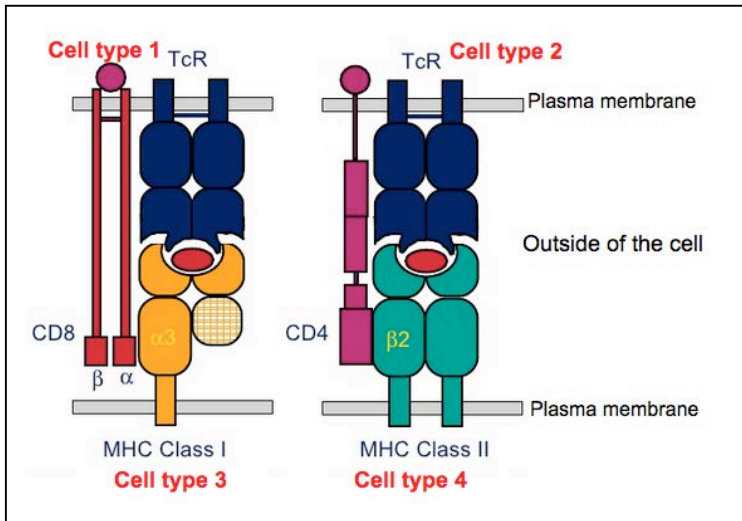


7.013 Problem Set 7- 2018

Question 1

The schematic below shows the interaction between the T cell receptors (**TcR**), Major histocompatibility complex Type I (**MHCI**) and II (**MHCII**) and the accessory cell surface molecules (**CD4** and **CD8**) located on the surface of **cell types 1-4**.



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a) Which cell type is likely a helper T cell (T_H): **Cell type 1/ 2/ 3/ 4**? Which cell surface marker(s) would this cell type have: **MHCI/ MHCII/ CD4/ CD8**?

b) Which cell type is likely a cytotoxic T cell (T_C): **Cell type 1/ 2/ 3/ 4**? Which cell surface marker(s) would this cell type have: **MHCI/ MHCII/ CD4/ CD8**?

c) Which cell type is most likely a professional antigen presenting cell (**APC**): **Cell type 1/ 2/ 3/ 4**? Which cell surface marker(s) would this cell type have: **MHCI/ MHCII/ CD4/ CD8**?

d) Identify the cell types that interact with each other to trigger ...

i. B cell activation and humoral (Antibody mediated) immune response: **Cell type 1/2/ 3/ 4**?

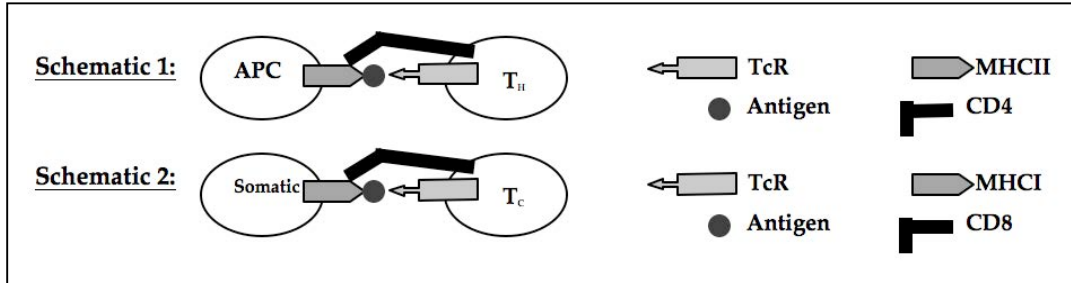
ii. Cytotoxic T cell mediated killing of an infected cell: **Cell type 1/2/ 3/ 4**?

e) An individual who is heterozygous for two alleles of the Antibody (Ab)/ Immunoglobulin gene (Ig) expresses only ONE of the two alleles for this gene. Briefly **explain** why this is critical.

Question 2

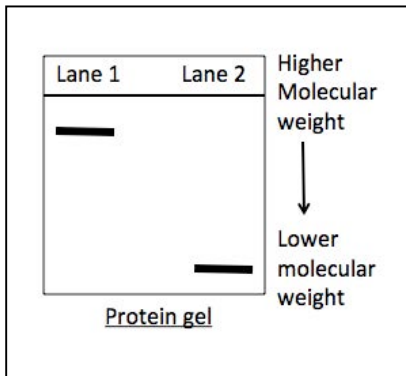
Gardasil is a preventive vaccine that was designed against the **surface proteins** of Human Papillomavirus (HPV), a **DNA virus** that causes cervical, head and neck cancer.

a) Which of the following schematics (1 or 2) represents the immune response that will be triggered following vaccination with Gardasil.



b) Following vaccination with Gardasil, why the secondary immune response against HPV is **faster and more effective** than the primary immune response?

c) During a primary and secondary humoral immune response to an antigen, the mature and memory B cells **produce surface antibodies**. Furthermore, the memory B cells, during secondary immune response can give rise to the **plasma B cells that produce secreted antibodies**. You isolate the antibodies that are specific to the HPV surface proteins and resolve them on a gel designed to separate proteins based on the difference in their molecular weight. The gel profile is shown below.



- i. Which class of antibodies is present in **Lane 2** of the gel: **secreted IgG OR IgM?**
- ii. From the gel, which B cell-type produces the antibody type shown in **Lane 2**?

d) If you compare the structure of secreted and surface antibodies that are specific to the **same epitope** (antigenic determinant) of an antigen, would you expect these antibodies to have ...

- i. The **same or different Variable** regions? **Why?**
- ii. The **same or different Constant** regions? **Why?**

Question 2 continued

e) Our immune system is capable of producing antibodies (IAb) and T- cell receptors (TcR), each of which has antigen-binding sites that are specific to a particular antigen. If our genome only has approximately 20,000 genes, **list three processes** by which our immune system can produce millions of Abs and TcRs.

Question 3

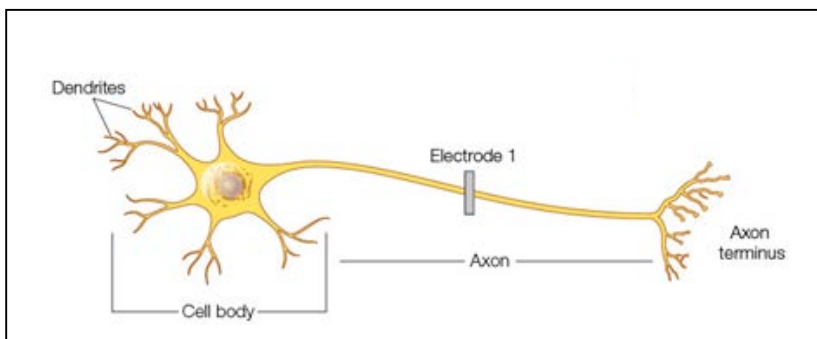
Multiple sclerosis (MS) is an autoimmune disorder in which the immune system attacks and destroys the myelin sheath of a neuron.

a) What immune mechanism is disrupted in MS patients, resulting in the production of self-reactive antibodies?

b) Immunosuppressive drugs are often prescribed to patients with autoimmune diseases. What would be the most common side effect of these drugs?

c) What happens to the speed of propagation of action potentials in a neuron when the myelin sheath is destroyed: **slows down/ speeds up/ shows no change**? **Explain** why you selected this option.

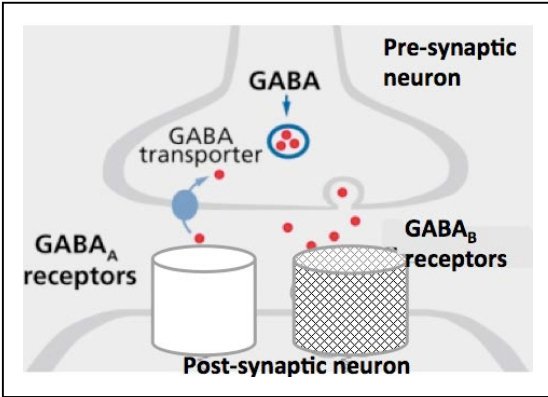
d) The schematic below a normal healthy neuron. Use an arrow(s) to show the propagation of the action potential (AP) after stimulating the neuron by passing current through electrode 1. **Explain** why it differs from the normal direction of propagation.



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Question 4

GABA is an inhibitory neurotransmitter in the central nervous system (CNS). It acts by binding to GABA-A receptors that are ligand gated chloride channels (Cl-) and GABA-B receptors that activate potassium channels (K+) 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.**

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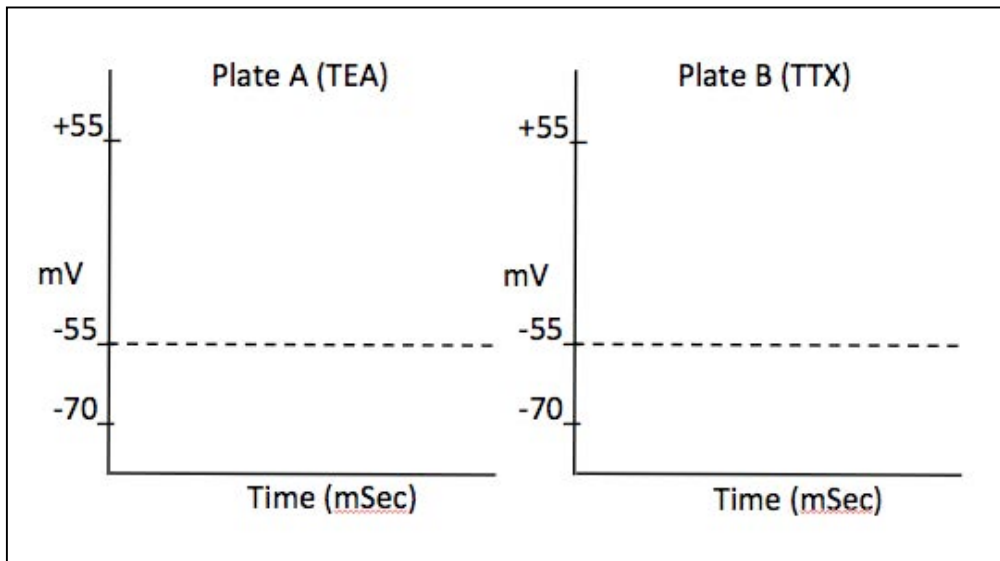
b) Note that the K⁺ concentration is high inside the neuron, while the Ca²⁺, Na⁺ and Cl⁻ ion concentrations are high outside. In what direction would Cl⁻ ions flow when the GABA-A receptor is activated: **into OR out of the neuron**? How does this flow alter the likelihood of an action potential in the post-synaptic neuron? **Explain.**

c) You culture a GABA producing neuron in the presence of the following neurotoxins in two separate cell culture plates (Plate A & Plate B). You then apply excitatory stimuli to both plates.

Plate A: Neuron is treated with tetraethylammonium (TEA), which **inhibits voltage gated K⁺ channels**.

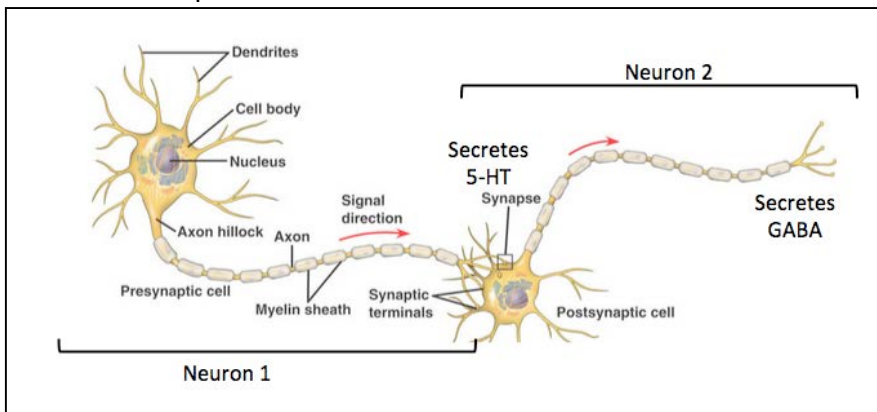
Plate B: Neuron is treated with tetrodotoxin (TTX), which **inhibits voltage gated Na⁺ channels**.

Sketch the alteration in the action potential following the treatment of the GABA producing neuron with each neurotoxin. **Note:** If there is no change, please write **“NO CHANGE”** on the graph. The resting and threshold membrane potentials are -70mV and -55 mV respectively.



Question 4 continued

d) Serotonin (5-HT) is an excitatory neurotransmitter. It acts by binding to 5-HT₃ (a ligand gated Na⁺ channel). In comparison, GABA is an inhibitory neurotransmitter, which acts by binding to the GABA-A receptors that act as Cl⁻ channels.



Neuron 1 secretes 5-HT and has GABA-A receptors

Neuron 2 secretes GABA and has 5-HT₃ receptors.

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You stimulate neuron 1 in the presence of Prozac (an inhibitor of 5-HT reuptake from the synaptic cleft) and let it synapse with Neuron 2. Would neuron 2 secrete GABA at a **higher/ lower/ at the same rate** as the synapse that has not been treated with Prozac? **Explain.**

e) Over time, the postsynaptic neuron shows a decrease in responsiveness to 5-HT. Propose an **alteration** in the **post-synaptic neuron** that would account for decreased responsiveness.

Question 5

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 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 the extracellular matrix (ECM).
- **Guidance cue 2: Ephrins**, which diffuse to form a concentration gradient.

a) Which guidance cue, **Fibronectin OR ephrin** is short range and **why**?

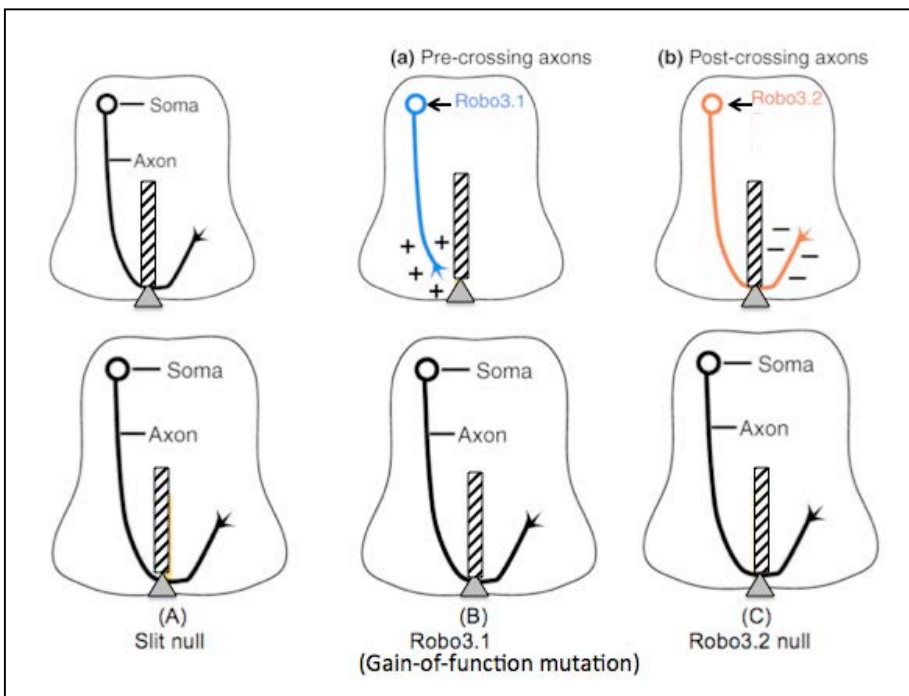
b) You do a stripe assay to determine if fibronectin serves as an attractive guidance cue. Briefly **explain** how this assay works.

Question 5 continued

As diagrammed below, in mice, spinal commissural axons (black) are attracted to grow towards the floor plate (shaded Δ) and then need to cross this to find their targets. The midline of the spinal cord expresses the **repulsive ligand Slit** (shown as striped rectangle).

- Before crossing the midline, the axons shown in blue express Robo3.1. Robo3.1 blocks the repulsive activity of Slit so the axons can cross.
- After midline crossing, the axons (shown in red) express Robo3.2, a second isoform of Robo3, in place of Robo3.1, which repels axons away from the midline so they do not grow back the wrong way. (Ypsilanti et al, 2010).

c) On the diagrams, draw in BLUE or RED or using a dashed line, how the axons would grow in the mutants indicated. **Note:** Normal axon growth is shown in each for reference.



Adapted from Ypsilanti, A., et al. "[Moving away from the midline: new developments for Slit and Robo.](#)" *Development* 137(2010): 1939-52.

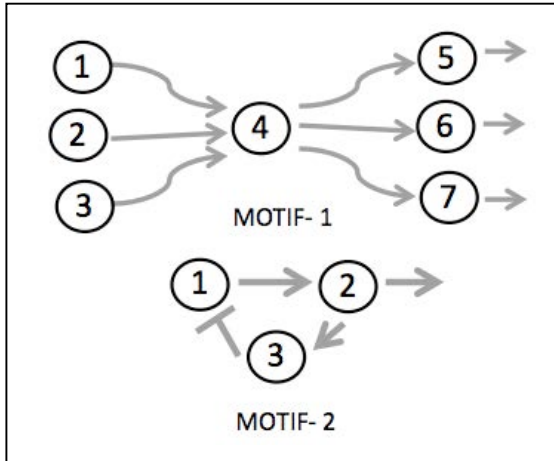
d) Nocodazole is a chemical that disrupts the microtubules. What would be the effect of nocodazole treatment on the growth of commissural neurons?

e) Slit is a secreted ligand acting at long-range. Would you be able to use a 'stripe assay' to monitor what regions of the spinal cord express Slit? **Why or why not?**

Question 6

C. elegans is a transparent nematode that has a total of 1031 cells of which 302 are neurons. All the neuronal connections in *C. elegans* have been mapped and many complex circuits have been defined.

The following are two motifs/ circuits in **C. elegans**. **Note:** The → represents activation and “T” represents inhibition. Each neuron is represented by a number.

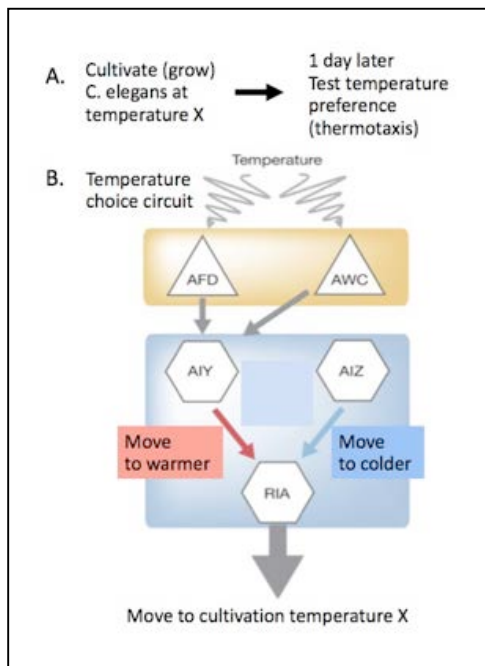


a) Would you see an action potential generated in neurons 5, 6 and 7 of motif 1? **Why or why not?**

b) How would the activity of neuron 1 change if neuron 2 were removed, in Motif 2? **Explain your answer.**

Thermotaxis is movement of an organism toward or away from a specific temperature. The worm *C. elegans* can be grown (cultivated) at a specific temperature and later will remember and choose to move towards that temperature through the process of thermotaxis. The specific neuronal circuitry involved is shown below.

You cultivate (grow) *C. elegans* at (temperature X for 1 day and then test their temperature preference. The temperature choice neuronal circuit for *C. elegans* is shown below (adapted from Nishida et al. [EMBO reports 12\(2011\): 855-62](#)).



- Temperature is detected by AFD and AWC neurons.
- The activated AIY–RIA circuit promotes movement to a temperature **higher** than cultivation temperature.
- The activated AIZ–RIA circuit accelerates movement to a temperature **lower** than the cultivation temperature.
- The RIA neuron integrates and promotes temperature choice.

c) In the circuit to the left...

i. Is there a sensory neuron shown? **Explain** your choice.

ii. Is there an interneuron shown? **Explain** your choice.

Question 6 continued

d) The circuit on Page 7 was defined by destroying (ablating) neurons and testing thermotaxis. Predict what would happen to the temperature memory from the following ablations. **Explain** your answers.

i. **AFD** ablated?

ii. **AIZ** ablated?

iii. **RIA** ablated?

e) Glutamate is an excitatory neurotransmitter normally produced by AFD. AIY produces a glutamate receptor. You engineer a mutant worm where both AWC and AFD produce glutamate. What would you predict would happen to thermotaxis? **Explain** your answer in terms of the action potential produced.

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7.013 Introductory Biology
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