## Bertram, Matveev - Calcium Cooperativity of Exocytosis



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highlighted (see Page 4)

http://www.ncbi.nlm.nih.gov/pubmed/21621748

The slope of the resulting log-log plot of transmitter release rate versus presynaptic Ca(2+) current is termed Ca(2+)current cooperativity of exocytosis, and provides indirect information about the underlying presynaptic morphology. In this review, we discuss the relationship between the Ca(2+) current cooperativity and the average number of Ca(2+) channels participating in the exocytosis of a single vesicle, termed the Ca(2+)channel cooperativity. We relate these quantities to the morphology of the presynaptic active zone. We also review experimental studies of Ca(2+) current cooperativity and its modulation during development in different classes of synapses.

Related: <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2784595/</u>Bertram, Matveev 2009

Marcotti - Ca currents (numbers of calcium channels/voltage dependency)

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highlighted (see Page 11)

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2817446/

As for the 4th power stuff, I don't remember where/when I learned that, but I think it's well established? Here's a current-ish paper that has references (#1-6) related to vesicle fusion and calcium:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3686347/

And here is another paper that I haven't had time to read but has lots of good info/refs on cooperativity at synapses: http://www.pnas.org/content/97/25/13955.full.pdf

This is the original paper and it's the NMJ (neuromuscular junction), in some ways the hair cells of neuromasts are like the NMJ. Maybe if the model shows the 4th power can account for things, that would be a novel outcome of our project?

http://www.ncbi.nlm.nih.gov/pubmed/6065887

Assumptions?:

We use Mch (Matveev), a measure of how many channels contribute to NT

release. We generate Nopen (number of channels open) and use cooperativity Hill function to generate probability of release, assuming that each channel contributes an equal amount of calcium no matter how many channels are open.

Catterall - 3rd or 4th power dependency of NT release to Ca input http://cshperspectives.cshlp.org/content/3/8/a003947.full

## Molecular Mechanisms of Neurotransmitter Release - 4th power dependency

edited by Zhao-Wen Wang Excerpt:

The calcium dependence of neurotransmitter release has been investigated in numerous studies. Dodge and Rahamimoff's (13) seminal work demonstrated that the amount of evoked neurotransmitter release is steeply dependent on calcium concentration with release rates proportional to calcium concentration raised to the power of ~4 (see Chapter 4 for further discussion). This steep power dependence most likely evolved to minimize the likelihood of random activation of the release mechanism by small fluctuations in cytoplasmic Ca<sup>2+</sup> levels. Mutant analyses, and *in vitro* and molecular studies suggest that synaptotagmin-1 serves, or at least contributes to, the calcium sensing mechanism (reviewed extensively in refs. 14 to 17).

## **Chemical and Cellular Architecture**

edited by N.S. Abel Lajtha

nerve terminals of the squid giant synapse.<sup>10</sup> Other studies at the motor nerve endings of the frog show that the rate of release of acetylcholine when an impulse arrives is highly dependent on  $[Ca^{2+}]_o$  and that there is a sigmoid relationship between transmitter release and  $[Ca^{2+}]_o$ .<sup>235</sup> Neurotransmitter release highly dependent on  $[Ca^{2+}]_o$  is also observed at the mammalian neuro-muscular junction<sup>236</sup> and at the squid giant synapse.<sup>237</sup> The simplest interpretation for the sigmoid relationship is that several  $Ca^{2+}$  ions have to cooperate in the release of a quantum of transmitter, and analysis of some of the data indicate that three or four  $Ca^{2+}$  ions may be necessary to release one quantum.<sup>11,235</sup> It is not known how  $Ca^{2+}$  induces release, but it is postulated that it binds at some site in the presynaptic terminal.<sup>238</sup>

Zebrafish CaV2.1, 2.2 channels - 2nd power dependency http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4317531/

## Sun - coupled release

http://www.jneurosci.org/content/35/26/9632.full
-Synaptotagmin activated by calcium, which leads to vesicle release activations
As a Ca<sup>2+</sup> sensor for synchronous release, Syt-2 has a low Ca<sup>2+</sup> affinity with cooperativity of 4–5 (Borst and Sakmann, 1996; Schneggenburger and Neher, 2000; Sun et al., 2007; Kaeser and Regehr, 2014).
It was argued that Syt-2 might have an allosteric modification that reduces the cooperativity at low Ca<sup>2+</sup> concentrations (Lou et al., 2005). However, the apparent Ca<sup>2+</sup> dependence of minis at Syt-2 KO synapses displayed a similar apparent Ca<sup>2+</sup> cooperativity, indicating that the absence of Syt-2 does not affect the Ca<sup>2+</sup> cooperativity.

<u>http://www.jbc.org/content/278/31/29231.full</u> Syntaxin modulation <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1304492/</u> Hill function for voltage gated channels <u>http://www.jneurosci.org/content/21/2/462.full.pdf</u> Relevant? Auditory synapse