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pH Dynamics within the *Drosophila* Synaptic Cleft During Activity

The pH sensitivity of neural mechanisms affects neurotransmission and makes it vulnerable to changes in the extracellular pH. While it was believed that the synaptic cleft acidifies during neurotransmission due to the co-release of neurotransmitters and protons, our findings using fluorescent pH reporters in Drosophila larvae show that conventional synapses actually undergo alkalinization instead. This alkalinization is dependent on the exchange of protons for calcium at the postsynaptic membrane. A computational model of pH dynamics at the larval neuromuscular junction was developed to support these experimental findings, revealing a dynamic pH landscape with rapid acid transients followed by a prolonged period of alkalinization. Furthermore, the pH sensitivity of voltage-gated calcium channels varies among different classes and subclasses. This variability presents an opportunity to study plasticity and diseases related to acid-base imbalances. A bichromatic fluorescence reporter was developed to assess the abundance of splice isoforms of the cacophony gene in various parts of the Drosophila nervous system. The study found differences in exon ratios between different terminals and cell bodies, indicating potential functional variations in these regions.

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