Efficient Analysis of Evoked Potentials using Linear Mixed-Effects Regression

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Introduction

One in five adults suffer from chronic pain, which is the result of disturbed processes in the central nervous system.

- *Early detection of these disturbances enables better treatments and less clinical efforts per patient.*
- *Disturbances in nociceptive processing can be studied by estimation of the evoked potential in response to a stimulus.*

The maximum number of stimuli in experiments with human subjects is limited.

- *Stimulus selection methods are used for a more efficient probing of the stimulus parameter space.*
- *This results in different amounts of trials per stimulus property, which is problematic for conventional averaging.*

An analysis method which is robust to variations in the amount of trials is provided by a linear mixed model.

Experiment

Quantitative assessment of nociceptive sensitivity

- *Detection probability of stimuli*
- *Neurophysiological response to stimuli*

1. Specific stimulation of nociceptive nerve fibers.
2. Tracking of the nociceptive detection probability and threshold using an adaptive stimulus sequence (multiple threshold tracking, MTT).
3. Measurement of the subjective response with respect to every stimulus (detected or undetected).
4. Measurement of the EEG signal with respect to every stimulus.

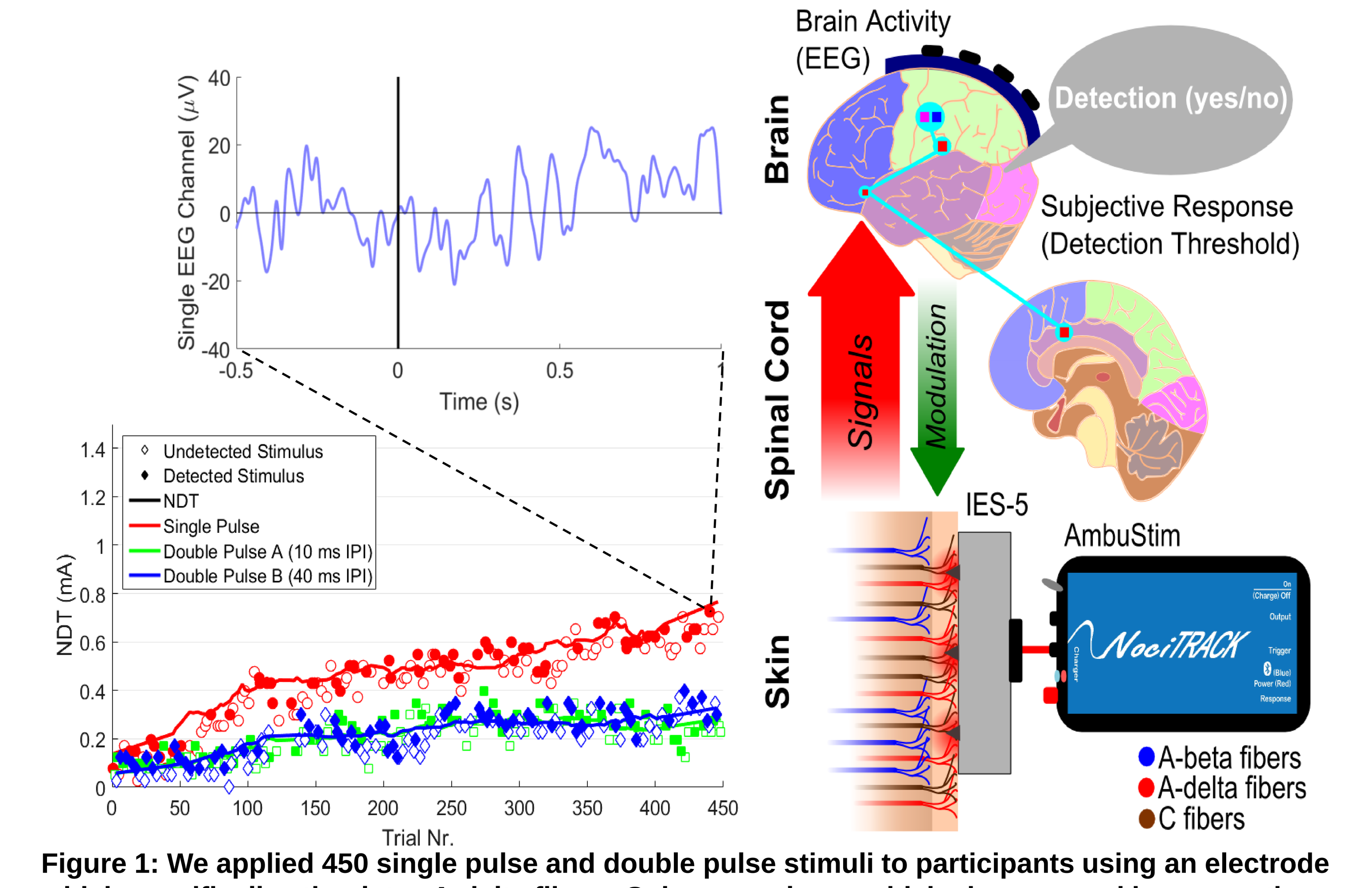

Figure 1: We applied 450 single pulse and double pulse stimuli to participants using an electrode which specifically stimulates A-delta fibers. Subsequently, sensitivity is assessed by computing stimulus detection probability and studying brain responses (EEG).

Analysis

During estimation of the detection probability stimulus parameters are constantly varied, leading to a very low number of trials per combination of parameters.

- *Very poor SNR ratio using conventional averaging.*
- *Pooling data provokes confounding and reduces the percentage of variance explained by our estimate.*

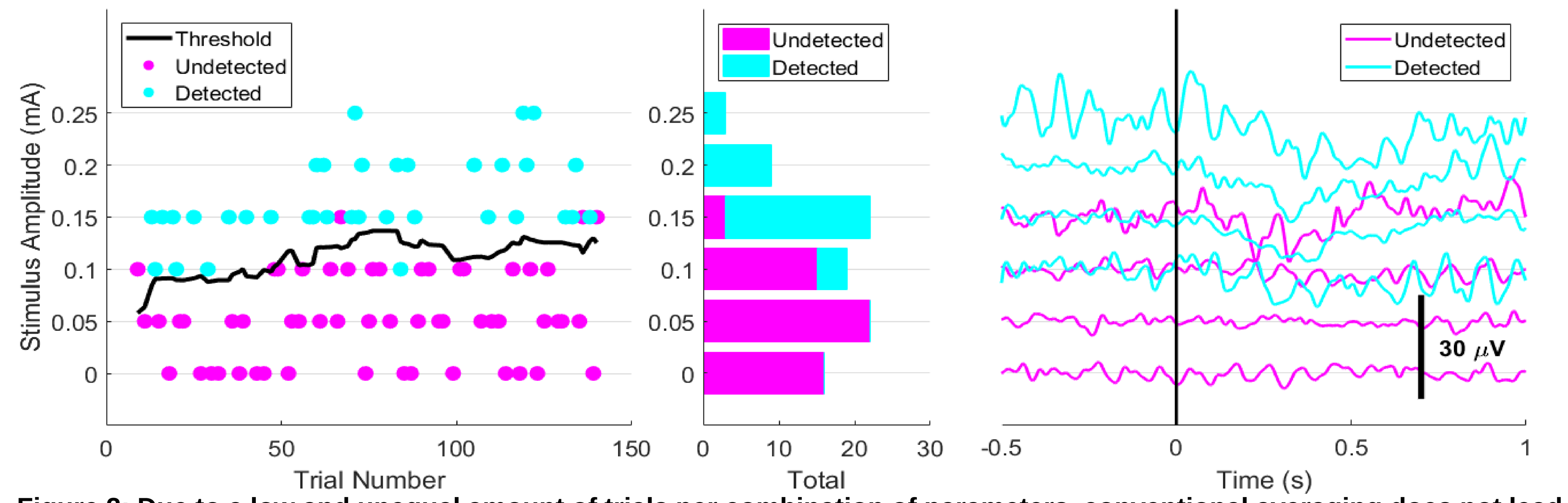

Figure 2: Due to a low and unequal amount of trials per combination of parameters, conventional averaging does not lead to an interpretable estimate of the evoked potential.

Averaging assumes that the signal in the j-th trial consists of the real signal and random trial-specific background activity.

$$y_j(\tau) = \beta_0(\tau) + \eta_j(\tau) \quad (1)$$

Real signal Noise/Background activity

We can improve averaging by accounting for variation of the signal.

- *With respect to stimulus parameters* $(\beta_0(\tau) + \sum_{k=1}^{p} \beta_k(\tau) x_{ijk})$.
- *With respect to the subject* $(v_{i0}(\tau) + \sum_{k=1}^{p} v_{ik}(\tau) z_{ijk})$.

$$y_{ij}(\tau) = \beta_0(\tau) + \sum_{k=1}^{p} \beta_k(\tau) x_{ijk} + v_{i0}(\tau) + \sum_{k=1}^{p} v_{ik}(\tau) z_{ijk} + \eta_{ij}(\tau) \quad (2)$$

Real signal Noise/Background Activity

We can analyze evoked potentials using a linear mixed model (Eq. 2).

1. Compute model coefficients for every point in time.
2. Use model coefficients to analyze variation of the evoked potential with respect to stimulus parameters.

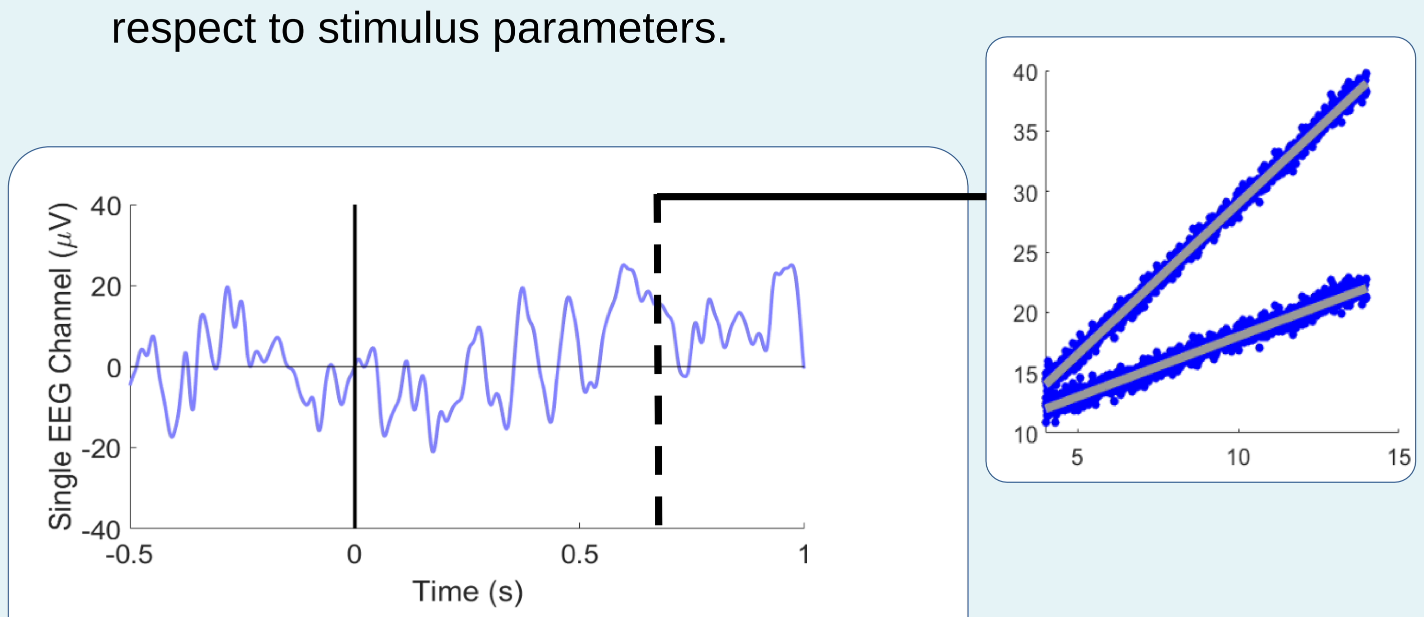

Figure 3: The evoked potential can be estimated by fitting a linear mixed model to the set of trials for every point in time.

Individual effect of stimulus parameters can be shown by prediction using the model coefficients (β_k).

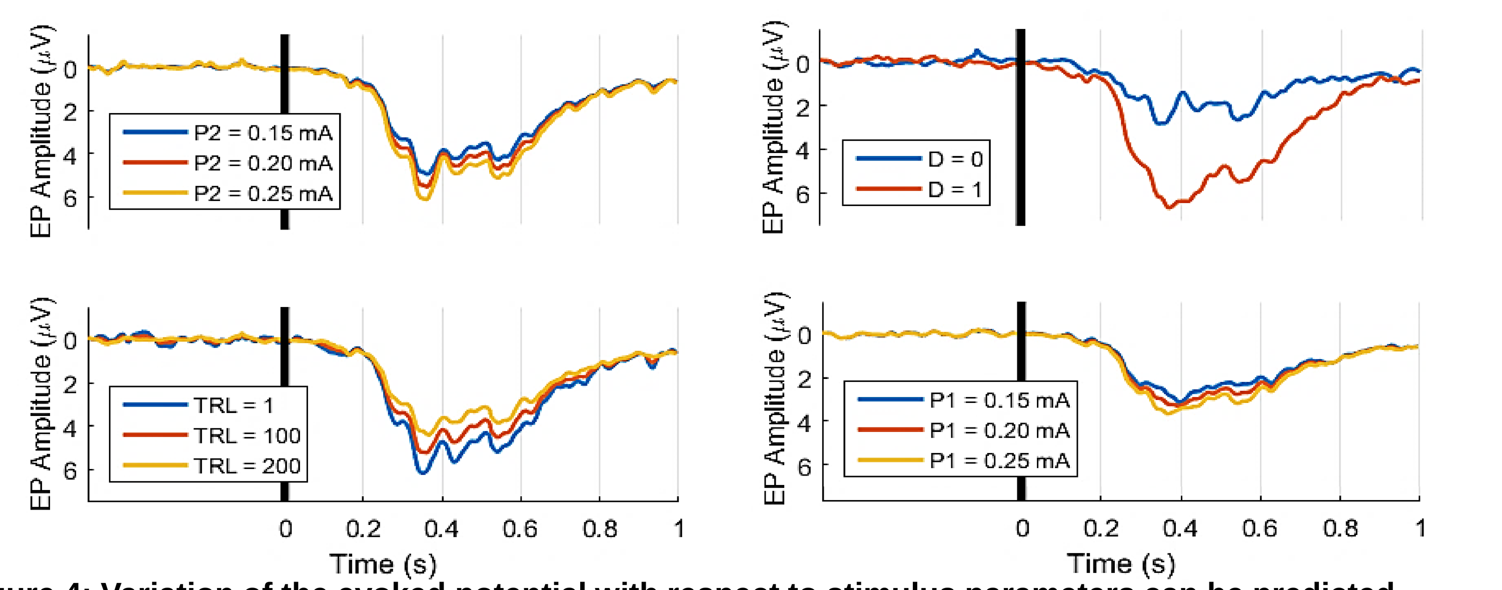

Figure 4: Variation of the evoked potential with respect to stimulus parameters can be predicted using the computed model coefficients.

Conclusion

- A linear mixed model can improve analysis of evoked potentials during multi-stimulus experiments (e.g. during multiple threshold tracking).
- The effect of experimental parameters can be analyzed using model coefficients.

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