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+}

> Divalent cations that permeate Ca^{2+} channels, such as Ba^{2+} and Sr^{2+}, support transmitter release, although only weakly. Cations that block Ca^{2+} channels, such as Co^{2+} and Mn^{2+}, block transmission (Augustine et al., 1987); Mg^{2+} reduces transmission, perhaps by screening fixed surface charge and effectively hyperpolarizing the nerve (Muller and Finkelstein, 1974).

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

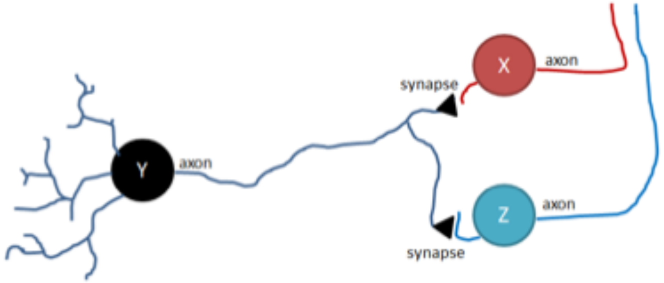
Vesicular transmitter transporters use an electrochemical proton gradient to concentrate transmitter in the vesicle.
True
False

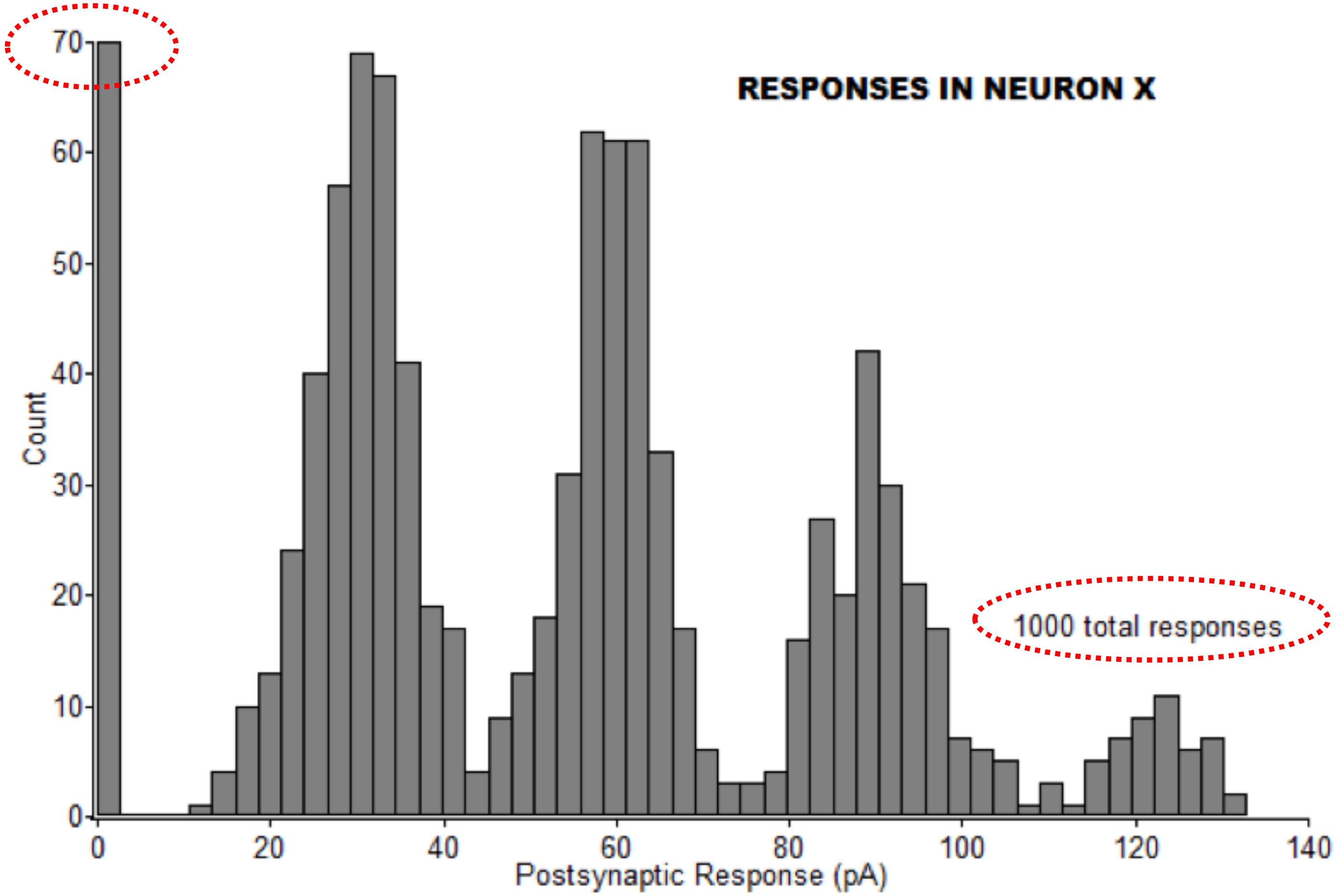
In the absence of SNARE complexes, vesicles readily fuse with the presynaptic membrane.
True
False

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





What fraction of the total responses were failures of transmission (hint: no transmission = no response)? 70/1000 = 7% or 0.07

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)

p = average probability of a vesicle to release; q = probability of release failure (1-p)

0 vesicles: 0.070 = q^4 = 0.514^4 , so if we want to know p, the 1-0.514 = 0.486 p=0.486

1 vesicle: 0.264 = $4pq^3$ = 4*0.486* 0.514^3

2 vesicles: 0.374 = $6pq^3$ = 6*0.486^2* 0.514^2

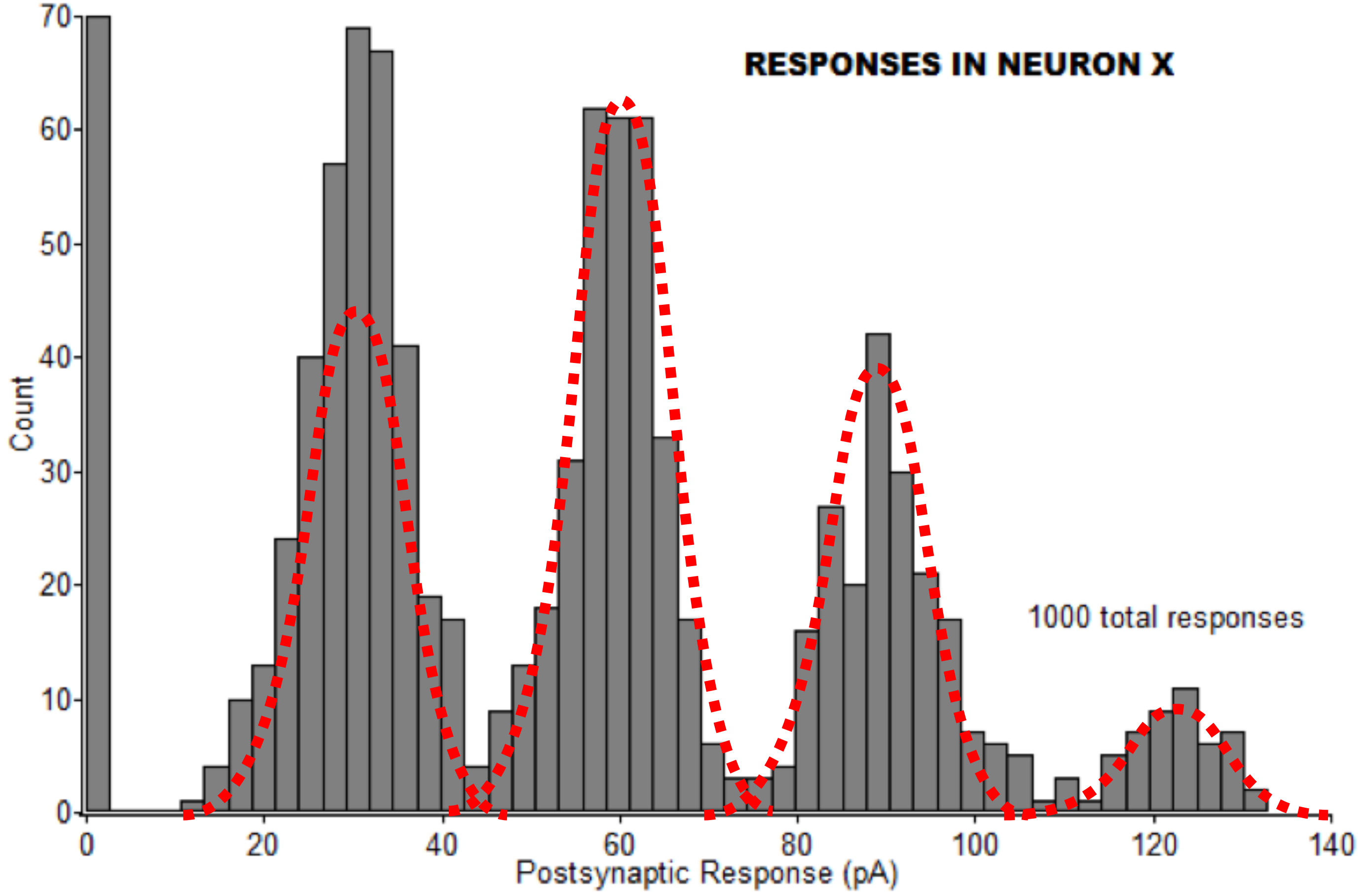
3 vesicles: 0.236 = $4p^3q$ = 4*0.486^3* 0.514

4 vesicles: 0.056 = p^4 = 0.486^4

$$P_x = \frac{n!}{(n-x)!x!} p^x q^{n-x}$$

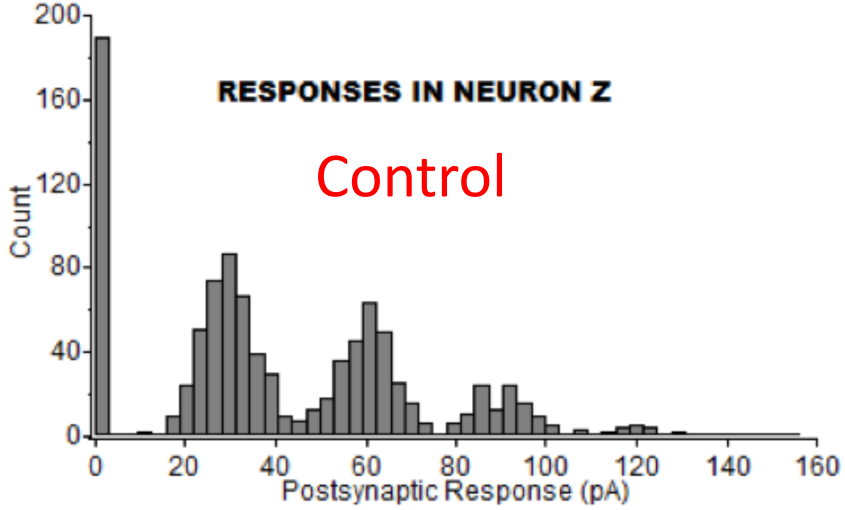
1
1 1
1 2 1
1 3 3 1
1 4 6 4 1
1 5 10 10 5 1

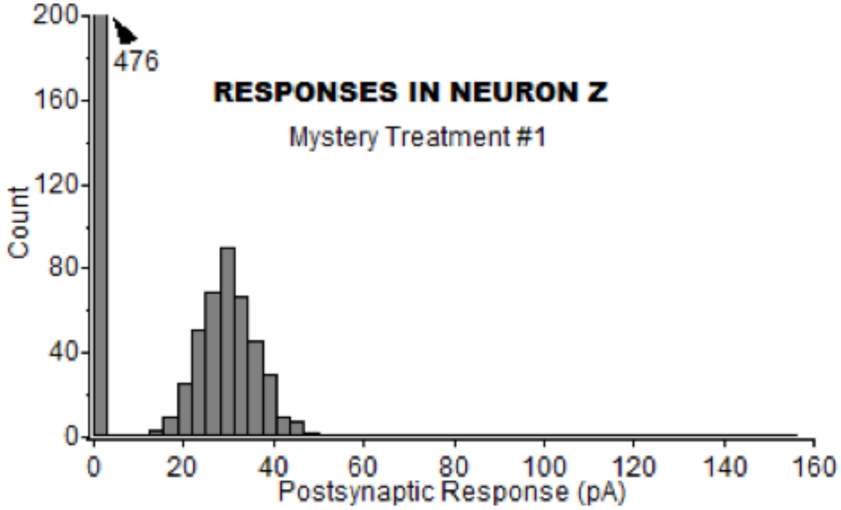
Does a binomial model describe your data well? In a few sentences, explain why or why not.



0 vesicles: 0.070
1 vesicle: 0.264
2 vesicles: 0.374
3 vesicles: 0.236
4 vesicles: 0.056

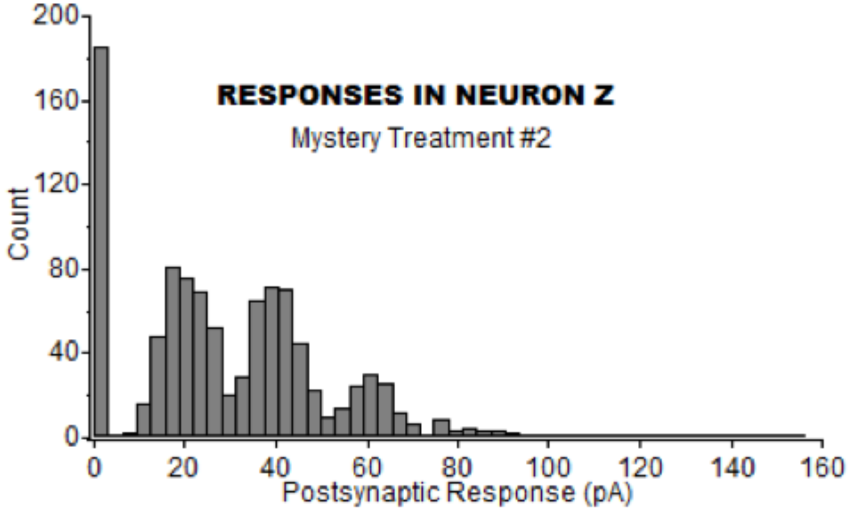
1 vesicle: 71
2 vesicles: 100
3 vesicles: 63
4 vesicles: 15

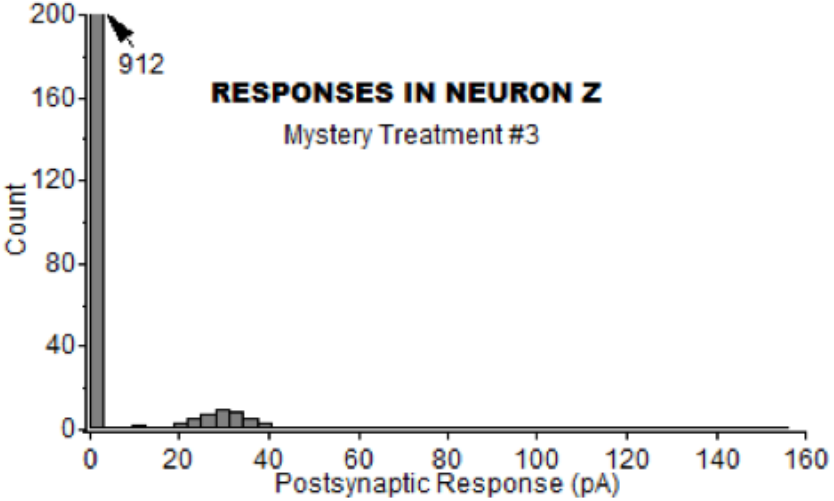




Lower p

1) No big events
2) High failure rate



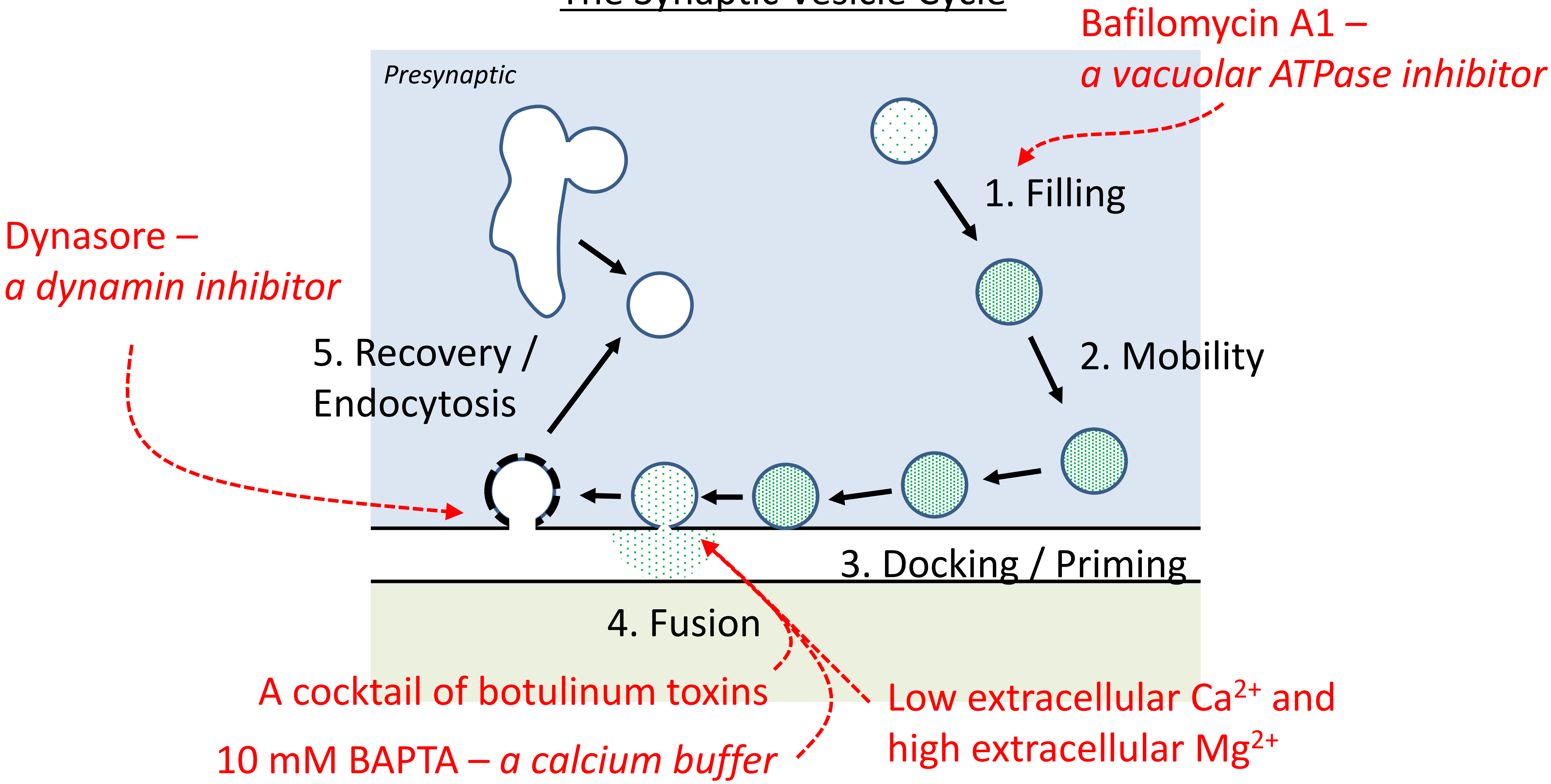


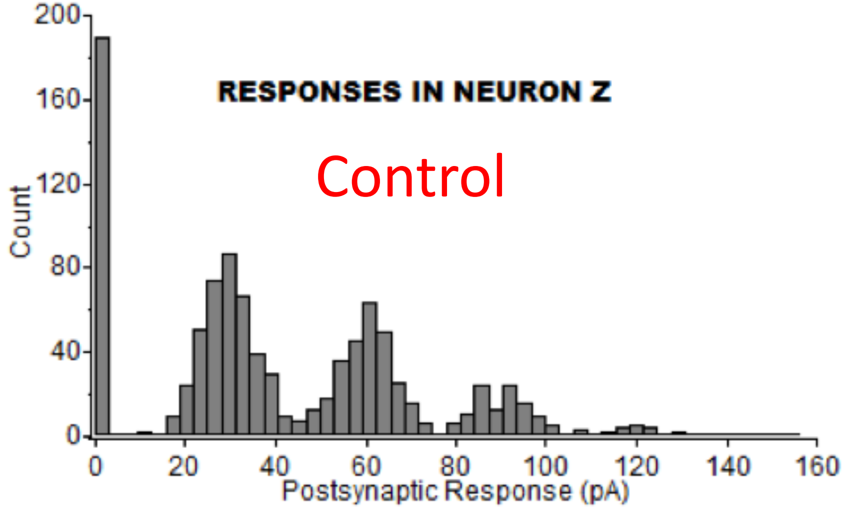
p ≈ 0 (or close to it)

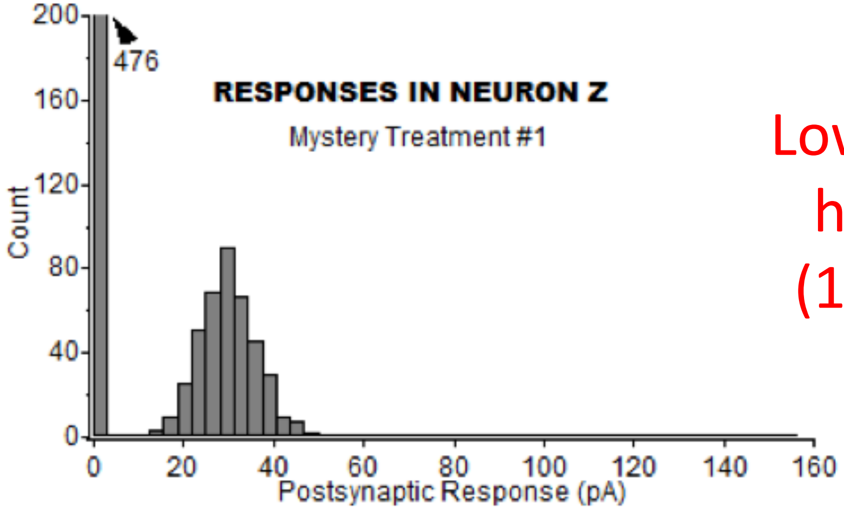
Lower Q (quantal size)

n and *p* look about the same

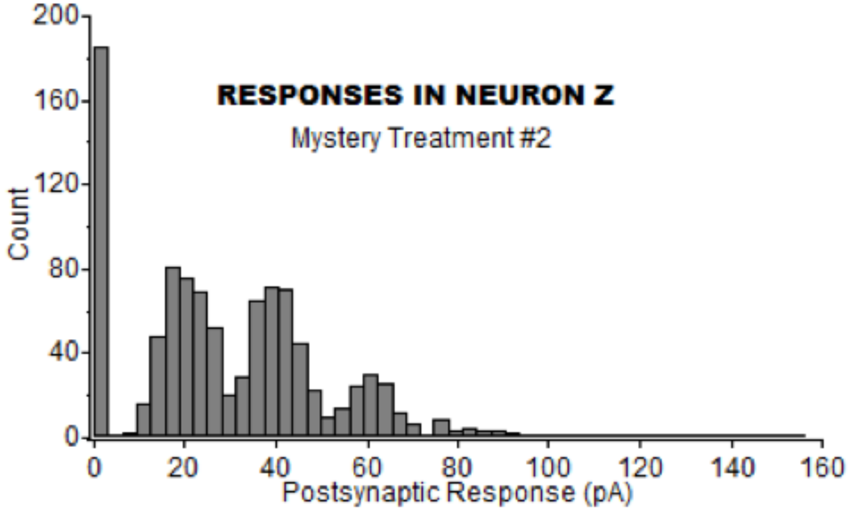
The Synaptic Vesicle Cycle

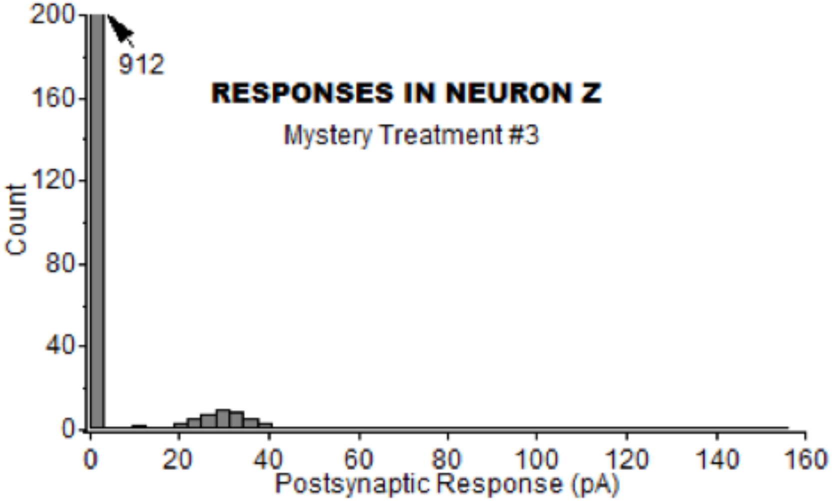






Low extracellular Ca^{2+} and high extracellular Mg^{2+} (10 mM BAPTA - maybe)



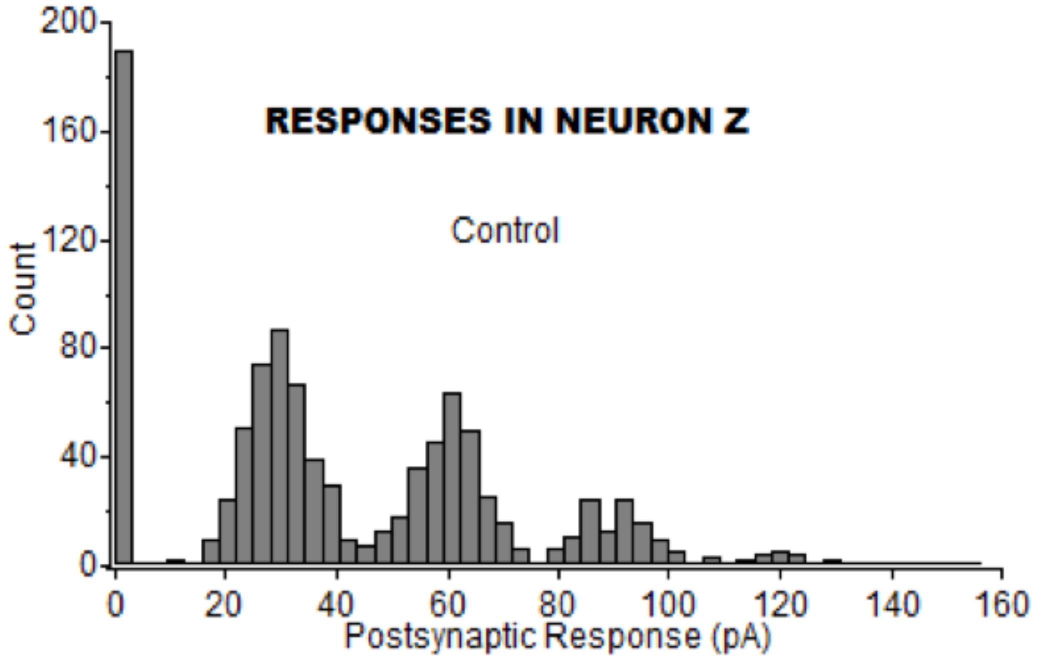


botulinum toxins
10 mM BAPTA

Bafilomycin A1

What would you expect with Dynasore?

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.**



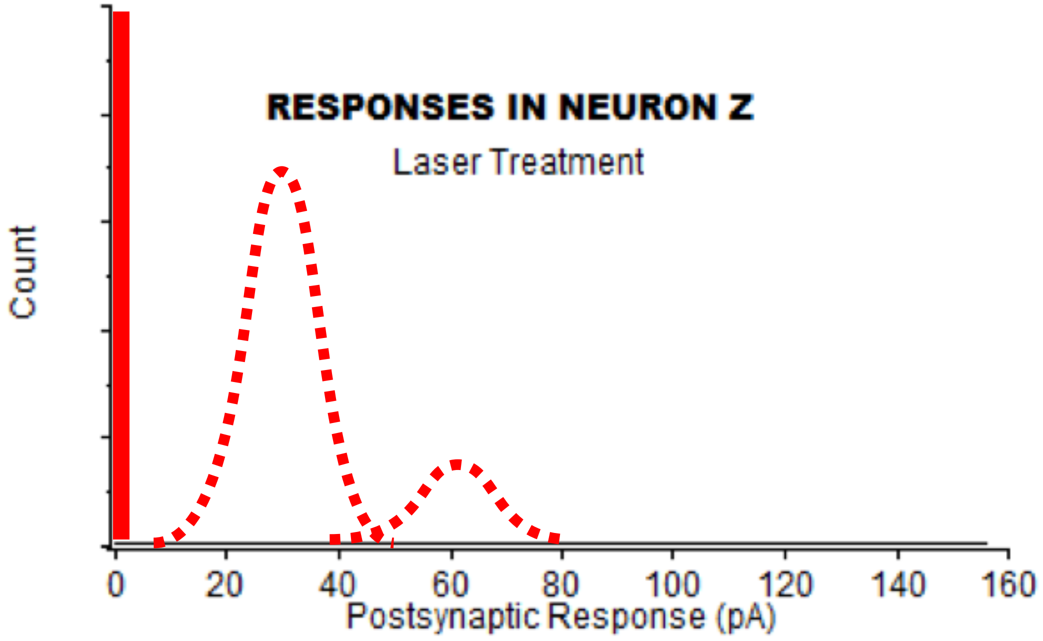
First, find p:

0 vesicles: ~190/1000 = 0.19 = q^5 = 0.717^5

so if we want to know p, the 1-0.717 = 0.283

p = 0.283

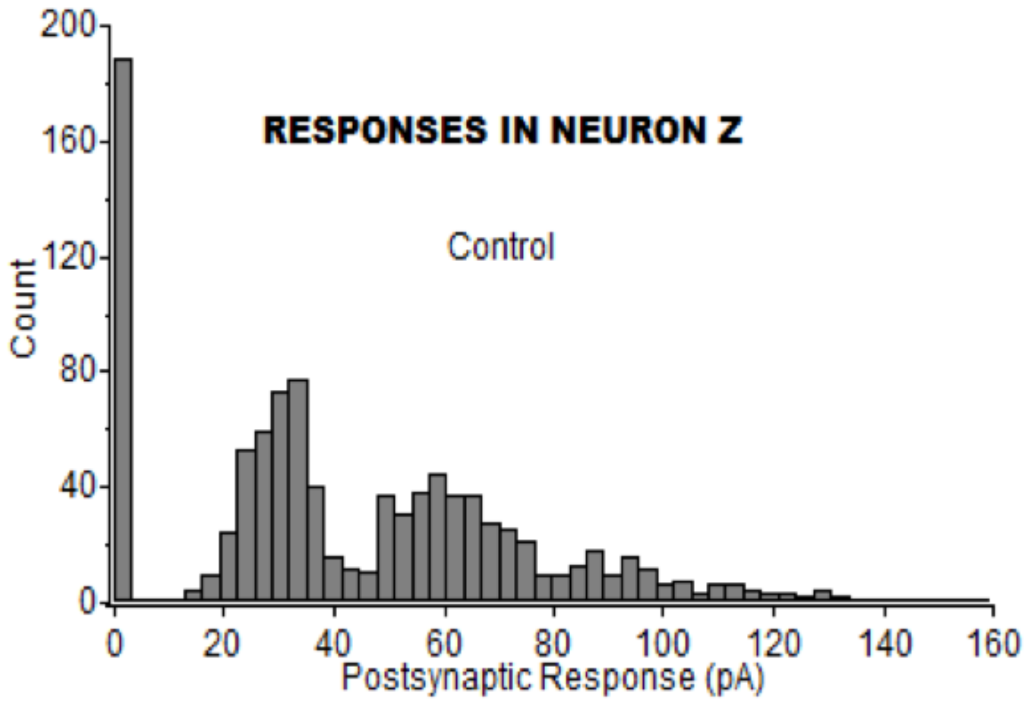
Exciting news! Your colleague working on Neuron Z (the one that can't label his files) says that he has determined that the Neuron Y-> Neuron Z is described quite well with binomial statistics, with n = 5 vesicles. Behind his PI's back, he has been secretly developing an extremely precise laser that 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.**



0 vesicles: 0.514 = $q^2 = 0.717^2$
1 vesicle: 0.406 = 2pq = 2*0.283* 0.717
2 vesicles: 0.080 = $p^2 = 0.283^2$

0 vesicles: 0.514 <- about 50% are failures
1 vesicle: 0.406
2 vesicles: 0.080 <- ~5x fewer than singles

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.



Normal Sum Distribution

If two normal, independent distributions:

Distribution 1:
Mean μ_1
Variance $\sigma^2{}_1$

Distribution 2:
Mean μ_2
Variance $\sigma^2{}_2$

$$\mu_{1+2} = \mu_1 + \mu_2$$

$$\sigma^2{}_{1+2} = \sigma^2{}_1 + \sigma^2{}_2$$

Variance increases with each additional vesicle