Novel method for reliably measuring miniature and spontaneous postsynaptic potentials/currents in whole-cell patch clamp recordings

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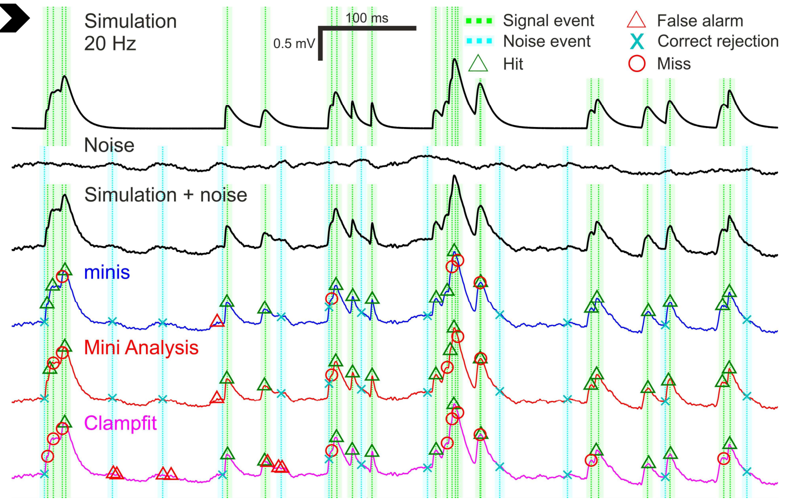
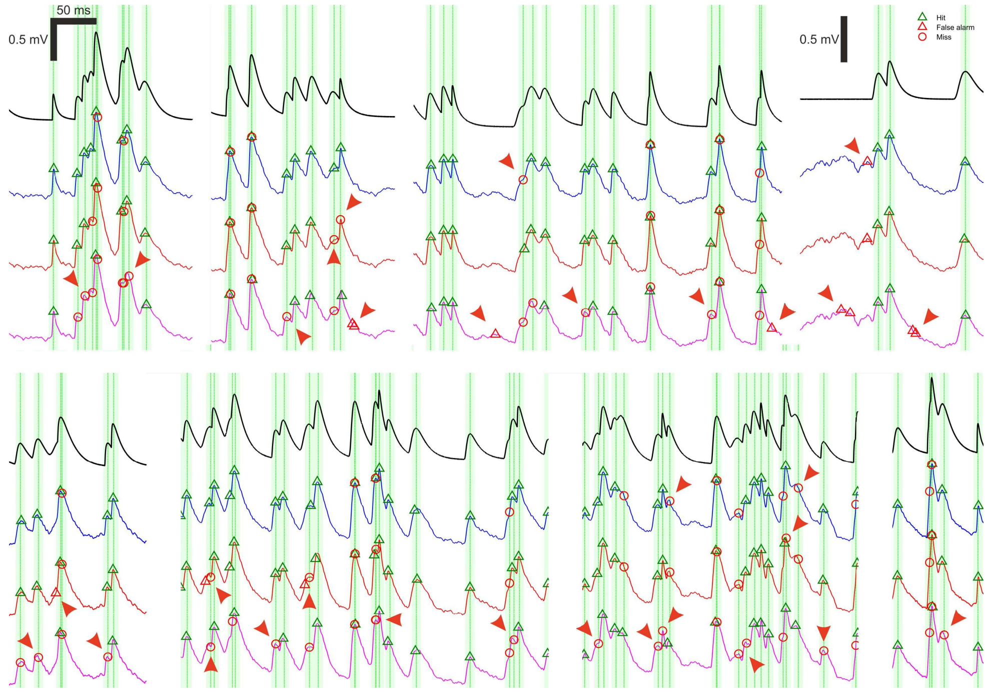
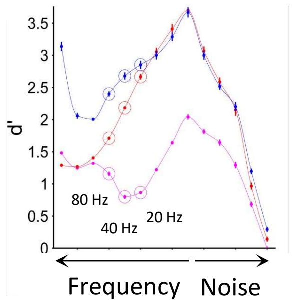
Background: Measurements of amplitudes of miniature postsynaptic currents (mPSCs) or potentials (mPSPs) (minis) combined with measurements of cell membrane potential noise fluctuations offer a technically straightforward way to estimate distributions of quantal sizes, a key synaptic transmission parameter, as each mini is elicited by the spontaneous release of a single neurotransmitter vesicle. With that in mind, we developed and present here a novel mPSP/mPSC detection algorithm as part of our quantal analysis software called 'minis'.

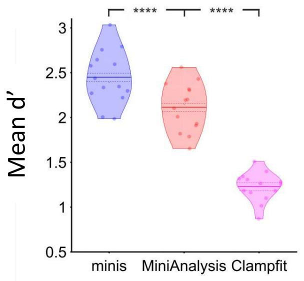
Methods: We used signal detection theory to evaluate algorithm's performance in detecting simulated minis added to real noise, using data from rat cortical slice whole-cell recordings, and compared it to the two most commonly-used minis detection algorithms in the field of synaptic function research: Mini Analysis (Blue Cell) and Clampfit (Molecular Devices).

Results: Simulated minis were often missed when occurring in close proximity to other minis and on the rise or decay phases of neighbouring minis (overshadowing). Alternatively, background noise could occasionally be misidentified as real events.





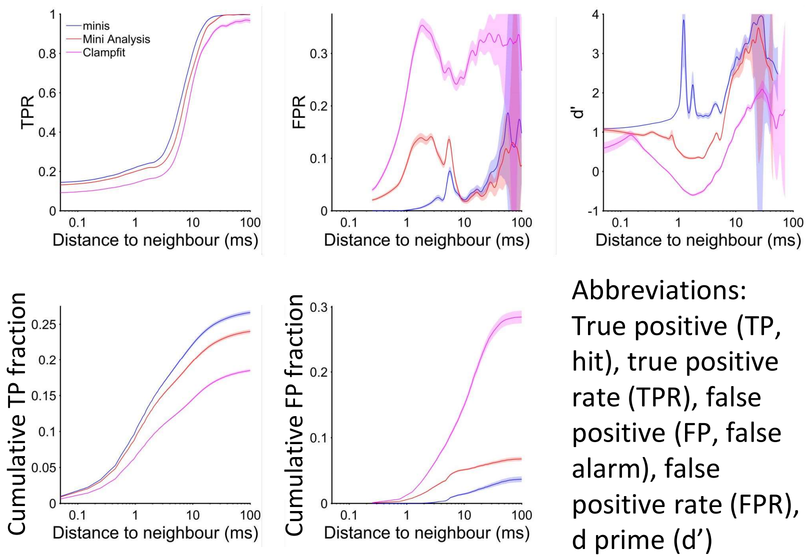




Overall detection performance

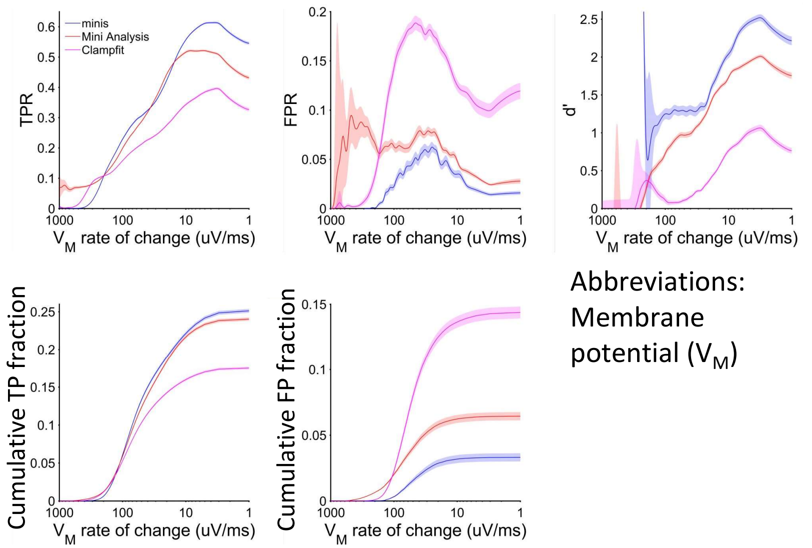
We compared the three algorithms on their likelihood of committing different types of detection errors.

Detection as a function of the nearest neighbour's onset time



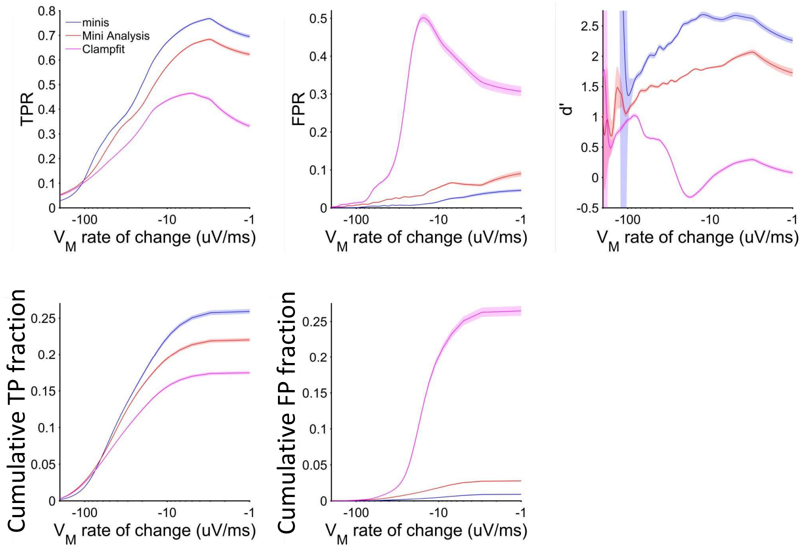
Abbreviations: True positive (TP, hit), true positive rate (TPR), false positive (FP, false alarm), false positive rate (FPR), d prime (d')

Detection as a function of the background V_M increase



Abbreviations: Membrane potential (V_M)

Detection as a function of the background V_M decay



Conclusions: Our mPSP/mPSC detection algorithm outperformed the other two most commonly used minis detection algorithms. The superior overall performance stemmed from a reduced likelihood of committing all types of different errors:

- Our algorithm was better at detecting closely overlapping minis.
- It was more likely to correctly identify minis appearing on the rising phase of another simulated mini.
- It was also more accurate at detecting a mini that coincided with the decay phase of the previous simulated event.

The superior performance was also maintained for realistic minis' incidence rates (circled frequency conditions on the left: 20, 40, and 80 Hz) and a wide range of simulated minis' amplitudes (Dervinis and Major, 2022, doi: https://doi.org/10.1101/2022.03.20.485046).

The detection algorithm comes as a part of the 'minis' quantal analysis software. It is available free of charge and can be used as a Matlab app, a Python package, or as a stand-alone application with a graphical user interface.

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Resources: https://github.com/dervinism/minis