman staining which classified them together as area 3.
Now considered to be two different areas for multiple reasons:

- Functional: Monkey cortical ablation studies- in 3b impairs tactile function, spatial form; in 3a impairs proprioception
- Anatomical: Parallel projections from thalamus to both areas (one gets projections from deep/shell-proprio (3a), other gets projections from core- cutaneous (3b))
- Anatomical: Different output pathways
- Functional: Differential activation in different tasks

+2 for Brodman staining explanation
+2 for at least one functional explanation
+2 for at least one anatomical explanation