P02

SAMPLE TITLE

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OVERVIEW

Background

- Extracellular micro-electrode recordings from the human brain have been feasible for some years
- **Spike-sorting** is necessary to identify contributions of individual neurons from raw recordings
- Multi-hour single-unit recordings would allow to study important questions regarding both epilepsy (e.g., ictogenesis (Gast et al. 2016)) and cognition (e.g., memory consolidation)
- **However**, no tools for the spike-sorting of multi-hour single-unit recordings have been available

Approach

- We developed **Combinato**, a data analysis framework for multi-hour single-unit recordings (Niediek et al. 2016). This framework handles
  - Artifact rejection
  - Automatic spike-sorting
  - Guided manual improvement of spike-sorting
- Combinato is based on spike-sorting in blocks followed by combination of clusters from blocks. Each block is sorted by superparamagnetic clustering (Quian Quiroga et al. 2004).

Evaluation

- When tested on simulations, Combinato outperformed manual operators of the wide-spread package WaveClus
- On data recorded from the medial temporal lobe of patients to find selective single-unit responses, Combinato again outperformed WaveClus
- Combinato was able to track selectively responding single-unit throughout entire nights

RESULTS: SIMULATED MODEL DATA

Evaluation on 10-minute simulations

- We used published simulated model data (Pedreira et al. 2012), consisting of 95 simulations of 10 minutes duration each.
- Spike-sorting performance was measured by the number of "hits", where a hit is a unit consisting of at least 50% of the spikes of a true unit, and with at most 50% contamination.
- We compared Combinato's results to published results (Pedreira et al. 2012) obtained by manual operators of WaveClus (Quian Quiroga et al. 2004).

Figure 1: **Results for one simulated channel. A** Automatically selected clusters at different "temperatures". **B** Performance at default parameters. **C** Clusters generated in one simulation. **D** Manually splitting unit C1 from C generated another hit.

Figure 2: **Performance at different parameter settings.** Displayed are results for 8 of the 48 parameter settings tested. Asterisks indicate that the percentage of hits is significantly higher than the optimum obtained by Pedreira et al. 2012. The fully automated Combinato outperformed manual operators of WaveClus at 24 of the 48 settings, indicating robustness of our algorithms. ***, P < .001; **, P < .01, *, P < .05; n.s., better but not significantly.

Evaluation on 10-hour simulations

- We concatenated simulations of 10 minutes duration to produce 19 simulations of 10 hours duration.
- To make the task harder, we added drift and Gaussian noise to the concatenated data.

Figure 3: **Simulated neuron with drift and added noise.** The unmodified unit is shown in orange in the bottom panel for comparison.

Figure 4: **Performance at different parameter settings. A** Numbers of hits for different numbers of units in the simulated data. Four parameter settings were tested. **B** Mean and standard deviation for each paramter setting.

METHODS & SOFTWARE

Automated data processing framework

Figure 5: **Schematic of data processing. A** Channels without unit activity are excluded. Action potentials are detected after bandpass filtering. **B** Detected artifact events are excluded according to three criteria. **C** Spike-sorting is performed in parallel in blocks of 20 000 by "superparamagnetic clustering" (Quian Quiroga et al. 2004). In each block, a second clustering step is applied to all large clusters. **D** Remaining spikes are assigned by Euclidean template matching. **E** Artifact clusters are removed. **F** Similar clusters are grouped both within each block and across blocks.

Graphical user interfaces

Figure 6: **Combinato's data viewer.** Both the raw signal (at several temporal resolutions) as well as the clustering result for each channel are displayed.

Figure 7: **Combinato's tool for result inspection.** Several graphical quality metrics are displayed for each cluster. Clusters can be manually discarded or manipulated.

RESULTS: RECORDINGS FROM EPILEPSY PATIENTS

Micro-electrode recordings

- Micro-electrode recordings from 10 neurosurgical patients undergoing epilepsy monitoring implanted with intracerebral micro-electrodes (as in Mormann et al. 2015). Electrodes were located bilaterally in the hippocampus, amygdala, entorhinal cortex, and parahippocampal cortex.

Figure 8: **Result of automatic sorting on one channel with noise. A** Bandpass filtered data. **B** Pre-sorting artifact removal. **C** Automatically selected clusters at different temperatures. **D** Clusters and artifacts as identified by Combinato. **E** Clusters as identified by WaveClus. **F** Raster plots from visual stimulus presentation. Cluster D2 responds to all four pictures. Three of the four responses remain undetected when using WaveClus.

Figure 9: **Examples of neurons tracked over an entire night. A** Stable waveform and response pattern. **B** Amplitude variations; no response to the written name. **C** Amplitude shift results in the detection of two different units. **D** Two resp. cclusters generated; no response to the written name. **E** Stable waveform; weak response in the morning. **F** Solid response in the evening and morning, but with separate units. **G** The blue and red clusters both contribute to the response; both tracked with a stable waveform. **H** The red, blue, and yellow clusters contribute to the response. All three clusters have a stable waveform.

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