Novel parameterization of event-related potentials: a step towards characterizing the biophysical origins

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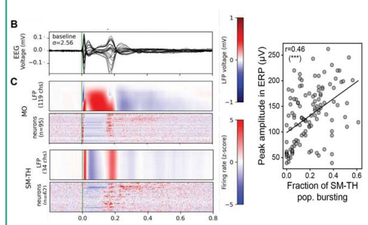
Background

- Despite the fact that **event related potentials (ERPs)** are highly studied electrophysiological signatures of brain activity, their biophysiological origins remain an active area of debate
- Recent evidence from animal models suggests that cortical ERP amplitudes are modulated by temporal synchrony of thalamocortical bursting activity
- Canonical ERP analyses entail averaging over pre-defined time windows and extracting amplitude/latency metrics -- commonly from difference waves (between conditions)
- Here, we introduce a novel **ERP parameterization method (ERPparam)** which over-parameterizes waveform shape features which may relate to underlying temporal dynamics

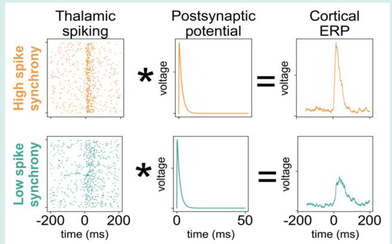
Hypothesis and LFP Model

Previous Findings

Claar et al. 2023 (eLife)

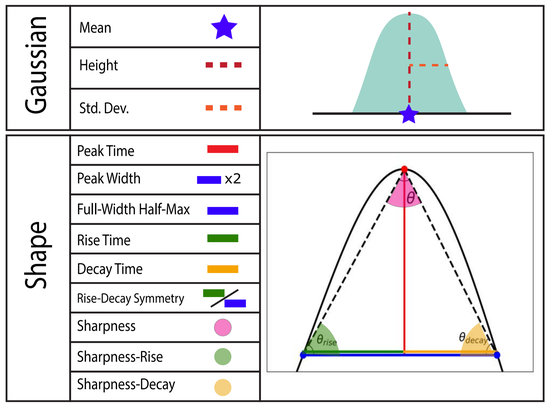


Biophysiological Model



- Previous findings have linked the amplitude of the cortical event-related potential (ERP) to local and thalamic spiking activity (Kandel, 1997; Clarr, 2023).
- Here, we leverage a physiologically-informed model of the cortical field potential (Miller, 2009; Gao, 2017) to characterize the relationship between the ERP and the underlying population spiking dynamics.
- We hypothesize that synchronized spiking activity is associated with higher amplitude and sharper ERPs.

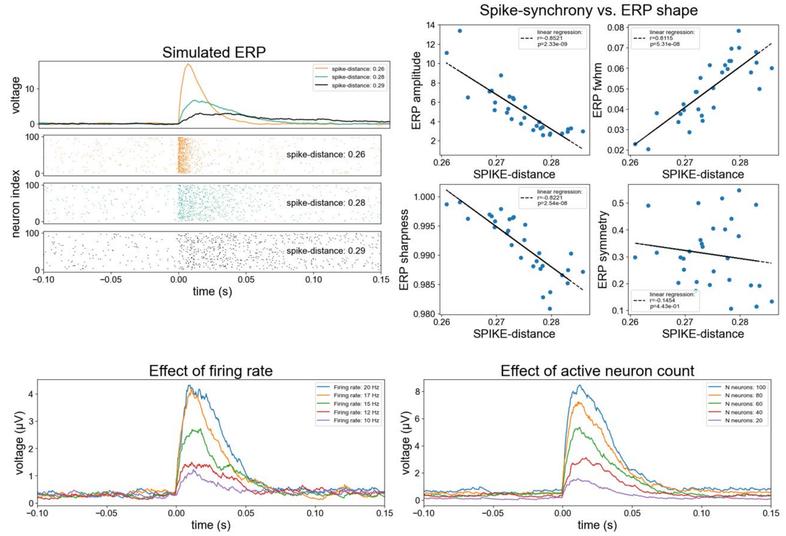
Novel ERP Parameterization Method



Methodology:

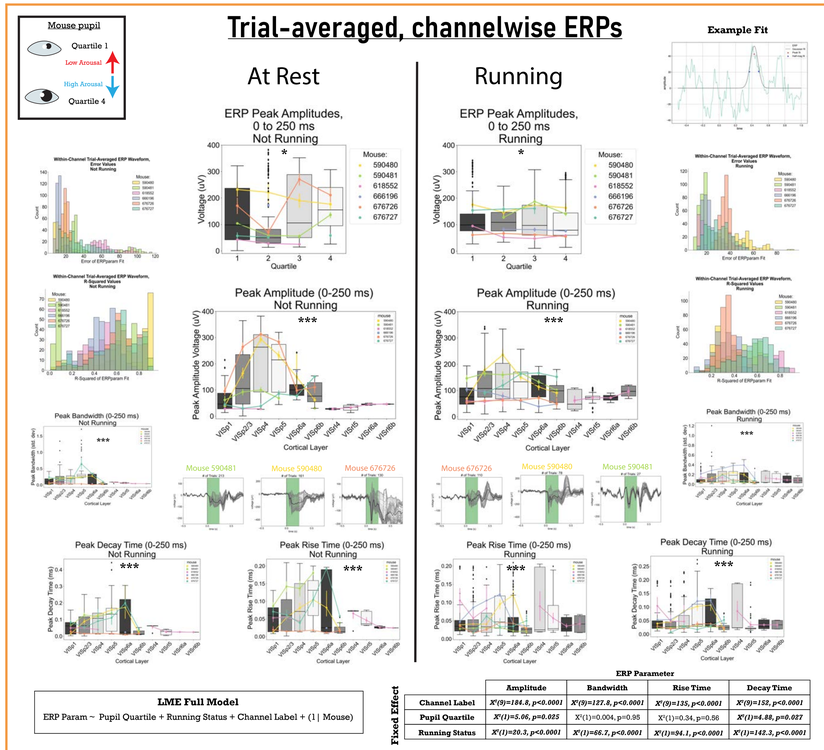
1. **Find peak**: identify signal maximum (above threshold)
2. **Remove peak:** fit Gaussian to peak and subract from signal
4. **Iterate:** repeat steps 1-2 until stop criterion is met (peak below threshold or max # of peaks found)
5. **Parameterize each peak:** compute shape metrics for each peak identified

Spike Statistics v. ERP Shape in Simulated ERPs



- Spike synchrony is positively correlated with ERP amplitude, width, and sharpness, but not symmetry.
- Both firing rate and the number of active neurons show the same relationship to ERP shape parameters.
- These results support our hypothesis that thalamic spiking activity underlies variability in the shape of the visual cortical ERP.

Trial-averaged, channelwise ERPs



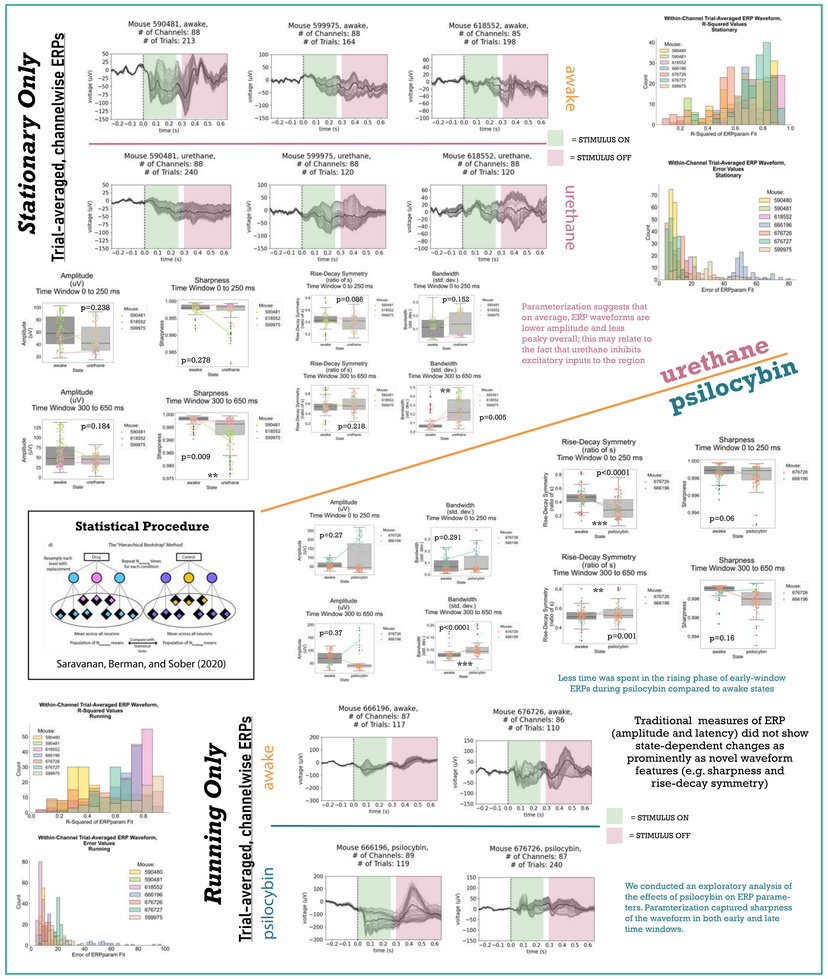
LME Full Model

ERP Param ~ Pupil Quartile + Running Status + Channel Label + (1| Mouse)

Fixed Effect

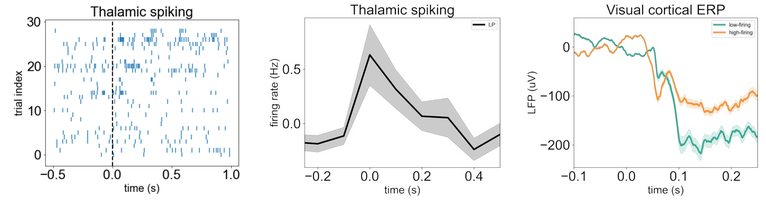
ERP Parameter	Amplitude	Bandwidth	Rise Time	Decay Time
Channel Label	$X^2(9)=184.8, p<0.0001$	$X^2(9)=127.8, p<0.0001$	$X^2(9)=135, p<0.0001$	$X^2(9)=152, p<0.0001$
Pupil Quartile	$X^2(1)=5.06, p=0.025$	$X^2(1)=0.004, p=0.95$	$X^2(1)=0.34, p=0.56$	$X^2(1)=4.88, p=0.027$
Running Status	$X^2(1)=20.3, p<0.0001$	$X^2(1)=66.7, p<0.0001$	$X^2(1)=94.1, p<0.0001$	$X^2(1)=142.3, p<0.0001$

Stationary Only — Trial-averaged, channelwise ERPs



Running Only — Trial-averaged, channelwise ERPs

Future directions: thalamic spiking contribution to ERP shape



CONCLUSIONS

- Our novel parameterization method allows us to relate ERP waveform shape to underlying physiology.
- We find that ERP amplitude, width, and sharpness are positively correlated with spiking activity in a biophysically-informed model of the LFP.
- ERP waveform shape parameters vary across cortical layers which are most directly receiving inputs from thalamus.
- Finally, we find significant differences in novel ERP waveform shape parameters across states: awake vs. anesthetized (urethane), and awake vs. psilocybin.
- Future work will address the relationship between waveform shape and the physiological generators of these different states.

References: Leslie D **Claar**, Irene Rembado, Jacqulyn R Kuyat, Simone Russo, Lydia C Marks, Shawn R Olsen, Christof Koch (2023) Cortico-thalamo-cortical interactions modulate electrically evoked EEG responses in mice *eLife* 12:RP84630 | **Kappenman,** E. S., Farrens, J. L., Zhang, W., Stewart, A. X., & Luck, S. J. (2021). ERP CORE: An open resource for human event-related potential research. *NeuroImage, 225*, 117465.| **https://courses.erpinfo.org/courses/Intro-to-ERPs** | **Kandel,** A., & Buzsáki, G. (1997). Cellular–synaptic generation of sleep spindles, spike-and-wave discharges, and evoked thalamocortical responses in the neocortex of the rat. *Journal of Neuroscience, 17(17),* 6783-6797. | **Luck,** S. J. (2014). An introduction to the event-related potential technique. MIT press. | **Makeig,** S., Westerfield, M., Jung, T. P., Enghoff, S., Townsend, J., Courchesne, E., & Sejnowski, T. J. (2002). Dynamic brain sources of visual evoked responses. *Science, 295*(5555), 690-694. | **Gao,** R., Peterson, E. J., & Voytek, B. (2017). Inferring synaptic excitation/inhibition balance from field potentials. Neuroimage, 158, 70-78.|**Donoghue,** T., Haller, M., Peterson, E. J., Varma, P., Sebastian, P., Gao, R., ... & Voytek, B. (2020). Parameterizing neural power spectra into periodic and aperiodic components. Nature neuroscience, 23(12), 1655-1665.