# Setting spike boundaries: The effectiveness of three neuronal spike validation methods

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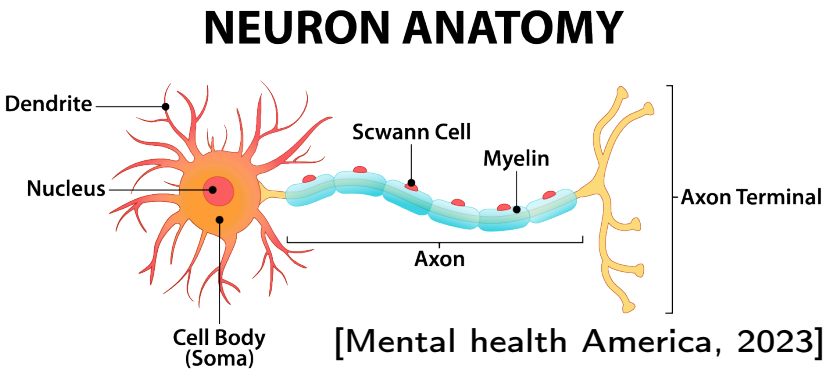
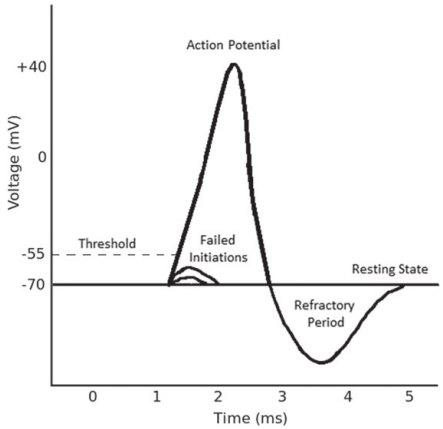
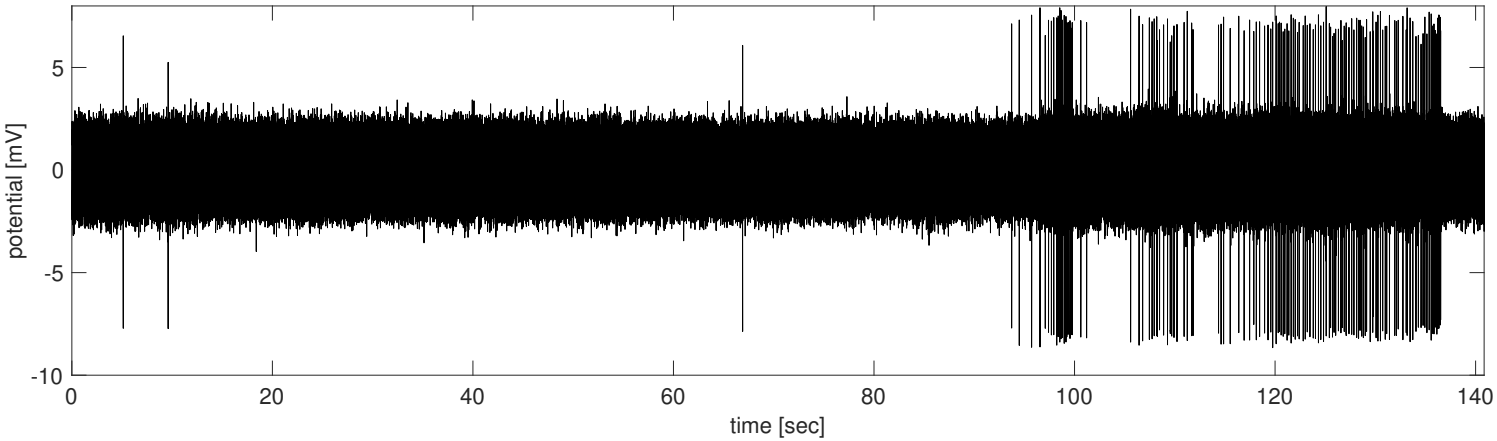
# Neural spikes




[Mental health America, 2023]

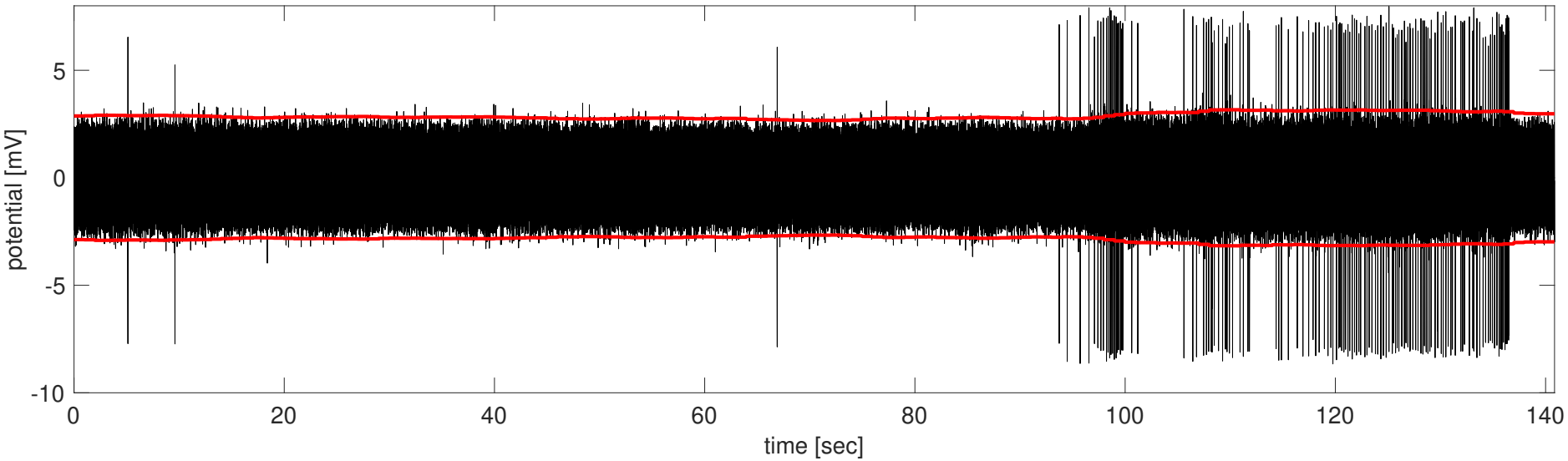



[Ajayan and James, 2021]



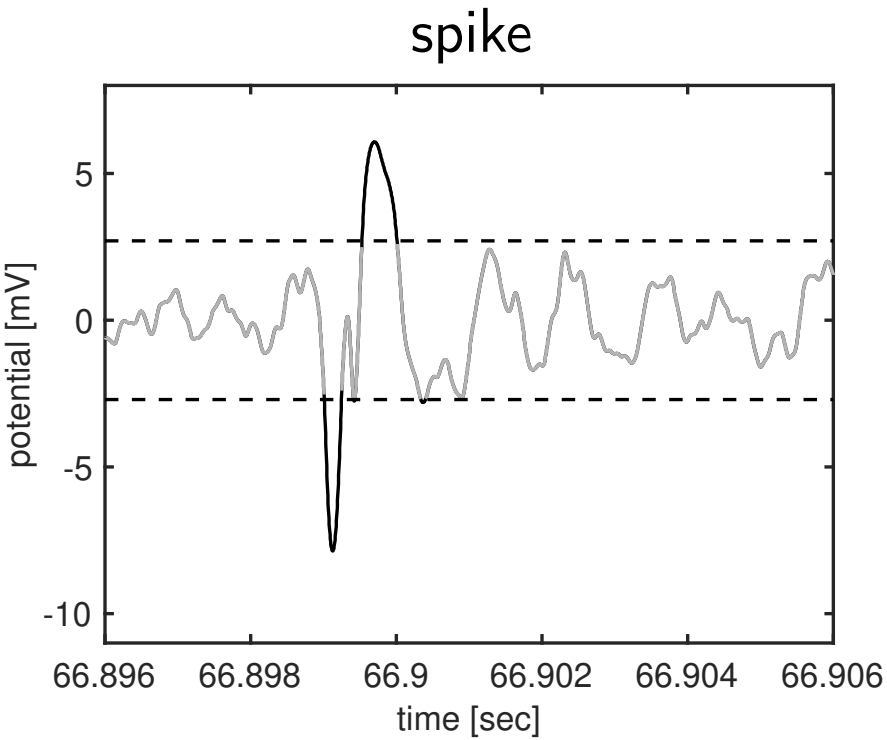

- neuron spiking activity $\rightarrow$ identification + treatment of brain diseases:
  - epilepsy, Parkinson's disease, ...
  - depression, psychiatric abnormalities, memory loss, ...

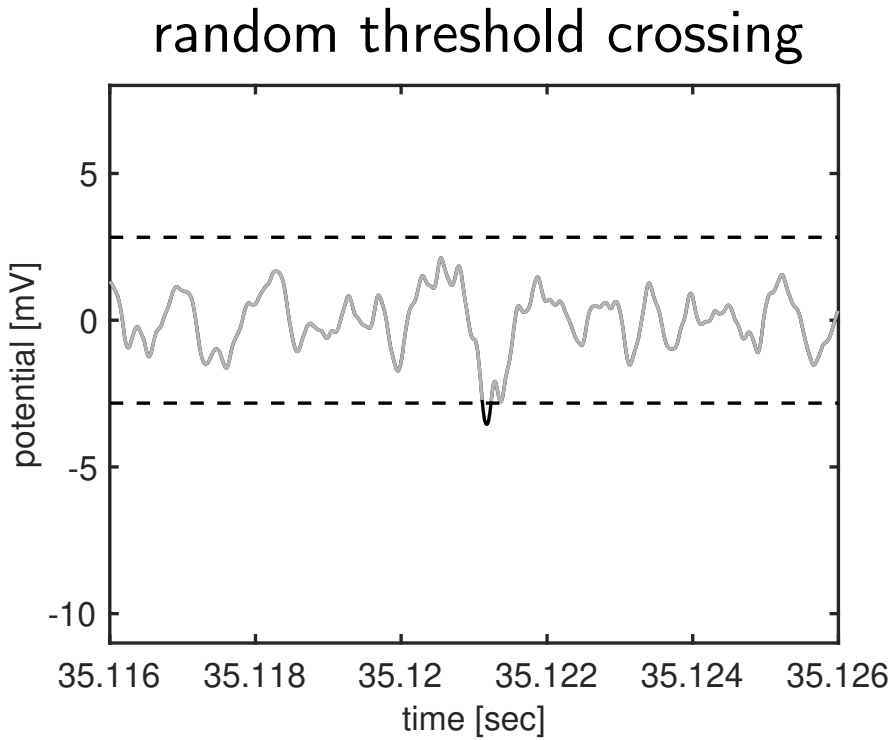
# How to detect spiking activity of a neuron?




- **AdaBandFlt** [Biffi et al., 2010] $\rightarrow$ adaptive thresholding method
  - 1 = threshold crossing  0 = no threshold crossing
  - indicator vector (0,0,0,0,0,0,1,1,1,1,0,0,...)

# Which threshold crossings form the same spike?



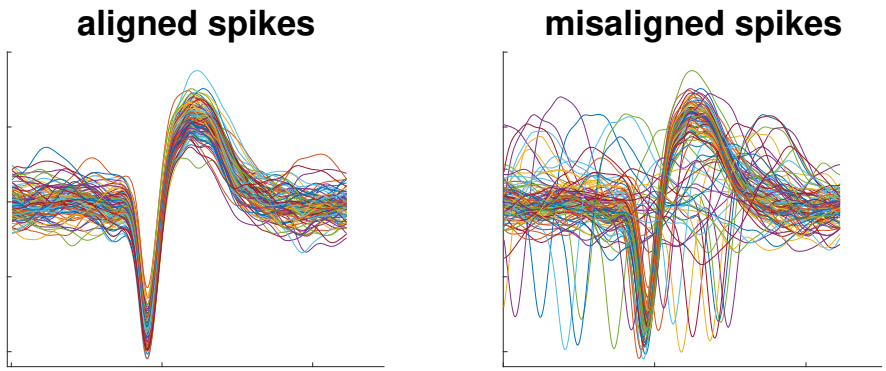

$$\text{spike} = x \pm K$$

- x = "spike center", different definitions among methods
- $K \approx 1$ ms
- refractory period $\rightarrow$ distance between two spike centres $> \theta_{refrac}$

# Spike validation methods

- method of Wagenaar [Wagenaar et al., 2005, Biffi et al., 2010]
- method of Toosi [Toosi et al., 2021]
- method of Nenadic [Nenadic and Burdick, 2005]

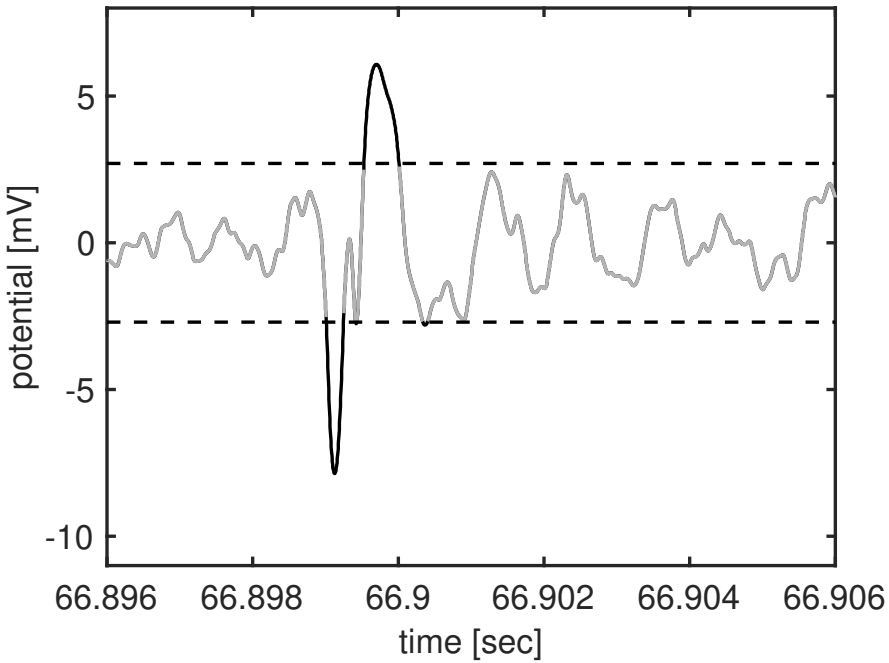
- comparison focused on:

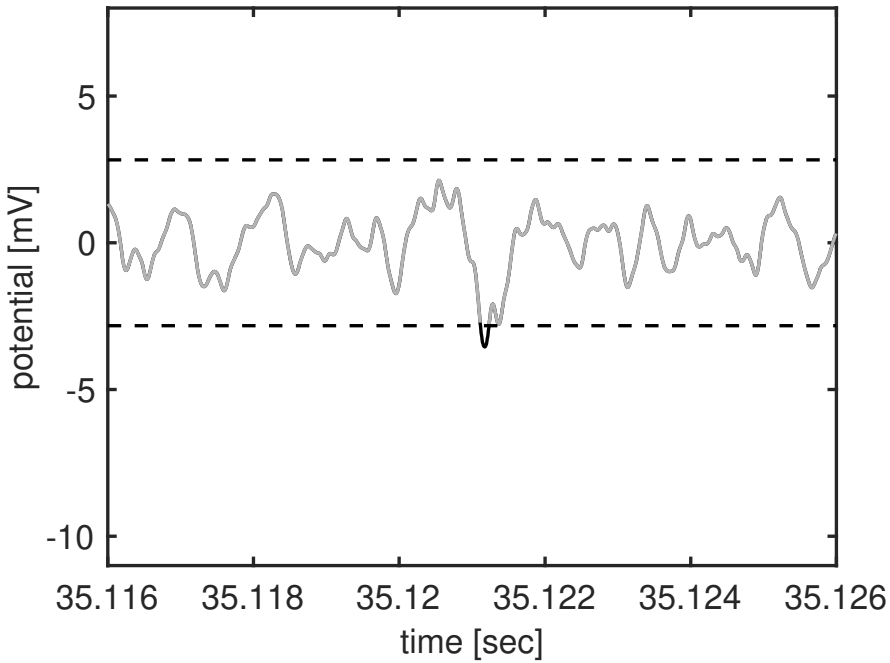



1. spikes alignment
2. ability to distinguish an actual spike from a random threshold crossing
3. sensitivity to presence of noise
4. distance between actual spike centre and detected spike centre ($mD$)

# Spike validation: method of Wagenaar

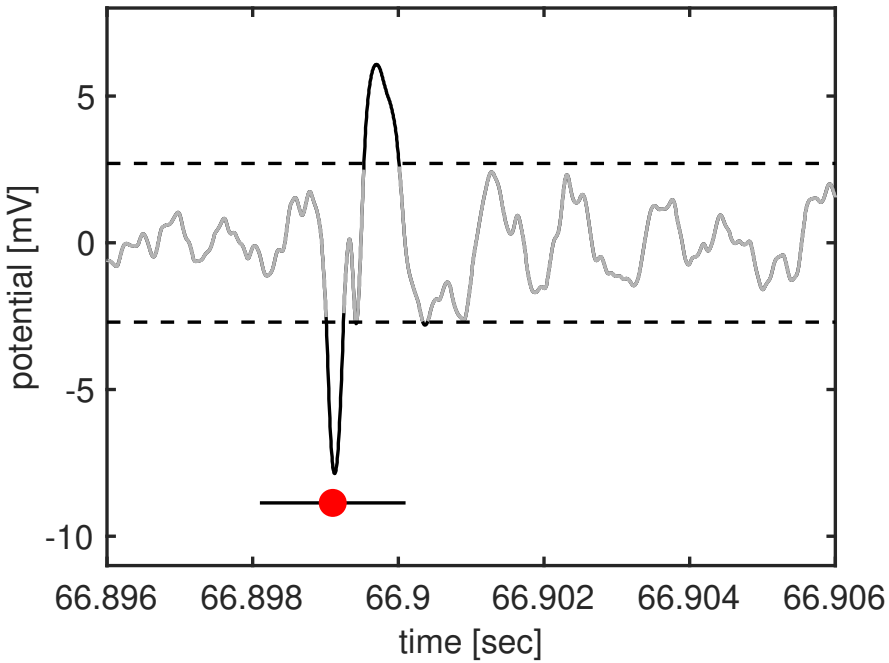
- **input:** indicator vector + original electrophysiological signal
- a threshold crossing = spike center if:

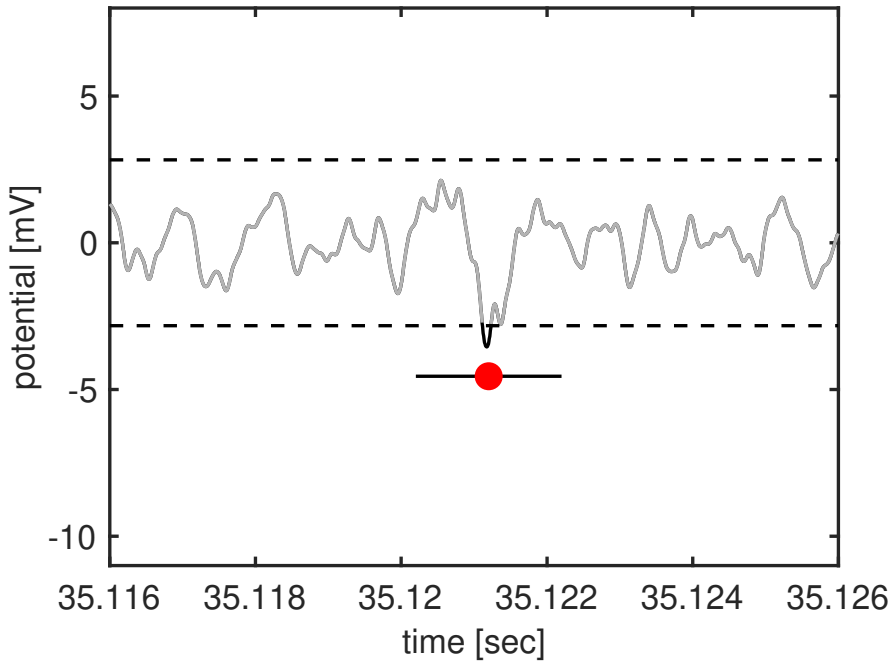


# Spike validation: method of Wagenaar

- **input:** indicator vector + original electrophysiological signal
- a threshold crossing = spike center if:
  - C1: it forms the highest peak of either polarity over the $\pm 1$ ms interval $\Rightarrow$ **spikes are aligned to their dominant extremum**
  - C2: its amplitude $> 2 \times$ amplitude of the $2^{nd}$ highest peak with the same polarity on this interval
  - C3: $|x_i - x_{i+1}| > \theta_{refrac}$



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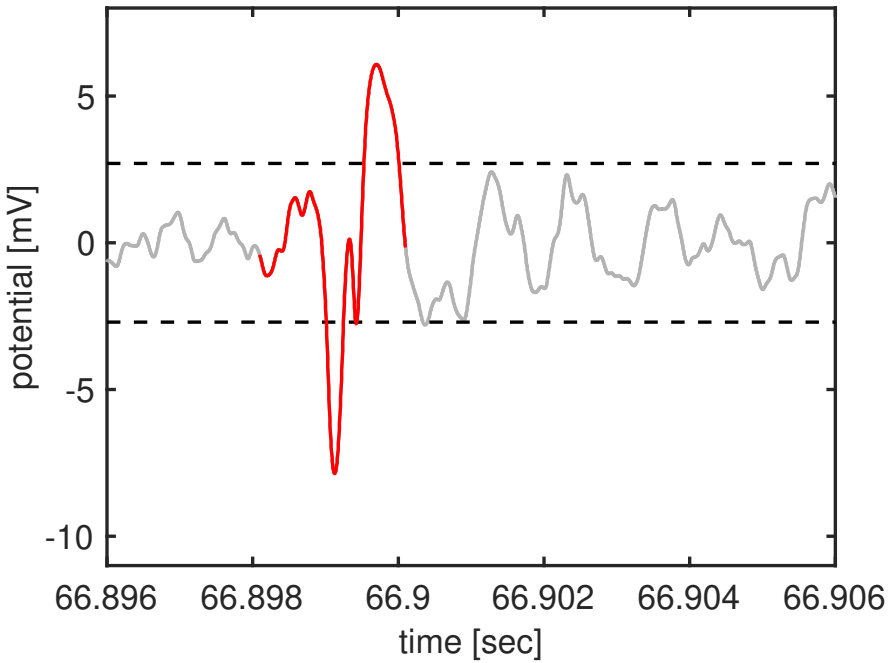
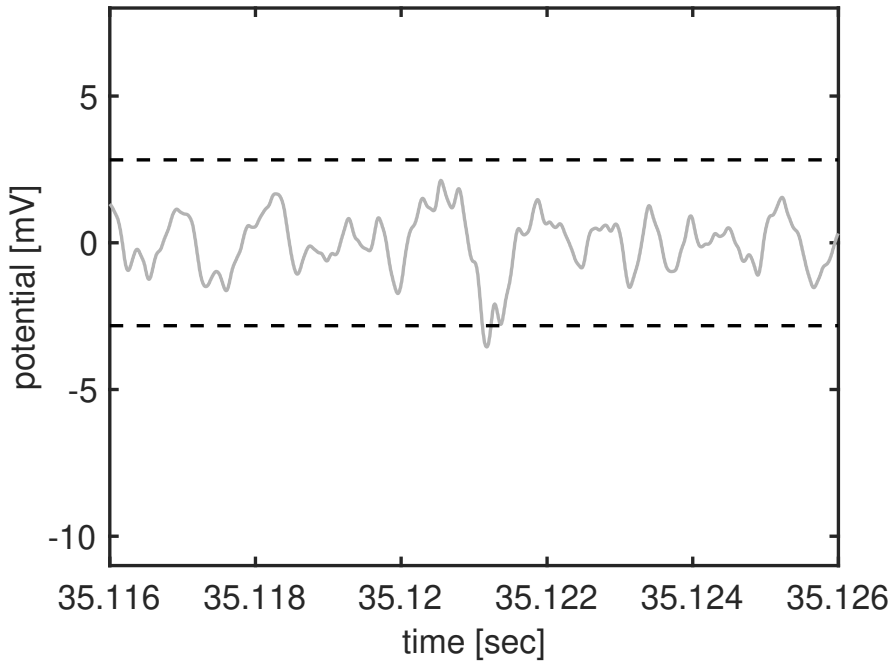
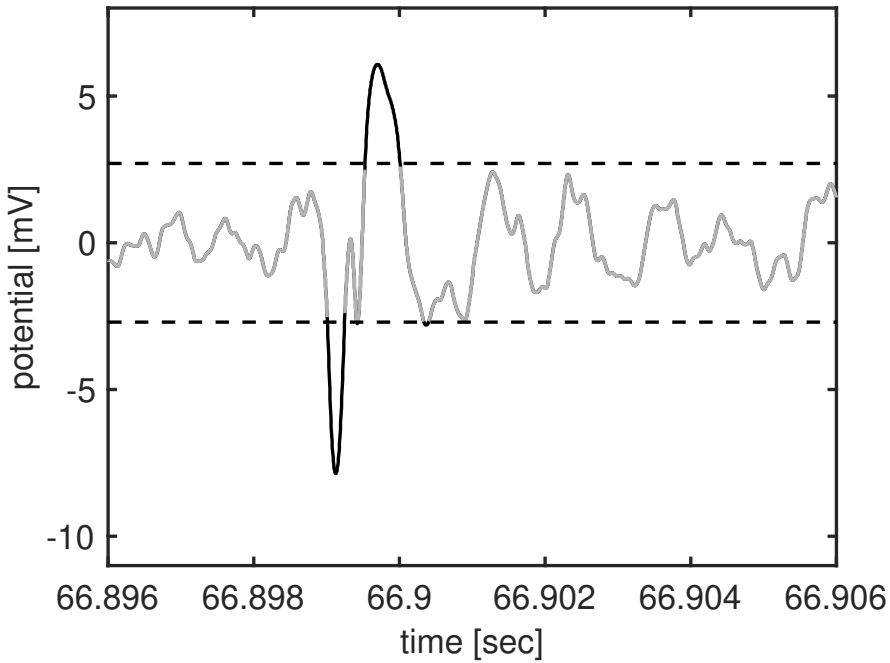


# Spike validation: method of Toosi

- [Toosi et al., 2021]



# Spike validation: method of Toosi

- [Toosi et al., 2021]

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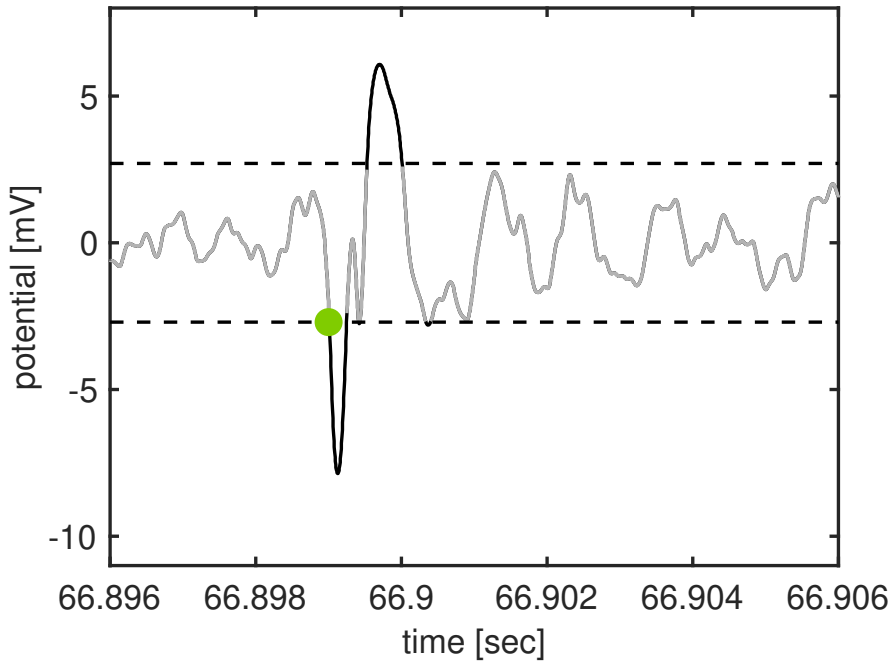

# Spike validation: method of Toosi

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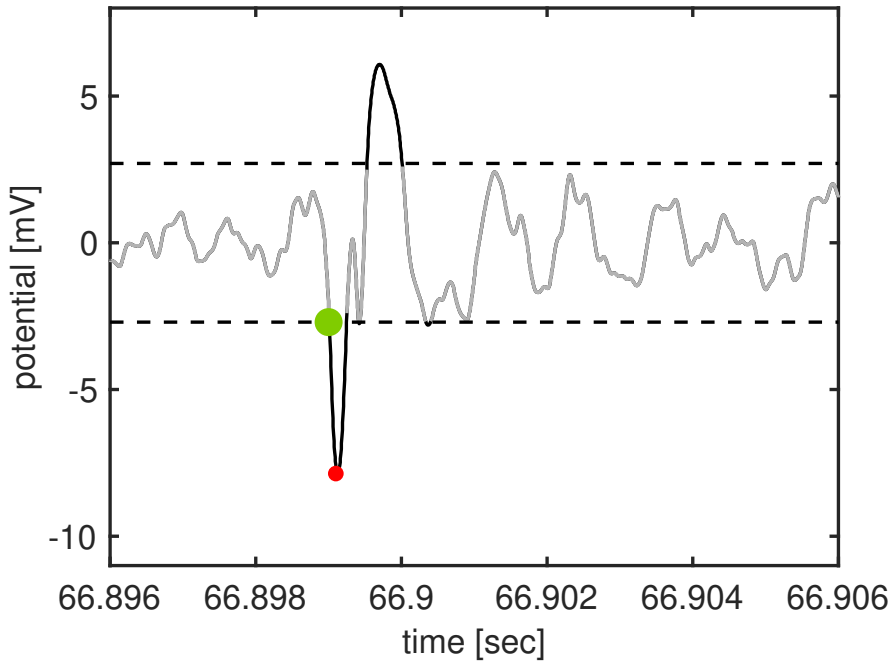
1. find the first threshold crossing
2. spike center $x$ = local minimum to the right of



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1. find the first threshold crossing
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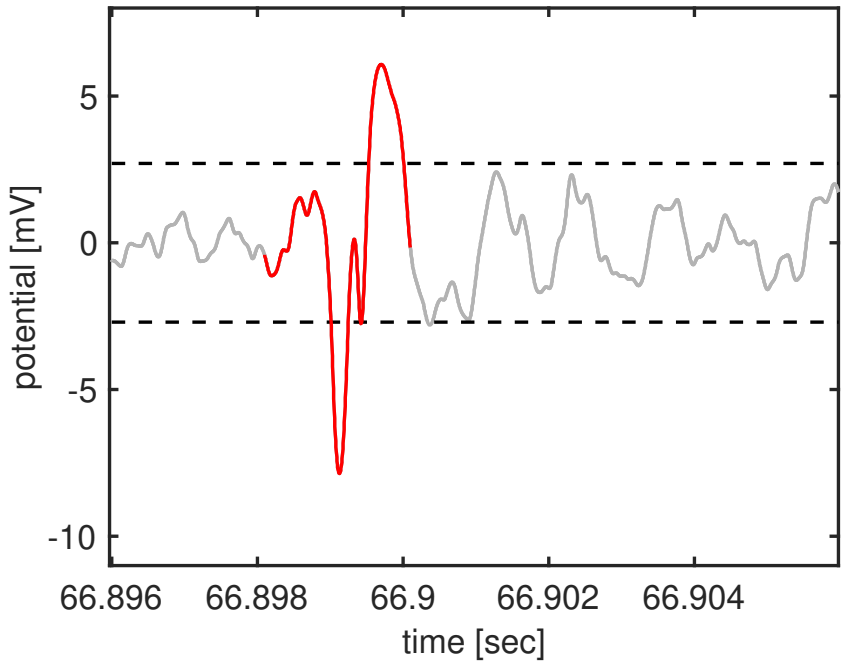
3. spike: $x \pm K$ ms



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1. find the first threshold crossing
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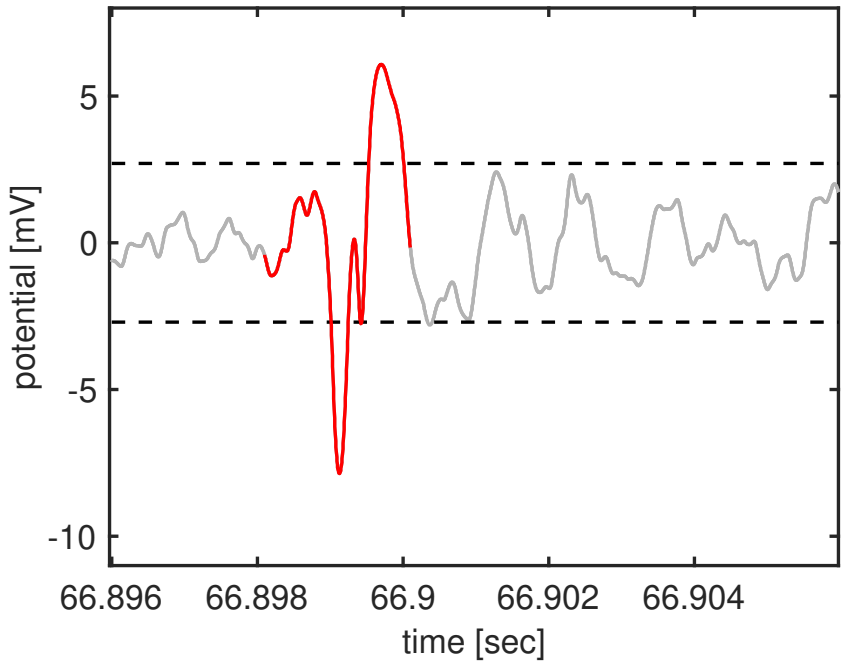

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2. spike center $x$ = local minimum to the right of
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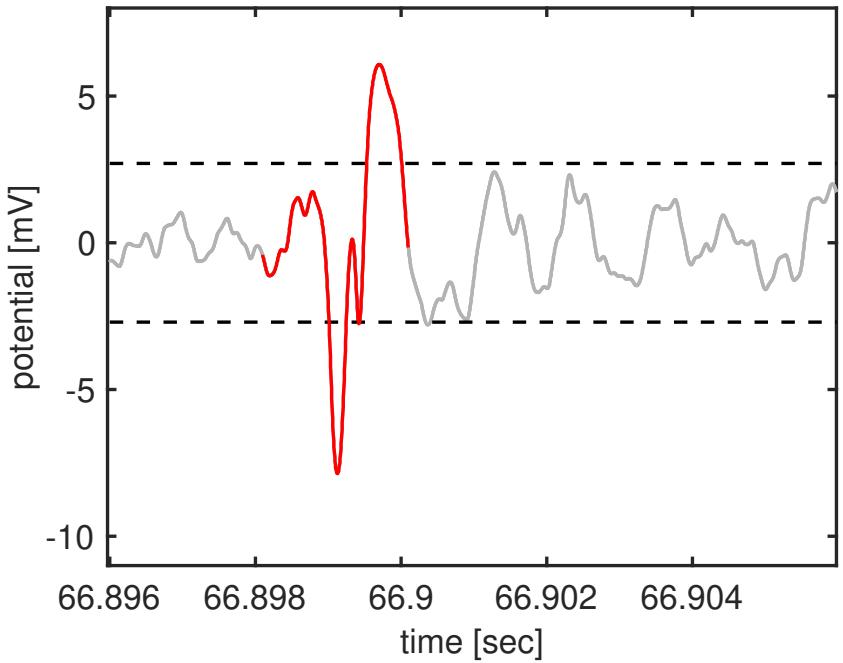
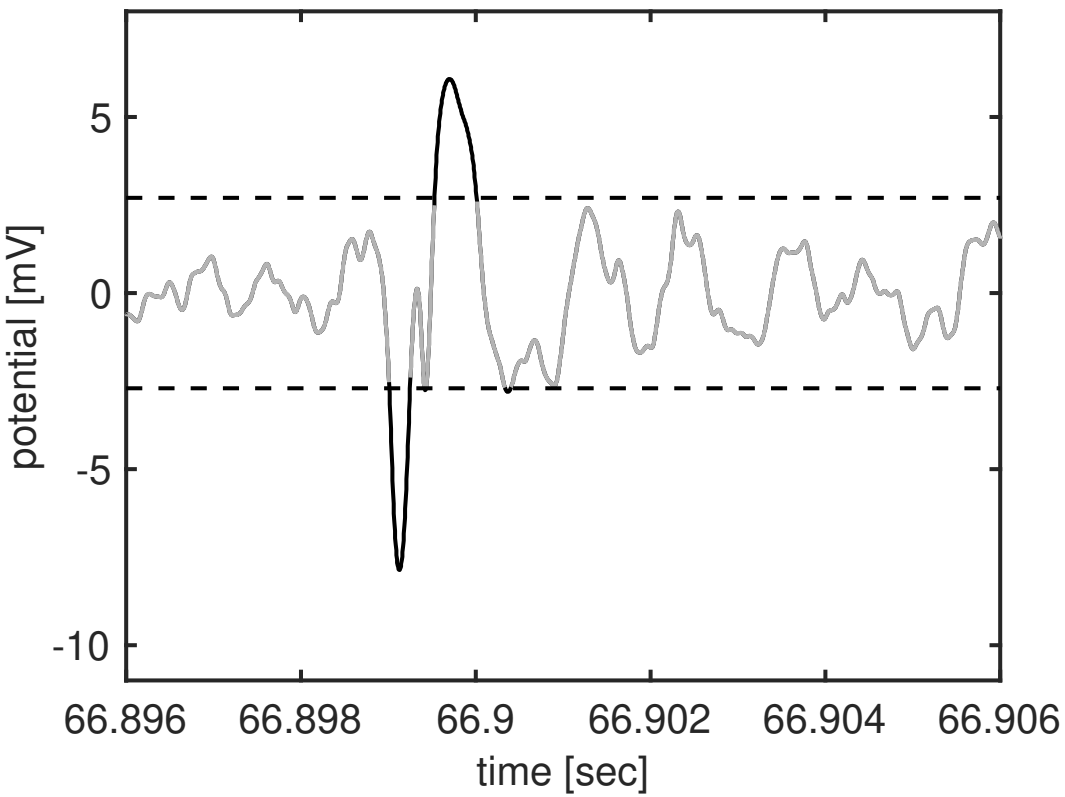
- repeat steps 1.-4. with the next (not discarted) threshold crossing

- **spikes are aligned to their global minimum**



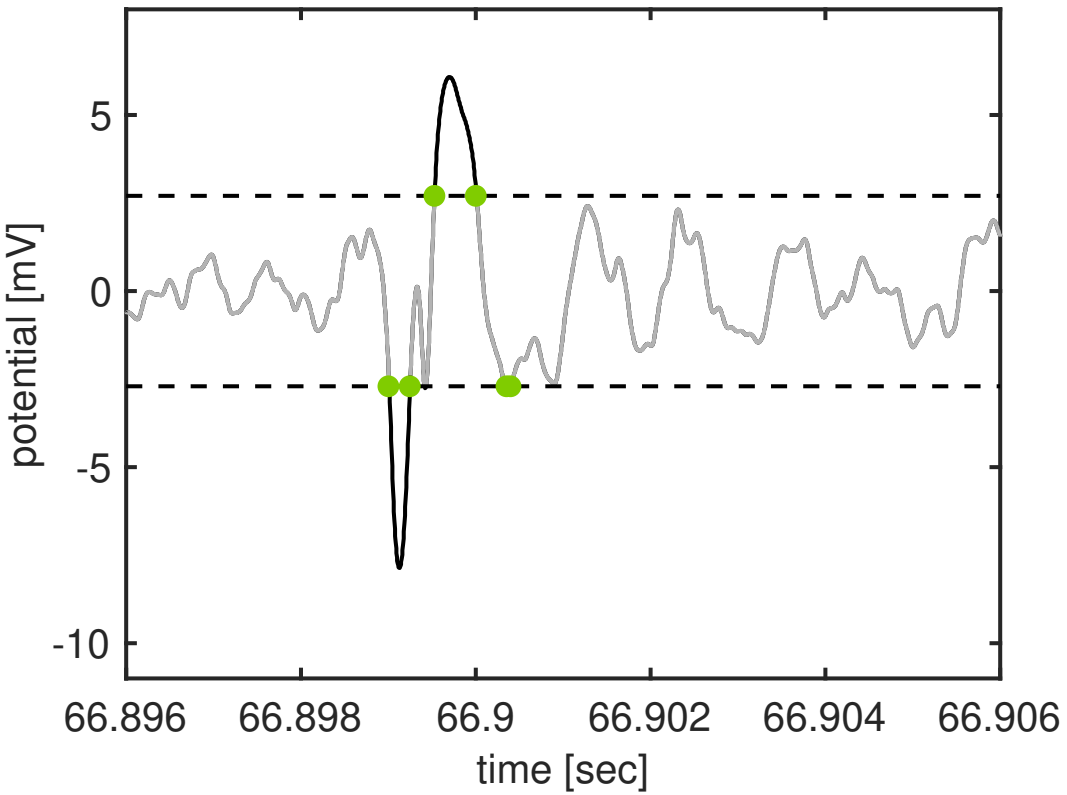
# Spike validation: method of Nenadic

- [Nenadic and Burdick, 2005]



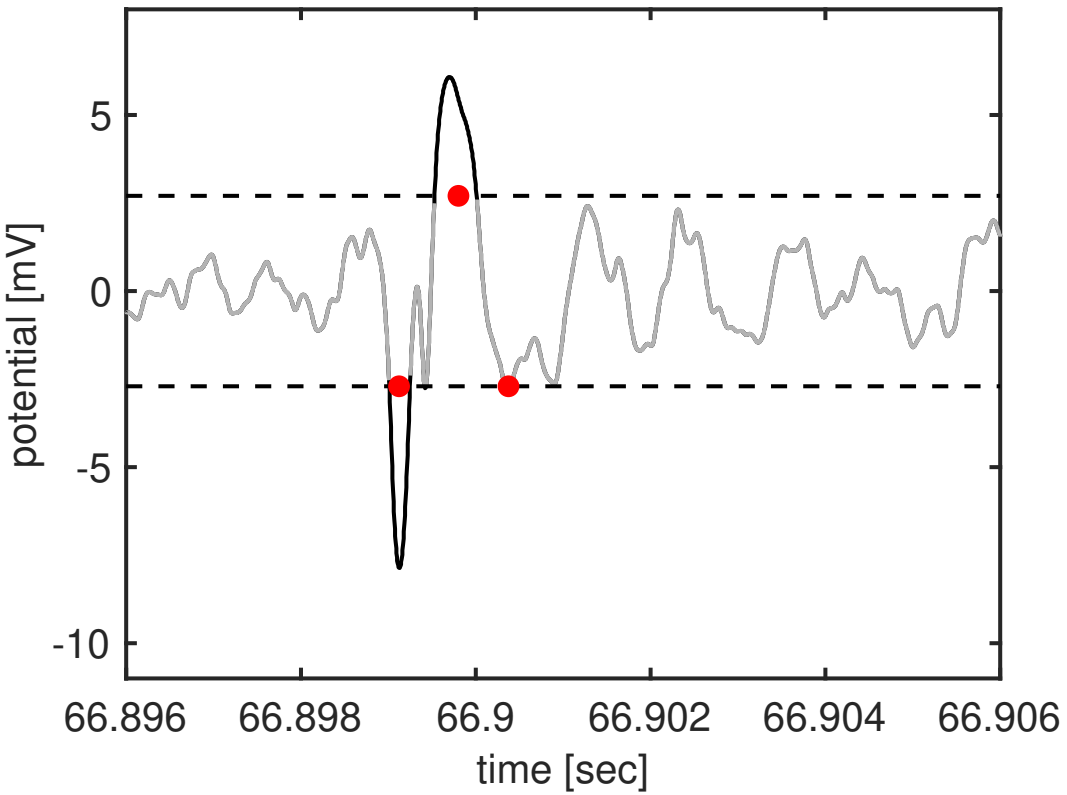
# Spike validation: method of Nenadic

- [Nenadic and Burdick, 2005]
- indicator vector - 1 = threshold crossing, 0 = no threshold crossing
- $0 \rightarrow 1 \quad \Rightarrow$ possible spike starting point
- $1 \rightarrow 0 \quad \Rightarrow$ possible spike ending point



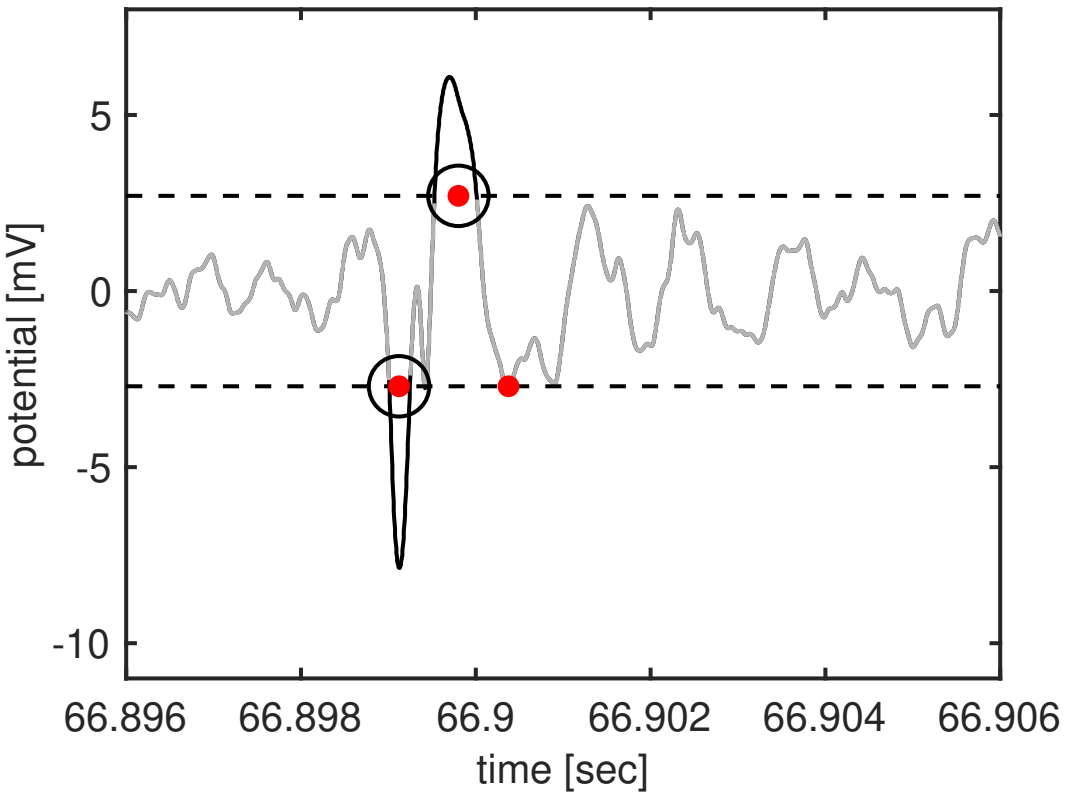
# Spike validation: method of Nenadic

- [Nenadic and Burdick, 2005]
- candidate spike centre $x$
  = mean between consecutive starting and ending points



# Spike validation: method of Nenadic

- [Nenadic and Burdick, 2005]
- consecutive candidate spike centres $x_i$ and $x_{i+1}$ are analysed sequentially



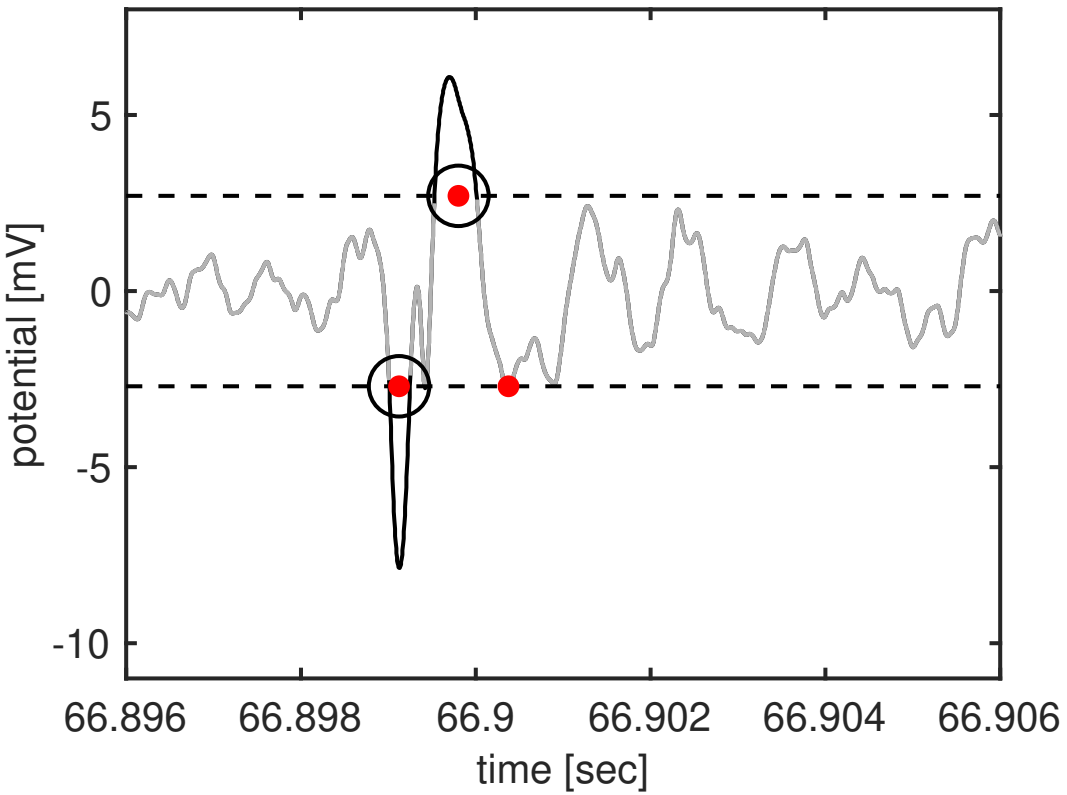
# Spike validation: method of Nenadic

- [Nenadic and Burdick, 2005]

1. $|x_i - x_{i+1}| \leq \theta_{merge}$

$\Rightarrow$ $x_i$ and $x_{i+1}$ represent one spike

$\Rightarrow$ new candidate spike center $x_i^{new} = \left\lceil \frac{x_i + x_{i+1}}{2} \right\rceil$



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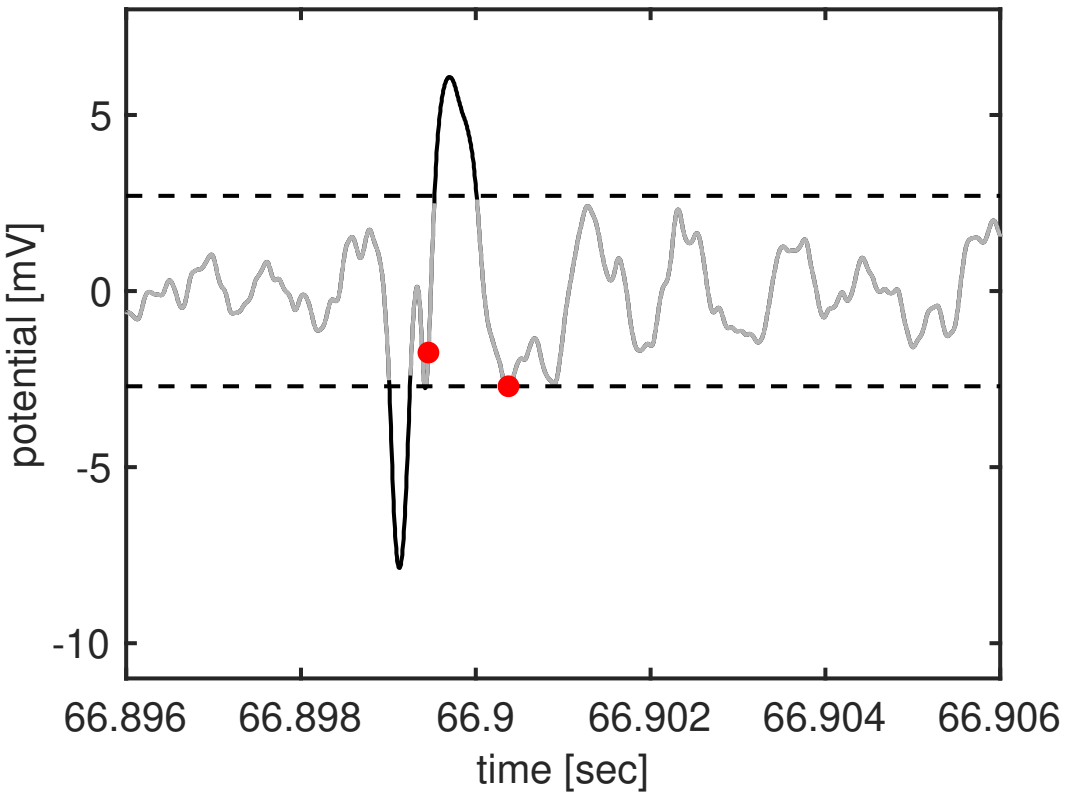
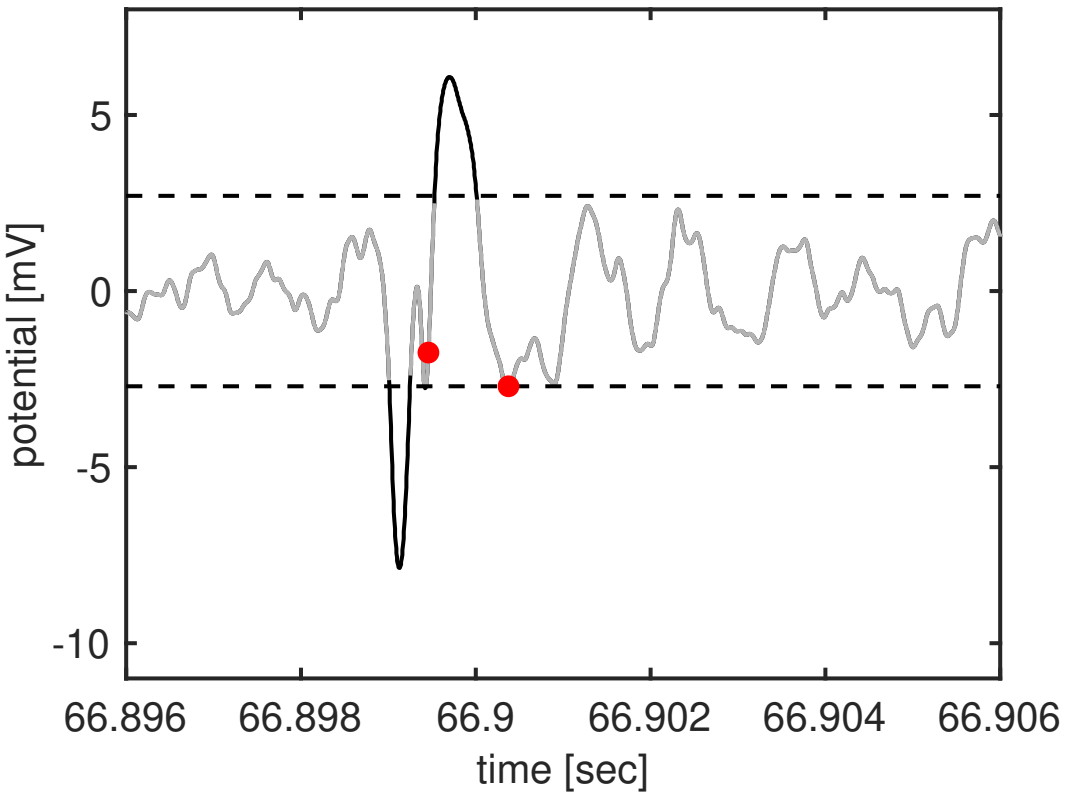


# Spike validation: method of Nenadic

- [Nenadic and Burdick, 2005]

2. $|x_i - x_{i+1}| > \theta_{merge}$ and $|x_i - x_{i+1}| \leq \theta_{refrac}$

$\Rightarrow$ $x_{i+1}$ is discarded



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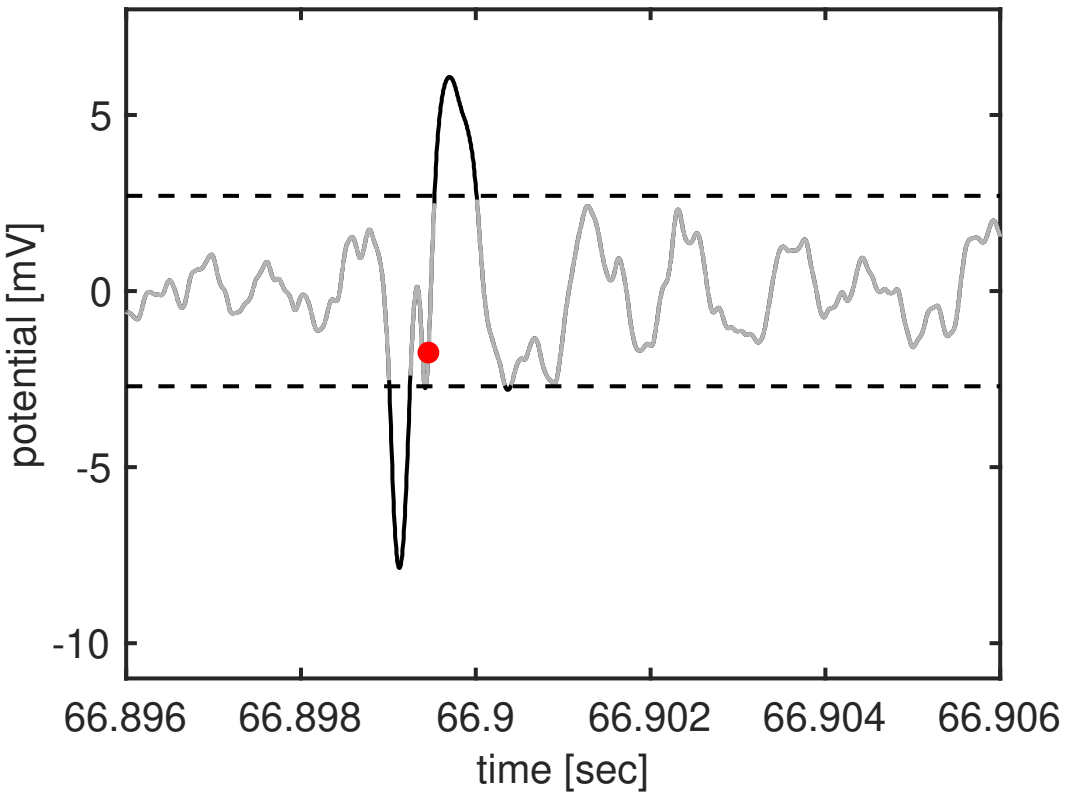

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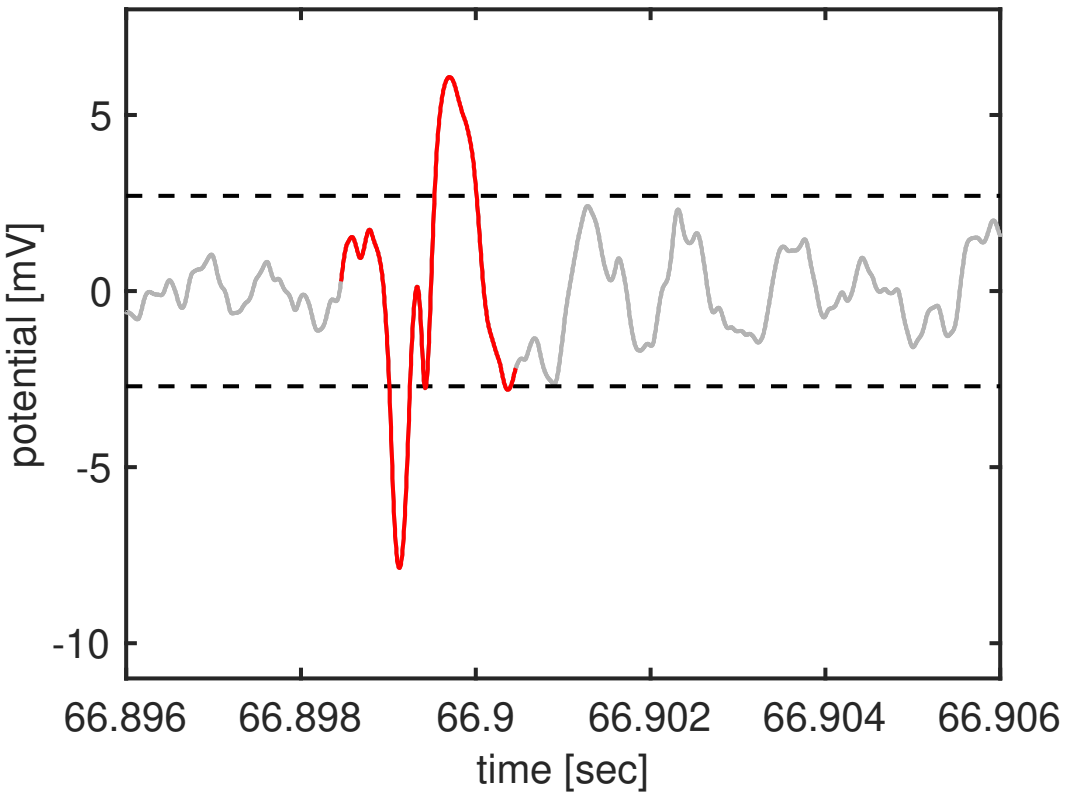


# Spike validation: theoretical comparison

| | Wagenaar | Toosi | Nenadic |
|---|---|---|---|
| spikes alignment | partially | yes | no |
| rejecting random threshold crossings | yes (C2) | no | no |
| presence of noise | ? | ? | ? |
| $\lvert x_{true} - x_{detected} \rvert$ | ? | ? | ? |

$\Rightarrow$ simulated data with different levels of signal-to-noise ratio (SNR)

# Simulated data

- inspired by the work of [Smith and Mtetwa, 2007]
- duration: 5 seconds, sampling rate: 100 kHz
- **target neuron**
  - Naundorf model [Naundorf et al., 2006] , Poisson distribution of spike times
  - spike duration: 4, 44 ms, refractory period: 10 ms
- **background electrophysiological activity**
  - 7 neurons - firing in line with the target neuron
  - 100 neurons - firing independently of target neuron
- **Gaussian noise** $\rightarrow$ $SNR \in \{50, 35, 25, 10, 0, -5\}$ dB

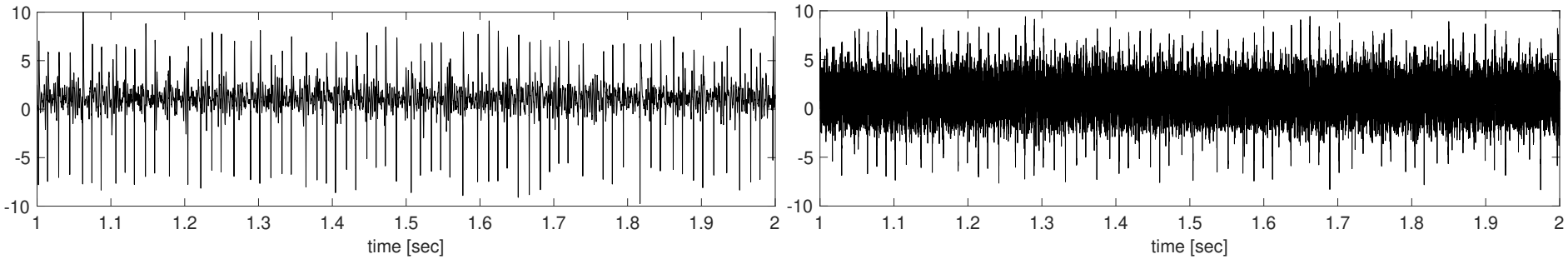
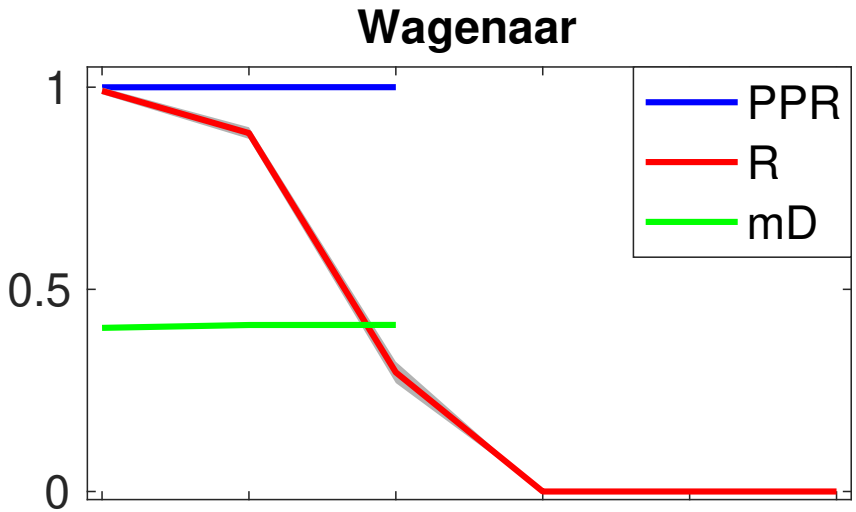
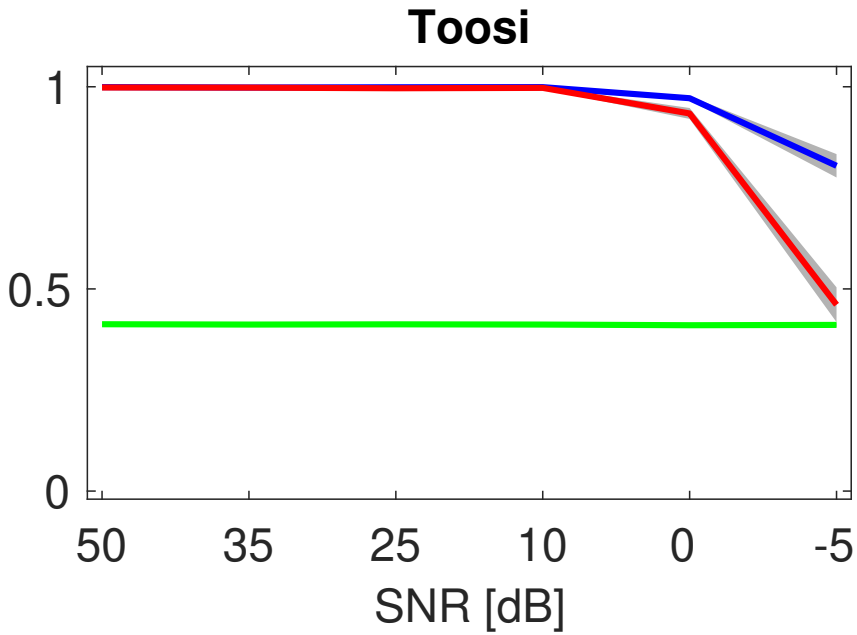


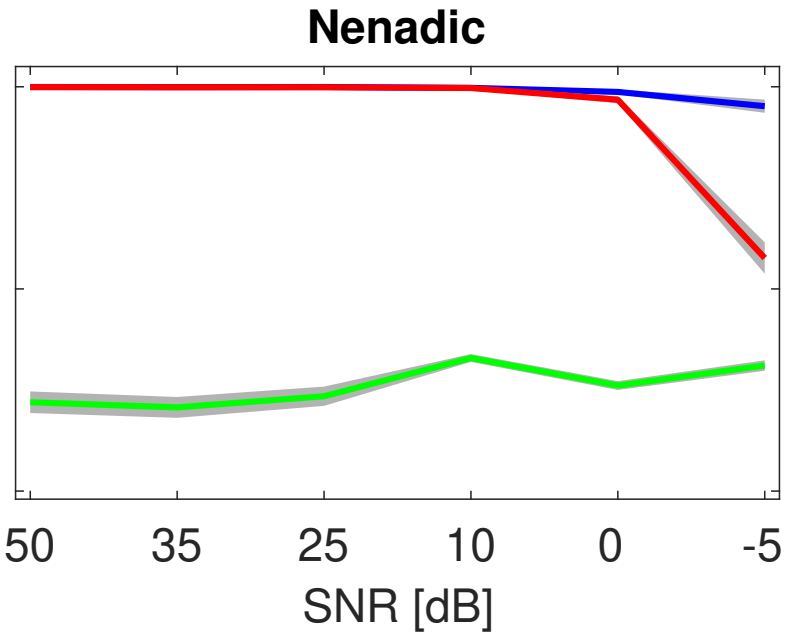

Figure: Simulated data with SNR = 50 (left) and SNR = 0 (right).

# Results

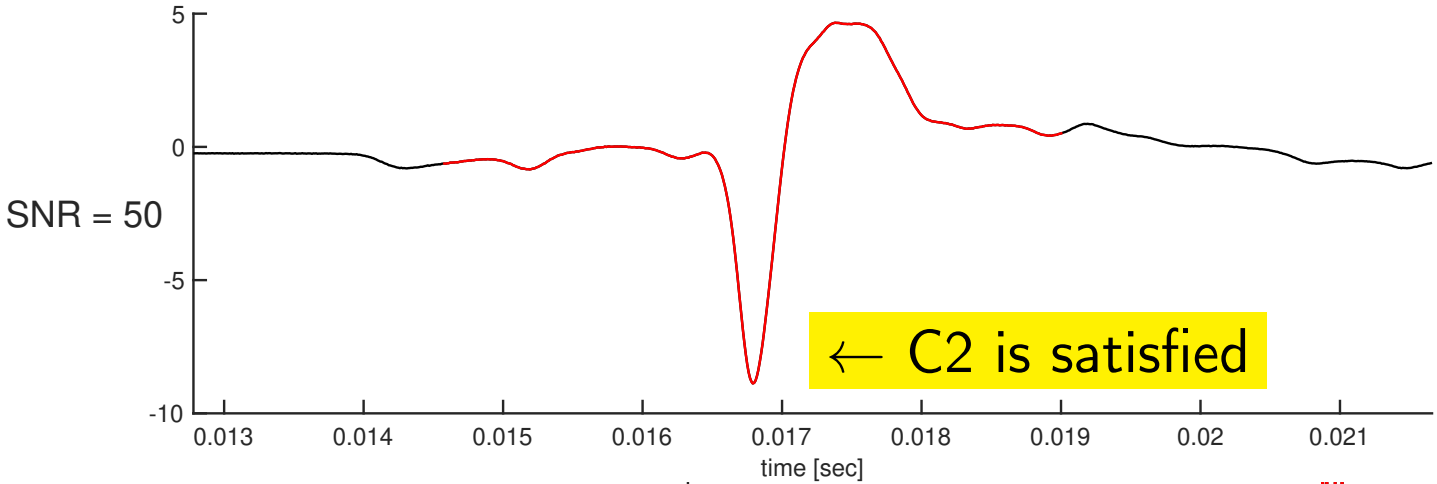


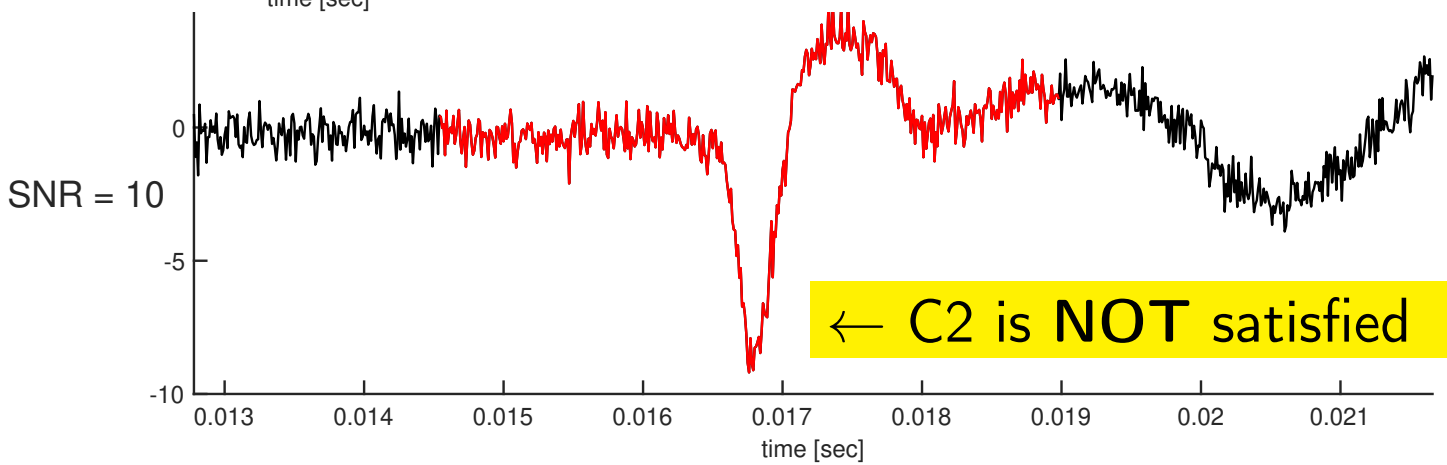

- spike $= x \pm 2,22$ ms
- **mD** $= \|x_{detected} - x_{actual}\|$
- **PPR** $= \dfrac{\#\text{ correctly identified spikes}}{\#\text{ detected spikes}}$
- **R** $= \dfrac{\#\text{ correctly identified spikes}}{\#\text{ actual spikes}}$



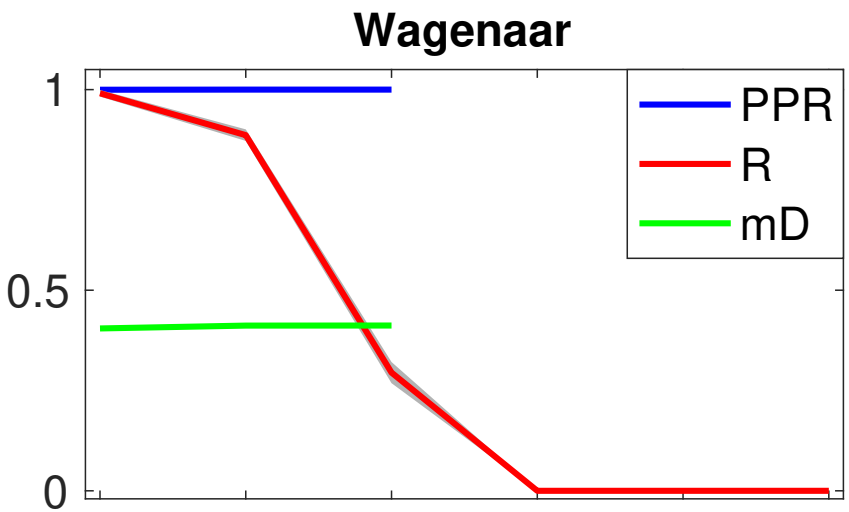
# Results - problem in Wagenaar's method

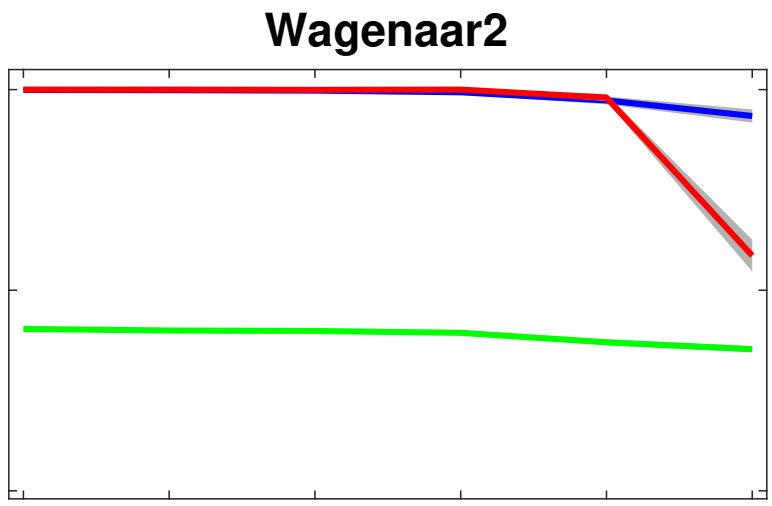


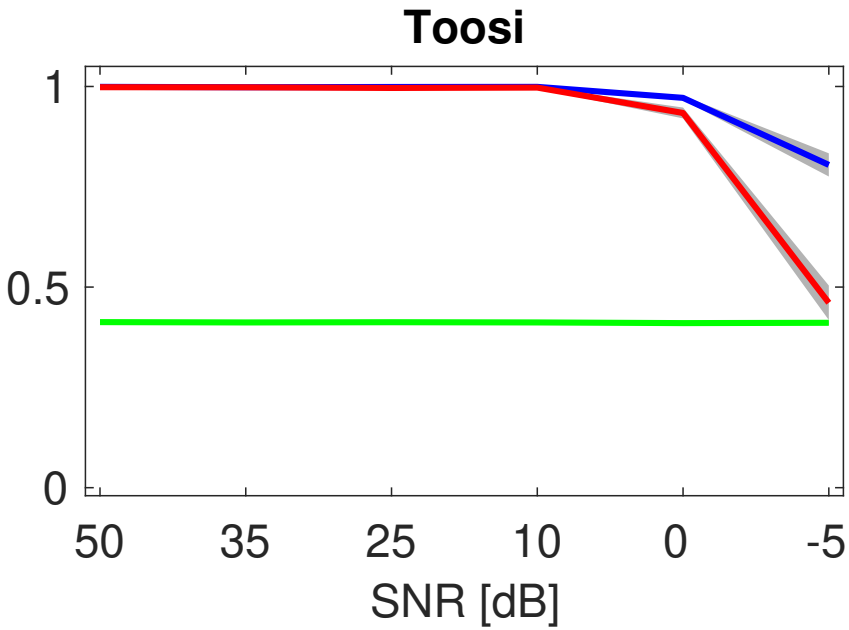



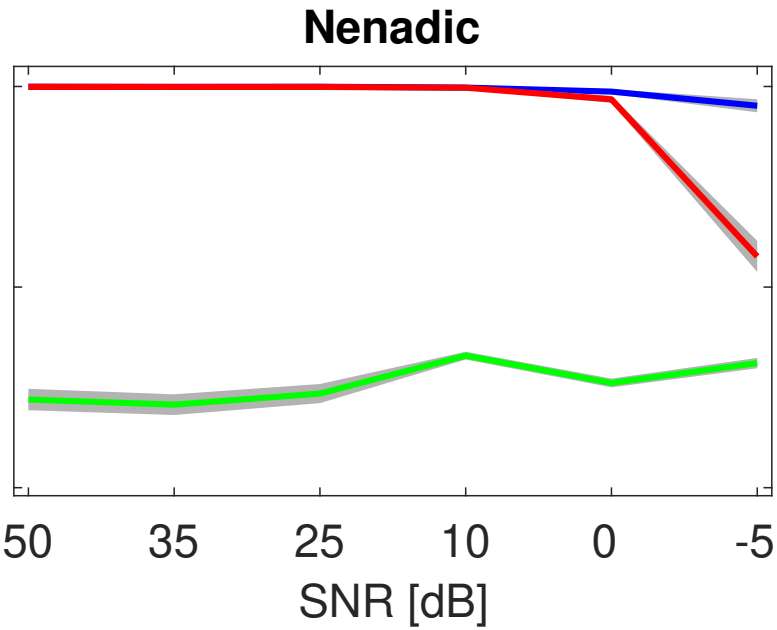

- **solution 1** → zero-phase bandpass filter between 300 Hz and 3000 Hz
- **solution 2** → removing condition C2 → **Wagenaar2**

# Results


Wagenaar
PPR
R
mD
1
0.5
0

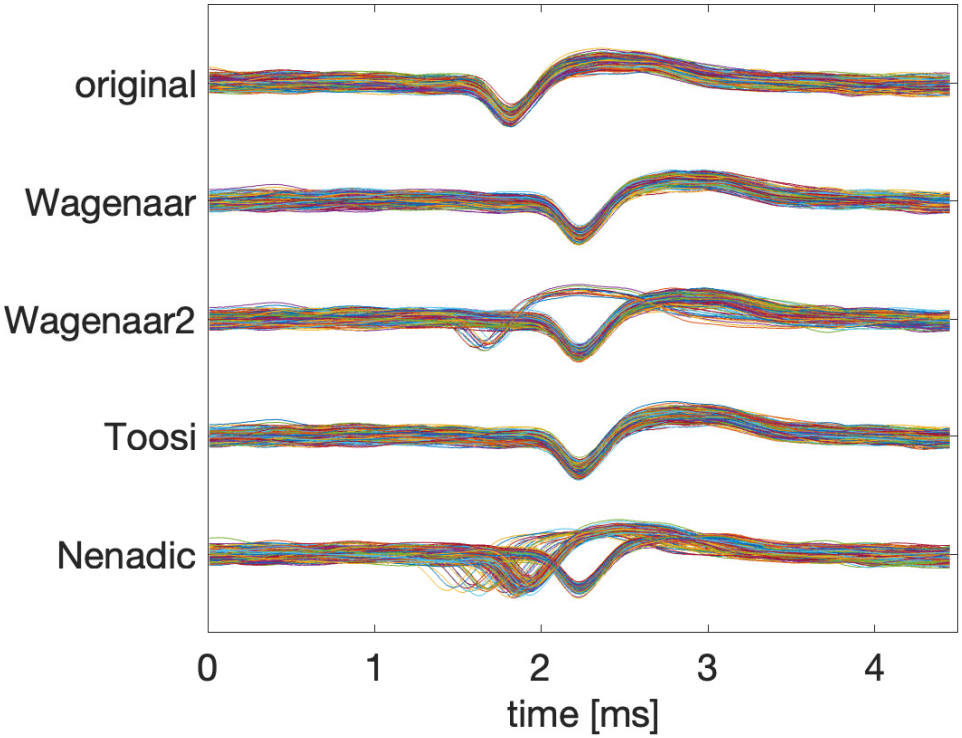

Wagenaar2


Toosi
1
0.5
0
50
35
25
10
0
-5
SNR [dB]

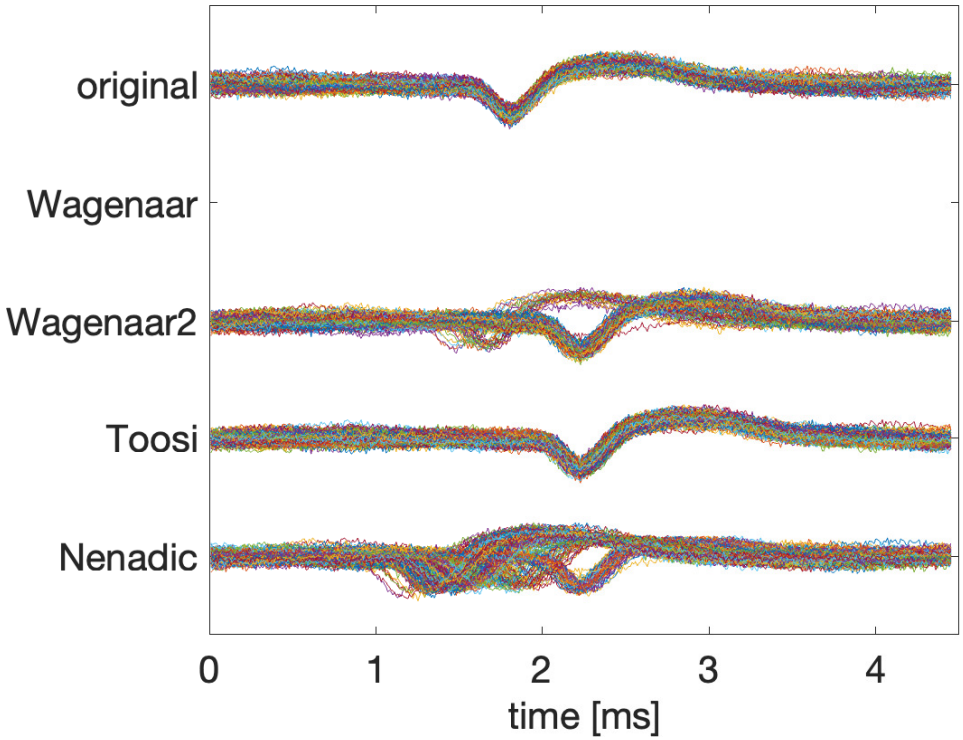

Nenadic
50
35
25
10
0
-5
SNR [dB]

# Results spikes alignment

SNR = 35 dB




SNR = 10 dB



# Conclusion

| | Wagenaar | Wagenaar2 | Toosi | Nenadic |
|---|---|---|---|---|
| spikes alignment | partially | partially | yes | no |
| rejecting random threshold crossings | yes (C2) | no | no | no |
| presence of noise | problem | deteriorates alignment | ok | ok |
| $\lvert x_{true} - x_{detected} \rvert$ | $\approx$ const. | $\approx$ const. | const. | non-const. |

- **future work** $\rightarrow$ methods' comparison on simulated data with:
  - spikes with varying amplitude
  - lower refractory period or overlapping spikes
  - ...

# Literature I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# Literature II


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