Synaptic Transmission I: Presynaptic Mechanisms
Problem Set

You want to completely block release from a synapse by replacing Ca^{2+} outside the cell with another cation. Which would work? (Circle all that apply)

A. Ba^{2+}
B. Co^{2+}
C. Mg^{2+}
D. Mn^{2+}
E. Sr^{2+}

Increases in presynaptic Ca^{2+} influx cause a linear increase in the release of neurotransmitter.

True
False

Vesicular transmitter transporters use an electrochemical proton gradient to concentrate transmitter in the vesicle.

True
False

In the absence of SNARE complexes, vesicles readily fuse with the presynaptic membrane.

True
False

Transmitter release is quantal. This means that one vesicle has only one transmitter molecule (i.e. a "quantum" of transmitter)

True
False

At the presynaptic terminal, vesicle release is triggered by:

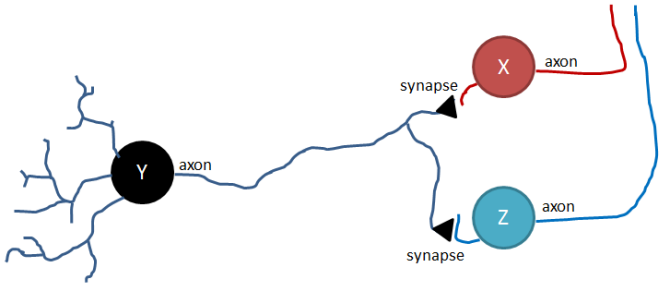
A. Na+ influx from an action potential
B. Membrane depolarization
C. K+ efflux through voltage-gated potassium channels
D. Ca2+ influx through voltage-gated calcium channels
E. All of the above

Miniature end-plate potentials, or mEPPS, are produced

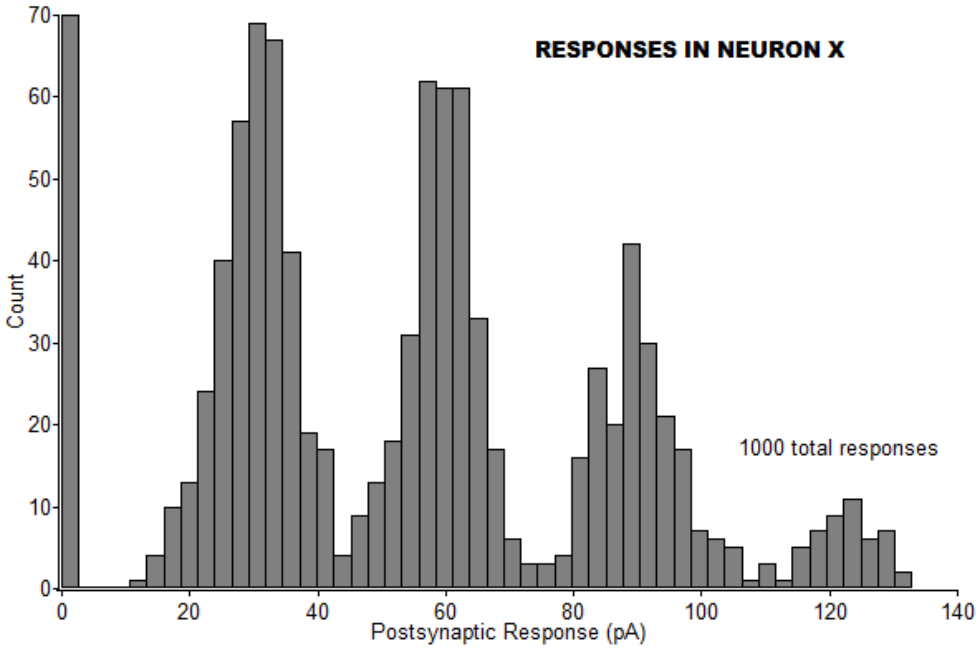
A. by the smallest axons
B. by spontaneous release of neurotransmitter
C. in response to weak stimuli
D. by the smallest neurotransmitters
E. at miniature end-plates

Quantal Analysis Problem

Your lab is working on a special group of neurons: Neuron X, Neuron Y, and Neuron Z. What makes these neurons special is that Neuron Y makes only a single synapse onto both Neuron X and Neuron Z. Neuron X and Neuron Z are also special, because they have a single, very short dendrite that ONLY receives the ONE synapse from Neuron Y.



You recently figured out a way to stimulate the axon on Neuron Y so that you can make it produce an action potential. After many stimulations, you created a histogram of the postsynaptic events that you saw in Neuron X.



What fraction of the total responses were failures of transmission (hint: no transmission = no response)?

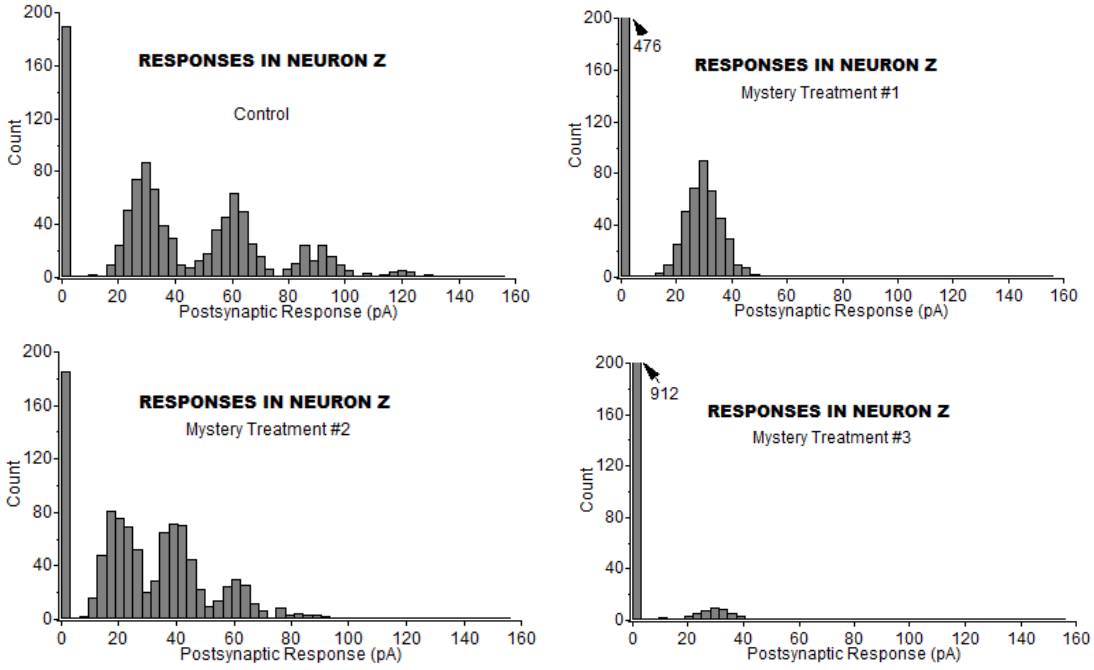
70/1000 =
7%

An electron microscopist colleague has reconstructed several of the Neuron Y-> Neuron X synapses. She says that each synapse has about 50 vesicles in the cytoplasm, and about 4 vesicles touching the presynaptic membrane. Now that you know how many vesicles are at the synapses, and the fraction of total responses that were failures, **calculate the probability that one (two, three…etc) vesicle will be released during a stimulation using a binomial model. Show the math.** (Hint: Box 15.4 on pg 469)

n = quanta released = 1000
q = probability quanta not discharged = 7%
p = probability quanta released = 100%-7% = 93%

Does a binomial model describe your data well? In a few sentences, explain why or why not.

Another colleague, who is working on Neuron Z, has sent you an email with some of the data he has collected. Just like you, he has generated postsynaptic response histograms, each with 1000 data points.



You see from the files that some of the data was collected during the application of some drugs/treatments to the neurons (Mystery Treatments #1-3). Unfortunately, none of those files had labels. In the email, the colleague mentioned that he was planning to test the following drugs/treatments:

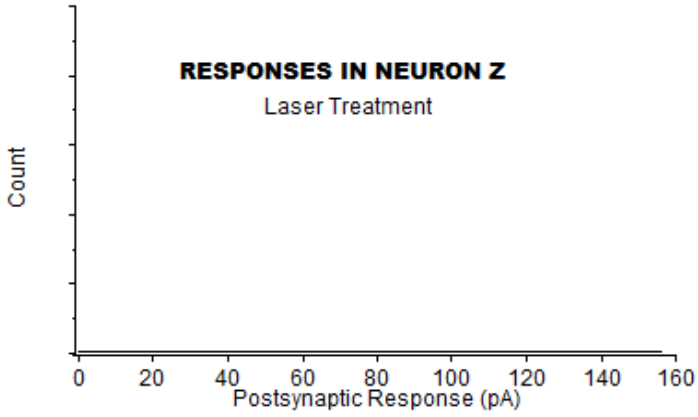
10 mM 1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid (BAPTA) – *a calcium buffer*
Bafilomycin A1 – *a vacuolar ATPase inhibitor*
A cocktail of botulinum toxins
Dynasore – *a dynamin inhibitor*
Low extracellular Ca^{2+} and high extracellular Mg^{2+}

For each mystery histogram, which treatment might produce results like those observed? Give a brief (1 sentence or less) reason for each treatment you list. There might be more than one (or none). Assume all treatment effects are only presynaptic (i.e. there is no effect on the postsynaptic cells).

Low extracellular Ca2+ and high extracellular Mg2+, A cocktail of botulinum toxins: mystery treatment #3

Bafilomycin A1 – a vacuolar ATPase inhibitor: mystery treatment #2

Exciting news! Your colleague working on Neuron Z (the one that can't label his files) says that he has determined that the Neuron Y-> Neuron Z is described quite well with binomial statistics, with n = 5 vesicles. Behind his PI's back, he has been secretly developing an extremely precise laser that can target individual vesicle release sites. He claims that he can reduce the n=5 vesicles to n=2 vesicles without changing the other release properties (e.g. the probability of release, etc). **1) Use binomial statistics to calculate the probability that 0, 1, or 2 vesicles are release with a single action potential, and 2) fill in the histogram below with the distribution that you expect.**



BONUS question: To make the histograms in this problem set look realistic but also be fairly easy to interpret, I have given each peak in a distribution the same width. In reality, the peak representing 2 vesicles should be wider than the peak for one vesicle, the peak for 3 vesicles even wider, etc. (See histogram below and compare to the "Control" Histogram above). In a few sentences, explain why the width increases for each vesicle.