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

Model Description & Parameterization

Biophysiological Model

Kandel and Buzsaki, 1997 (JoN)

Claar et al. 2023 (eLife)

- Mouse LFP recording using neuropixels
- Found correlation of thalamic bursting (spike synchrony) & cortical spike rate with ERP amplitude

- Recording of extracellular currents in rat somatosensory cortex
- The temporal variability of spiking across cortical layers results in a wider, lower amplitude potential on cortical surface (B) compared to (A)

Parameters

Fitting Procedure

1. **Find** candidate peak: defined as max point in signal
2. **Fit** guess gaussian around peak
3. **Subtract** guess gaussian from signal
4. **Repeat** steps 1-3 until the user-specified max number of peaks is reached, or until highest point in the signal is lower than noise threshold
5. **Define** Shape Parameters

Application in simulations with colored noise

Application in mouse LFP data

Results of repeated-measures ANOVA (67 Chs)

We see significant differences in all waveform shape parameters across pupil quartiles.

In line with our hypotheses, the trials with larger pupils have higher ERP amplitudes. Larger pupils are indicative of a higher E:I balance, which may result in more thalamic spiking and a higher amplitude ERP in visual regions.

Data Description

- Data acquired in collaboration with Allen Brain Institute
- Neuropixels contact in visual cortex
- 1 mouse
- 93 channels
- 119 trials (~29 trials per quartile)
- Mouse running consistently

Application in Human EEG: P300 data

Data Description

- ERPCore P300 dataset
- N=40
- Oddball task requiring subject response to target (rare) stimulus
- Data epoched and preprocessed according to practices set forth in Kappenman et al. 2021

	Rare	Frequent
Time	0.308594	0.324219
Sharpness	5.8e-05	4.1e-05
Amplitude	1.2e-05	1e-05
Decay Time	0.210938	0.089844
Rise-Decay Symmetry	0.15625	0.410256

	Rare	Frequent
Time	0.378906	0.289062
Sharpness	5.8e-05	3.4e-05
Amplitude	1.4e-05	1e-05
Decay Time	0.046875	0.082031
Rise-Decay Symmetry	0.8	0.553191

	Rare	Frequent
Time	0.394531	0.367188
Sharpness	2.2e-05	1.2e-05
Amplitude	8e-06	3e-06
Decay Time	0.121094	0.070312
Rise-Decay Symmetry	0.483333	0.6

Trial Averaged

Single Trial

Model Fitting Parameters	
Max Num. Peaks	10
Peak Width Limit Lower	0.1
Peak Width Limit Upper	40
Peak Amp. Threshold (std. devs)	2
Peak Overlap Threshold (std. devs)	1.75

Application in Human iEEG: Oddball data

Data Description

- Data recorded from one electrode in human V1
- N=1
- 497 trials (117 Rare, 380 Frequent)
- Oddball task requiring subject response to infrequent stimuli only
- Data acquired by Bradley Voytek

These results are the opposite of what we might expect given the mouse LFP results, but may indicate that pre-stimulus excitability modulates temporal precision in the human V1

Reaction time showed no significant linear relationship to peak amplitude or sharpness (only for Rare trials)

smaller -> larger

more obtuse -> more acute

Pre-stimulus aperiodic activity may act as a proxy for the excitability of cortical networks at the time of stimulus onset

ERP amplitude quantiles calculated on the maximum peaks fit between 0 and 50 ms

Relating ERPparam to other ERP methodologies

Empirically Tested	Biologically Interpretable	Parameter
✓	?	Fractional Area Latency
✓	?	Mean Amplitude
✓	✓	Peak Amplitude
✓	✓	Peak Latency
?	✓	Rise-decay Symmetry
?	✓	Sharpness
?	✓	Full-width Half Max.

Adapted from ERP Bootcamp Slides by Steve Luck

ERPparam Metrics
Established Metrics
Both

What parameterization approach do you prefer?

- ***Common ERP parameterization approaches seek to obscure/overcome issues of temporal variability and between-subject variability***
- ***This variability may not be exclusively due to noise/randomness, but likely reflects underlying biophysiological states***
- ***Over-paramterization of the waveform shape enables richer signal descriptions***
- ***These novel parameters may or may not prove to be empirically relevant for the common use case of ERP analysis***
- ***Signal parameterization may also give additonal dimensions along which machine-learning algorithms can discriminate between different inputs***

- ***Future initiatives:***
  - Sensitivity analysis of hyperparameters used in ERPparam
  - Potential incorporation of more established ERP metrics for ease of comparison
  - Application of ERPparam tool in empirical datasets to bridge scales of analysis
- ***Open questions:***
  - Can we account for confounding oscillations prior to fitting (esp. for single trial, invasive data)?
  - Can the trial-averaged ERP waveform act as a template for model assessment of single trials?
  - How empirically valid are the specific parameters ERPparam is fitting?
  - How can our biological models, which relate to activity at the level of spiking and LFP, inform or influence theories at the level of non-invasive EEG?

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QR CODE

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