Name: _____

Neuroscience 201A Exam, October 7, 2014

Question #1 7.5 pts

Consider a spherical neuron with a diameter of 20 μm and a resting potential of -70 mV. If the net negativity on the inside of the cell (all of the "excess" anions) were uniformly distributed within the volume of the cell rather than being "glommed" onto the inner surface of the plasma membrane, what would the concentration of these ions be (in M)? Assume that these are all univalent ions. Assume that the capacitance of the plasma membrane is the standard 1 $\mu F/cm^2$.

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Question #2 12.5 pts

Imagine that you have a squid neuron with a single population of leak channels, which are cation channels with permeability to only Na^+ and K^+. The concentrations of permeant ions on each side of the membrane are as follows:

Ion	Na^+	K^+
Outside	550 mM	20 mM
Inside	55 mM	440 mM

a) If the resting membrane potential of the cell is -63 mV, calculate g_{Na}/g_K for the leak channels. (You are encouraged to use conductances for this problem (not permeabilities).

b) If the squid neuron is spherical with a diameter of 200 μm, if the leak conductance of its membrane is 0.3 mS/cm^2, and if the conductance of a single leak channel is 10 pS, calculate the average density of leak channels in the membrane, as # per μm^2.

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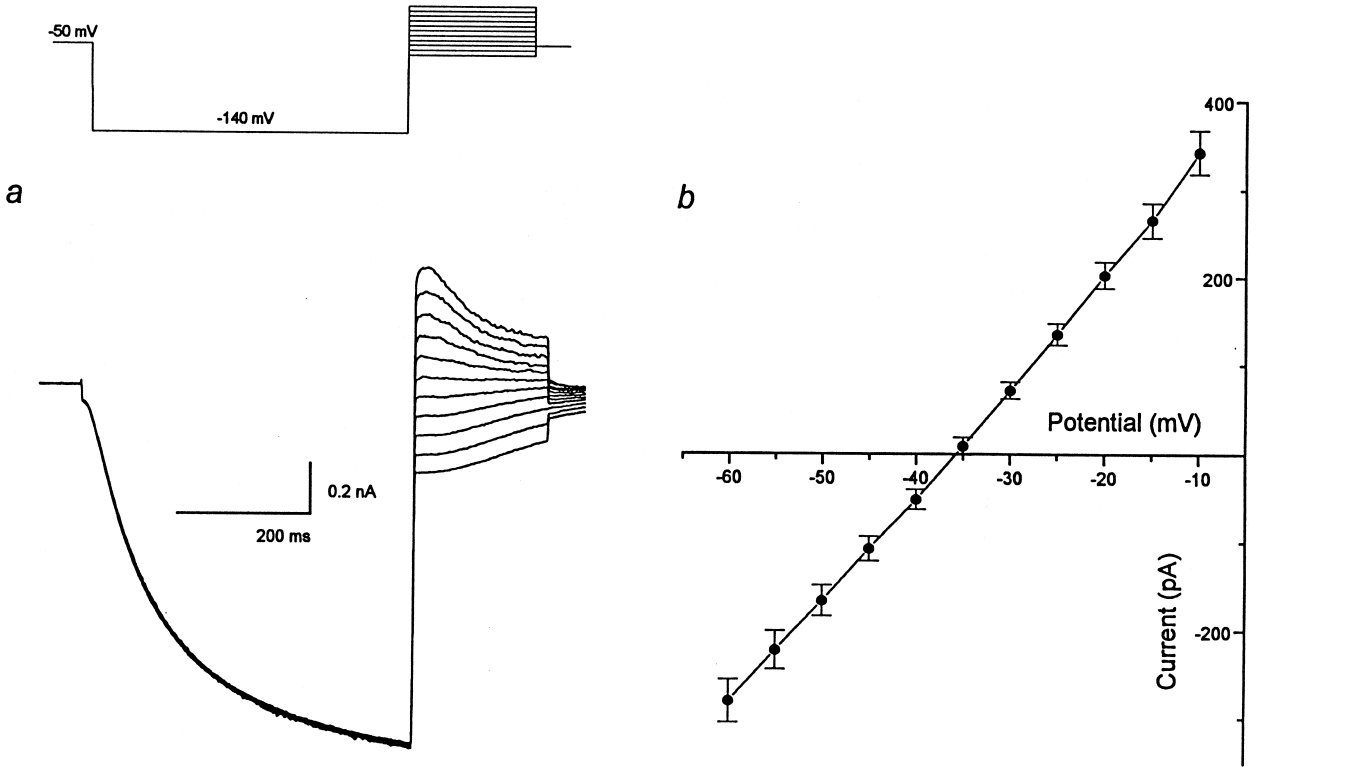
Question #3 12.5 pts



The above figure illustrates a set of current responses (a, lower traces) to voltage steps (a, top traces) for a population of channels in a neuron with physiological solutions bathing the inside and outside of the cell. (Conventional graphics – inward current is downward and negative in sign). There are leak channels in this cell's membrane in addition to the voltage dependent channels.

a) What is the leakage conductance of this cell (the conductance attributable to all of the leak channels)? Assume that the resting potential is -50 mV.

b) In part b is shown an IV curve for the early current after the potential is stepped from -140 mV to the indicated value in the graph. What is the reversal potential for this channel? To what ion or ions do you suspect that this channel is permeable? How would you test your hypothesis? If you think that this channel is permeable to multiple ions, how would you measure the permeability ratios (P_1:P_2, where 1 and 2 represent different ions).

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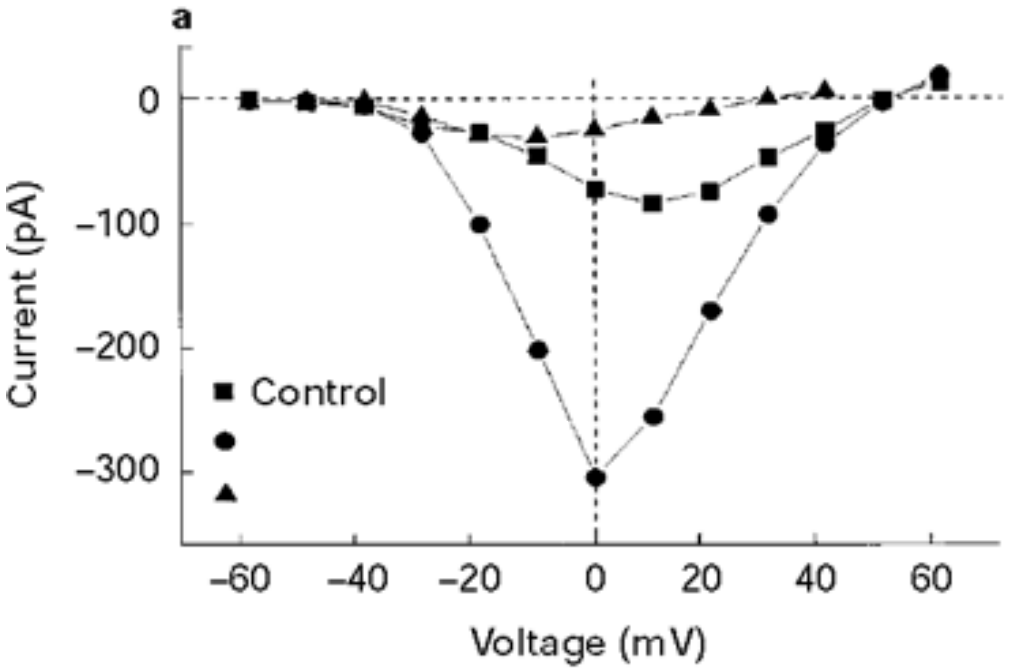
Question #4 15 pts

The following figure is taken from a paper on voltage-dependent calcium channels and shows the peak current-voltage relation for a single population of channels.



a) Data shown as **squares** were collected under control conditions. From these data, construct a curve of peak conductance vs. voltage for this channel, over the range of -60 mV to +60 mV.

b) The data shown in **circles** were collected using a drug (the "circle drug"). Provide a plausible hypothesis about what the "circle drug" does to alter the IV curve for this channel. What sort of evidence (obtained in an experiment of your choosing) would support this hypothesis?

The data shown in **triangles** were collected in the presence of a different drug (the "triangle drug").

c) The figure supports the possibility that one of the two drugs (circle, triangle) alters the ion selectivity of the channels. Which drug is this, and on what do you base your assertion?

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Question #5 12.5 pts

The following passage recently appeared in the "News & Views" section of one of the journals with a one word name. "Gliomas, a common brain tumor, frequently induce epileptic seizures as they grow, but it is not clear why. LastName et al. (XXXX) show that the epileptic activity in the brain around gliomas happens because neurons respond anomalously to the neurotransmitter γ-aminobutyric acid (GABA). Usually GABA turns neurons off, but when gliomas are nearby, it turns them on instead."

What do you hypothesize that gliomas are doing to neurons that would allow GABA to depolarize them enough to fire them? Describe an experimental test of your prediction. Assume that you can whole cell record/clamp from neurons in slices with gliomas nearby and that you can activate GABAergic inputs onto these cells.

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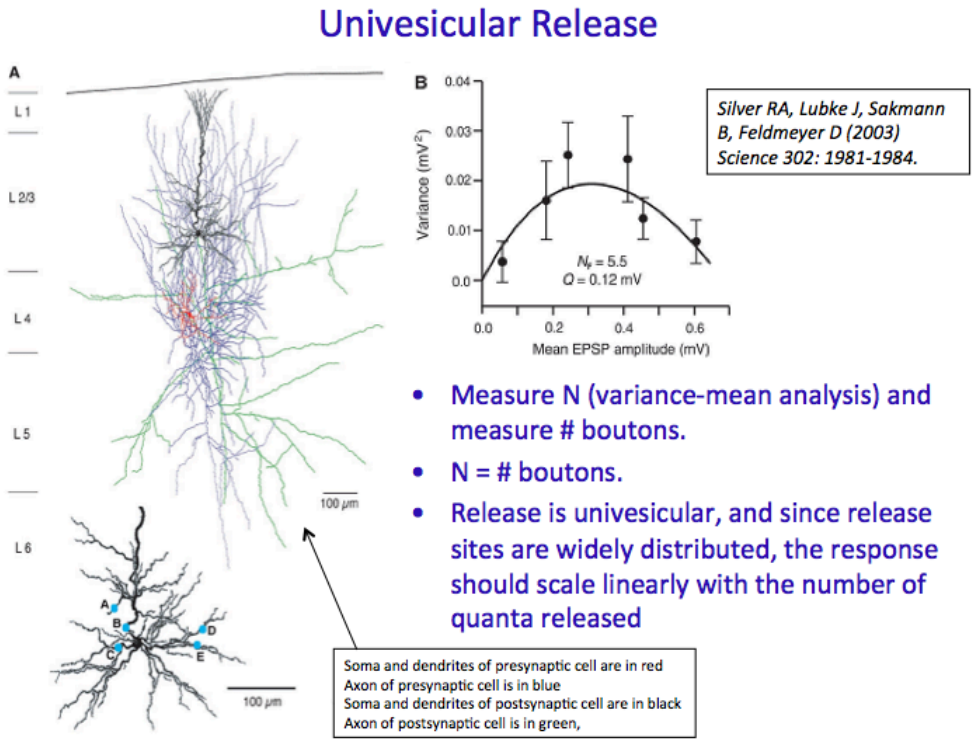
Question #6 10 pts



The figure above, taken from the slide set on synaptic transmission, illustrates an example of a result in which N, the physiologically measured number of releasable quanta, was equal to the number of synaptic boutons (each of which is thought to contain a single active zone).

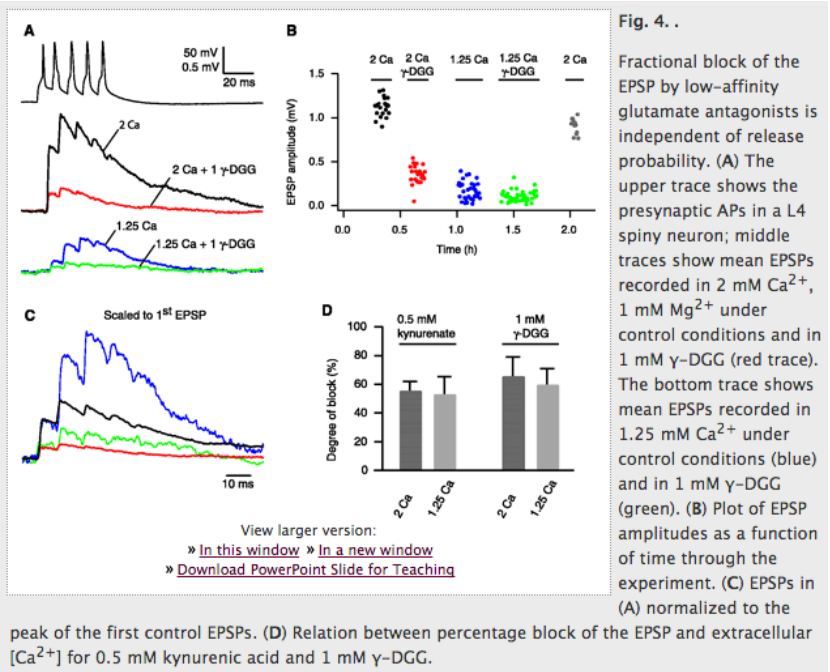


Fig. 4. .

Fractional block of the EPSP by low-affinity glutamate antagonists is independent of release probability. (**A**) The upper trace shows the presynaptic APs in a L4 spiny neuron; middle traces show mean EPSPs recorded in 2 mM Ca^{2+}, 1 mM Mg^{2+} under control conditions and in 1 mM γ-DGG (red trace). The bottom trace shows mean EPSPs recorded in 1.25 mM Ca^{2+} under control conditions (blue) and in 1 mM γ-DGG (green). (**B**) Plot of EPSP amplitudes as a function of time through the experiment. (**C**) EPSPs in (**A**) normalized to the peak of the first control EPSPs. (**D**) Relation between percentage block of the EPSP and extracellular [Ca^{2+}] for 0.5 mM kynurenic acid and 1 mM γ-DGG.

The data above is interpreted as supporting a univesicular release model for this synapse.

a) An alternative possible explanation for the data above is that release is multivesicular, but that a single quantum of transmitter saturates the AMPA receptors at the synaptic site. The data shown on the left (Fig. 4) argue against this possibility. Explain why.

b) What sources of intersite quantal variance are likely to be at play in this experimental arrangement?

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Question #7

(Please write your response to this question on a separate page, if you are completing the exam in paper format.)

How are high selectivity and high rate of transport through ion channels achieved simultaneously? Do you think Na^+ can permeate through a Ca^{2+}-selective ion channel? If yes, under what conditions? Please explain your answers.

15 pts

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Question #8

(Please write your response to this question on a separate page, if you are completing the exam in paper format.)

What is the role of S1, S2 and S3 transmembrane helices of the voltage-gated ion channels in the mechanism of voltage sensitivity? Do you think it would be possible to construct a simpler voltage-sensor domain that would consist of S4 domain only? Please explain your answers.

15 pts