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A model-based framework for the analysis of miniature post-synaptic currents

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Miniature post-synaptic currents (mPSCs) have become a primary measure of synaptic modification during development, plasticity, and disease. 'Minis' represent the response of postsynaptic receptors to the spontaneous fusion of vesicles. They are a useful assay for the number and strength of synaptic connections, as mini event frequency is related to the number of functional release sites, and event amplitude is a measure of synapse strength [1]. Thus, accurate characterization of synapse dynamics relies critically on statistical analyses of event frequency and amplitude.

We develop a new paradigm for mPSC analysis that uses likelihood methods [2] and formal goodness-of-fit assessments [3] to derive accurate statistical descriptions of their frequency and amplitude properties. In particular, we demonstrate that mPSC inter-event intervals and amplitudes within individual cells are well described by exponential and log-normal models. These characterizations allow us to analyze mPSCs at the single-cell level. We employ a parametric bootstrap based on these models to make accurate assessments of uncertainty within and between groups in the setting of small samples. This enables accurate estimation of responses for individual cells or groups, and paired comparisons of before- and after- manipulations in single cells.

We illustrate this approach in the analysis of excitatory mPSCs from acute slices of sensory midbrain. We show that the method may be broadly applicable to excitatory and inhibitory PSCs in other CNS regions, and is robust to changes in event selection parameters and recording conditions.

Our method preserves information about the variability of events within individual cells and allows the summary of information across cells in order to make between-group comparisons. The use of an accurate model maximizes the efficiency of the resulting statistics, by taking advantage of the high degree of structure in the data. The framework allows accurate inferences to be made from studies of spontaneous activity, and for the first time extends analysis of synaptic function to the single cell level.

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