Question 1. (10 points total)
a) Pretend you are doing an experiment in which you are patching a mammalian neuron in the current clamp configuration. Your neuron is bathed in a solution containing physiological ionic concentrations. Describe qualitatively what happens to the membrane potential \( V_m \) of that neuron if you increase the extracellular potassium concentration \([K^+]\). (1 point)

\[ V_m \approx E_{K} \]

b) Assume that in the previous experiment you increased \([K^+]\) from 2.5 mM (physiological concentration) to 15 mM. If this experiment is being done at a physiological temperature of mammals (i.e., near 37° C), what potential will the membrane reach after you increased \([K^+]\)? The intracellular \([K^+]\) is 140 mM. For this problem assume the membrane of the neuron is permeable to \( K^+ \) only. (2 points)

\[ E_{K} = 62 \log \left( \frac{[K^+]_{in}}{[K^+]_{out}} \right) = -60.14 \, mV \]

c) The extracellular chloride concentration \([Cl^-]\) is 150 mM and the intracellular \([Cl^-]\) is 9 mM. Assume that the intra and extracellular \([K^+]\) are 140 mM and 15 mM, respectively, as mentioned earlier in the problem. Now assume that the membrane is permeable to \( Cl^- \) as well as \( K^+ \) (but not to sodium; i.e., \( g_Na = 0 \)) and that the conductance of potassium ions \( (g_K) \) is twice that of the conductance of \( Cl^- \) \((g_{Cl^-})\), i.e. \( g_K = 2 g_{Cl^-} \).

What is the membrane potential \( V_m \) of the cell? Note that we are still at mammalian physiological temperature. (4 points)

\[ E_{Cl^-} = -62 \log \left( \frac{[Cl^-]_{out}}{[Cl^-]_{in}} \right) = -62 \log \left( \frac{150 \, mM}{9 \, mM} \right) = -75.75 \, mV \]

\[ V_m = \frac{g_K E_K + g_{Cl^-} E_{Cl^-}}{g_K + g_{Cl^-} + g_{Cl^-}} \]

\[ g_{Cl^-} = 0 \quad \text{and} \quad g_K = 2 g_{Cl^-} \]

\[ V_m = \frac{2 g_{Cl^-} E_K + g_{Cl^-} E_{Cl^-}}{2 g_{Cl^-} + g_{Cl^-}} = \frac{4 g_{Cl^-} E_K}{3 g_{Cl^-}} = \frac{2 E_K + E_{Cl^-}}{3} = \frac{-75.75 + 75.75}{3} = 65.34 \, mV \]

d) Given \( V_m \) calculated in c) and an intra and extracellular \([K^+]\) of 140 mM and 15 mM, respectively (as above): What is the driving force for \( K^+ \)? Is potassium flowing in or out of the cell? Explain your reasoning. (3 points)

\[ \text{K}^+ \text{Driving force: } V_m - E_K = 65.34 \, mV - (-60.14 \, mV) = 5.2 \, mV \]

\( K^+ \) flows into the cell because \( V_m \) is more negative than \( E_K \).
**Question 2** (15.5 points)
a) Name three properties of action potentials, and for each assign a corresponding realistic value (number and unit). (3 points)

- **Amplitude**: -100 mV
- **Duration**: ~1 ms
- **Threshold**: -60 to -40 mV

**Propagation Velocity**: 0.25 - 100 m/s

**Absolute Refractory Period**: ~1 ms

b) Which conductance contributes to the rising phase of an action potential?
Draw the I/V plot for this conductance for membrane potentials between -100 and +100 mV.
Mark the equilibrium potential of this conductance on the I/V plot.
Mark the point of maximum conductance of that ion on that I/V plot as well.
Label both axes of your graph with the relevant units and tick mark the x-axis. (4.5 points)

![I/V plot for Na⁺ conductance](image)

-100 -80 -60 -40 -20 0 20 40 60

-80 0 80

V_m (mV)

E_Na

c) On that same I/V plot circle the section at which the conductance is constant.
Why does the current change over this range? (2 points)

![Change in Conductance](image)

**Change in Driving Force**

-100 -80 -60 -40 -20 0 20 40 60

-80 0 80

V_m (mV)

d) The conductance of which ion contributes to the falling phase of an action potential? Draw an activation curve for this conductance between -100 and +100 mV. Label both axes of your graph with the relevant units and tick mark the x-axis. (3 points)

![I/V plot for K⁺ conductance](image)

-100 -80 -60 -40 -20 0 20 40 60

-80 0 80

V_m (mV)

e) Pretend that you are doing an experiment in which you are recording from a giant squid axon using the voltage clamp method. The recording is made in the presence of a blocker for voltage-gated potassium channels. You step the membrane potential from -80 mV to +20 mV for 10 ms (as shown in the schematic below).
Draw the time-course of the current that you would record in response to that step.
On the same graph, draw the corresponding current response you would record in a hypothetical squid mutant in which voltage-gated sodium channels inactivate more slowly than normal. Be sure to label which current response corresponds to the normal and the mutant. (4 points)

![Time-course of current](image)

\[ V_m \]

\[ +20 \text{ mV} \]

\[ -80 \text{ mV} \]

\[ \text{time} \]
Question 3. Equipped with what you learnt from class, you are prepared to conduct the following series of experiments: (10.5 points total)

a) You are recording from an axon in the current clamp (I-clamp) configuration. TTX is present in the extracellular solution. You inject a rectangular depolarizing current step into an axon and record simultaneously the time-course of the membrane voltage ($V_m$).

Draw the time-course of the current you inject.
Draw the time-course of the $V_m$ that you would record in response to that current step injected into a non-myelinated axon.

On the same graph draw the time-course of $V_m$ that you would record in response to that current step injected a myelinated axon. Be sure to label which $V_m$ time-course corresponds to the myelinated and non-myelinated axon. (5 points)

![Graph showing $V_m$ vs. time for myelinated and non-myelinated axons.]

Remember: $T_{mem} = RC$

with myelin $C$ decreases (and $R$ may increase).

b) Now, you conduct the following experiment in a non-myelinated axon. TTX is no longer present in the extracellular solution.

You inject a depolarizing rectangular current pulse at position 1 and record $V_m$ at positions 1 and 2 simultaneously (see schematic below for experimental set-up).

![Schematic showing current injection and recording at two positions.]

Draw the time-course of $V_m$ recorded at position 1 and at position 2 on the same graph for a sub-threshold (below threshold) current pulse injected at position 1. Label both axes of your graph with the relevant units. Be sure to label which $V_m$ time-course corresponds to position 1 and 2. (2 points)

c) Using the same recording configuration illustrated in b) draw the time-course of $V_m$ recorded at position 1 and at position 2 for a supra-threshold (above threshold) current pulse injected at position 1. Label both axes of your graph with the relevant units. Be sure to label which $V_m$ time-course corresponds to position 1 and 2. (3.5 points)
Question 4. After graduation, you joined Dr. Theodor Alami's laboratory as a graduate research associate. After some training, you are qualified to record from the thalamus of an intact animal. (13 points total)

In the first experiment, you record the membrane voltage ($V_m$) from a thalamic neuron of an animal which is awake.

a) Draw the time-course of $V_m$ of the thalamic neuron. (1 point)

b) Now, you apply nickel to the extracellular fluid. Describe any change you expect to observe. (1 point)

No change because T-type Ca$^{2+}$ channels are inactivated.

In the second experiment, you record the membrane voltage from a thalamic neuron of an animal which is in slow-wave sleep.

c) Draw the membrane potential time-course. (2 points)

d) Indicated with an arrow where Ih activates and deactivates on your drawing in c). (2 points)

e) Draw the membrane potential time-course in the presence of nickel in the extracellular fluid. (1 point)

You are now ready to present your data at the Society for Neuroscience Meeting 2006 in Atlanta. Your advisor asks you to prepare the following plots for your presentation.

f) Draw the I-V plot for the T-type Calcium conductance for membrane potentials between -100 and 300 mV. Label both axes of your graph with the relevant units and tick mark the x-axis. (3 points)

g) On the graph above, draw the I-V plot for the N-type Calcium conductance. (3 points)
Question 5. You are a third-year medical student at UCSD. You are interning in the neurology department and you wish to study the synaptic transmission between neurons. (12 points total)

(a) Describe the sequence of events that begins with an Action Potential that reaches the axon terminal and ending with response in the endplate potential. (3.5 points)

1. AP reaches presynaptic terminal → depolarization → opening of Na⁺ channels
2. influx of Ca²⁺ in presyn terminal → vesicle fusion → release of NT in synaptic cleft → diffusion of NT across → NT binds to post terminal → in channels open → depolarization

(b) What part of the sequence described in part (a) would you interfere with if TTX were applied? Where does TTX act? (2 points)

AP propagation
Blanks Na⁺ channels

(c) The spontaneous release of a quantum of transmitter from the axon terminal of a motor neuron results in the miniature end plate potentials (mEPP or "mini") in the postsynaptic muscle fiber. If you reduce the extracellular Ca²⁺ concentration, would you reduce the amplitude of the mini? How about if curare were applied? (2 points)

No. Amplitude of mini remains the same in low extracellular Ca²⁺
Yes. Curare reduces amplitude of mini since it is an antagonist for ACh

(d) Congratulations! You have received your first patient. After an extensive examination, you diagnose him with Myasthenia Gravis. Describe the symptoms of the disease and the mechanics behind it? What are possible treatments that you would propose? (3 points)

Ptosis: Drooping of eyelids
Diplopia: Double vision
Fatigue: muscle weakness
Autoimmune Disease: attacks one's own ACh
Possible Treatments: ACh esterase inhibitor
Immuno suppressant

(e) A few days later, the attending physician corrects your diagnosis and tells you that the patient was actually poisoned by curare. What are the principle differences? How do you cure someone with curare poisoning? Can curare be used for healthcare purposes? (1.5 points)

Curare is an antagonist for ACh
Causes muscle relaxation/reduced EPP
Treatment: inhibit ACh esterase
Can be used during surgery to inhibit twitching
Question 6. Let's shift gears a bit. You did really well in Dr. Scanziani's class and now you're out in industry working for a research company that studies neurobiology. (14 points total)

(a) Your first task is to describe a gap junction. Describe the structure of the channel. (2 points)

- Composed of proteins named connexins. 13 different genes exist in newborn for connexins. Neuron 4 proteins with 6 transmembrane domain lined up. Functional gap junction consists of 6 connexins on each side. 12 connexins comprise a connexon. Size is between 1.5-2 nm.

(b) Compare and contrast an electrical synapse from a chemical synapse. (2 points)

- Directionality: Uni. vs. Bi
- Delay vs. No Delay
- Inhibitory or excitatory vs. Sign Conserving

(c) You have a living slice of cortex under your microscope. With patch recording electrodes you record from two neurons (neuron 1 and neuron 2). Describe an experiment you would conduct to determine whether or not these two neurons are electrically coupled. Specify if you would record the neurons in the current clamp or voltage clamp configuration, what type of current or voltage steps you would apply to either neuron 1 or neuron 2 and what you expect to observe in the case that the two neurons are coupled via gap junctions and in the case that they are not. (3 points)

- Any sub-threshold change in Vm of neuron 1 that leads to a change in Vm of neuron 2 is an indication for gap junction coupling. Record neurons in I-clamp. Inject a negative current pulse in neuron 1 and monitor change in neuron 2. If Vm of neuron 2 does not change, then the neurons are not coupled.

(d) You are given a channel permeable for both Na+ and K+.

- The current through that channel reverses at potential $E_{rev} = -30$ mV.
- The equilibrium potentials for K+ and Na+ are: $E_{K+} = -100$ mV, and $E_{Na+} = +60$ mV. What is the relationship between $g_{Na}/g_{K}$ for the particular channel? (4 points)

$$
\begin{align*}
g_{Na} & (V_{m} - E_{Na}) = g_{K} (V_{m} - E_{K}) \\
g_{K} & = \frac{g_{Na} (V_{m} - E_{Na})}{(V_{m} - E_{K})} = \frac{(-30 + 100)}{(-30 - 60)} = 70 \Rightarrow \frac{70}{90} = \frac{7}{9}
\end{align*}
$$

(e) Draw an I-V plot for a nonselective cationic conductance that is triggered by ACh. It is permeable to K+ and Na+. How does it change when you remove extracellular Na+. Label both axes of your graph with the relevant units and tick-mark the x-axis. (3 points)

- $I (pA)$
- Remove $[Na+]_o$
- Shift to left