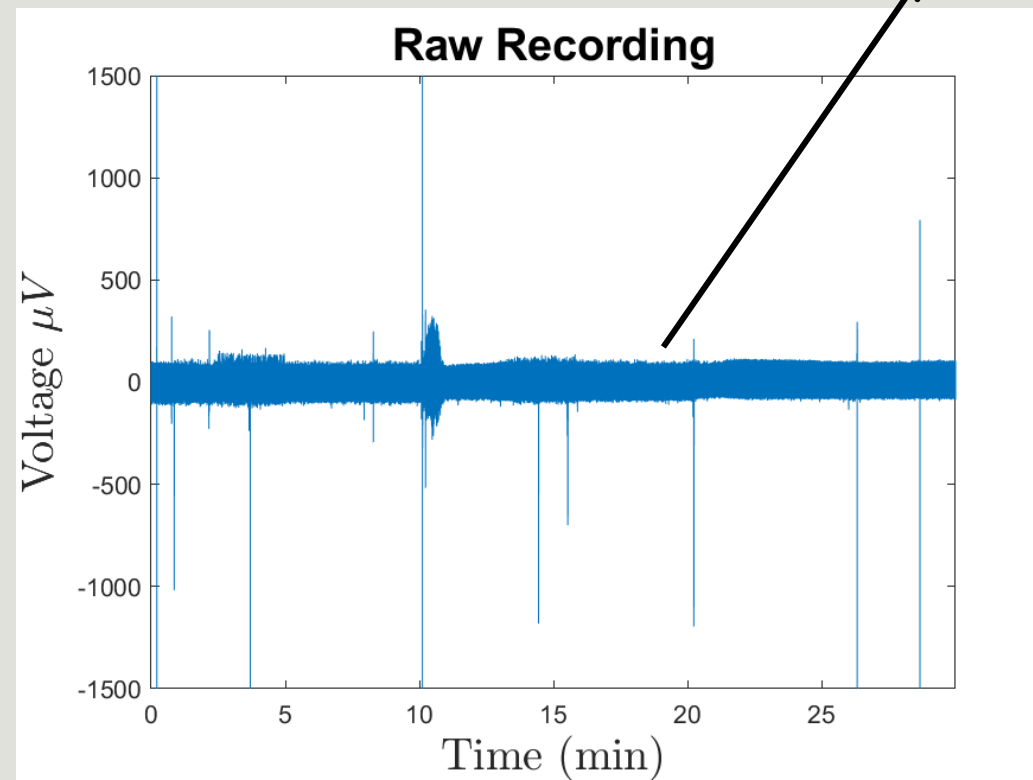
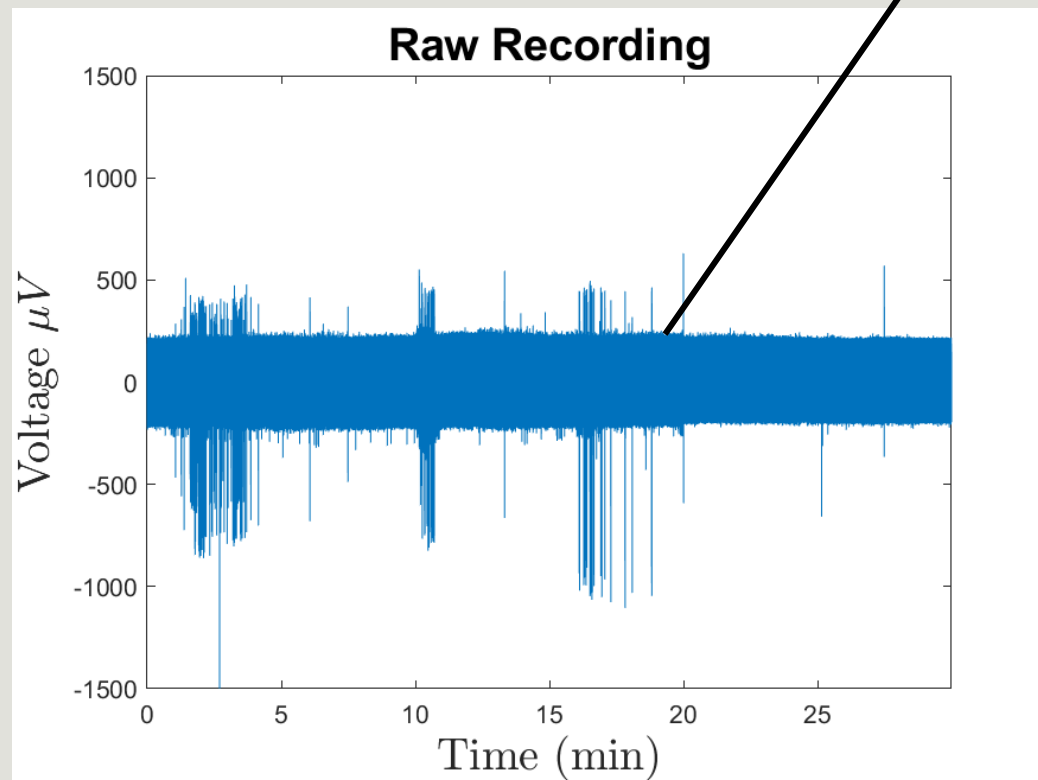
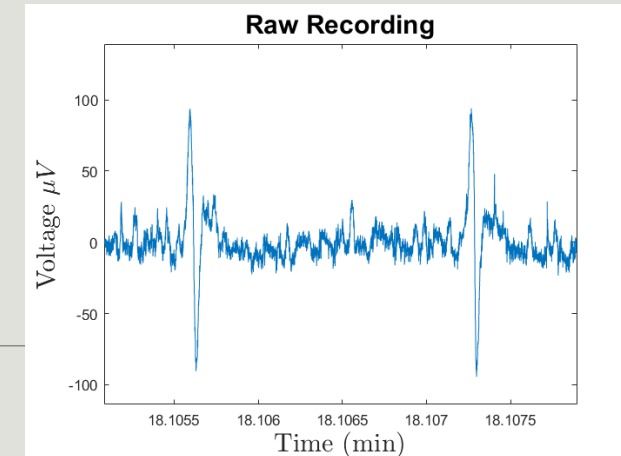
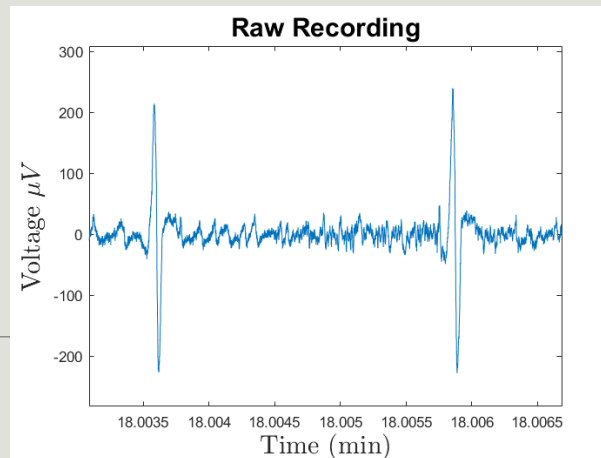


Identifying Neural Waveforms From Vagus Nerve Recordings

- METHOD TO EXTRACT NEURAL EVENTS FROM RAW RECORDING.
- IDENTIFYING NEURAL WAVEFORMS “CORRELATED” WITH INJECTION-EVENT

GABRIEL ANDERSSON 2021-06-30

Pre-processing Raw Signal



Main Steps in Pre-processing

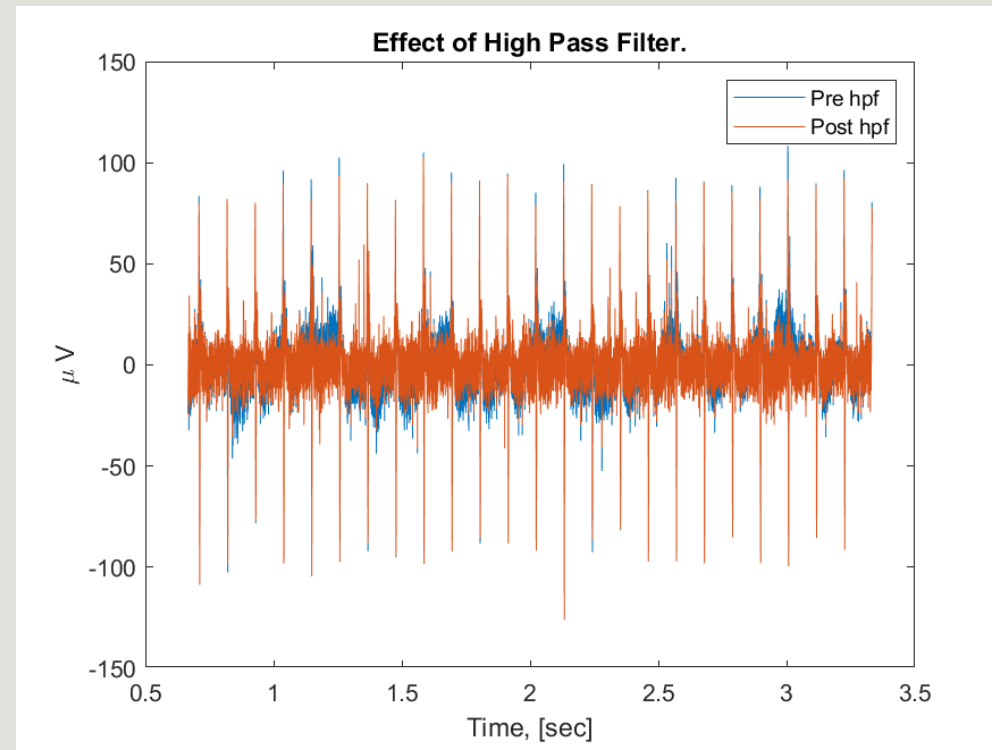
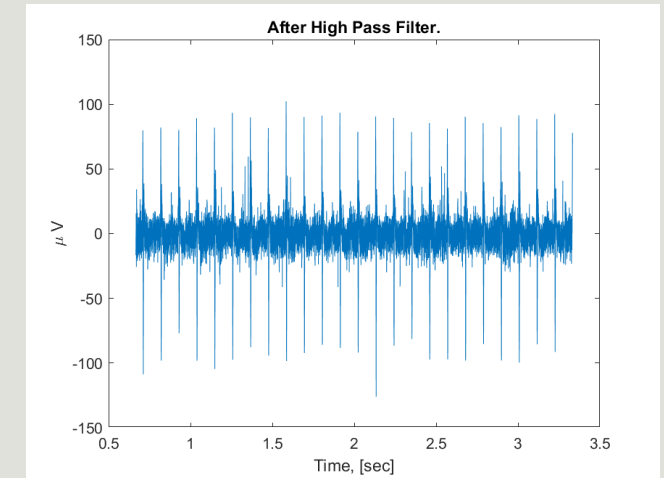
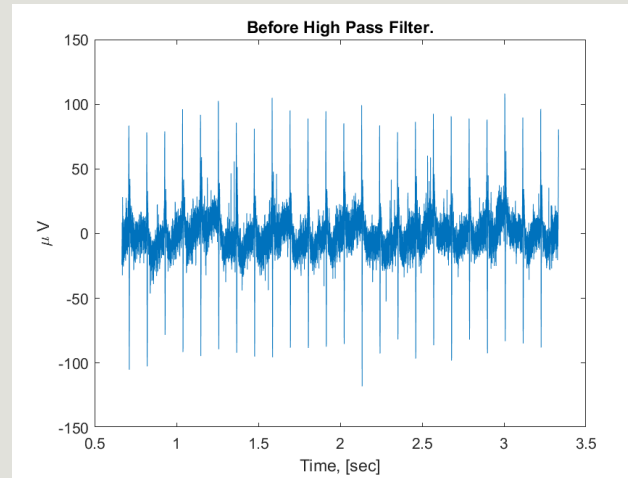
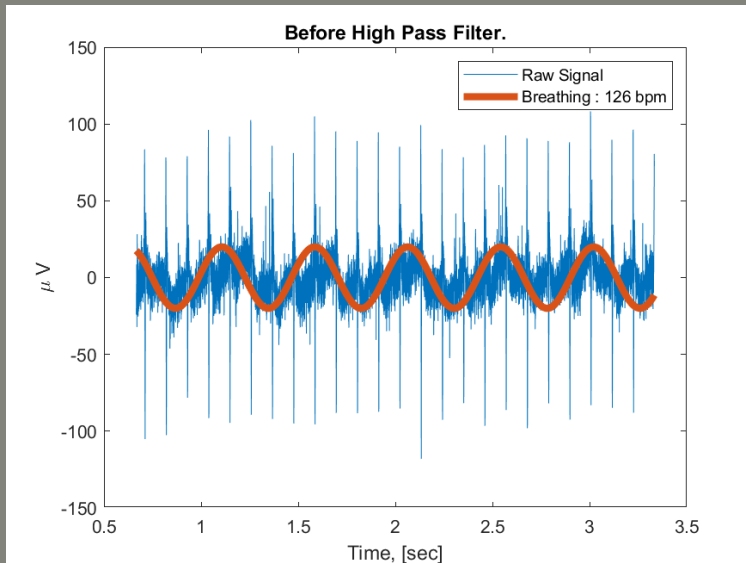
Aim to find all Compound Action Potentials (CAPs) from raw recording.

- High pass filter – Removes low frequencies from raw signal
- (Downsample – Solve memory issues and speed up computations.)
- **Adaptive Threshold** – Extracting the Neural Event from noise and other sources of interference. (e.g. cardiac events)

Pre-processing

1. High Pass Filter (hpf)

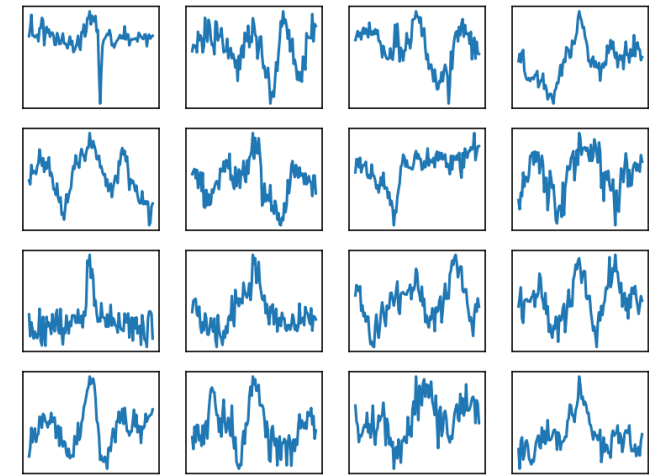
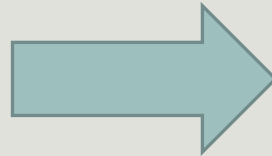
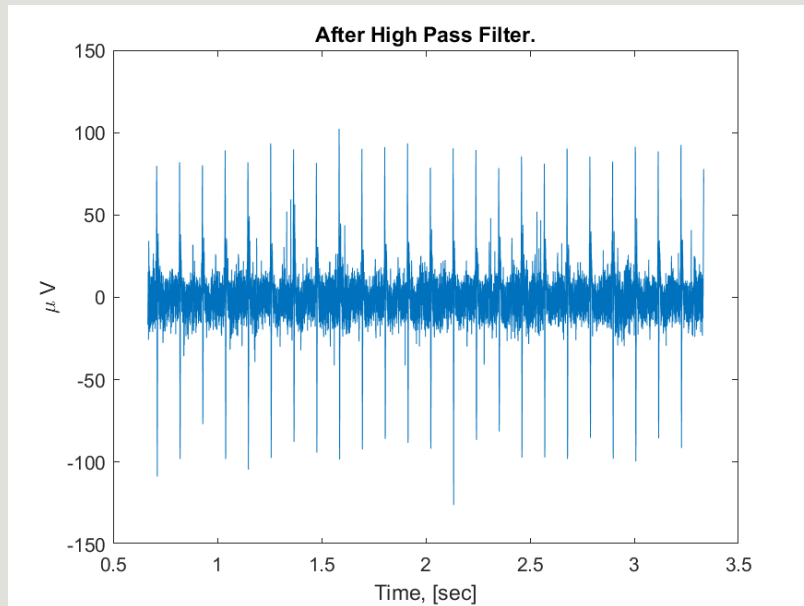
- Remove frequencies in signal below 10Hz.
- Assumes that this remove noise sources related, e.g. to micromovements of electrode caused by respiratory movements
- Respiratory rate in mice 80-230 bpm. (1.3 – 3.8 Hz)



Pre-processing

2. Adaptive - Threshold

Overview -- Extracting signal (CAPs) from noise and other sources of interference:

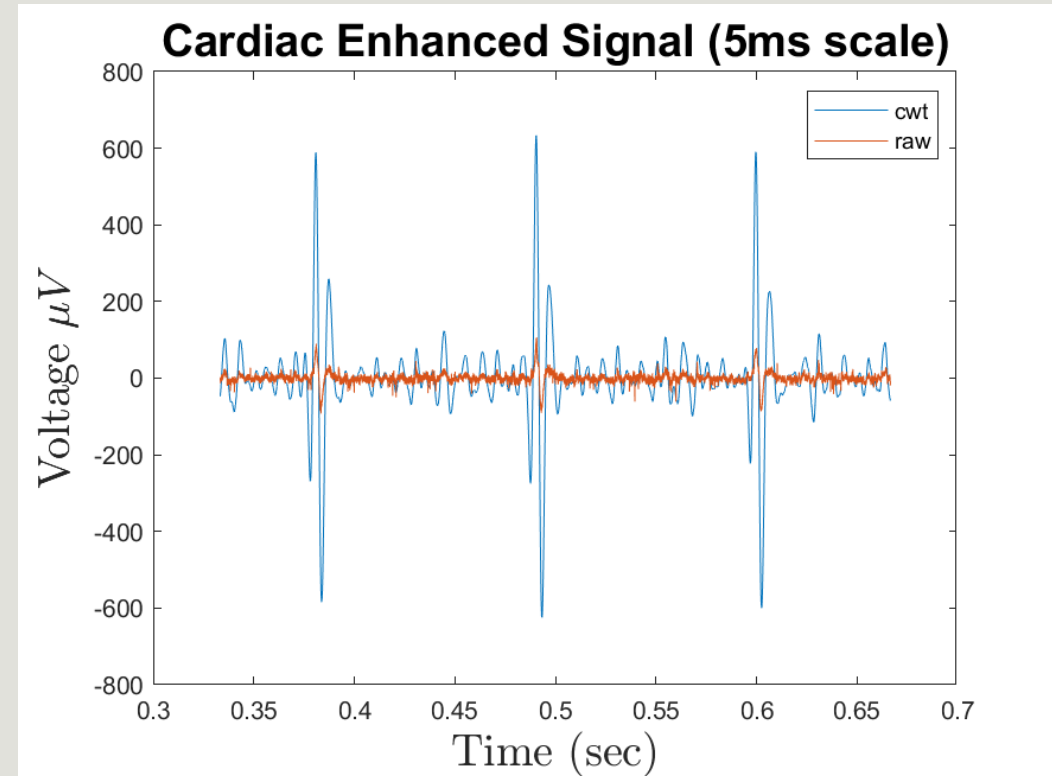


Pre-processing

2. Adaptive - Threshold

Includes:

- Get signal where cardiac events are emphasized -- event of the 5ms scale. (Wavelet transform)

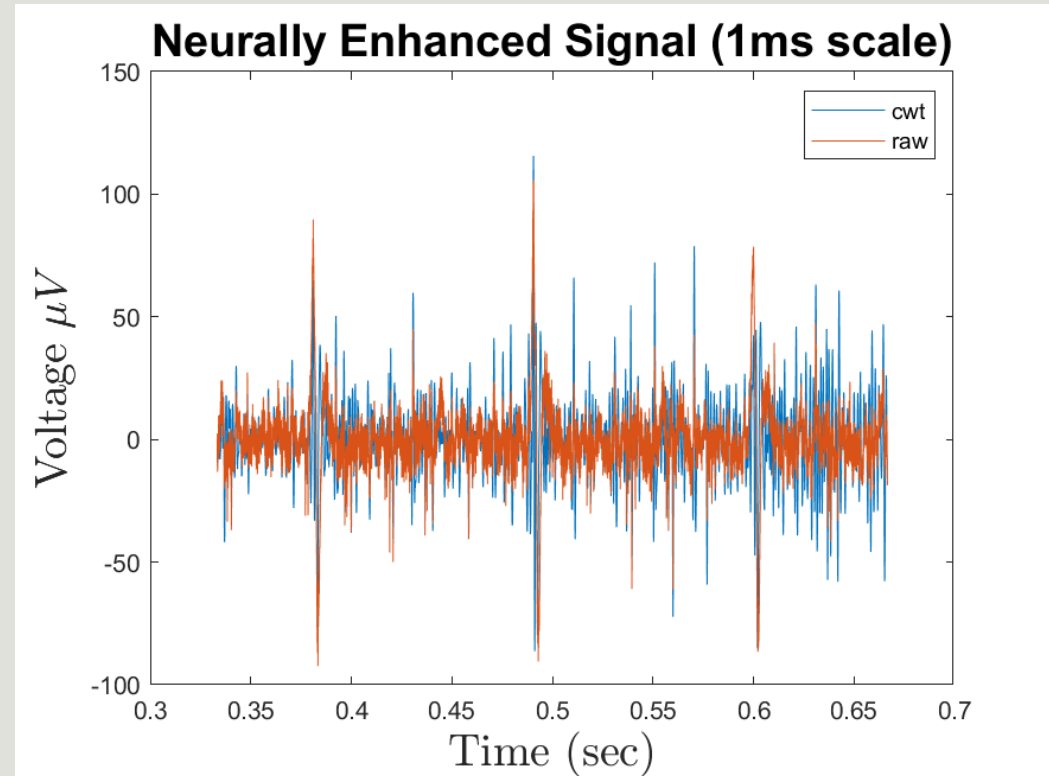


Pre-processing

2. Adaptive - Threshold

Includes:

- Get signal where cardiac events are emphasized -- event of the 5ms scale. (Wavelet transform)
- Get signal where neural events are emphasized - event of the 1ms scale. (Wavelet transform)

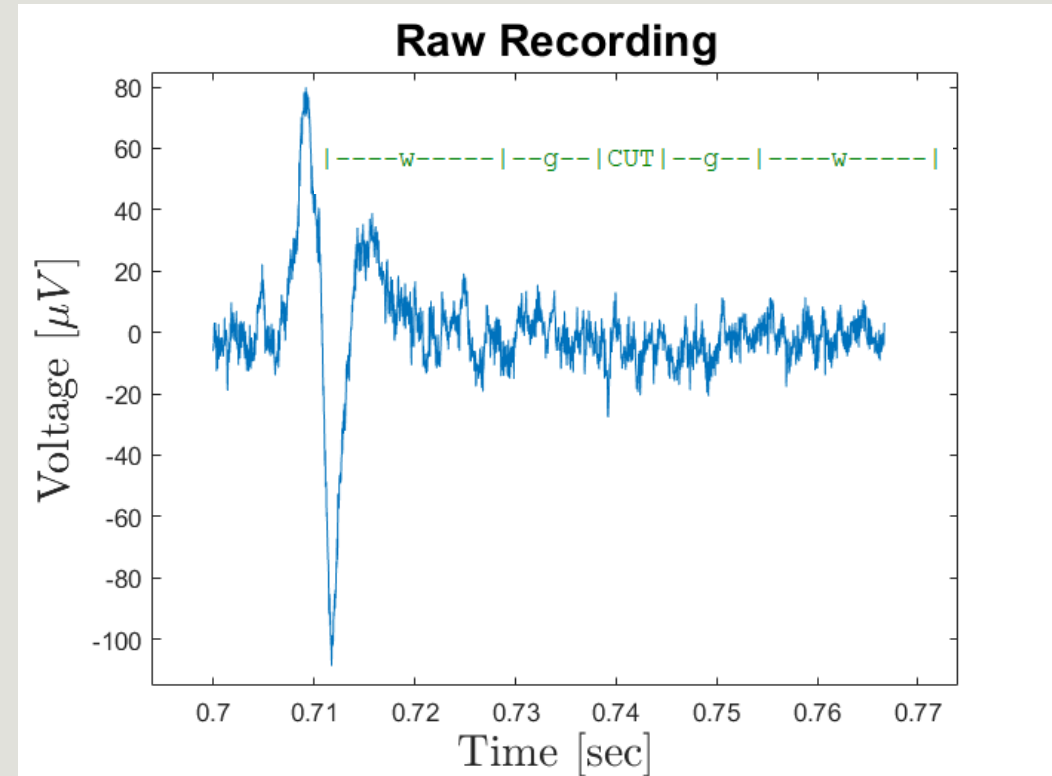


Pre-processing

2. Adaptive - Threshold

Includes:

- Get signal where cardiac events are emphasized -- event of the 5ms scale. (Wavelet transform)
- Get signal where neural events are emphasized - - event of the 1ms scale. (Wavelet transform)
- Use a sliding window, calculating the local-in-time noise-level for the two signals. (background statistics)
 - “CUT” : “Cell Under Test”.
 - w : windows where the standard deviation is estimated
 - w = 188ms
 - g : “guard” regions – a possible signal in the “CUT” should not corrupt the SD-estimate.
 - g = 13 ms

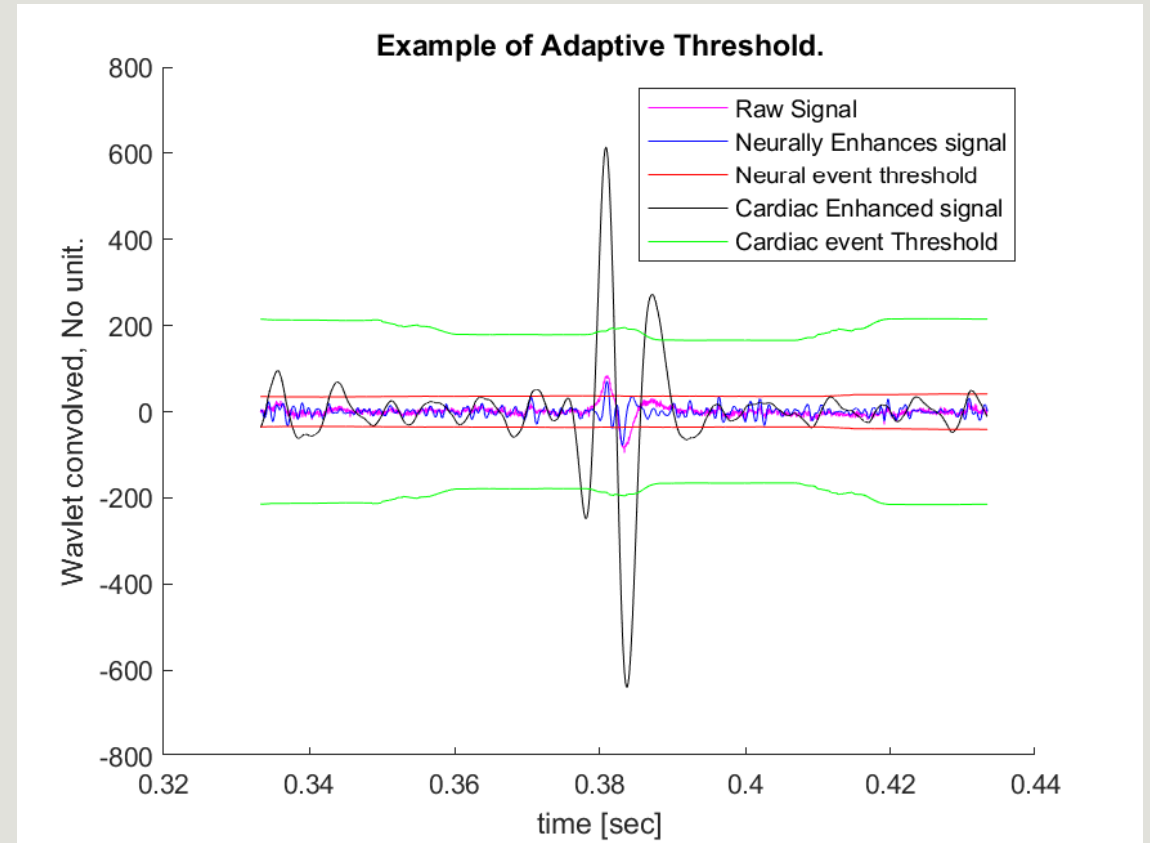


Pre-processing

2. Adaptive - Threshold

Includes:

- Get signal where cardiac events are emphasized -- event of the 5ms scale. (Wavelet transform)
- Get signal where neural events are emphasized - - event of the 1ms scale. (Wavelet transform)
- Use a sliding window, calculating the local-in-time noise-level for the two signals. (background statistics)
- Extract cardiac- and neural events that deviated more than 3 SD from mean for both signals.

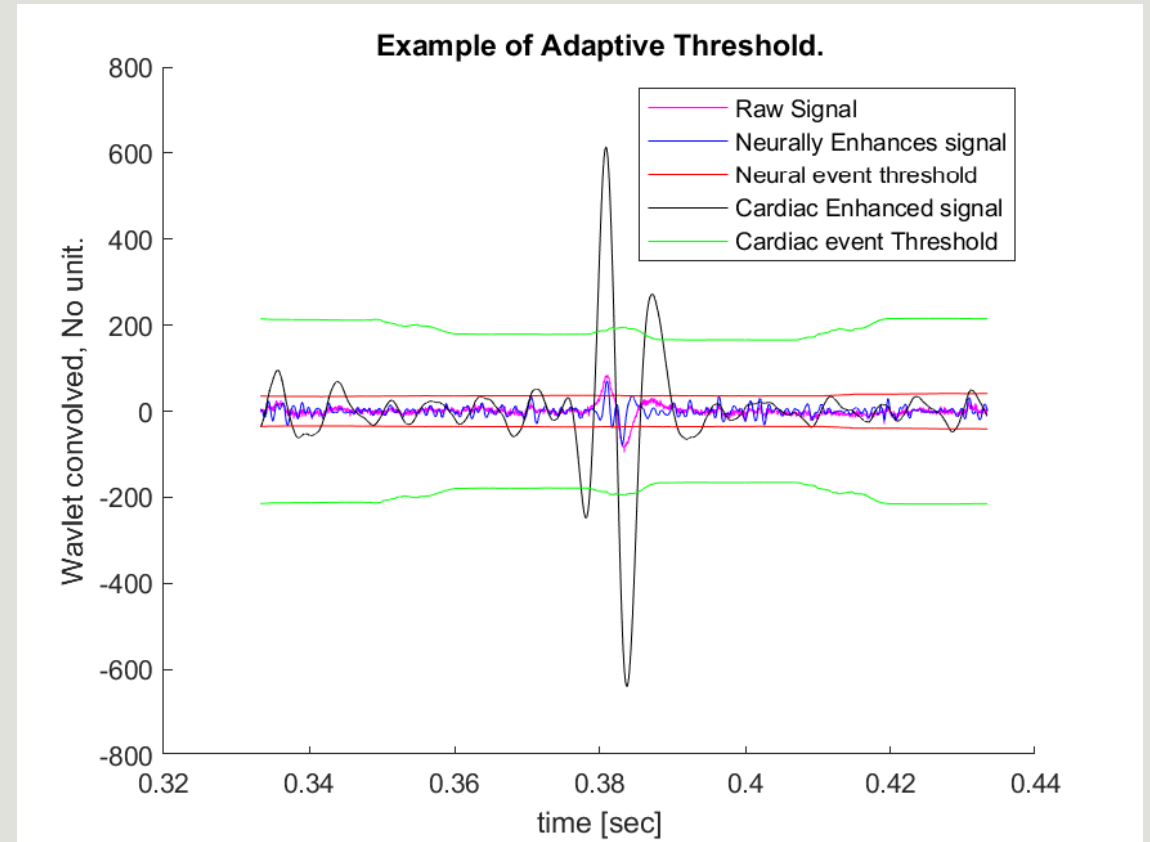


Pre-processing

2. Adaptive - Threshold

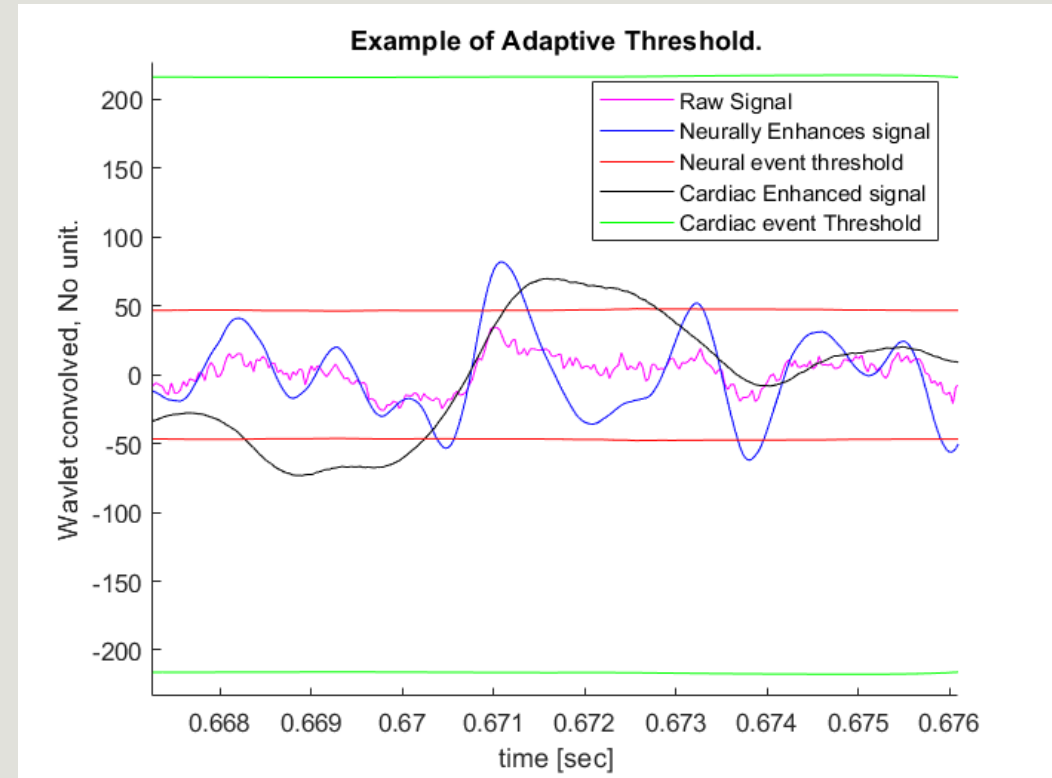
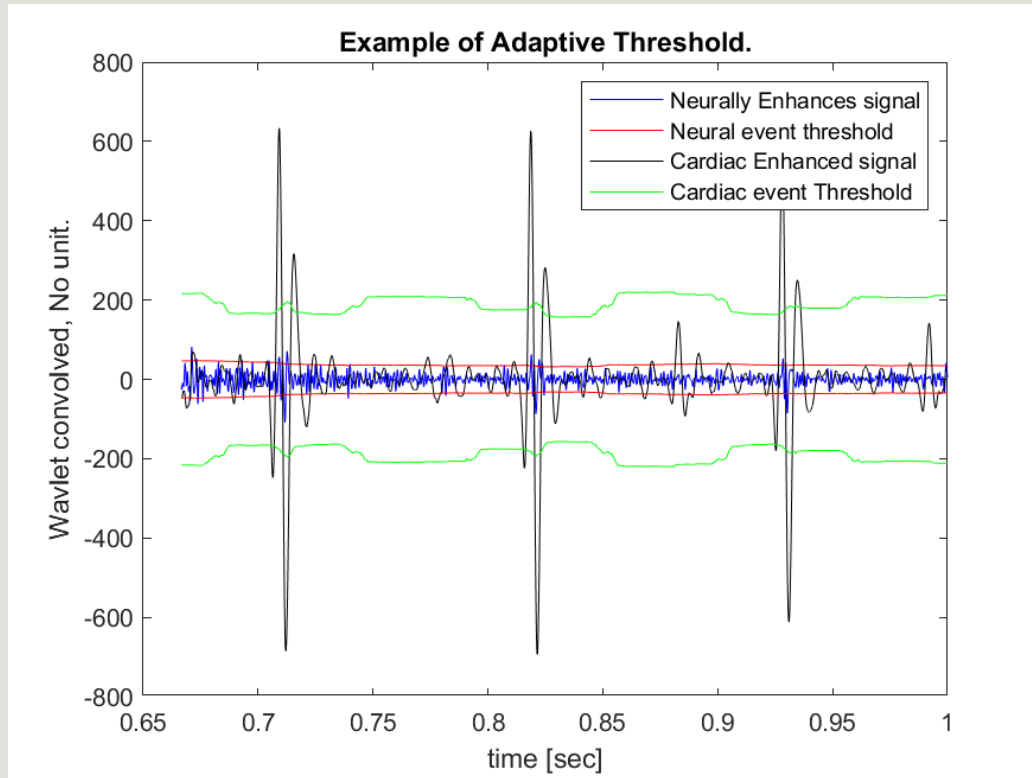
Includes:

- Get signal where cardiac events are emphasized -- event of the 5ms scale. (Wavelet transform)
- Get signal where neural events are emphasized - - event of the 1ms scale. (Wavelet transform)
- Use a sliding window, calculating the local-in-time noise-level for the two signals. (background statistics)
- Extract cardiac- and neural events that deviated more than 3 SD from mean for both signals.
- Discard neural events that cooccur with cardiac events.



Pre-processing

2. Adaptive - Threshold

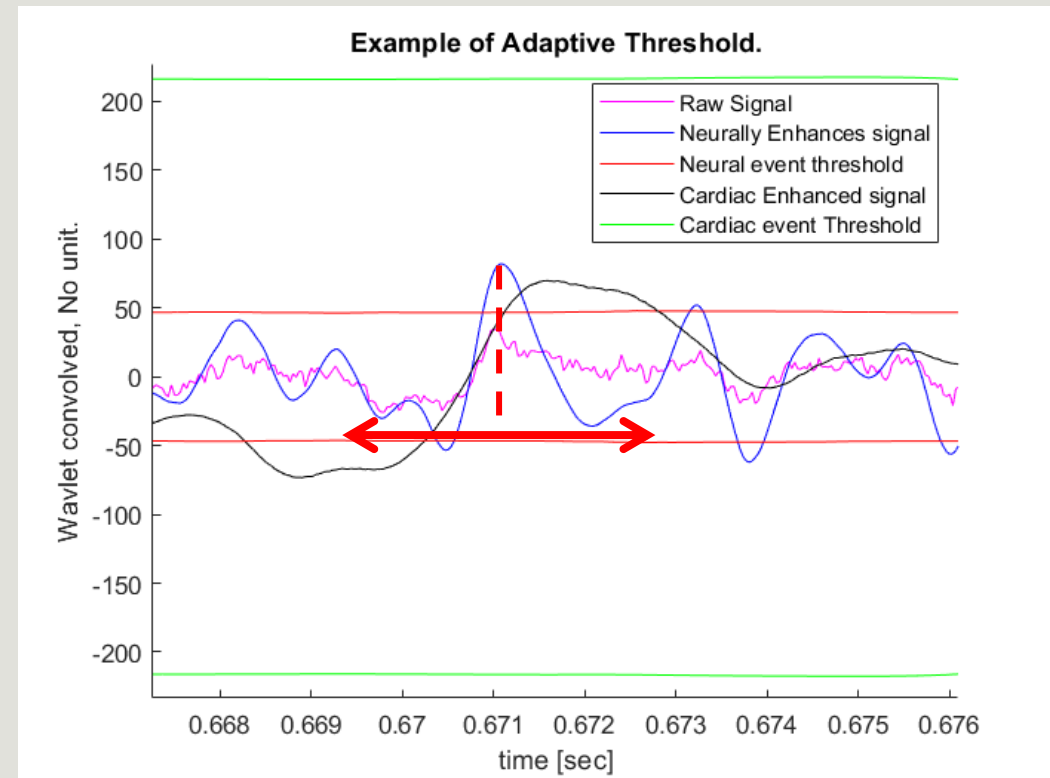
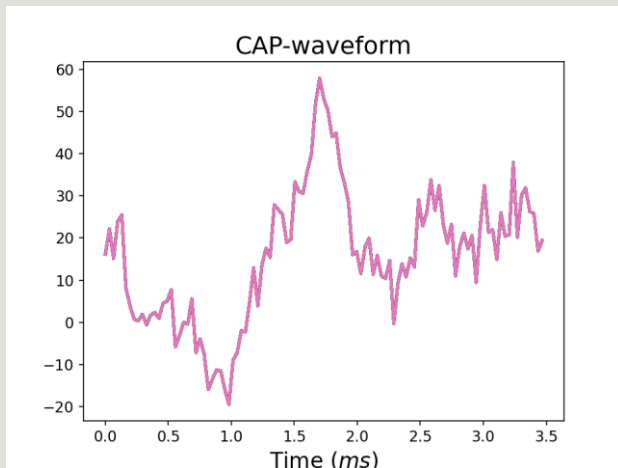


Pre-processing

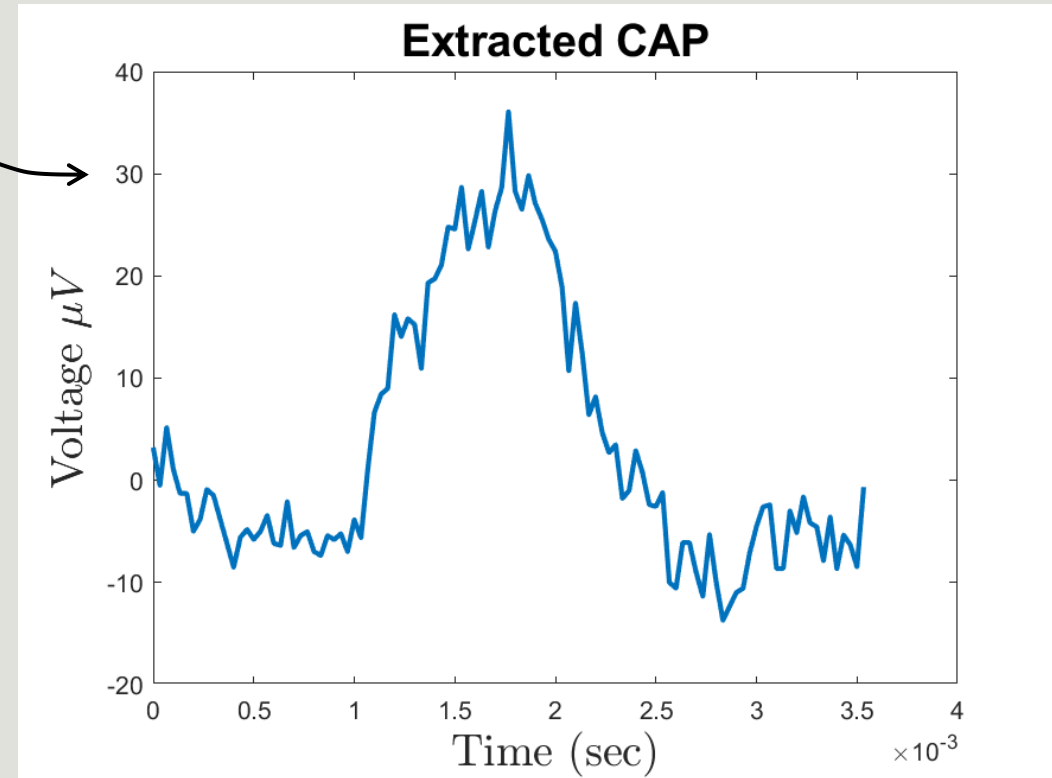
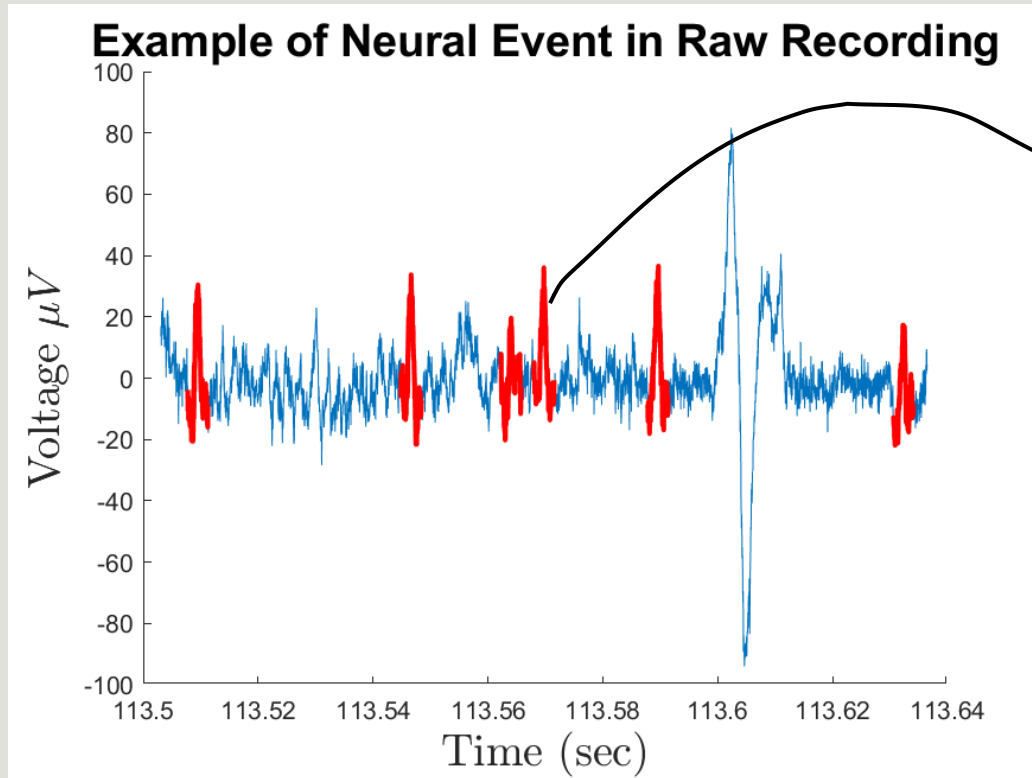
2. Adaptive - Threshold

The extracted CAPs / waveforms are:

- Assumed to be 3.5 ms in duration
- "max-centered" – the max peak is placed at the 1.75 ms mark.
- Example: (Not corresponding to right figure ->)



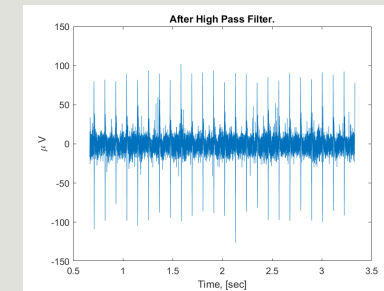
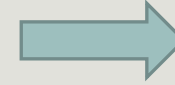
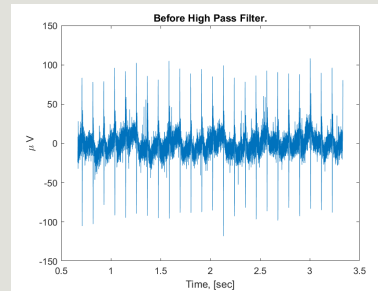
Example of Extracted Waveforms



Summary – Identifying CAPs

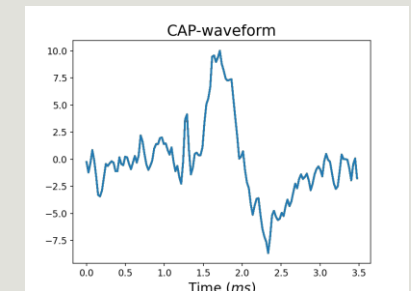
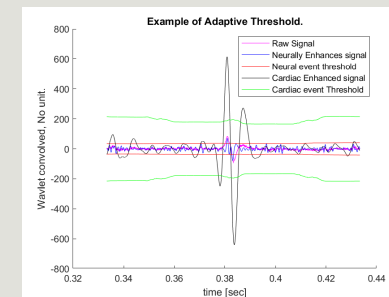
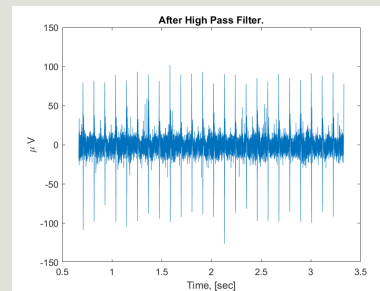
High Pass Filter

- Remove low frequencies



Adaptive Threshold

- Emphasize Neural/Cardiac events
- Apply threshold
- Disregard CAPs that cooccur with cardiac events.



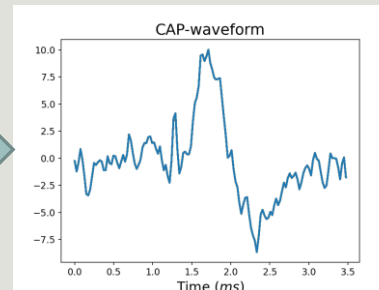
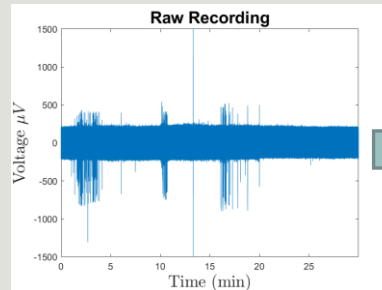
Amplitude threshold

- Waveforms with a max-amplitude larger than a specific value are discarded.

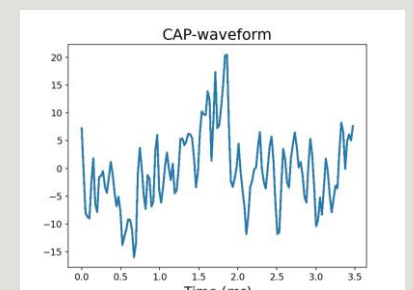
Finding Shapes “Correlated” With Injection-Event

Preprocess

- Extract individual waveforms.

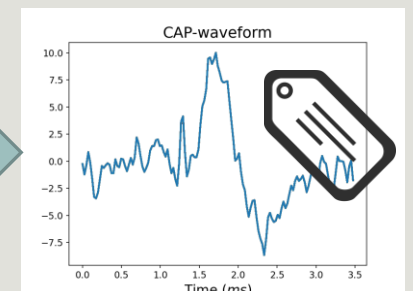
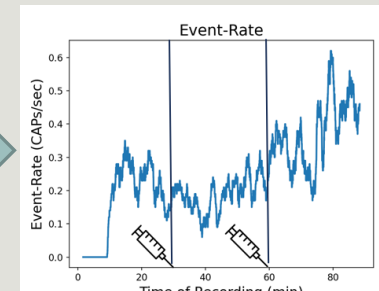
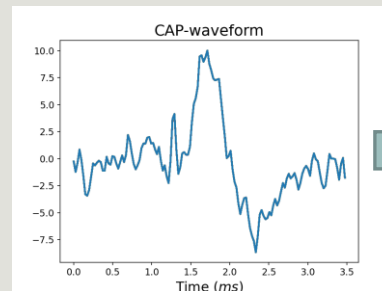


...



Incorporate Prior Belief

- Estimate event-rate.
- Label waveforms.

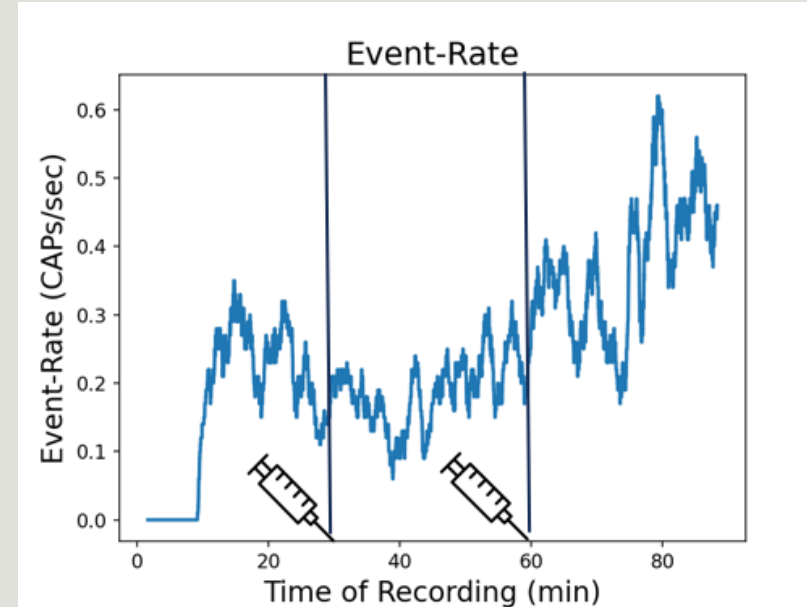
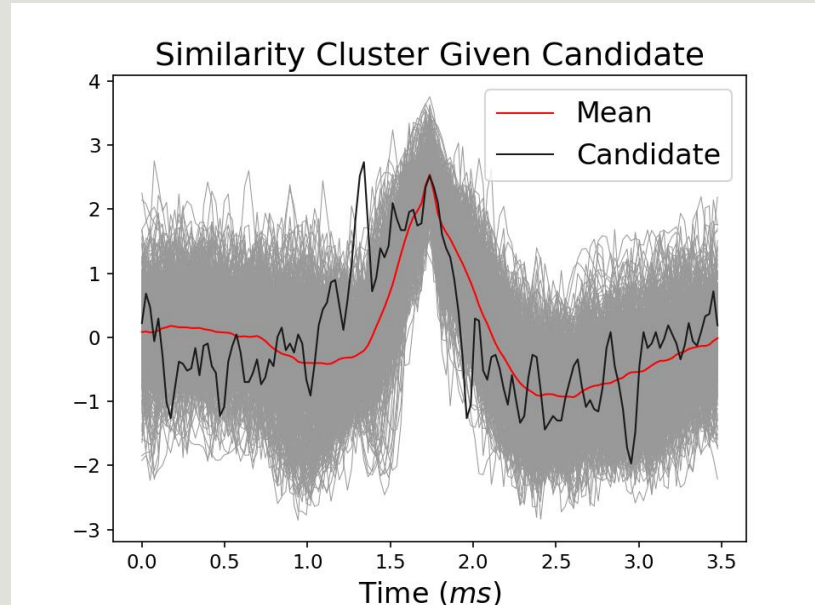


Build Probabilistic Model of Labeled Data

- Study maxima of

$\mathbb{P}(x \mid \text{"Increased event-rate after first/second cytokine injection"})$.

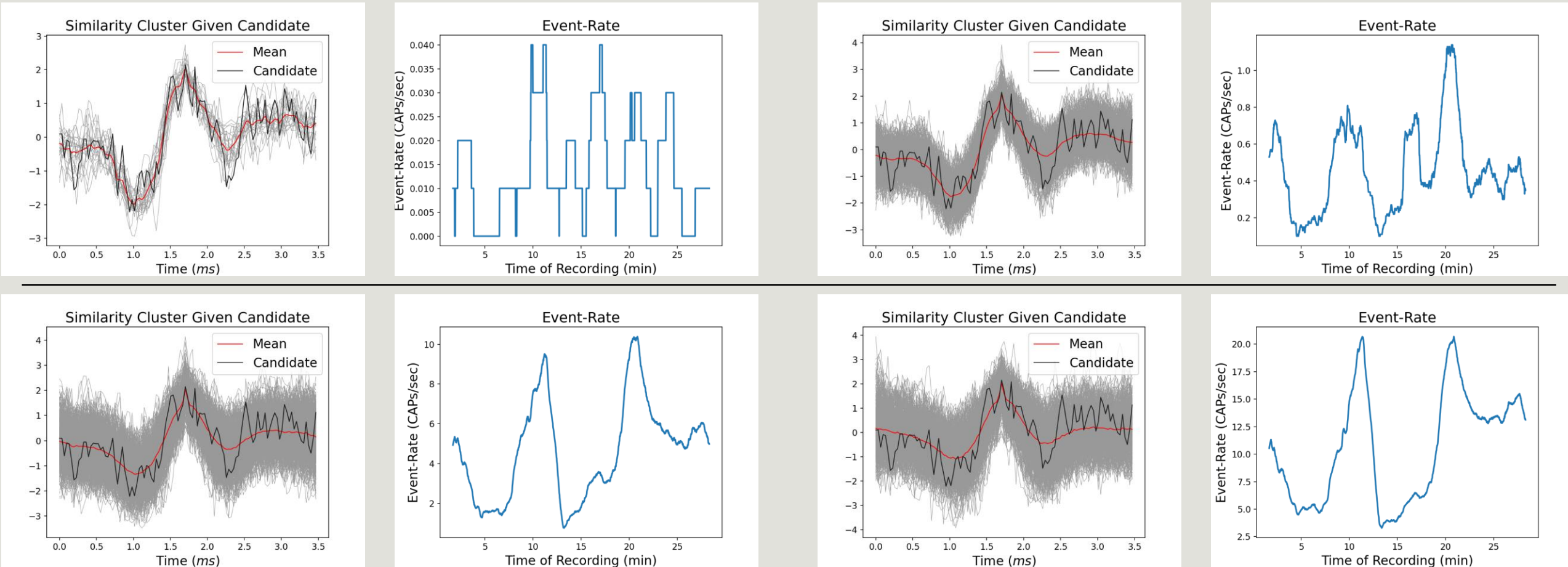
Similarity Measure – Similar CAPs Assumed to Encode Similar information



Event Rate : How often is a specific CAP-shape observed during time of recording.

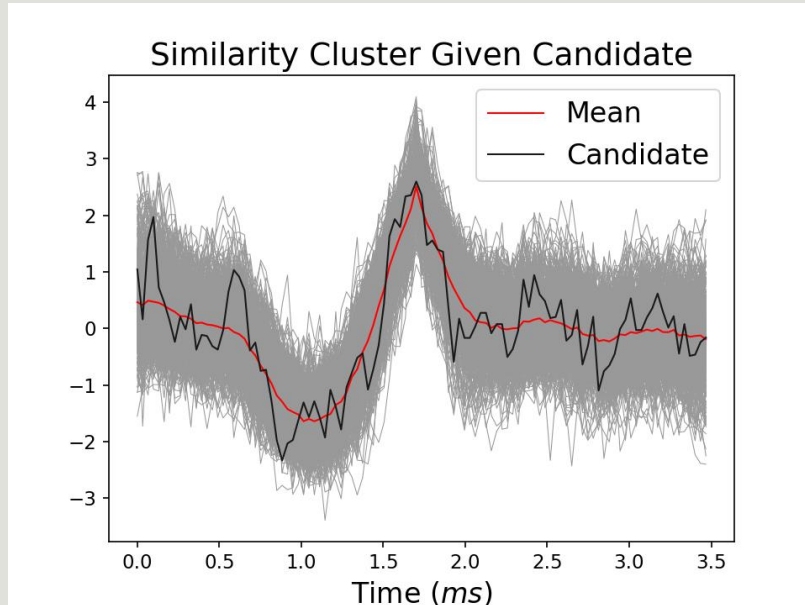
Similarity Measure –

Balance between: “CAPs being similar enough” and “obtaining informative event-rates”.

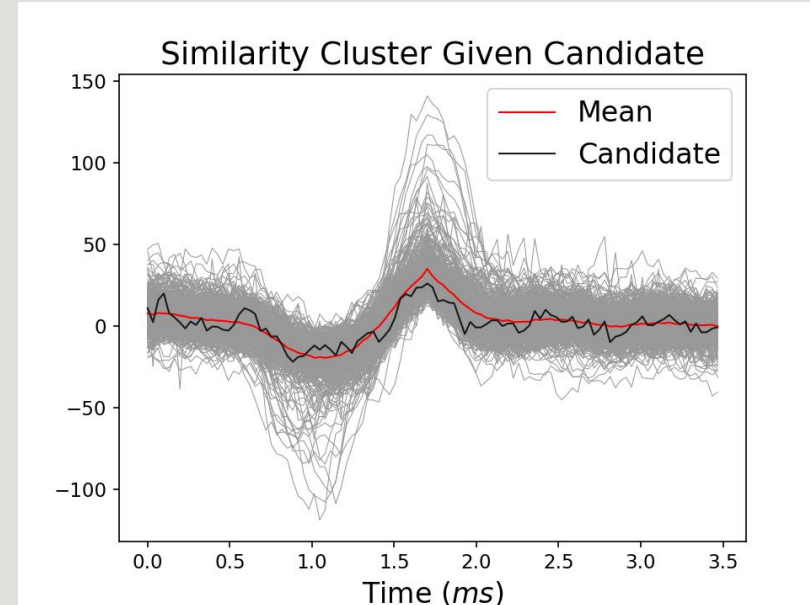


Similarity Measure –

Normalised Waveforms. Amplitude is not taken into consideration



Normalised CAPs.

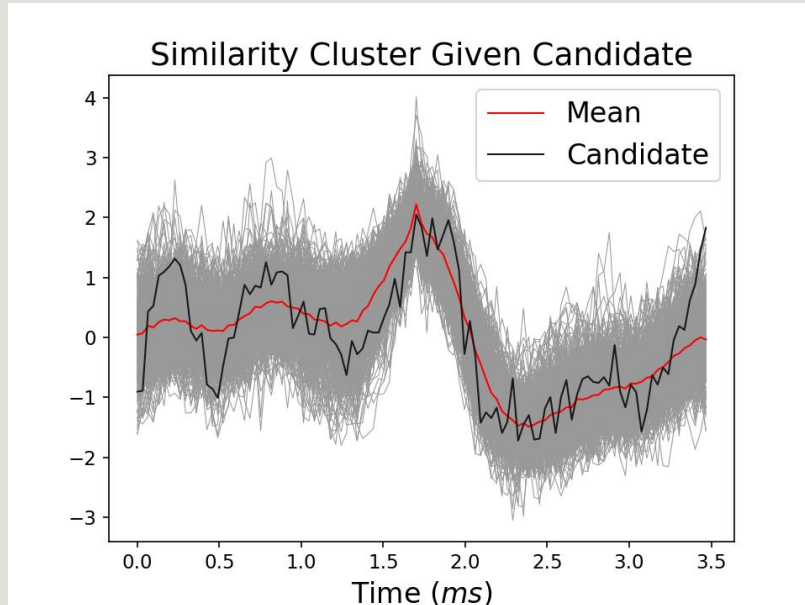


Raw CAPs. (μV)

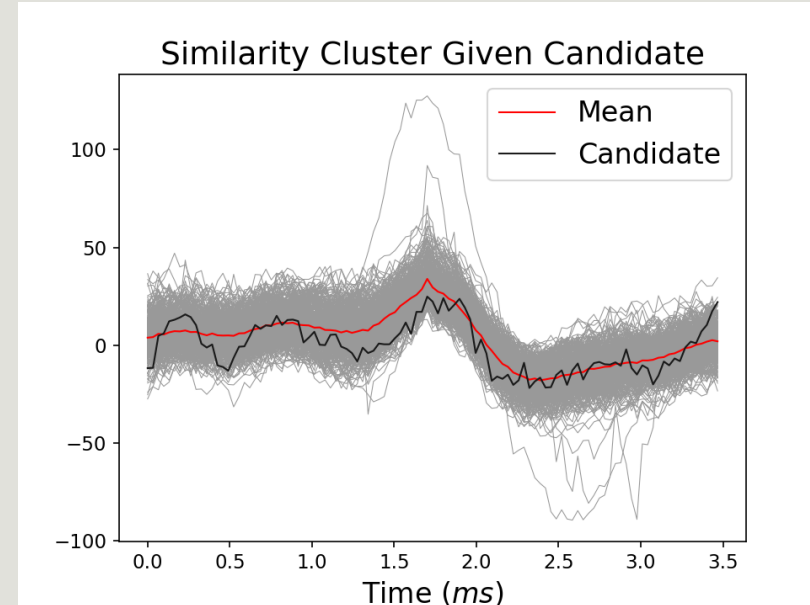
- Including the amplitude in the similarity measure either leads to a small number of observations, or very limited shape consistency.

Similarity Measure –

Normalised Waveforms. Amplitude is not taken into consideration



Normalised CAPs.

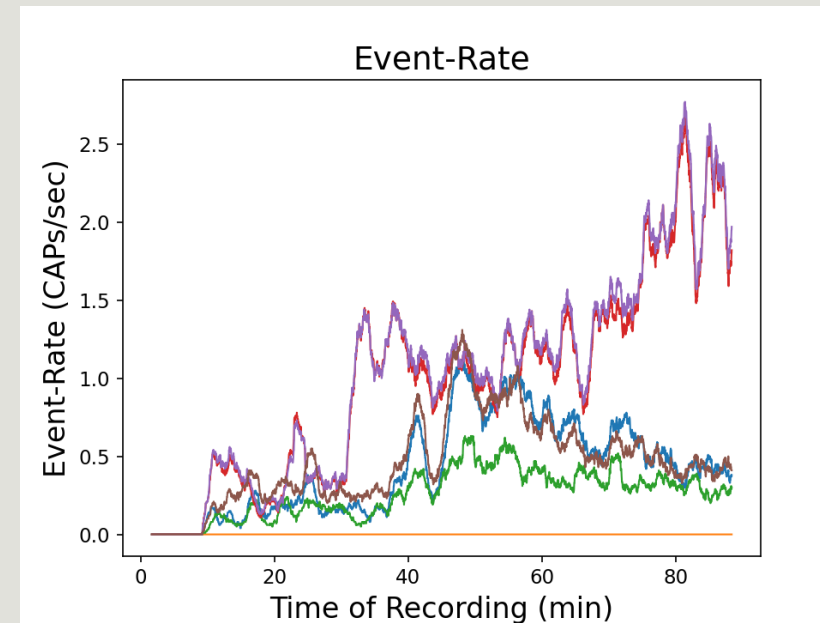
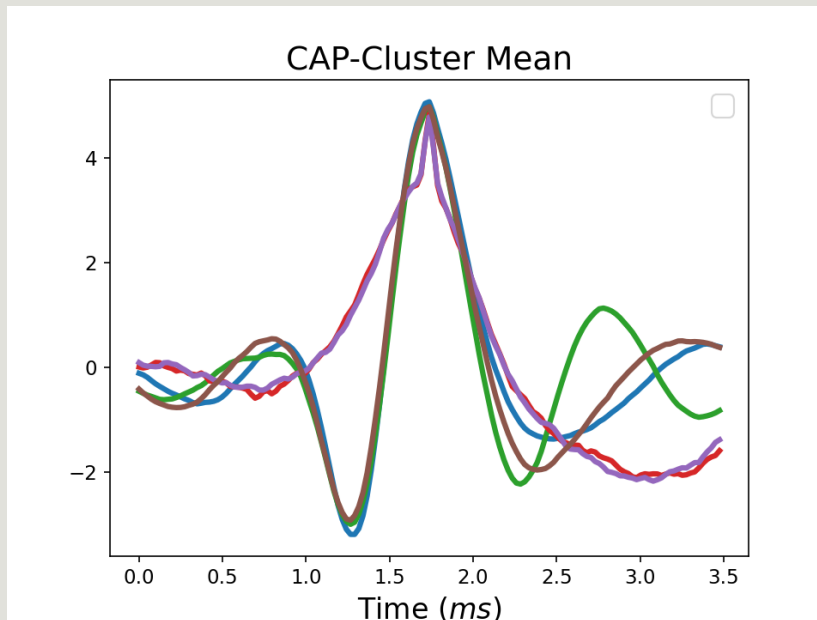


Raw CAPs. (μV)

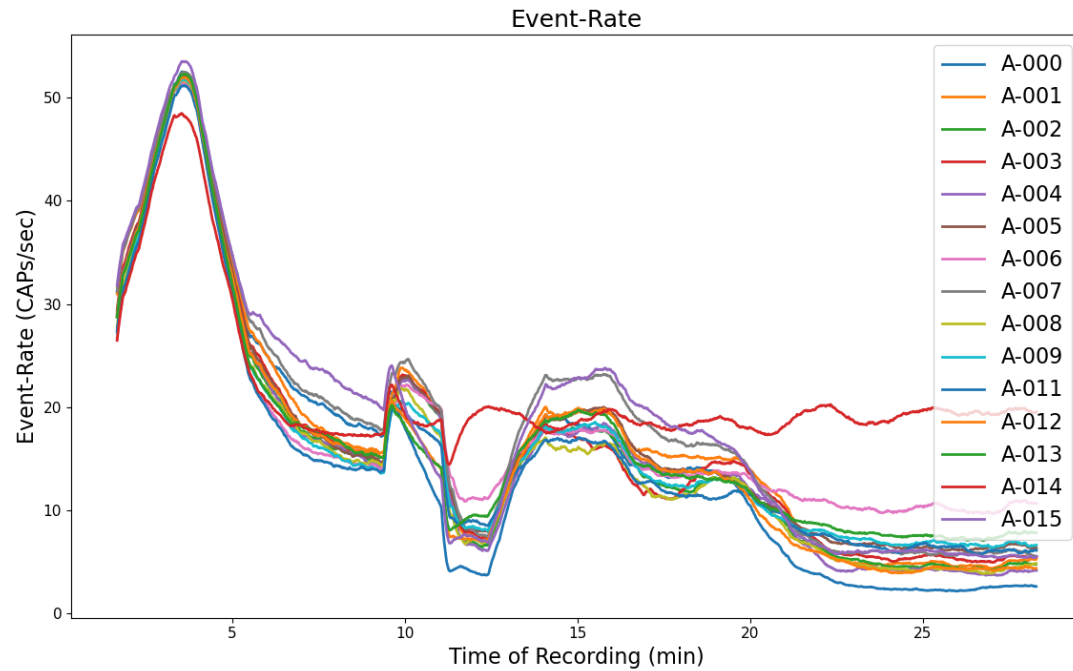
- Including the amplitude in the similarity measure either leads to a small number of observations, or very limited shape consistency.

Example Results from “Zanos et. al.” Recordings –

The most likely shapes, given some increase of event-rate after first injection.

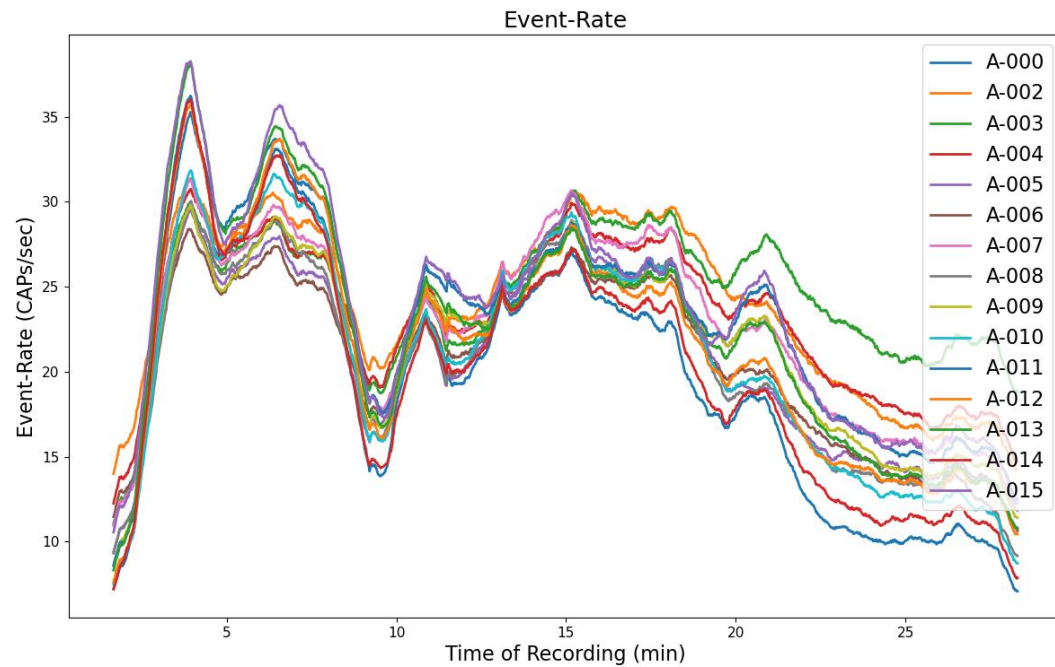


- Left: Candidate CAP-shapes to encode TNF-information.
- Right: Their corresponding event-rate using similarity measure.



New Data: Total event-rate for all channels

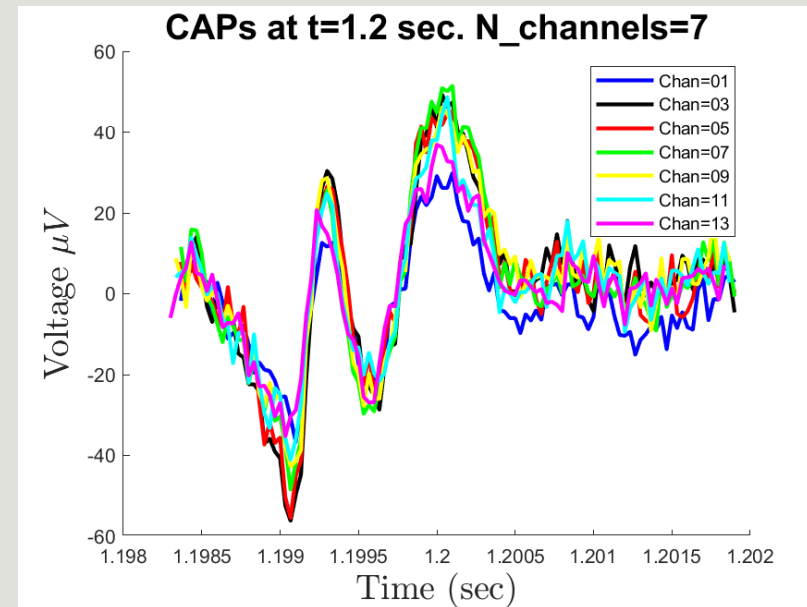
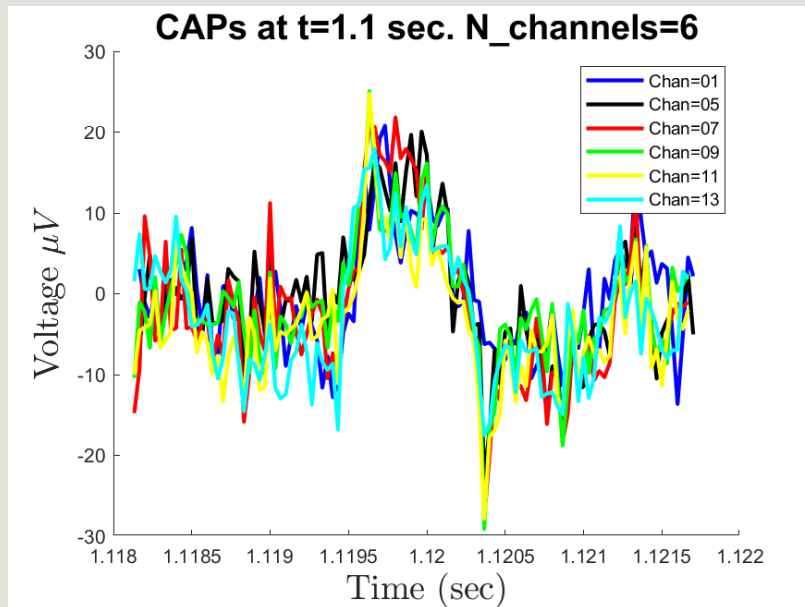
Baseline_10min_LPS_10min_KCl_10min_210617_142447



New Data: Total event-rate for all channels

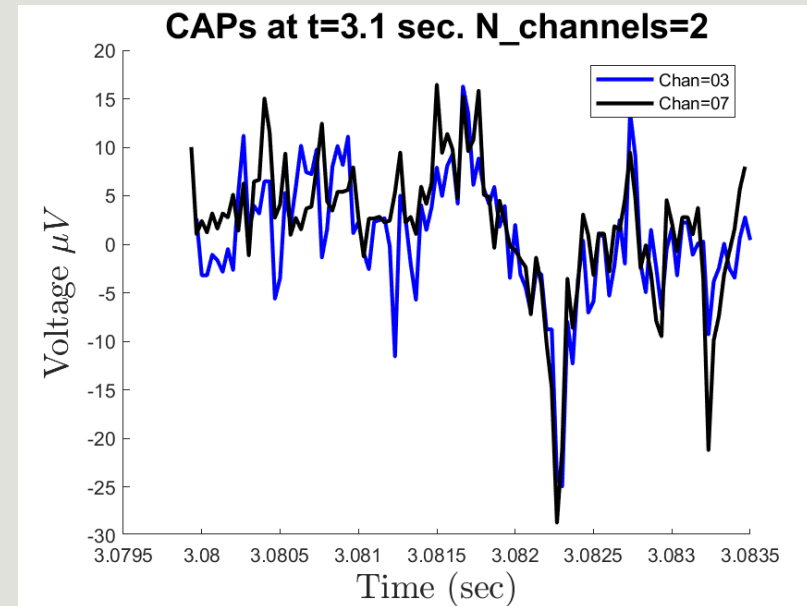
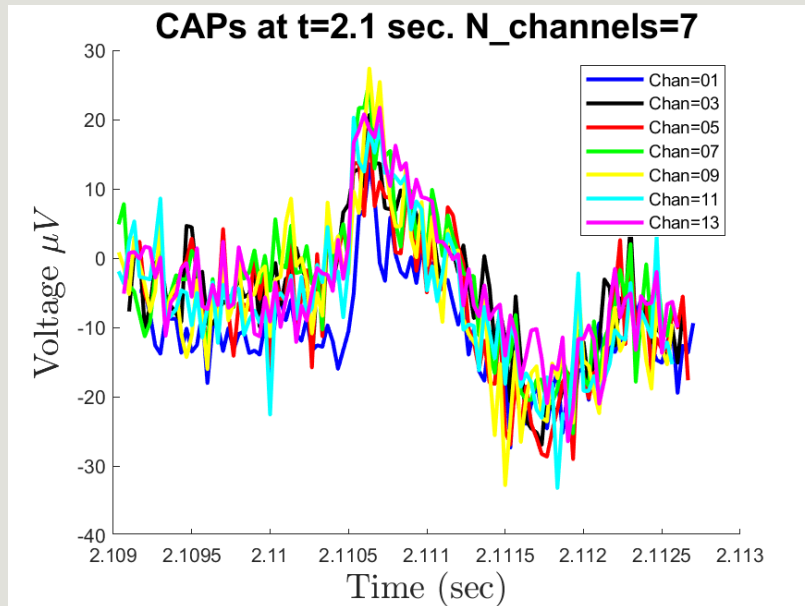
Baseline_10min_LPS_10min_KCl_10min_210617_103421

Comparing CAPs From Different (7) Channels



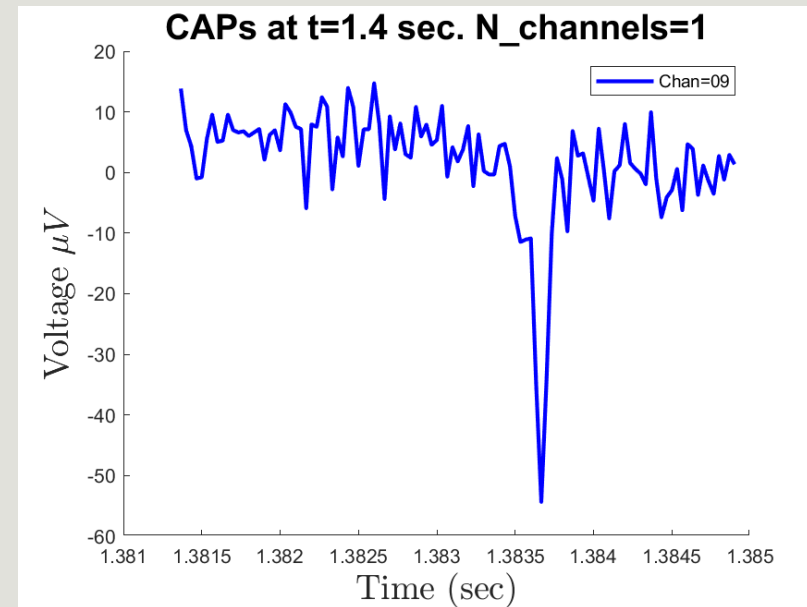
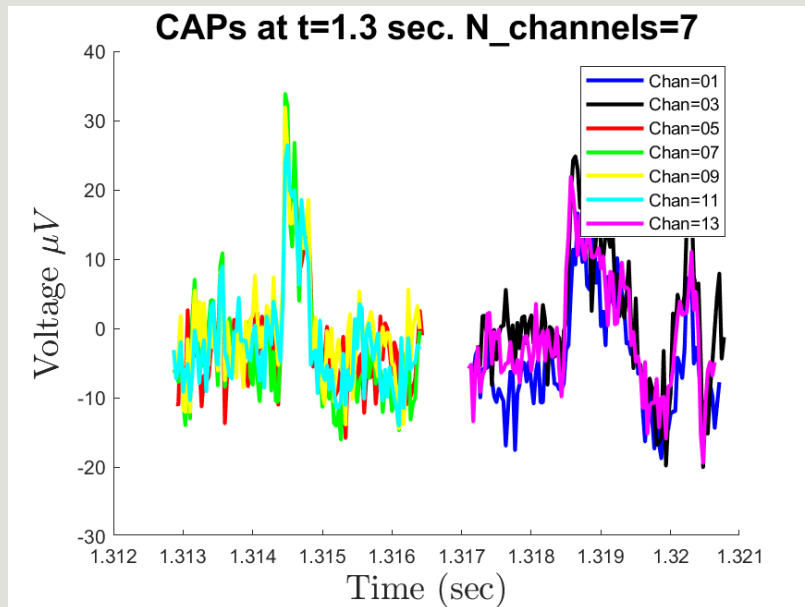
- Specified time, t .
- Find the channel with a CAP closest in time to t , denote : $t_{closest}$.
- All Channels with a CAP within 5 ms from $t_{closest}$ is plotted.

Comparing CAPs From Different (7) Channels



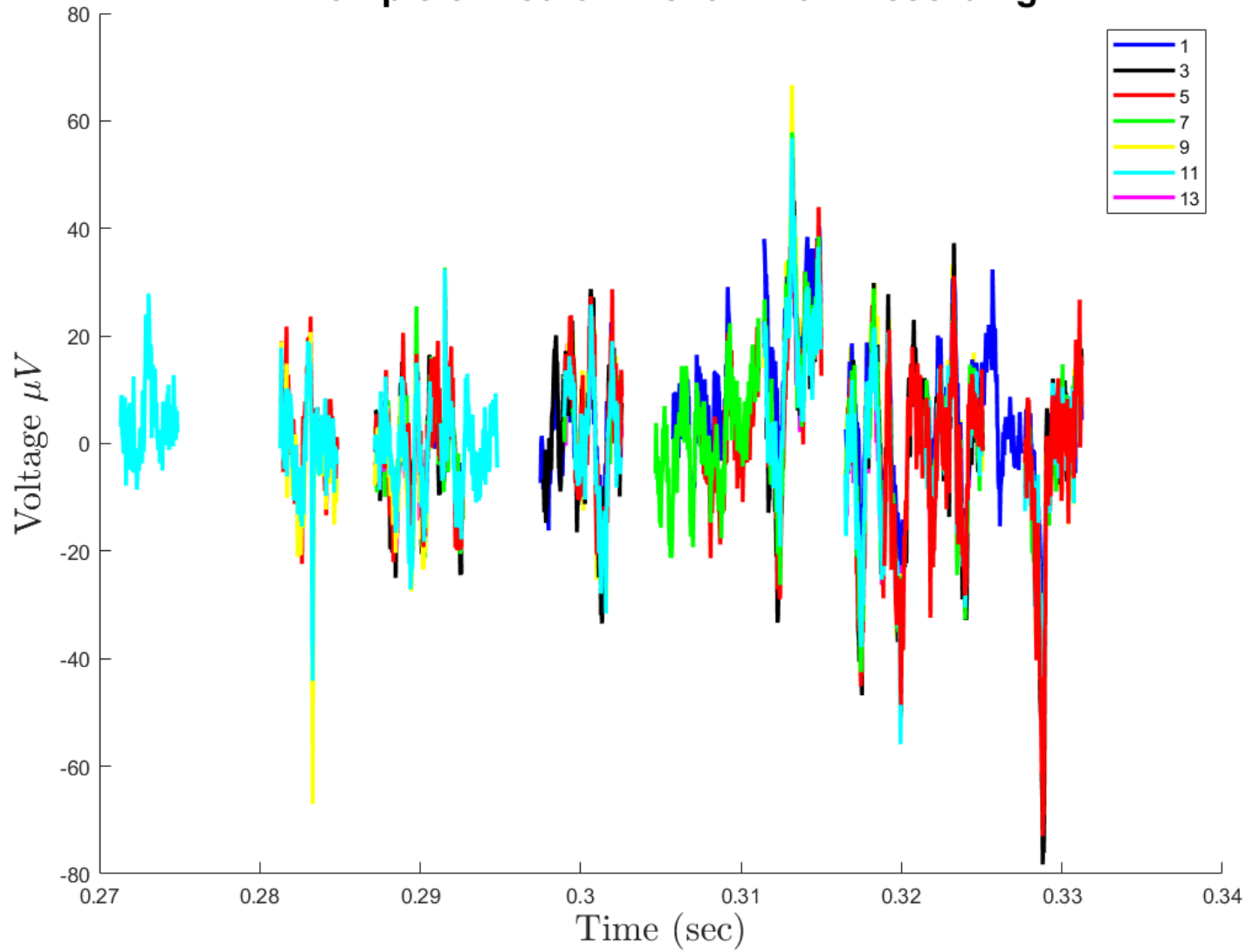
- Specified time, t .
- Find the channel with a CAP closest in time to t , denote : t_{closest} .
- All Channels with a CAP within 5 ms from t_{closest} is plotted.

Comparing CAPs From Different (7) Channels



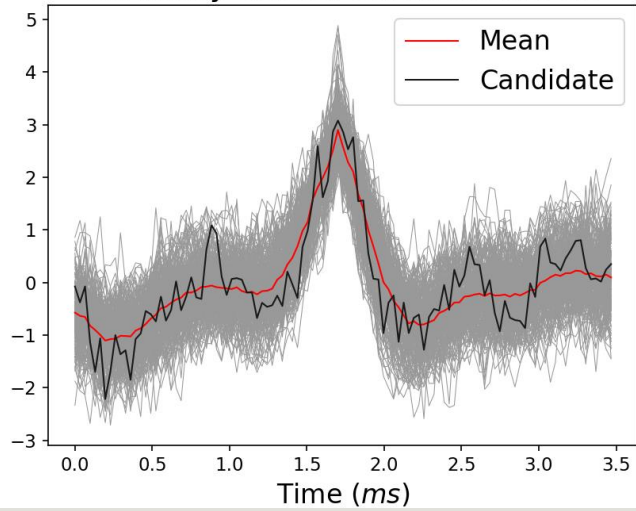
- Specified time, t .
- Find the channel with a CAP closest in time to t , denote : t_{closest} .
- All Channels with a CAP within 5 ms from t_{closest} is plotted.

Example of Neural Event in Raw Recording

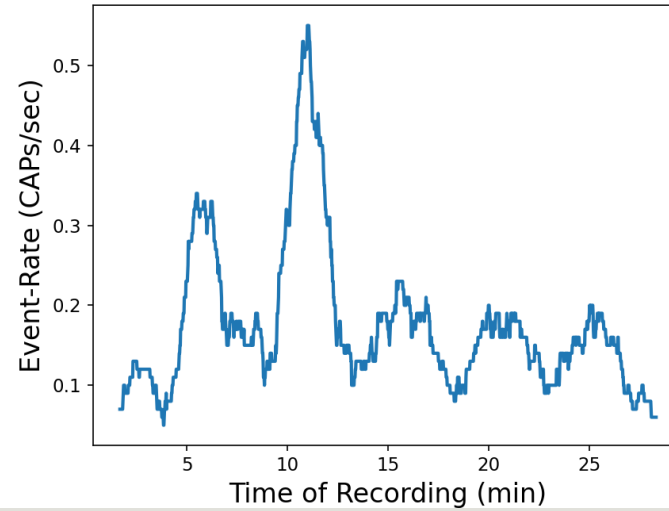


Observed CAPs
for Different
Channels
During First
Part of
Recording

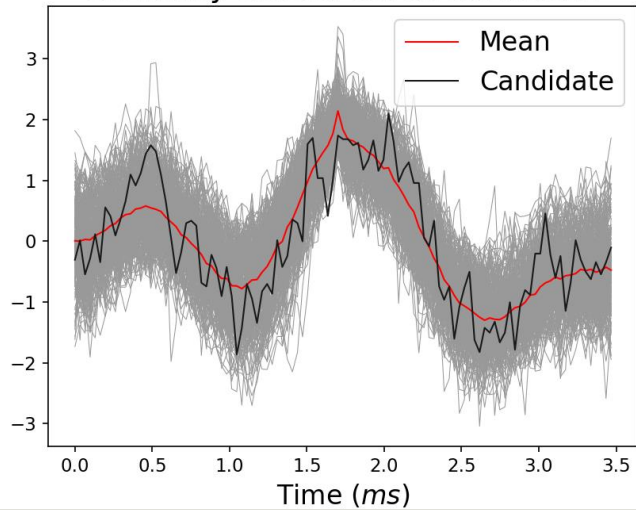
Similarity Cluster Given Candidate



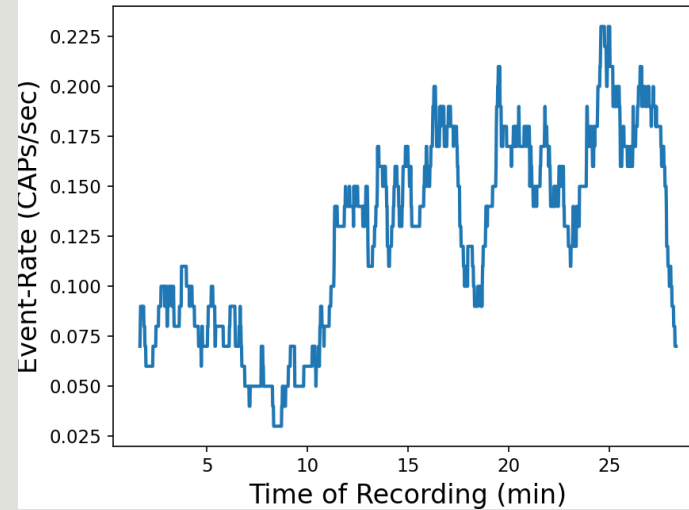
Event-Rate



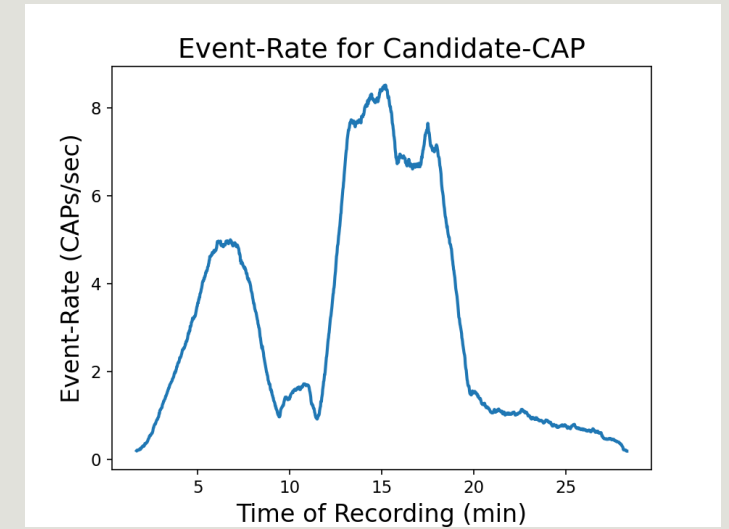
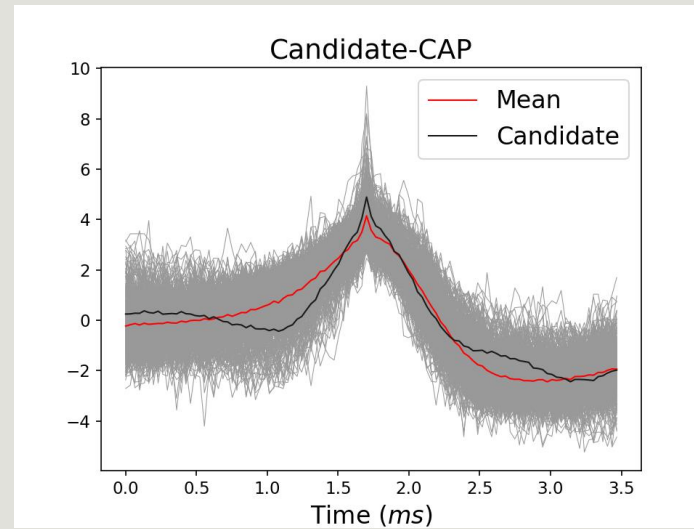
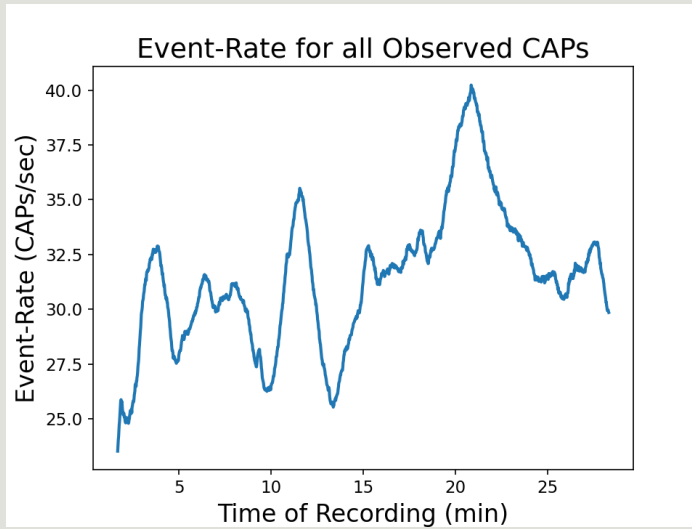
Similarity Cluster Given Candidate



Event-Rate

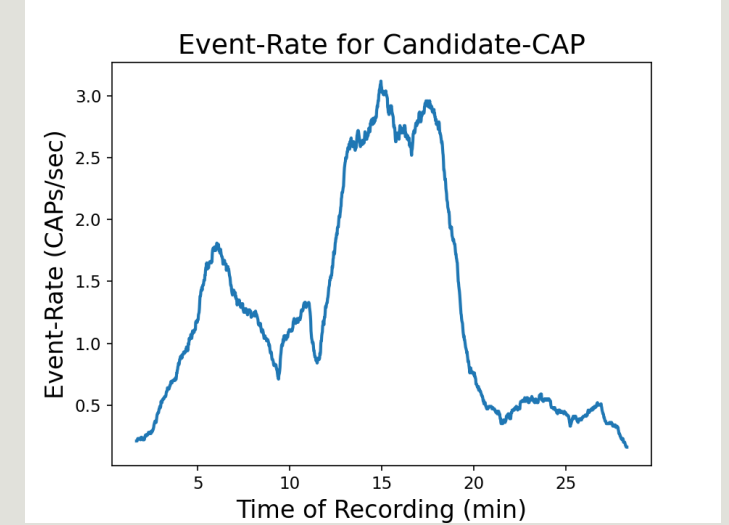
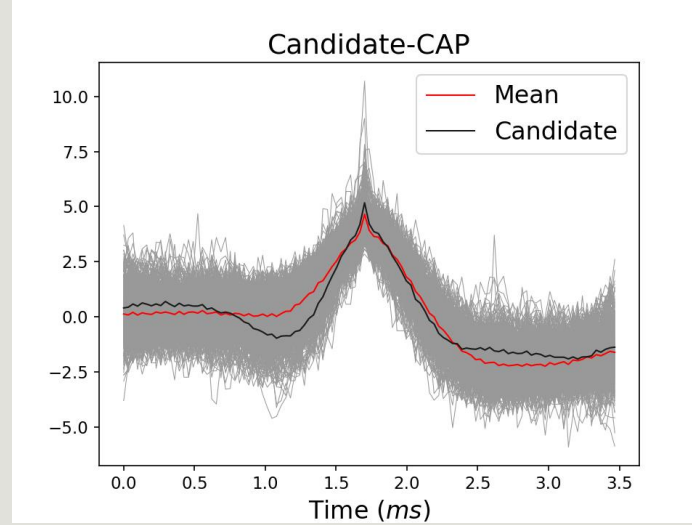
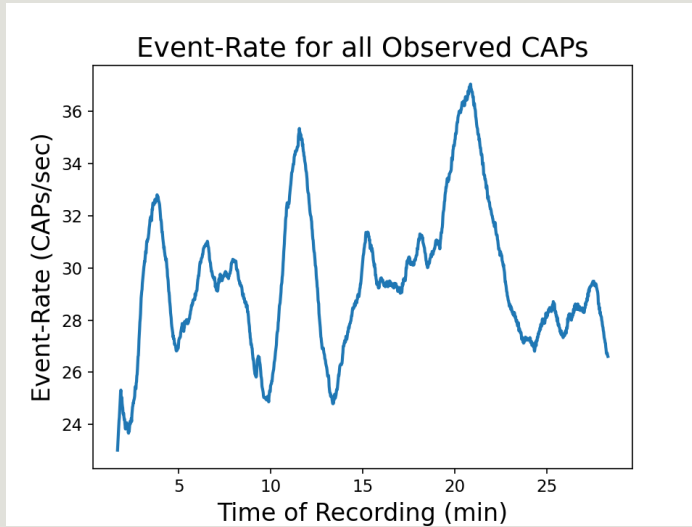


New Data
Example of
occurrence of
waveform shapes



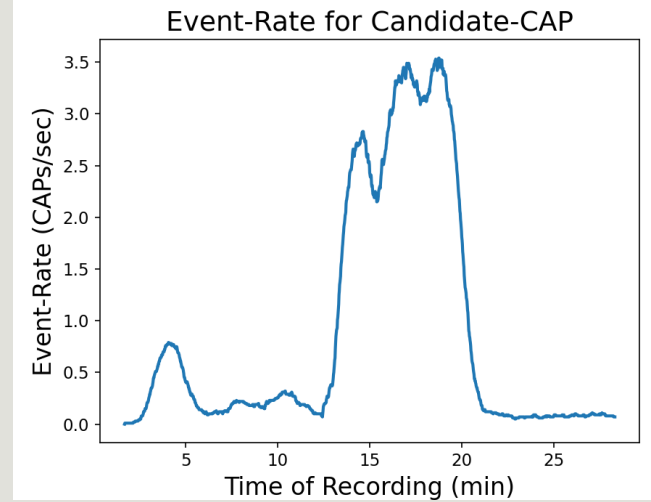
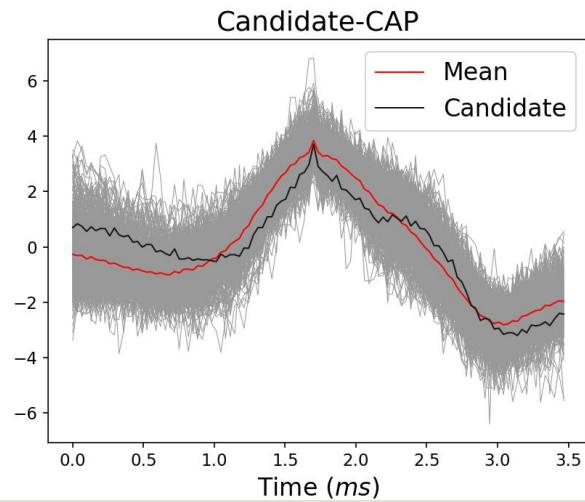
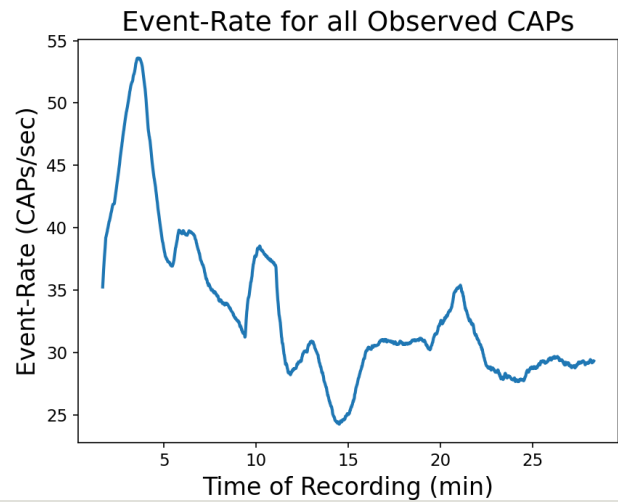
Preliminary Results

Baseline_10min_LPS_10min_KCl_10min_210617_103421-A-003



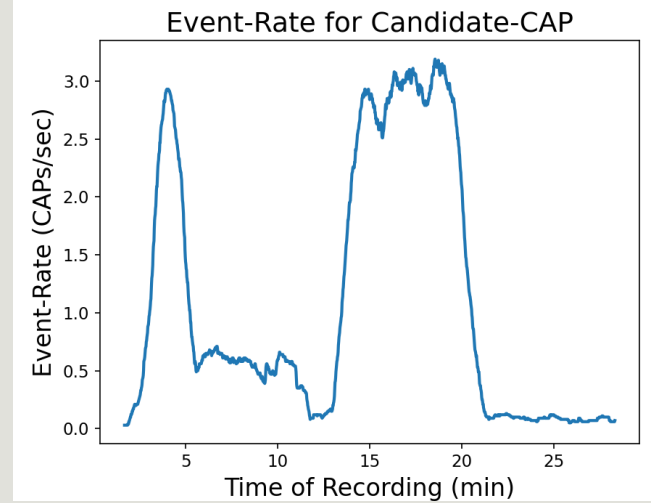
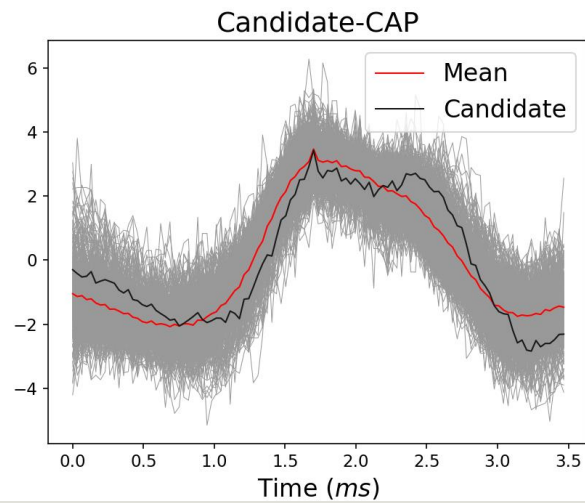
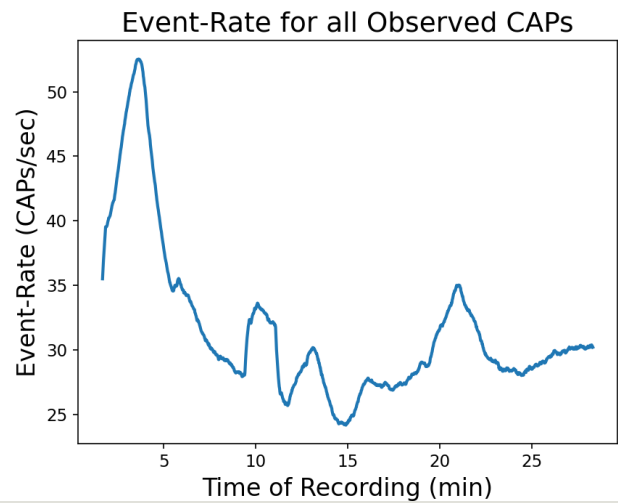
Preliminary Results

Baseline_10min_LPS_10min_KCl_10min_210617_103421-A-005



Preliminary Results

Baseline_10min_LPS_10min_KCl_10min_210617_142447-A-015

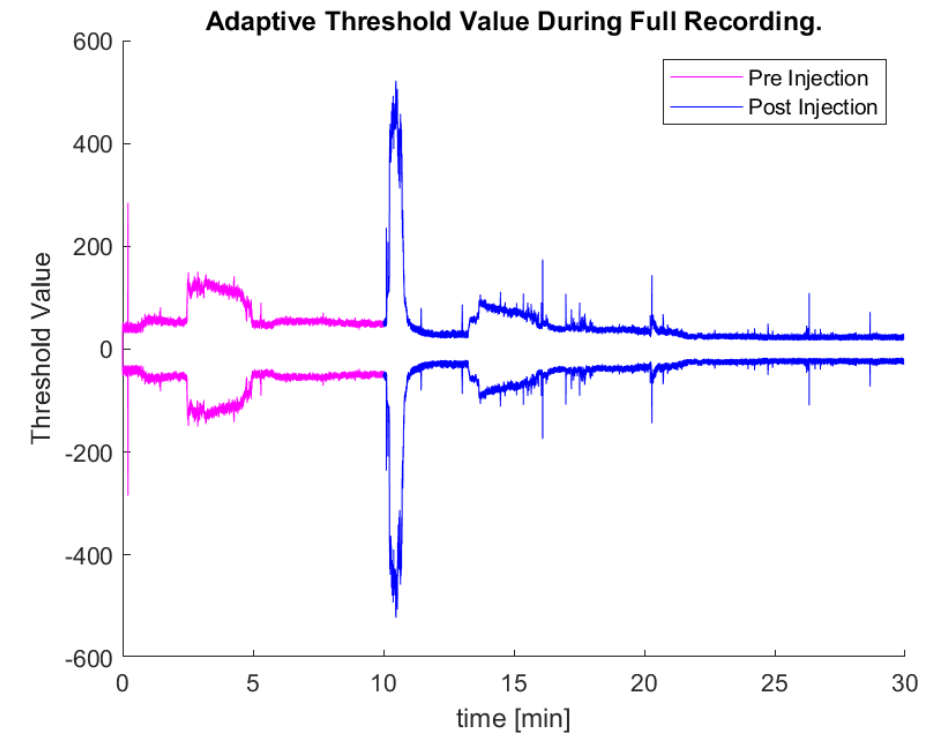
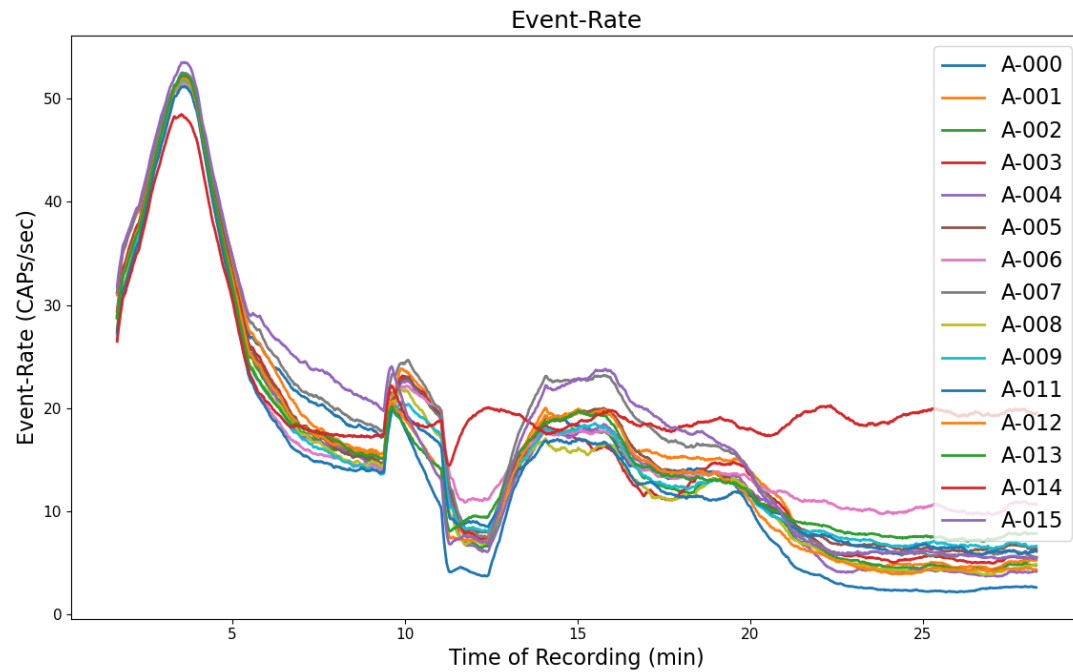


Preliminary Results

Baseline_10min_LPS_10min_KCl_10min_210617_142447-A-007

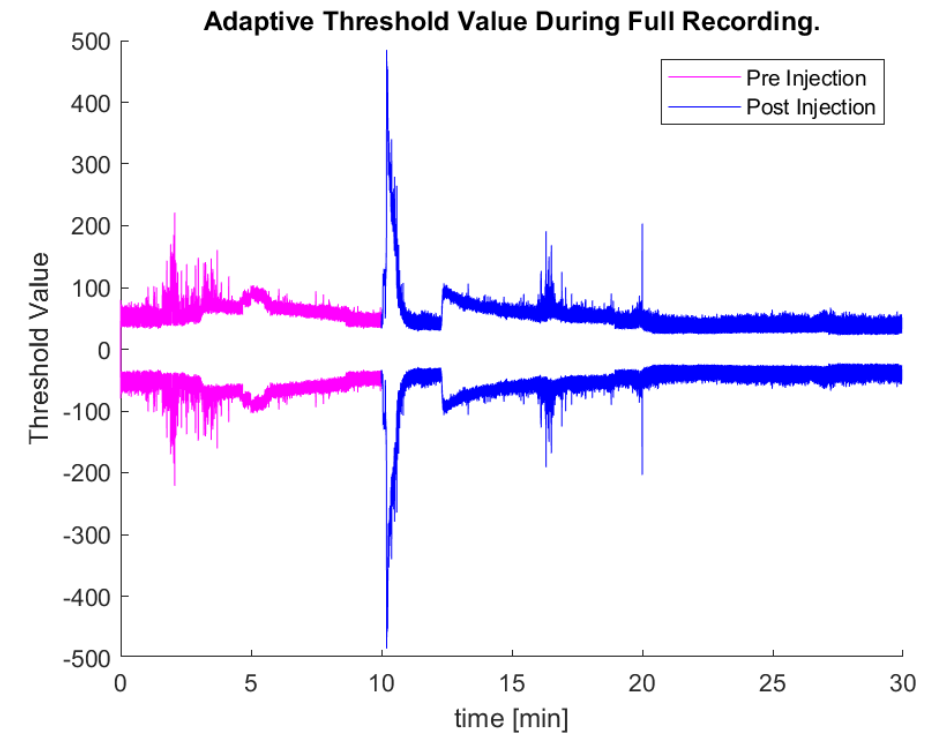
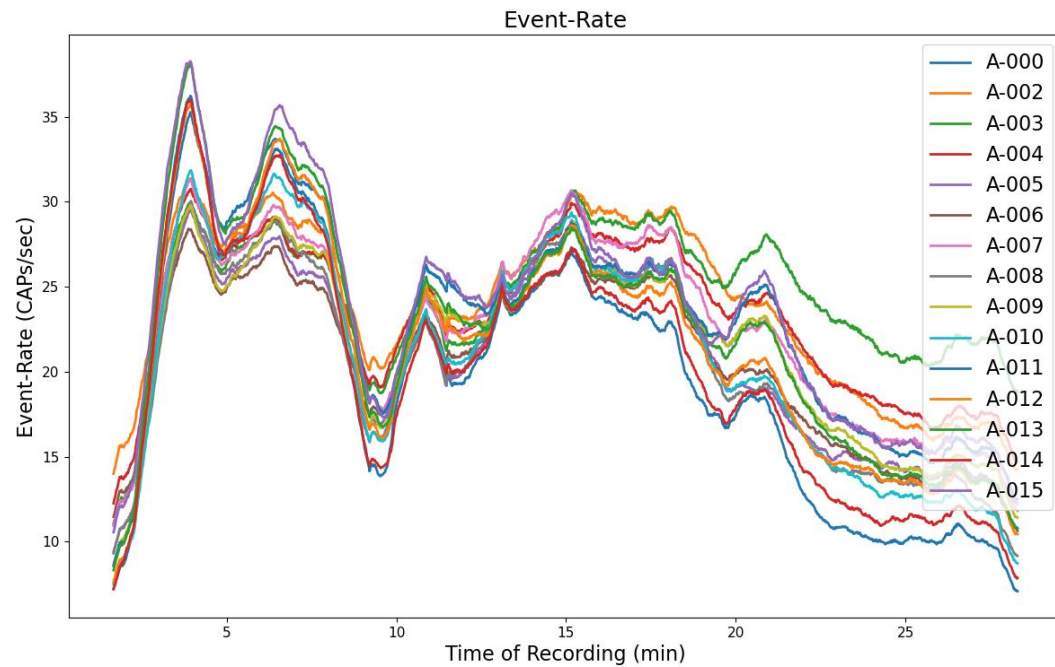
How to proceed?

- Duration of recording-periods, pre/post injection.
- Other sources of interference to take into consideration?
- Making use of all Channels:
 - Instead of using single electrode signal to describe a CAP – use all 16?
 - E.g. Only consider CAPs that are observed in at least 7/15 channels
 - Estimate propagation-speed / direction?
- Regarding Parameters:
 - How large/small CAP amplitude - thresholds are reasonable?



Duration of recording-periods, pre/post injection -- Longer Recording times?

Baseline_10min_LPS_10min_KCl_10min_210617_142447



Duration of recording-periods, pre/post injection -- Longer Recording times?

Baseline_10min_LPS_10min_KCl_10min_210617_103421