Solutions to 7.012 Quiz III

Class Ave = 70.5
Standard Dev = 12.5

Approximate grade	Range	%
A	83 - 100	19%
B	70 - 82	37%
C	56 - 69	30%
D	45 – 55	12%
F	0 – 43	2%

Initials_____

Question 1 (14 points)

You discover several new viruses.

a) Virus A is a positive-stranded (mRNA-like) RNA virus, but is **not** a retrovirus. The viral genome is enclosed by nucleocapsid proteins and enveloped by a membrane that contains surface viral glycoproteins.

- Would this virus need to package within the viral particle any additional protein or proteins to successfully reproduce within a host cell? If the answer is yes, state why additional protein(s) must be packaged and what protein(s) must be packaged. If the answer is no, explain why no additional protein needs to be packaged.
  No. Although this virus must encode an RNA-directed RNA polymerase, it does not have to package it, because the genome can be directly translated into the needed protein.

- Name the type of enzyme that this virus would use to copy its genome. Is this enzyme encoded by the virus or the host?
  RNA-directed RNA polymerase encoded by the virus.

b) Virus B is a negative-stranded RNA virus and it **does not integrate** into the host genome. The viral genome is enclosed by nucleocapsid proteins, which form an icosahedral capsid.

- Would this virus need to package within the viral particle any additional protein or proteins to successfully reproduce within a host cell? If the answer is yes, state why additional protein(s) must be packaged and what protein(s) must be packaged. If the answer is no, explain why no additional protein needs to be packaged.
  Yes. This virus must encode an RNA-directed RNA polymerase, and because the genome is can not be translated within the host cell, it must package this enzyme.

c) Virus C is a small double-stranded DNA virus and it **does not integrate** into the host genome. The viral genome is enclosed by nucleocapsid proteins, and no additional proteins are packaged within the viral particle. To maintain a small genome, this virus encodes only proteins that are absolutely required.

- Name the type of enzyme that this virus would use to copy its genome. Is this enzyme encoded by the virus or the host?
  DNA directed DNA polymerase from the host cell.

- You know that some viruses, like the influenza viruses change over relatively short periods of time. You examine the genomes of the new virus particles for viruses A, B, and C, and find that the mutation rate for one of the viruses is much less than that for the other two viruses. Which virus do you expect will have the lowest mutation rate? Explain why you made this choice.
  Virus C uses the host DNA polymerase which has proofreading capabilities and thus will make fewer mistakes resulting in mutations.

Initials_____

Question 2 (31 points)

Exposure to certain compounds can cause cancer. The Ames Test is used to evaluate the carcinogenic potential of chemical agents based upon mutagenicity.

The Ames test employs a specific strain of bacteria that has a defect in a gene required for synthesis of histidine, a his- strain. A compensatory mutation to this gene can reverse the effects of the mutation that caused histidine dependence. You evaluate compounds W, X, and Y and obtain the following results.

Compound	**Results of the Ames Test**
Control	10 colonies on test plate
Compound W	No colonies on test plate
Compound X	1000 colonies on test plate
Compound Y	2000 colonies on test plate

a) What type of media would be contained in the test plates?
The test plate would contain Media that does not contain histidine.

b) You use water without any added compound as the control for this experiment. You see 10 colonies on the control plate. How do you explain these colonies?
These colonies result from spontaneous mutations (reversions) in the his- cells that reverse the effects of the original mutation which caused the histidine dependence.

c) Given only the above data, which compound or compounds are certainly mutagens?
Compound X and Compound Y

d) Some of these compounds have the potential to be carcinogenic.

- Which one of these compounds has the greatest potential to be carcinogenic?
  Compound Y

- Explain why chemicals that cause mutations can be carcinogenic.
  Chemicals that cause mutations can result in a gain-of function mutation in proto-oncogenes or loss of function mutations in tumor suppressor genes. An accumulation of such mutations with a cell can result in a cell that has lost control of cell division. The cell that divides out of control can be the beginning of cancer.

- Not all chemicals that are shown to be mutagens in the Ames test are carcinogens in vivo. Briefly explain why some mutagenic compounds do not cause cancer in animals.
  Some mutagens are broken down by the enzymes (often liver enzymes) found in animals to form compounds that are not harmful.

Initials_____

Question 2, continued

Exposure of a human cell line to mutagens produced the five mutant human cells described below.

Cell	Affected Gene	Normal function of protein	Allele1	Allele 2
1	Gene M	Protein M is a G-protein linked growth factor receptor	A mutation causing a growth factor receptor to activate a G-protein in the absence of growth factor	Wild-type
2	Gene N	Protein N functions to halt cell division	A nonsense mutation that replaces the fourth codon with a stop codon	A mutation that inactivates the promoter for the gene N.
3	Gene O	Protein O phosphorylates and inactivates a tumor suppressor protein	A mutation such that protein O has no kinase activity	Wild-type
4	Gene P	Ras-like protein that turns on a signal cascade that promotes the cell cycle.	A loss of function mutation	Wild-type
5	Gene Q	Protein Q stimulates apoptosis when present.	A translocation that puts the coding region of gene Q next to a strong promoter, resulting in gene Q over-expression	A deletion of the entire gene

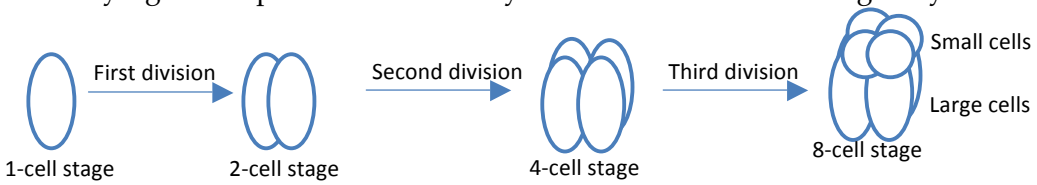
e) Given the table above, identify the normal version of Gene M, N, O, P or Q as a either a **tumor suppressor gene** or a **proto-oncogene** and give the phenotype of the cell that carries both allele 1 and allele 2 as described above. Choose **transformed** (i.e., has characteristics of a cancer cell and can form foci) **or NOT transformed**. *(Please note: The cells of this cell line do not need to have many different genes mutated to see a transformed phenotype.)*

Cell	Normal Gene functions as	Phenotype of cell carrying both alleles 1 and 2 above
1	Gene M: *proto-oncogene*	*Transformed*
2	Gene N: *tumor suppressor*	*Transformed*
3	Gene O: *proto-oncogene*	*Not Transformed*
4	Gene P: *proto-oncogene*	*Not Transformed*
5	Gene Q: *tumor suppressor*	*Not Transformed*

Initials_____

Question 3 (18 points)

You are studying development in a model system that has the following early cell divisions.



a) In experiments, you find that each of these at the 4-cell stage is pluripotent and each can form all the cells types of the organism.

- Would you expect that each of these four cells have all the same DNA?
  Yes
- Would you expect that each of these four cells have all the same RNA?
  Yes
- Would you expect that each of these four cells have all the same proteins?
  Yes

b) At the 8-cell stage, you find that the smaller cells are committed to form ectoderm and the larger cells are committed to form endoderm.

- Would you expect that each of these eight cells have all the same DNA?
  Yes
- Would you expect that each of these eight cells have all the same RNA?
  No
- Would you expect that each of these eight cells have all the same proteins?
  No

c) Some of the genes expressed in the cells at the 8-cell stage encode transcription factors.

- In the 8-cell stage, the genes for these transcription factors would best be described as ___*Regulatory*___ genes.
- Explain what a transcription factor is, and how it functions to determine the final fate of a cell.
  A transcription factor is a protein that binds to specific DNA sequences and controls transcription of genetic information from DNA to mRNA. Transcription factors (either alone or with other proteins) promote or block the recruitment of RNA polymerase to specific genes. In fate determination, a specific transcription factor will activate (either directly or indirectly) cell-type specific genes (effector genes) that give the cell its unique fate.

d) If the small cells from the above diagram are committed to form ectoderm as a result of an **mRNA** determinant, in which cells would you find the determinant? Choose one:

Small cells large cells both cells Can't tell

e) If the small cells from the above diagram are committed to form ectoderm as a result of a **protein** inducer, in which cells would the protein inducer be produced? Choose one and explain.

Small cells large cells both cells Can't tell

If the small cells form ectoderm due to an inducer, then the large cells would be the cells producing the inducer.

Initials_____

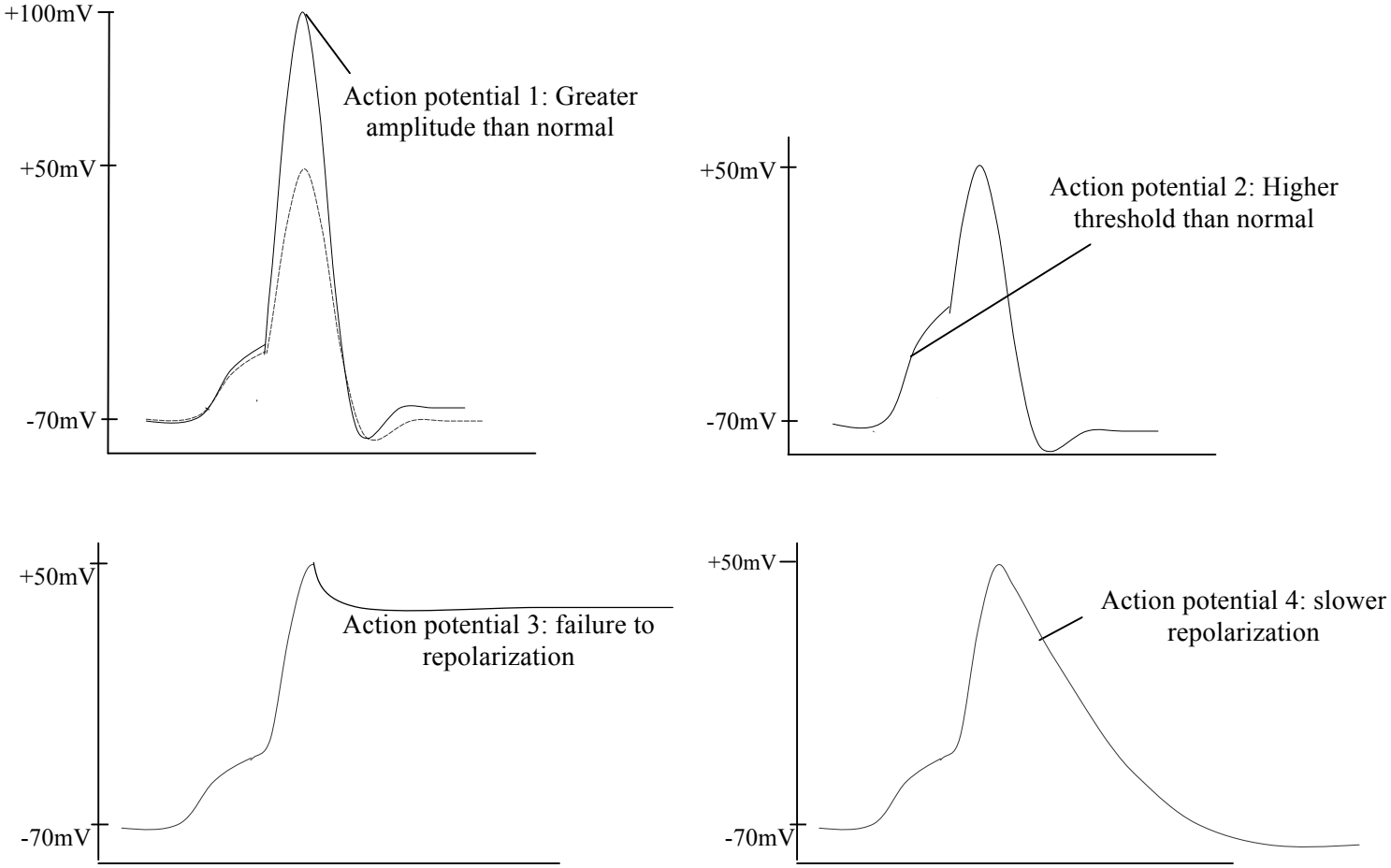
Question 4 (37 points)

a) In human neurons, the resting membrane potential is about -70 mV. Circle the true statements from below.

In a normal neuron where the resting membrane potential is a stable -70 mV…

- In a normal neuron at -70 mV, there is a higher concentration of Na^+ in the cell as compared to outside the cell.
- In a normal neuron at -70 mV, there is a higher concentration of K^+ in the cell as compared to outside the cell.
- In a normal neuron at -70 mV, the flow of Na^+ into the cell equals the flow of Na^+ out of the cell.
- In a normal neuron at -70 mV, the flow of K^+ into the cell equals the flow of K^+ out of the cell.
- In a normal neuron at -70 mV, the flow of K^+ into the cell equals the flow of Na^+ out of the cell.
- In a normal neuron at -70 mV, the flow of K^+ into the cell is much greater than the flow of Na^+ out of the cell.

Potent neurotoxins act to prevent normal neuronal function. Tetraethylammonium (TEA) blocks only the voltage-gated K^+ channels and prevents K^+ movement through voltage-gated K^+ channels.



b) Which of the above action potentials 1, 2, 3 or 4, would be recorded in a single neuron after the neuron was treated with Tetraethylammonium. A normal action potential in this neuron is shown by the dotted line on the first graph. Explain in terms of ion movement and ion pumps and channels why the shape of the action potential in these treated cells differs from normal.

Action potential 4 would be seen in cells treated with TEA. The cells depolarize to threshold normally in response to a stimulus. At threshold, the voltage-gated Na^+ channels open and Na^+ influx depolarizes the cell. The voltage-gated Na^+ channels close, which allows repolarization of the membrane. In the absence of the voltage-gated K^+ channels, the repolarization is dependent upon the flow of K^+ out of the cell through the resting K^+ channel, and is much slower.

Question 4, continued

c) In Aplysia, there is an axo-axonal connection between a tail sensory neuron and a siphon sensory neuron. At this axo-axonal connection, serotonin is released from the tail neuron to the siphon sensory neuron, and this makes the siphon sensory neuron more permeable to Ca^{2+}. The siphon sensory neuron synapses onto a motor neuron that innervates the gill muscle.

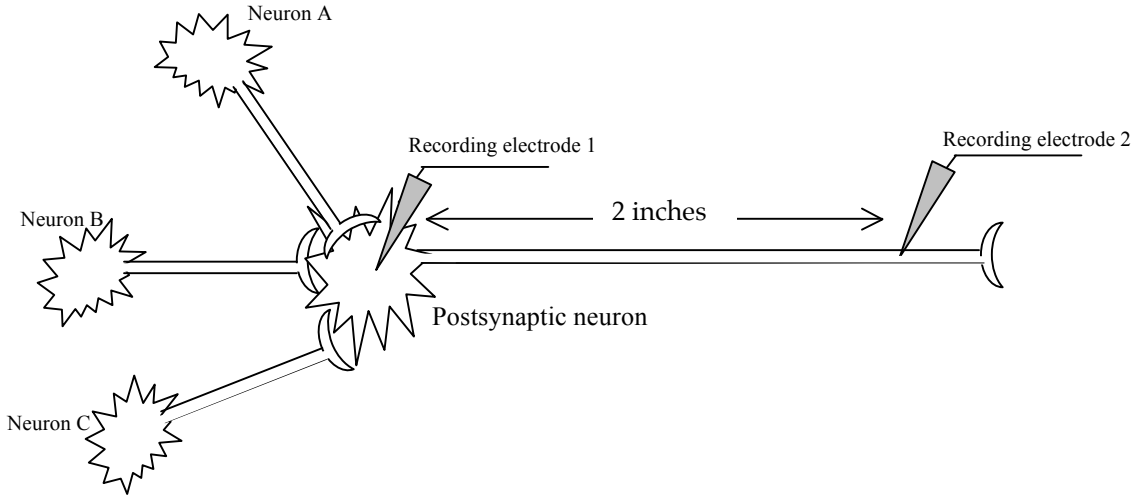
- Describe what is seen in each of the following cells, subsequent to serotonin release, when the siphon sensory cell fires an action potential.

  siphon sensory neuron: *As the action potential invades the terminal, the Ca^{2+} influx into the sensory neuron triggers phosphorylatyion of synapsin. This allows release of the vesicles containing neurotransmitters. The vesicles fuse with the membrane of the cell and release neurotransmitter into the synaptic cleft. Because there is extra Ca^{2+} influx, more neurotransmitter is released.*

  motor neuron: *The extra release of neurotransmitter will mean that more neurotransmitter is bound to the ligand-gated channels on the post-synaptic cell. This will result in a greater depolarization of the post-synaptic membrane and will increase the frequency of action potentials generated in the motor neuron.*

- What effect does serotonin release to the siphon sensory neuron have on the gill withdrawl response?
  Serotonin released to the siphon neuron will give a larger gill withdrawl in response to a touch to the siphon.

In the diagram below, the response of the postsynaptic neuron to input from the presynaptic neurons (neurons A, B, and C) can be recorded by placing small recording electrodes into the postsynaptic neuron. **Electrode 1 is in the cell body, electrode 2 is in the axon**.



Neurons A and C each make excitatory synapses using **Dopamine** as a neurotransmitter. Neuron B makes an inhibitory synapse using the neurotransmitter **Glycine**.

d) List an ion that can move across the postsynaptic cell membrane in response to Dopamine to facilitate the excitation. Would this ion move into or out of the cell?
Na^+ into cell or Ca^{2+} into cell

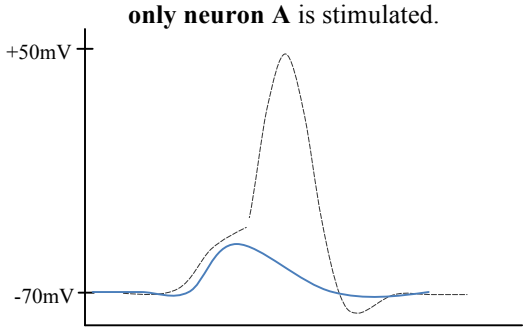
e) List an ion that can move across the postsynaptic cell membrane in response to Glycine to facilitate the inhibition. Would this ion move into or out of the cell?
Cl^- into cell or K^+ out of the cell

Initials_____

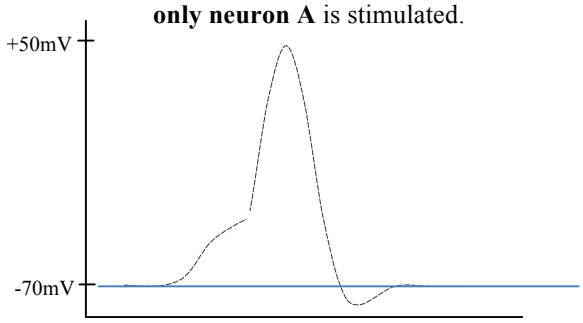
Question 4, continued

f) Neurons A and C make excitatory synapses using Dopamine as a neurotransmitter. You find that stimulating neuron A is not sufficient to trigger an action potential in the postsynaptic cell, but stimulating both neurons A and C is sufficient.

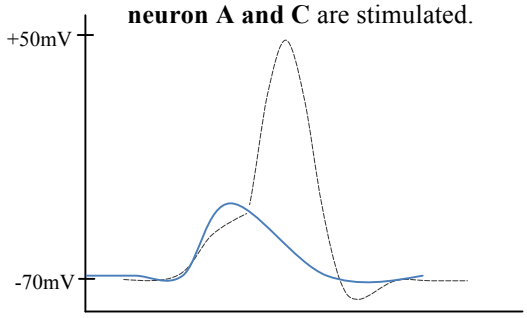
On the graph below, draw what you would record with **electrode 1** if **only neuron A** is stimulated.



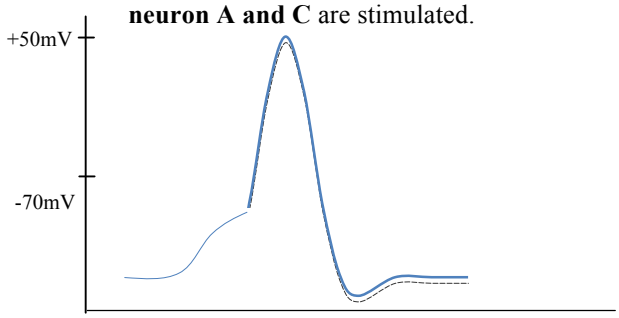
On the graph below, draw what you would record with **electrode 2** if **only neuron A** is stimulated.



On the graph below, draw what you would record with **electrode 1** if **both neuron A and C** are stimulated.

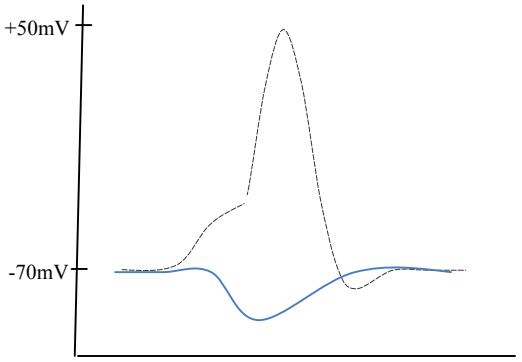


On the graph below, draw what you would record with **electrode 2** if **both neuron A and C** are stimulated.

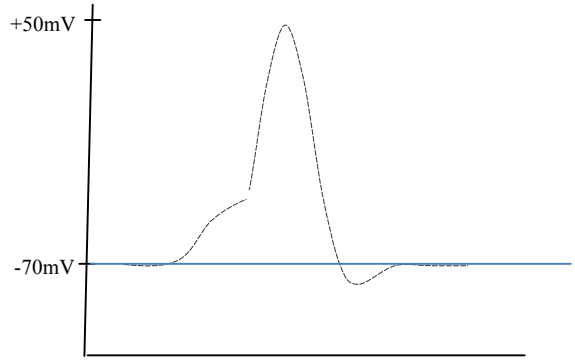


g) A normal action potential recorded from the postsynaptic neuron is shown by the dotted line on the graphs below. When Glycine is released from inhibitory Neuron B, the membrane potential in the postsynaptic cell changes.

On the graph below, draw what you would record with **electrode 1** if **only neuron B** is stimulated.



On the graph below, draw what you would record with **electrode 2** if **only neuron B** is stimulated.



Initials_____

Question 4, continued

h) Dopamine is a neurotransmitter used at many different synapses. Once released, dopamine is transported out of the synaptic cleft and back into the presynaptic neuron, where it is taken up into storage vesicles. Cocaine binds tightly to the dopamine transporter and blocks its function. Individuals that abuse cocaine find that, over time, the effects of cocaine are diminished. Describe a molecular change in the postsynaptic cells at dopamine synapses that explains the decreased response to cocaine.
The post synaptic cells have likely decreased the number of dopamine receptors in response to the chronically high levels of dopamine seen as a result of the loss of the reuptake mechanism.

i) Both α-bugarotoxin and β-bugarotoxin affect signaling at the neuromuscular synapse. α-bugarotoxin irreversibly binds to the acetylcholine receptor but does not activate it. β-bugarotoxin binds to cellular proteins and stimulates release of vesicles. One of these toxins results in rigid paralysis, where the muscles contract but do not relax. The other toxin results in flaccid paralysis, where the muscles fail to contract. Which of these toxins results in rigid paralysis? Explain your answer.
β-bugarotoxin would result in rigid paralysis because the muscles are receiving extra acetylcholine as a result of the stimulation of vesicle release.