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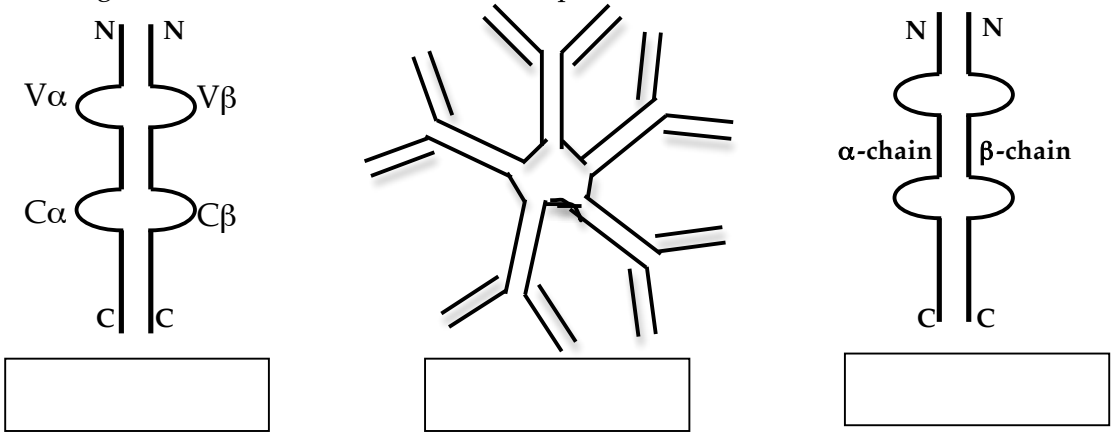
7.013 Problem Set 6 - 2013

Question 1

a) Our immune system is comprised of different cell types. Complete the table below by selecting **all** correct cell types from the choices provided.

Cells types that…	Choose from mast cells, macrophages, helper- T (T_H), cytotoxic- T (T_C), memory T_H and T_C, memory B and plasma B cells or ALL
Participate in the **innate immune response**.	
Bind directly to the **heat-killed antigen, circulating** in the blood stream.	
Secrete large amount of antibody in response to an infection.	
Provide **adaptive immunity** against **second exposure** to the **same virus**.	
Present the antigens to Tc cells during the Tc- mediated (CTL) immune response.	
Show rearrangement of specific gene(s) and do not have the same genome unlike other cell-types in the body.	

b) The following is a schematic of the structure of specific **cell surface molecules**.



i. Identify the above molecules as an antibody (Ab), T cell receptor (TcR) or major histocompatibility factor (MHC) by filling in the boxes.

ii. Which of the above cell surface molecule(s) …

- Can **directly** bind to a circulating antigen?
- Can present the antigen to a T_c or a T_H cell **after the antigen has been processed** either within an infected cell or by an antigen- presenting cell (APC)? On the schematic, show the antigen-presenting site of this molecule by drawing a **triangle**.
- Can recognize the antigen **after it has been presented** on the surface of an infected cell or an APC cell? On the schematic, **circle** the antigen- recognizing site(s) of this molecule.

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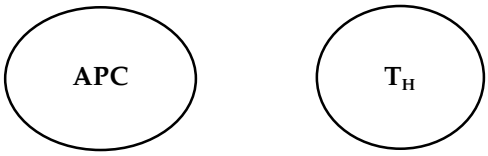
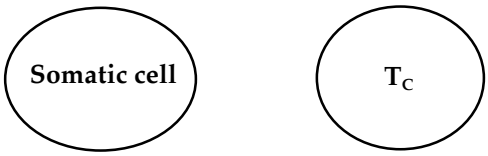
Question 1 continued

iii. Diagram the interaction of the molecules above with the antigens on…

- An **APC cell** that is interacting with and activating a **T_H cell**. ***Note:*** Include the relevant molecules on your schematic *(choose from antigen (Ag), TcR, MHC-1, MHC-II, CD4 and CD8).*



- A virus infected **somatic cell** interacting with and activating a **T_C cell**. ***Note:*** Include the relevant molecules on your schematic *(choose from antigen (Ag), TcR, MHC-1, MHC-II, CD4 and CD8).*



c) The diverse array of TcR and the antibodies is generated by DNA rearrangement. However this diversity is further enhanced by the function of enzymes like **terminal transferases**. Briefly **explain** how the activity of terminal transferase enzyme further contributes to antibody diversity.

d) Although the immune system has the IgG (secreted antibody) and the IgM (usually cell surface antibody) antibody molecules with the antigen- binding site against the same antigen these two classes of antibody have very different structure.

i. **Circle** the cells types that produce and secrete IgG (*choose from mature B cells, memory B cells, Plasma cells*).

ii. **Circle** the cells types that produce IgM (*choose from mature B cells, memory B cells, Plasma cells*).

e) Very rarely, the immune system in some individuals may produce cells that can recognize "self-antigens". These individuals therefore develop autoimmune diseases such as lupus, rheumatoid arthritis, Type 1 diabetic and multiple sclerosis. Briefly describe how the self-reacting T or B cells are eliminated during the development of immune system in a normal heatlthy individuals.

f) Organ transplant is required in various clinical conditions. One has to consider various criteria in order to reduce the chances of transplant rejection.

i. Name the surface molecule(s) that is critical in preventing transplant rejection.

ii. Is this molecule(s) expressed on the surface of **ALL** nucleated cell (*Yes/ No*)? **Explain** your choice.

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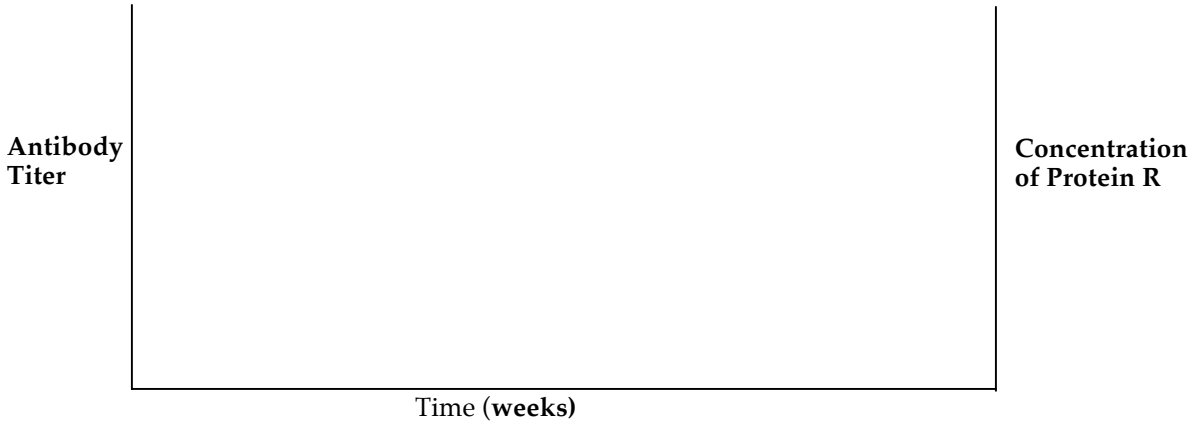
Question 2

You purify a **novel viral protein** (Protein R) and intend to further characterize it. Accordingly, you develop antibodies against Protein R. You inject Protein R into a rabbit, draw out some blood from the rabbit after a month and confirm the presence of Protein R specific antibody in the rabbit's blood. You wait for two months and then re-inject Protein R into the same rabbit. You observe a stronger and much rapid development of secondary immune response specific to Protein R.

a) On the graph below…

i. Draw the primary and secondary immune responses specific to Protein R **as a solid line (-)**.

ii. Draw the alteration in the concentration of Protein R **as a dashed line (------)** during the primary and secondary immune responses**.**



iii. Why is the primary immune response **slower** and **weaker** compared to the secondary immune response?

b) **Circle** all the correct options from the following choices. The **innate immune response**…

i. Occurs **only** in response to **first injection**.
ii. Occurs **only** in response to **second injection**.
iii. Occurs in response to **both injections**.
iv. Is **non-specific** unlike the adaptive immune response.

c) Briefly describe **two major mechanisms** by which the secreted antibodies destroy a virus circulating in the blood stream.

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Question 2 continued

d) Your friend decides to inject an **attenuated form of the virus** into a rabbit instead of injecting only Protein R derived from this virus.

i. What additional immune response specific to Protein R will be observed in this rabbit compared to your experimental rabbit?

ii. How does this additional immune response in part (i) destroy the virus- infected cells?

Question 3

a) You come across an online article titled "How Carrot-Chocolate Shakes Improve Memory?" The summary reads: "After drinking Carrot-Chocolate shake mix, mice show an immediate (within 10 seconds) increase in memory. The authors of the study claim that the shake…

i. Increases the amplitude of the action potential in hippocampal neurons (involved in memory) from +55mV to +90mV

ii. Changes the threshold potential from -50mV to -40mV.

iii. Furthermore, it works by targeting the metabotropic AMPA receptors.

For each of the claims made, indicate whether the claim is valid and **explain** your answer.

b) On the same site, you also read the following. "Recent data shows that…

i. Feeding mice the protein "Na^+K^+ATPase pump" improves their memory.

ii. This pump is essential for transmitting a signal along a neuron.

iii. It is not used anywhere else in the body."

For each of the claims made, indicate whether the claim is valid and **explain** your answer.

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Question 3 continued…

c) The depolarization phase of the action potential is generated by the passage of ions through…

i. The resting ion channels

ii. Voltage-gated ion channels

iii. G-protein coupled receptors that are associated with a ligand gated K+ channels.

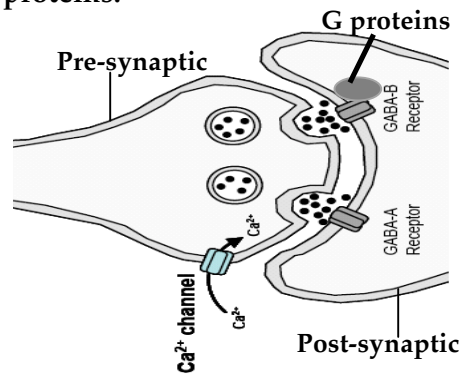
iv. The sodium potassium ATPase pump

d) Complete the following table for the two channels/pumps that play a critical role in establishing and maintain the resting membrane potential.

Channels/pumps	Direction of movement of ions (*choose from into the cell or out of the cell*)?	Default state (*choose from open, closed or always on*)?	Is this an example of *active transport or diffusion*?
Na^+K^+ ATPase pump	Na^+: & K+:		
Open K^+ channel	K^+:		

Question 4

GABA is a major inhibitory neurotransmitter in central nervous system (CNS). It acts by binding to **GABA-A receptors that are chloride channels and GABA-B receptors that activate K+ channels via G proteins.**



a) In response to GABA, would you expect both types of receptors to activate ion flow with the same time course? **Explain**.

b) K+ concentration is high inside the neuron, while Ca^{2+}, Na^+ and Cl^- ion concentrations are high outside. Passage of Na^+ into the neuron is responsible for an action potential.

i. In what direction will Na^+ ions flow when the GABA-A receptor is activated – *in or out* of the neuron?

ii. How does this flow alter the likelihood of an action potential in the post-synaptic neuron? **Explain**.

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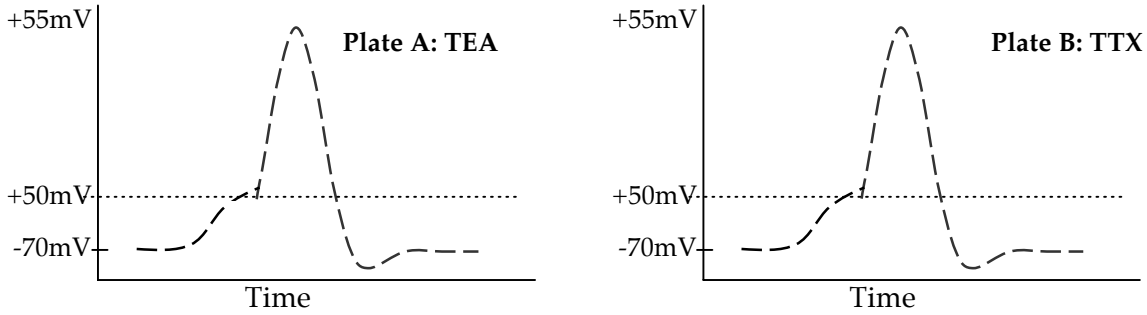
Question 4 continued

c) You culture a GABAergic neuron (i.e. one that produces GABA) in the presence of the following neurotoxins in two separate petri-plates (Plate A & Plate B).

- **Plate A:** Neuron is treated with tetraethylammonium (TEA), which **inhibits voltage gated K^+ channels.**
- **Plate B:** Neuron is treated with tetradotoxin (TTX), which **inhibits voltage gated Na^+ channels**.



A normal action potential in a GABA secreting neuron that has been stimulated **in the absence of any neurotoxin** has been drawn in each panel above. Sketch the alteration in the action potential following the treatment of the neuron with each neurotoxin. ***Note:*** *If there is no change please write* ***"NO CHANGE"*** *on the graph.*

d) Give two possible mechanisms by which GABA is removed from the synapse?

e) Consider the following synapse between two neurons.

- **Neuron 1** when stimulated secretes epinephrine. This neuron expresses the GABA-A and GABA-B receptors.
-
- **Neuron 2** when stimulated secretes GABA.

If neuron 2 is pre- synaptic and neuron 1 is post- synaptic would you expect Neuron 1 to secrete epinephrine? **Explain** your choice.

f) A functional neuron may receive both excitatory and inhibitory signals from multiple neurons at the synaptic junctions. In a post- synaptic neuron, where are the signals from all the pre- synaptic excitatory or inhibitory synapses integrated and the decision to fire an action potential made? **Circle** the correct options from the following choices and **explain** why you circled this option.

Cell Body ***Axon Hillock*** ***Myelin Sheath*** ***Synaptic Cleft***

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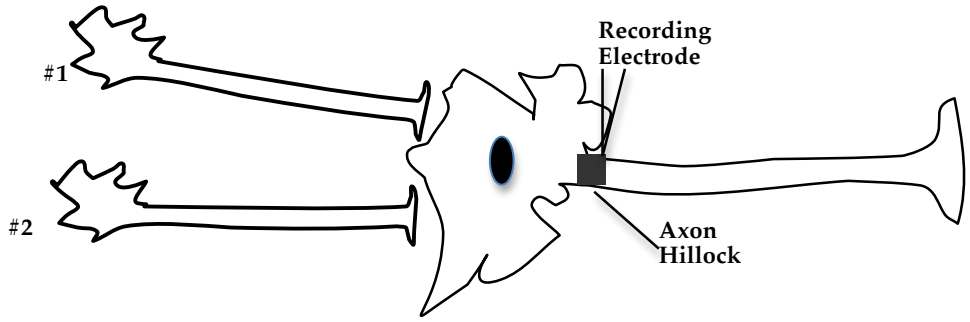
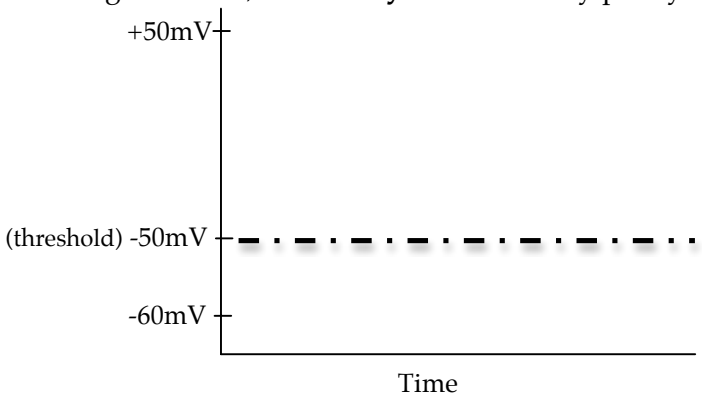
Question 4 continued

g) The following schematic shows **two excitatory pre-synaptic neurons** that independently converge on a post-synaptic neuron. The two pre-synaptic neurons can be stimulated individually. In the absence of any stimulation, the recording electrode in the post-synaptic neuron measures the membrane potential as -60mV.

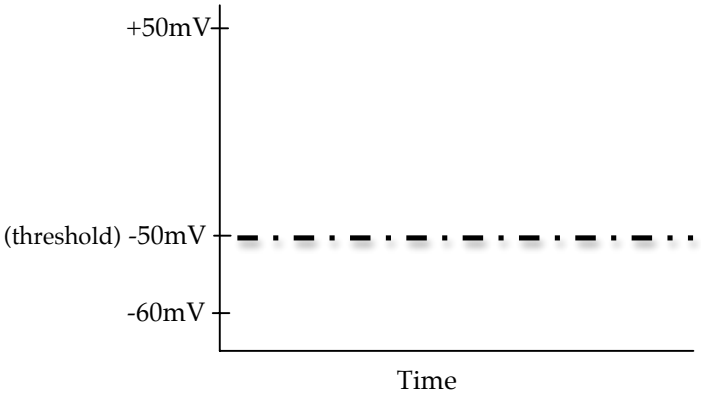


If **only one** excitatory pre-synaptic neuron is stimulated, you record a deviation from -60mV with the recording electrode in the post-synaptic neuron, but you do not record an action potential. If **both** the excitatory pre-synaptic neurons are stimulated, you record an action potential in the post-synaptic neuron.

i. On the graph below sketch the changes in the post-synaptic neuronal membrane potential, as measured by the recording electrode, when **only one** excitatory pre-synaptic neuron is stimulated.



ii. On the graph below sketch the changes in the post-synaptic neuronal membrane potential when **both** the pre-synaptic neurons are stimulated.



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Question 5

a) Neuronal path finding is crucial for structured cellular organization and development of neural circuits. The elongation or retraction of the growth cone is dependent on the guidance cues. You are looking at the response of the growth cone to the following guidance cues. ***Note:*** *In this example you may assume that both these guidance cues serve as* ***attractants****.*

- ***Guidance cue 1: Fibronectin*** *protein that is a part of ECM.*
- ***Guidance cue 2: Ephrins****, which diffuse along their concentration gradient.*

i. Classify the two guidance cues as **short-** or **long-** range signals.

Fibronectin: **Ephrins:**

ii. You do a stripe assay to determine if fibronectin and ephrins serve as attractive guidance cues. Briefly **explain** how this assay works, and what results you would get if one of these proteins is an attractive guidance cue.

iii. The stripe assay is an *in vitro* assay, that is, performed outside the body. You next need to determine whether fibronectin and ephrins are the normal guidance cue for these neurons in the brain. Give an experiment that can help you answer this question.

b) A key question in neurobiology is how neurons find their targets to generate circuits. Retinal neurons transmit information about the light that the eye perceives to the brain in the form of electrical signals. The cell bodies of these neurons are in the eye. During development they connect to a region of the brain known as the optic tectum. The goal of recent research has been to figure out how they do this. The following inhibitors disrupt innervation of the tectum by retinal neurons. Complete the table for each of the following treatments.

Treatments	What would be the effect of this treatment on axon elongation?
Nocodazole (disrupts microtubules)	
A collagen specific antibody that inhibits/ disrupts extracellular matrix (ECM)	

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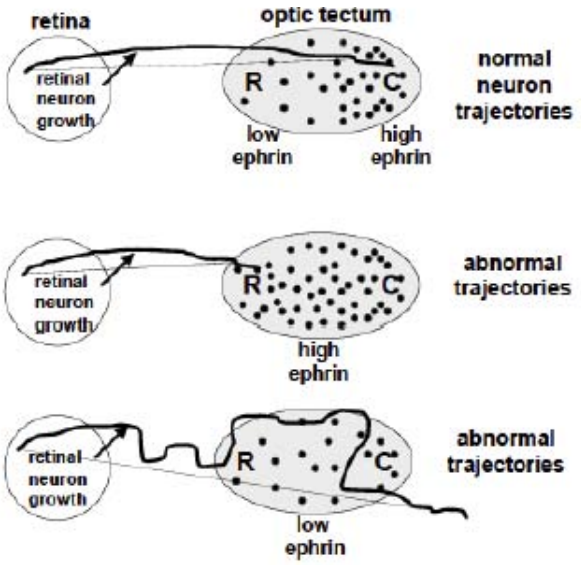
Question 5 continued

c) Ephrin is a ligand found in the optic tectum in a gradient, with more caudally (C), than rostrally (R). Temporally located retinal neurons (T) normally grow to the caudal tectum, as depicted below. When ephrin concentration is high throughout the tectum, retinal neurons stop in the rostral region (R). However, when ephrin concentration is low throughout the tectum, temporal retinal neurons grow past the tectum.



i. What part of the neuron grows, as neurons find their path?

ii. The receptor that binds ephrin is the Eph receptor. Where is the Eph receptor most likely to be expressed in the schematic above?

iii. Using the data in the schematic, explain why during normal development, the temporal retinal neurons grow to the caudal tectum.

iv. What would happen to the growth of retinal neurons in the absence of the Eph receptor? **Explain**.

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