Mitigating Neuropathic Pain: From Theory to Practice

Inhibiting Neuroma Pain *In-silico* and Measuring Neural Activity *In-vivo*

Final Colloquium
Thesis M.Sc. Systems and Control | Thesis M.Sc. Technical Medicine
Hubald Verzijl
26 October 2021

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Why mitigating neuropathic pain?

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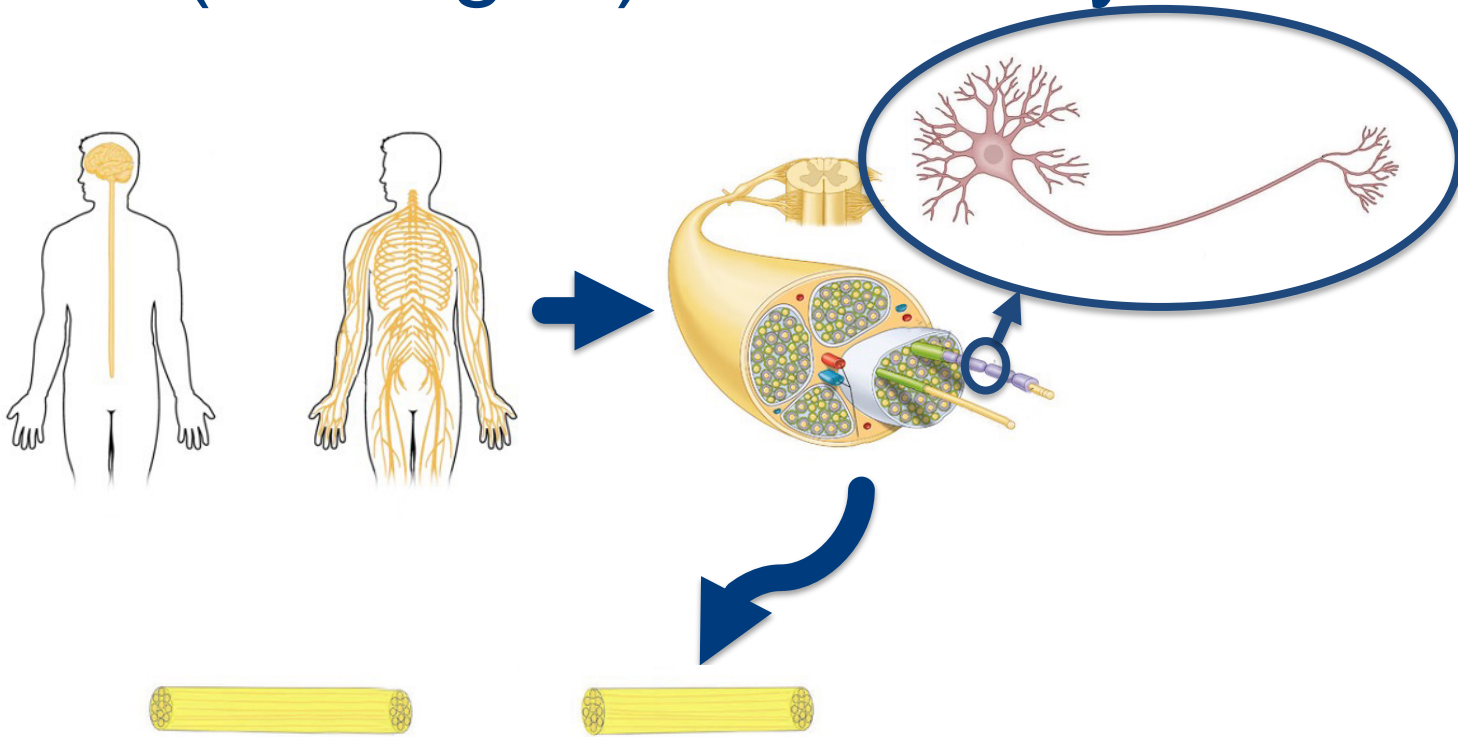
The (damaged) nervous system



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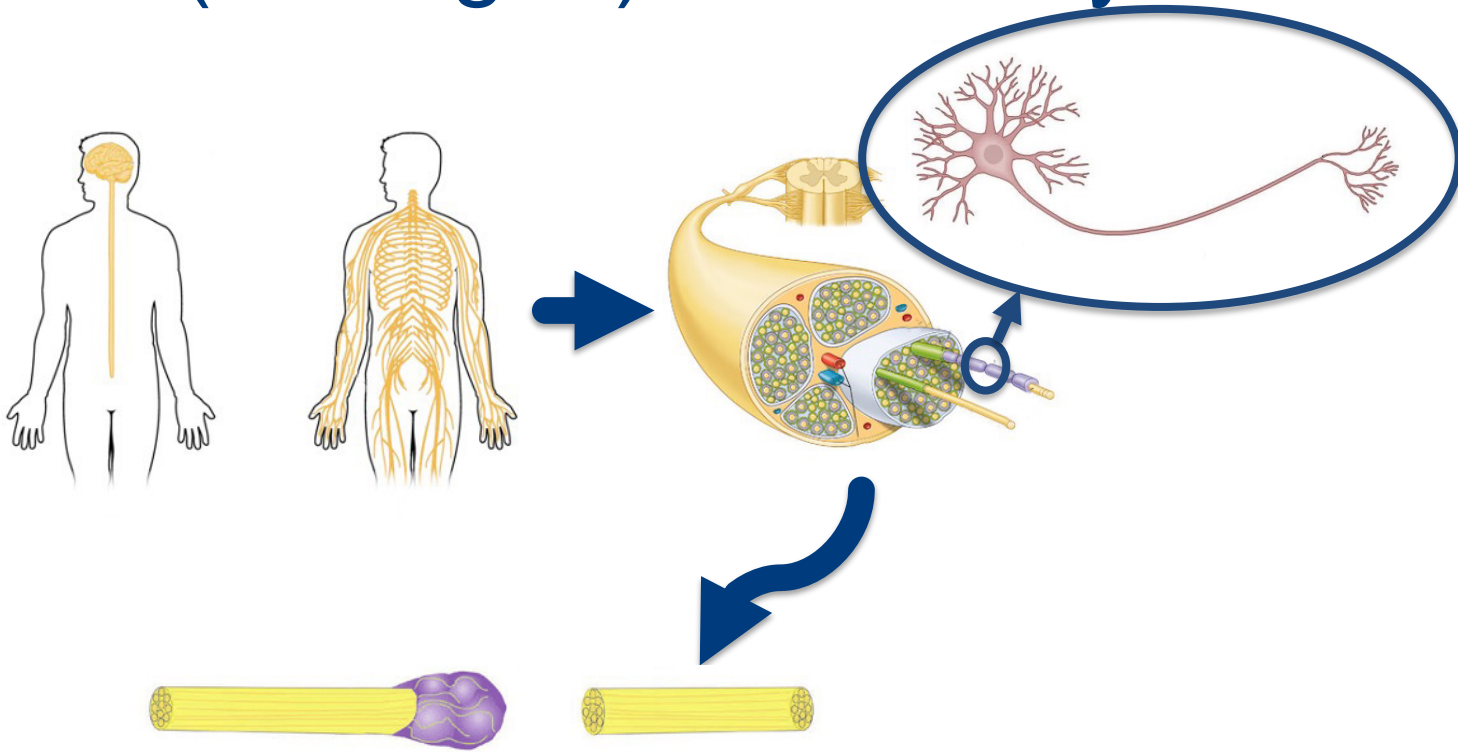

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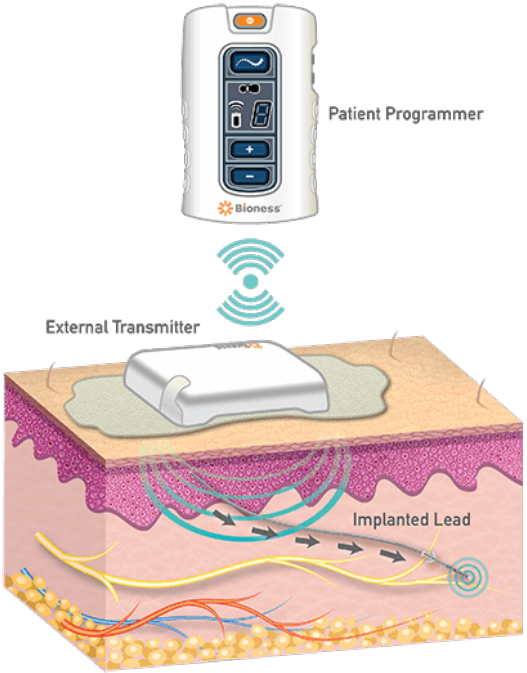
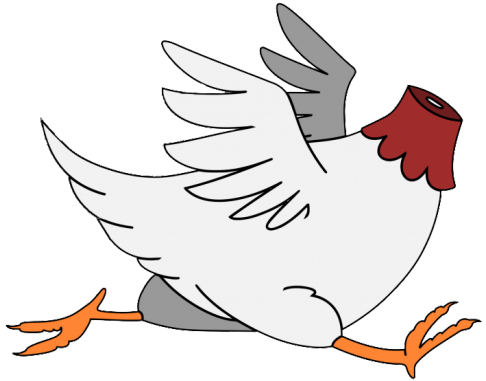
Open-loop stimulation





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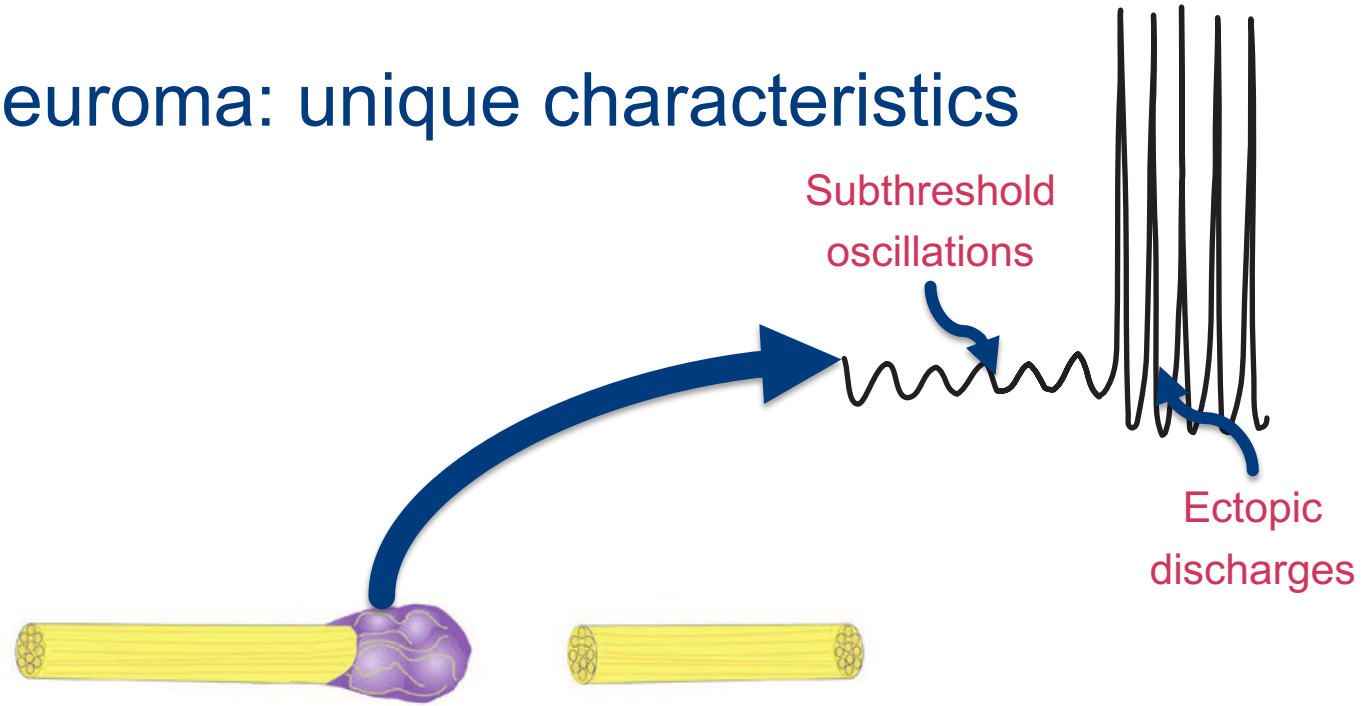
Neuroma: unique characteristics



Working hypothesis: *By neutralizing subthreshold oscillations and ectopic discharges, the generation of neuropathic pain could be mitigated.*

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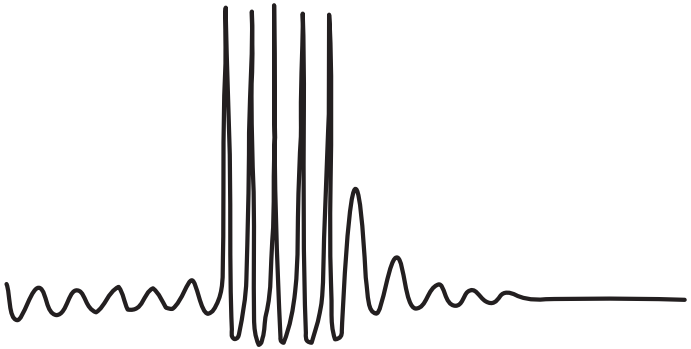
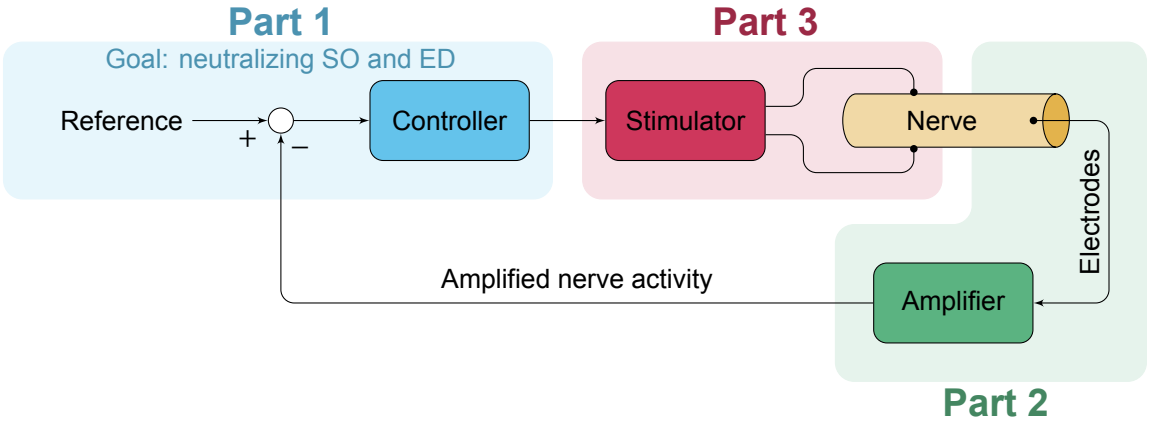
Our strategy: electrical neurostimulation





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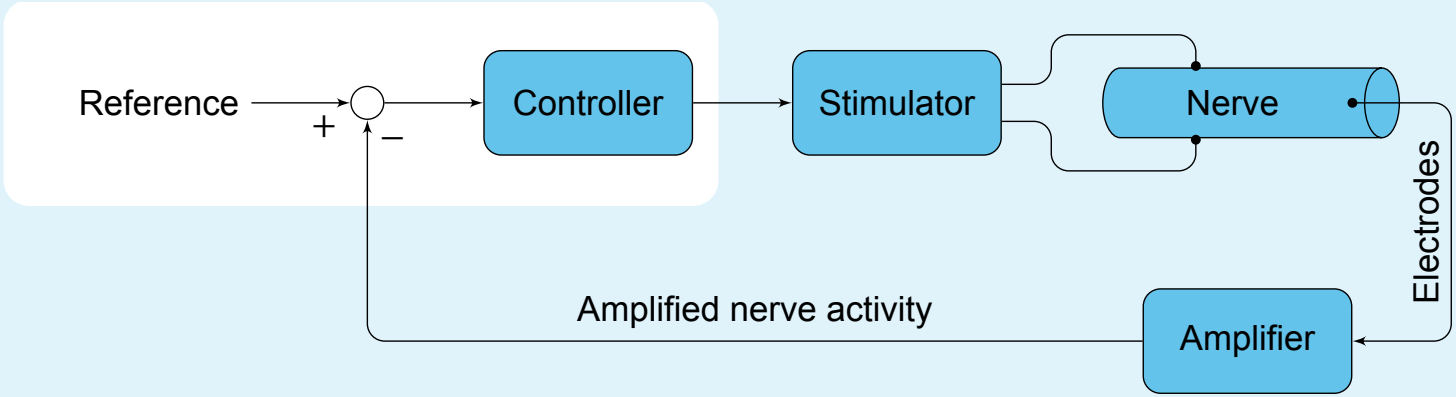
Part 1



Mitigating neuropathic pain **at the neuron** level through **electrical neurostimulation**: a **model predictive control** approach with **fractional-dynamics proxy**

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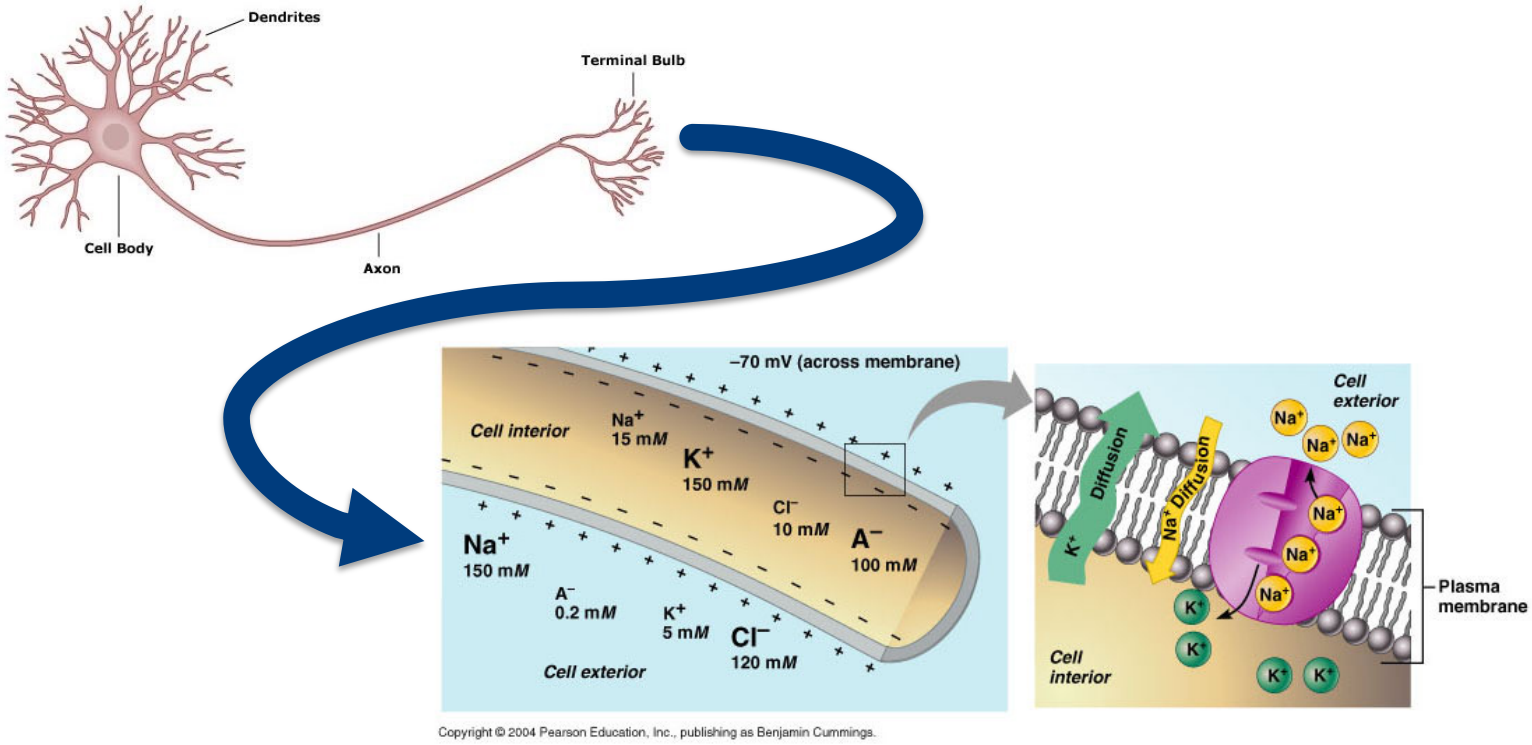
The cell membrane



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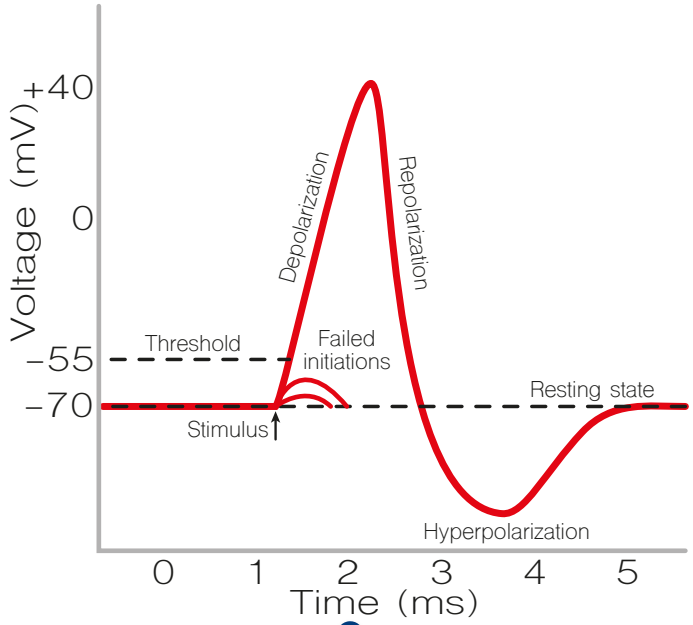
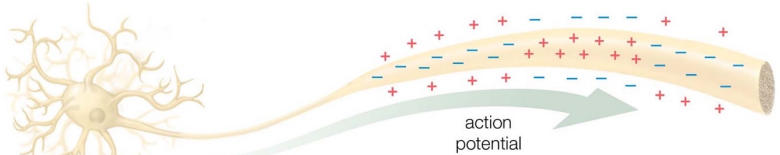
The action potential





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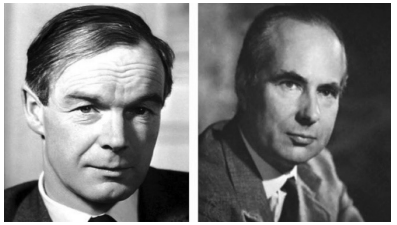
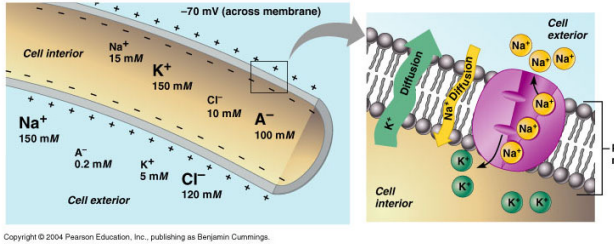
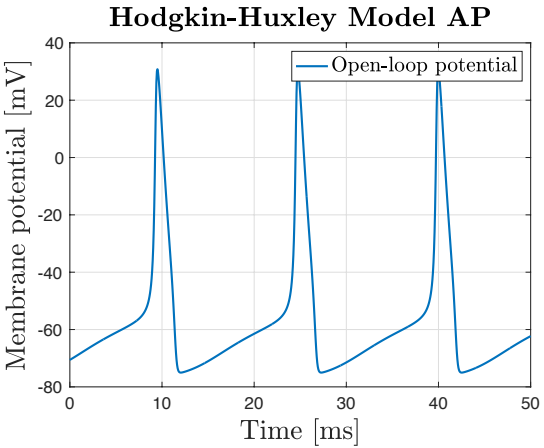
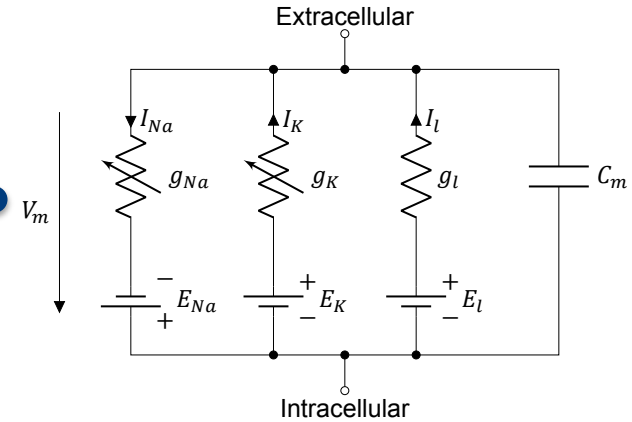
Hodgkin and Huxley



Stimulation current [μA] → ? → Membrane potential [mV]







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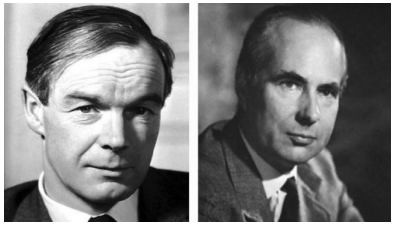

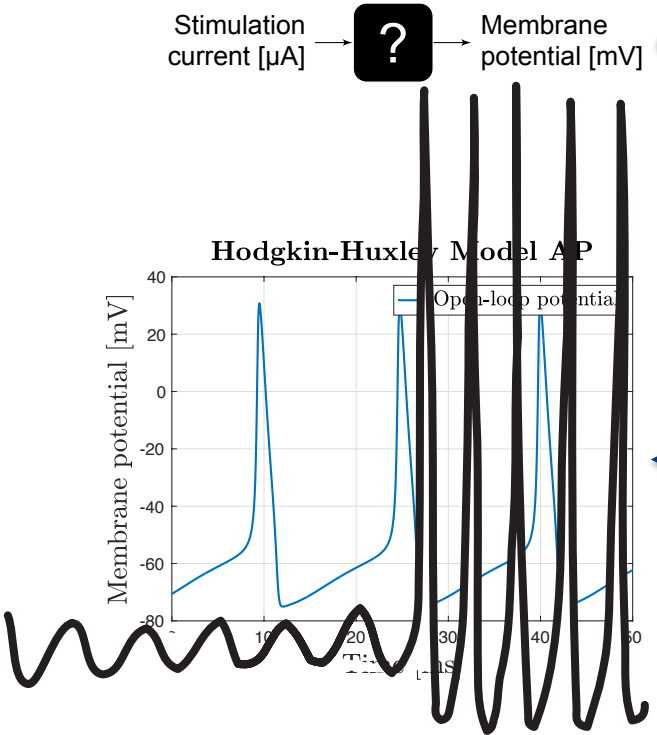

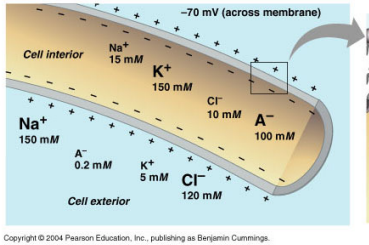

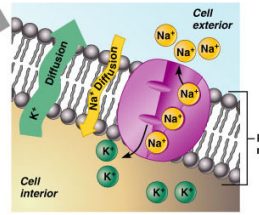

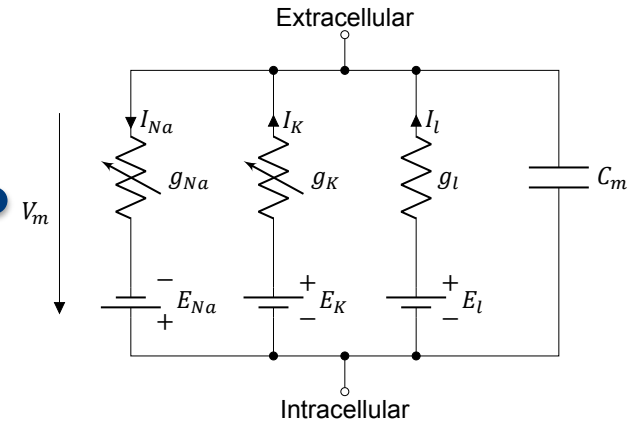

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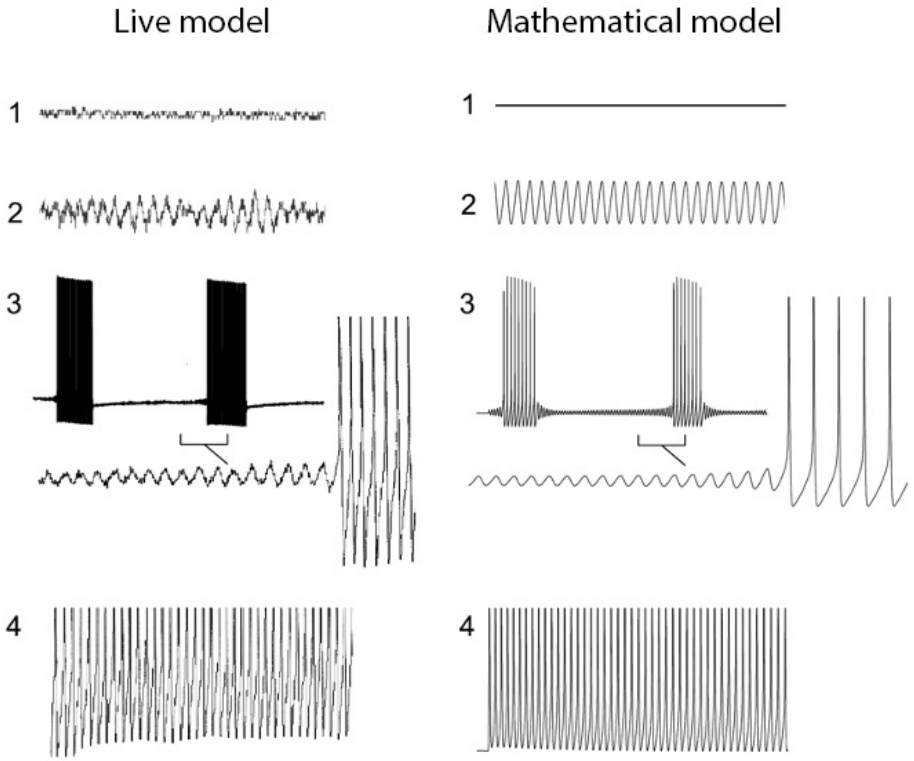
Modeling neuropathic pain

Stimulation current [μA] → ? → Membrane potential [mV]

- Addition of sodium channels
- Fast, intermediate and slow current



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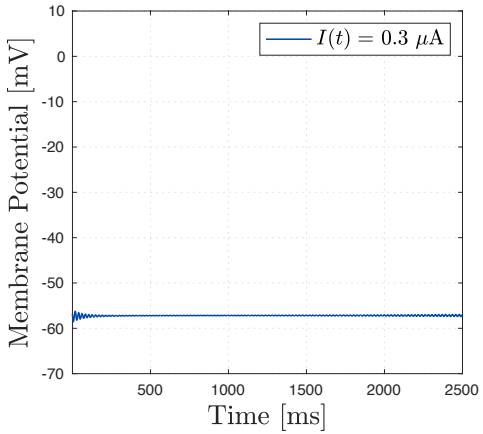
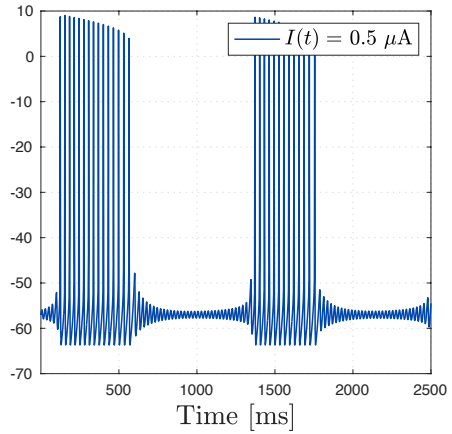
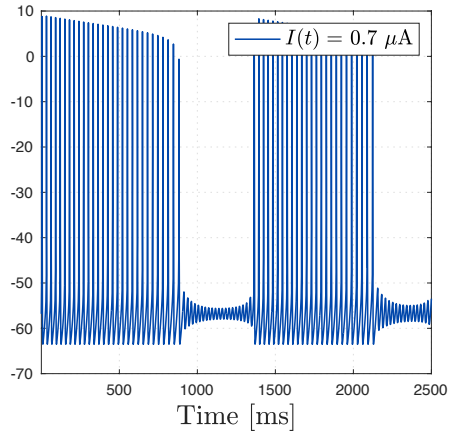
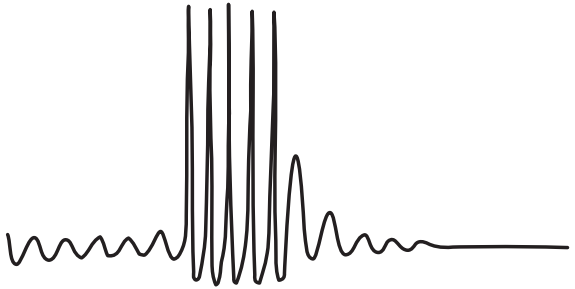
Modeling neuropathic pain







Increased stimulation current



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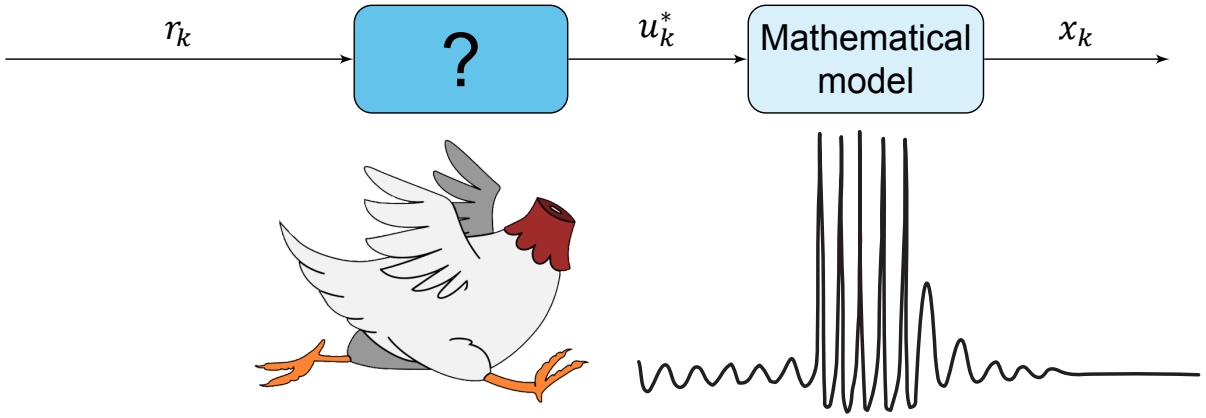
Dynamical system-based feedback control



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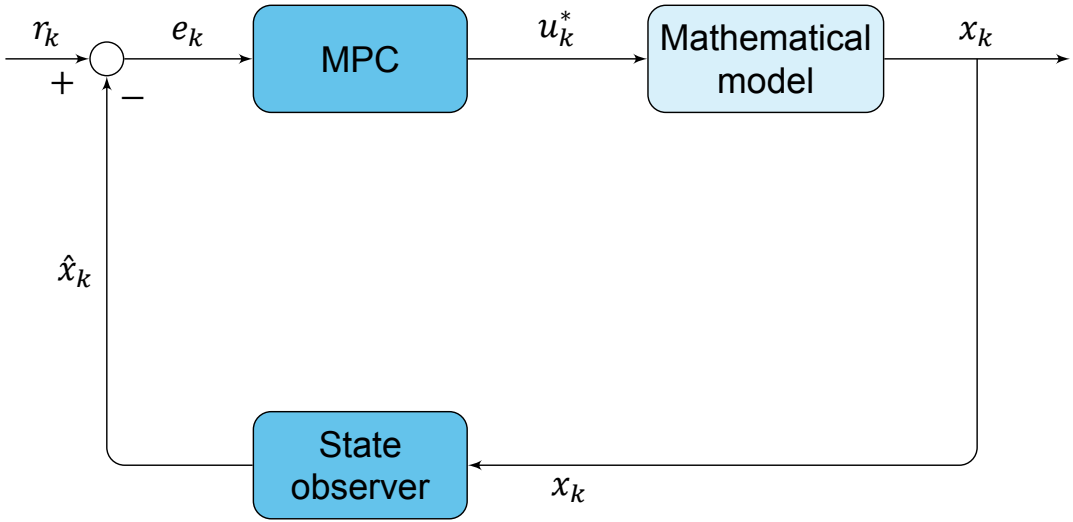

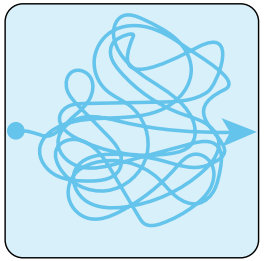

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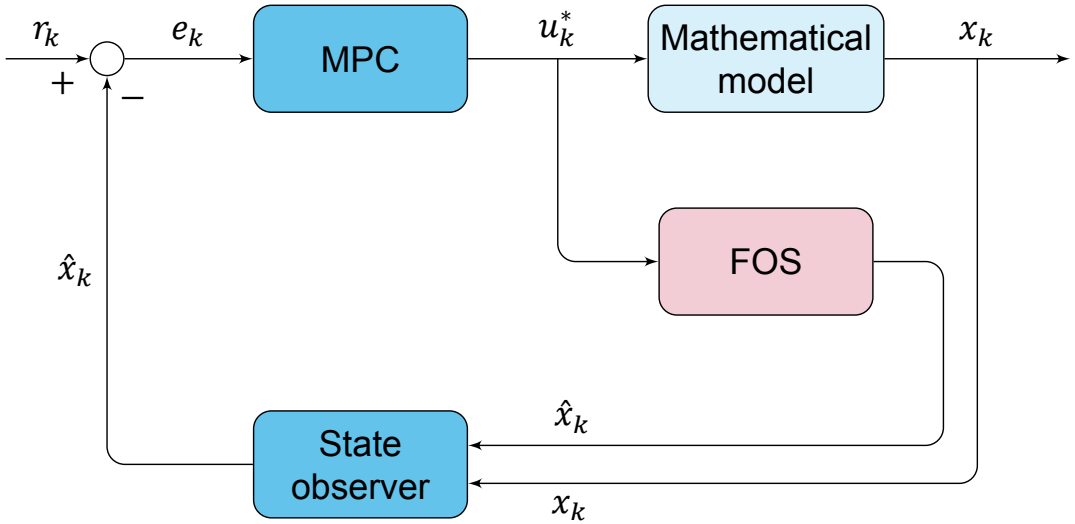
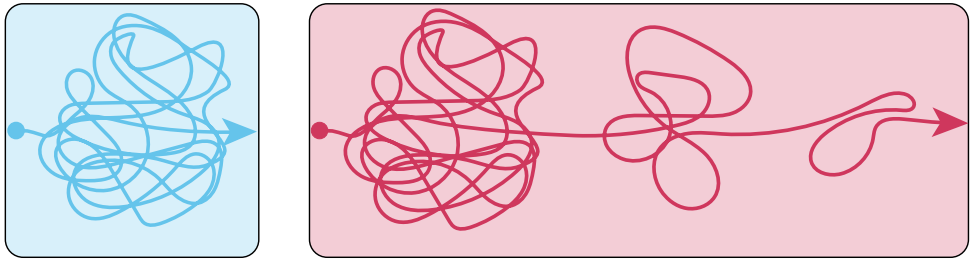
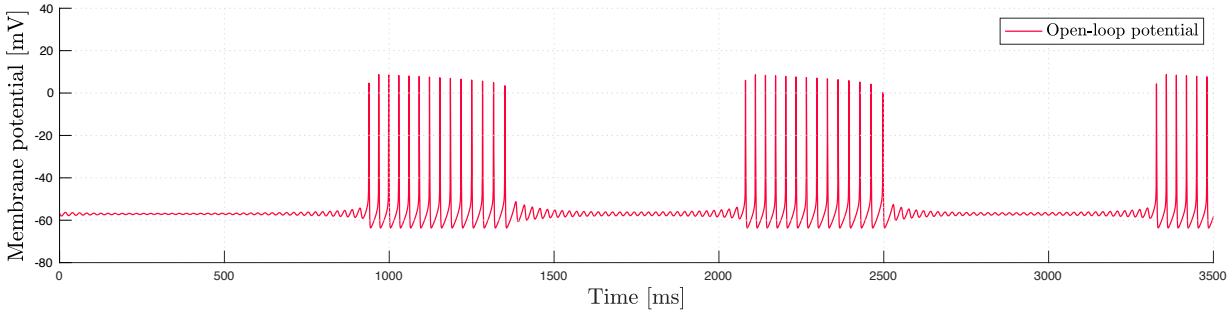
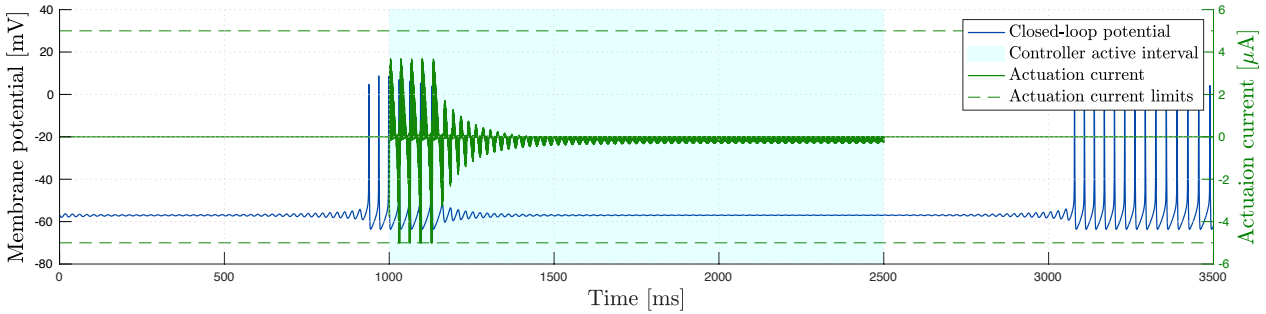




In-silico results: Hodgkin-Huxley based





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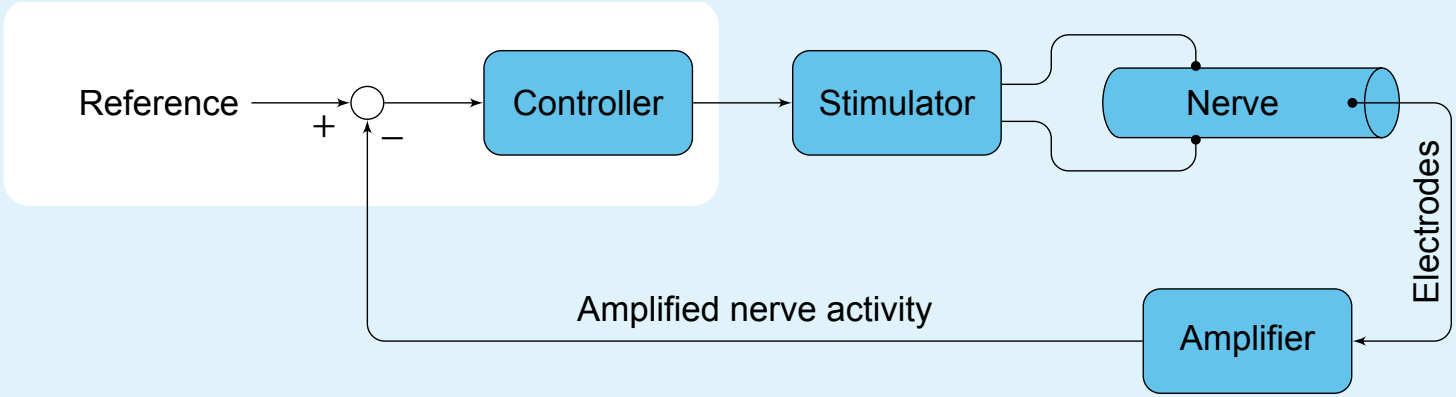
Part 1



Mitigating neuropathic pain **at the neuron** level through **electrical neurostimulation**: a **model predictive control** approach with **fractional-dynamics proxy**

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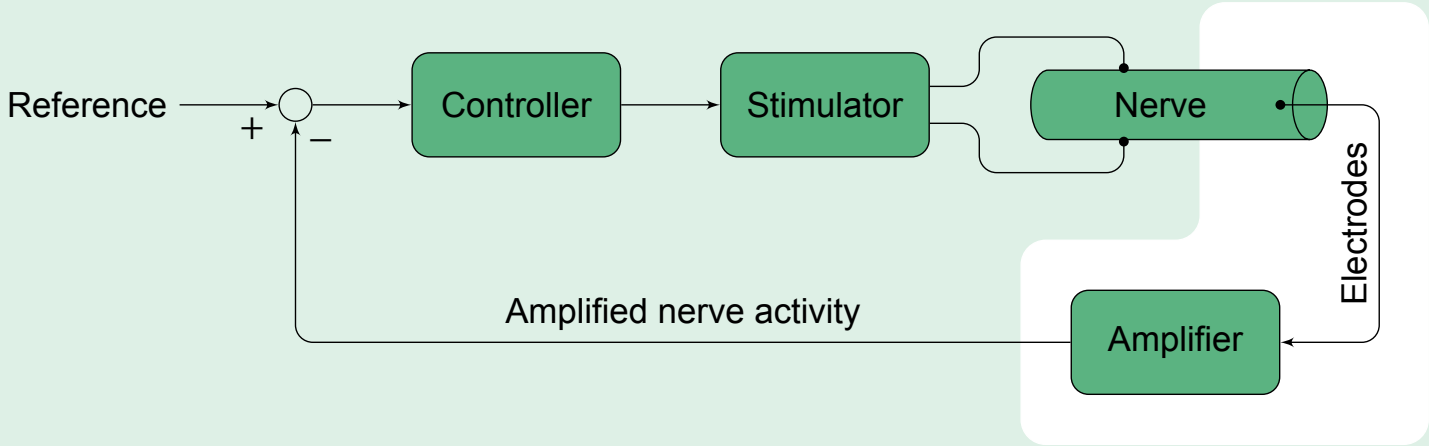
Part 2



Design of an **extended signal amplifier** for **microneurography**

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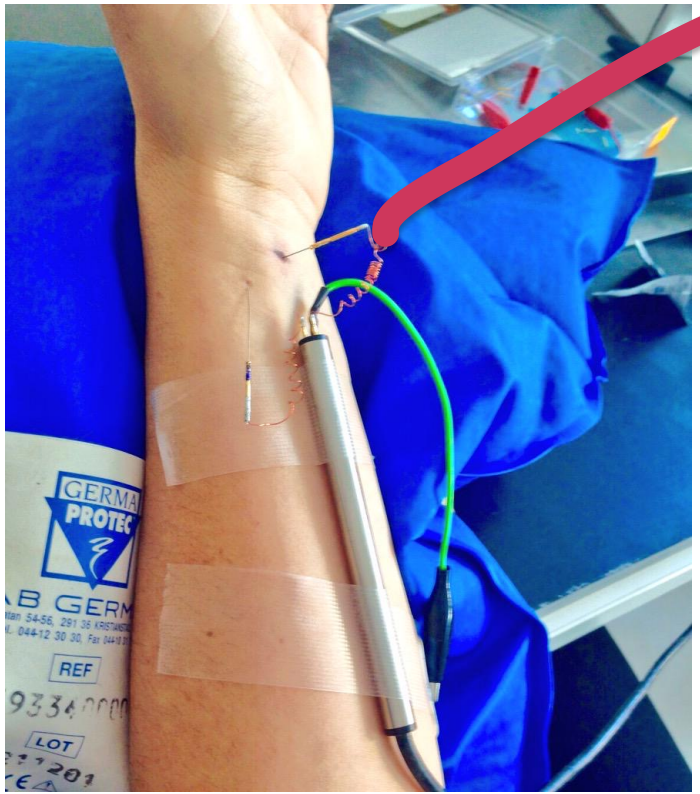
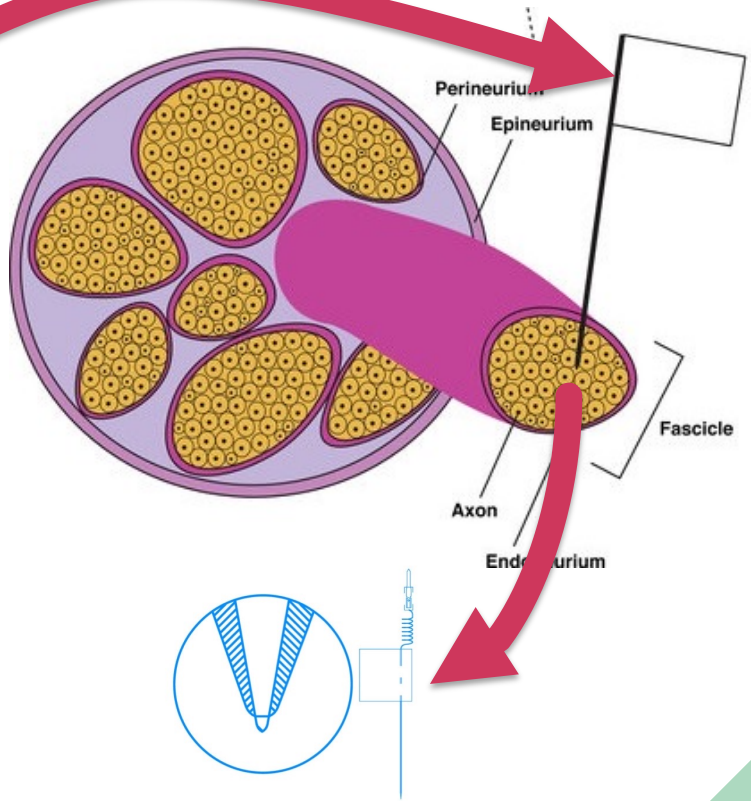
Recording neuronal activity





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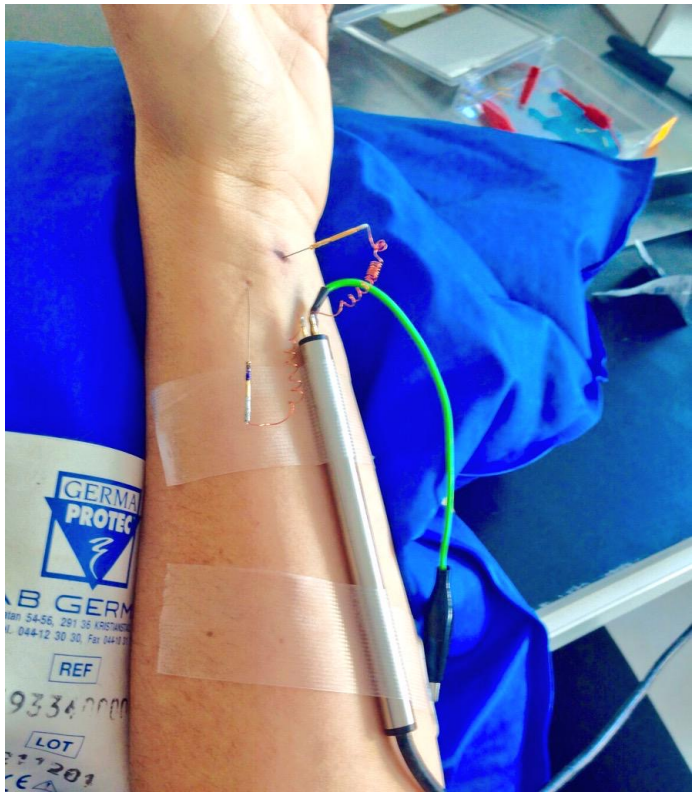

Impulses from a cutaneous sense organ in response to touch

→ Only capable of measuring

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Hardware requirements

- Microneurography amplifier
  - $\pm 10\ \mu V$
  - 500 – 5000 Hz
  - Interference rejection
- Graphical user interface
- Processing power and stimulator control

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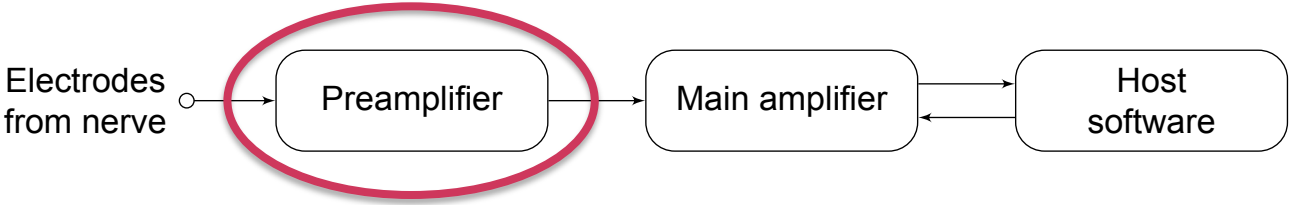
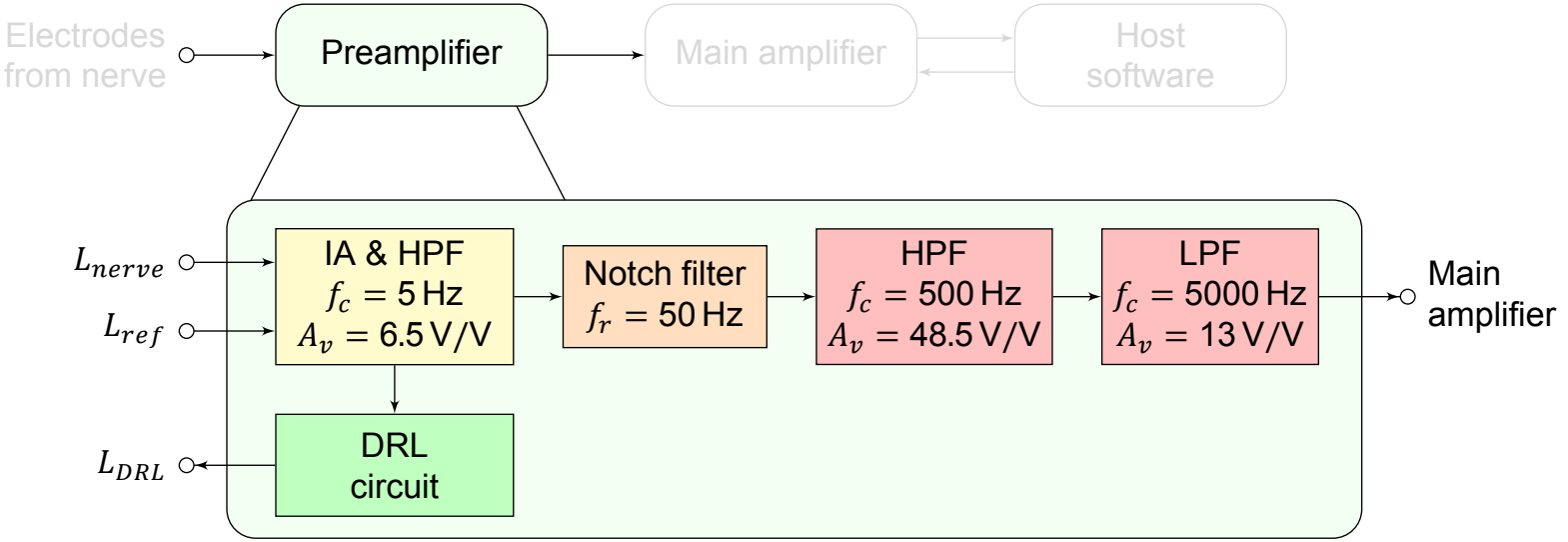
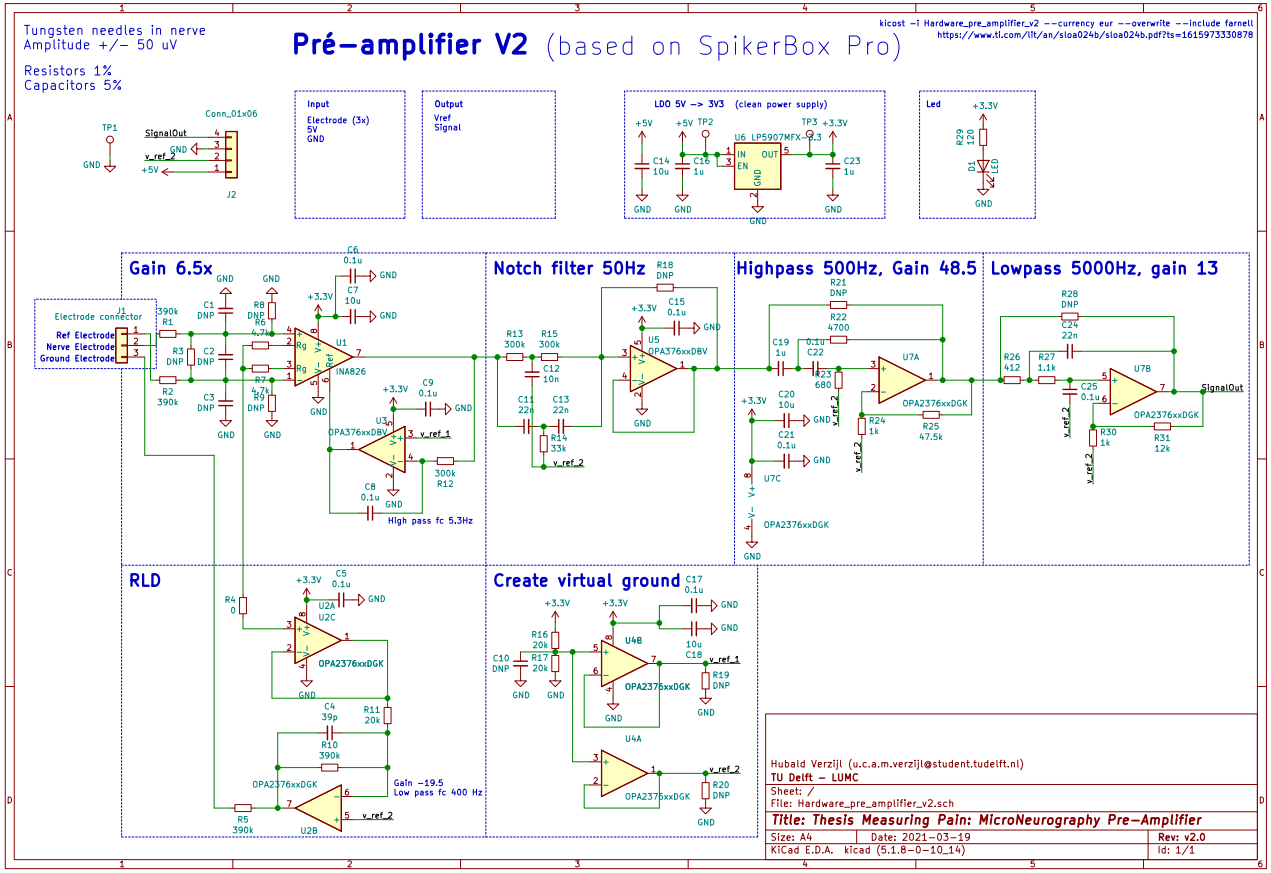
Proposed hardware



Preamplifier | Design



Preamplifier | Design



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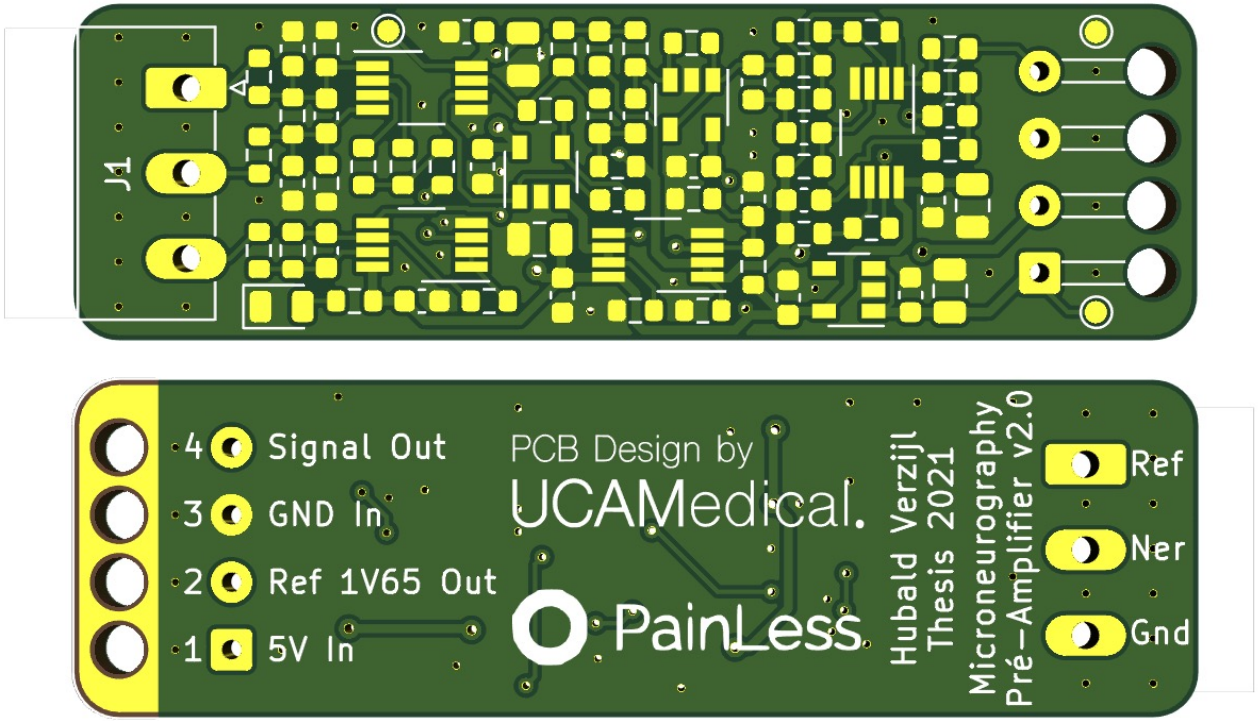
Preamplifier | Design



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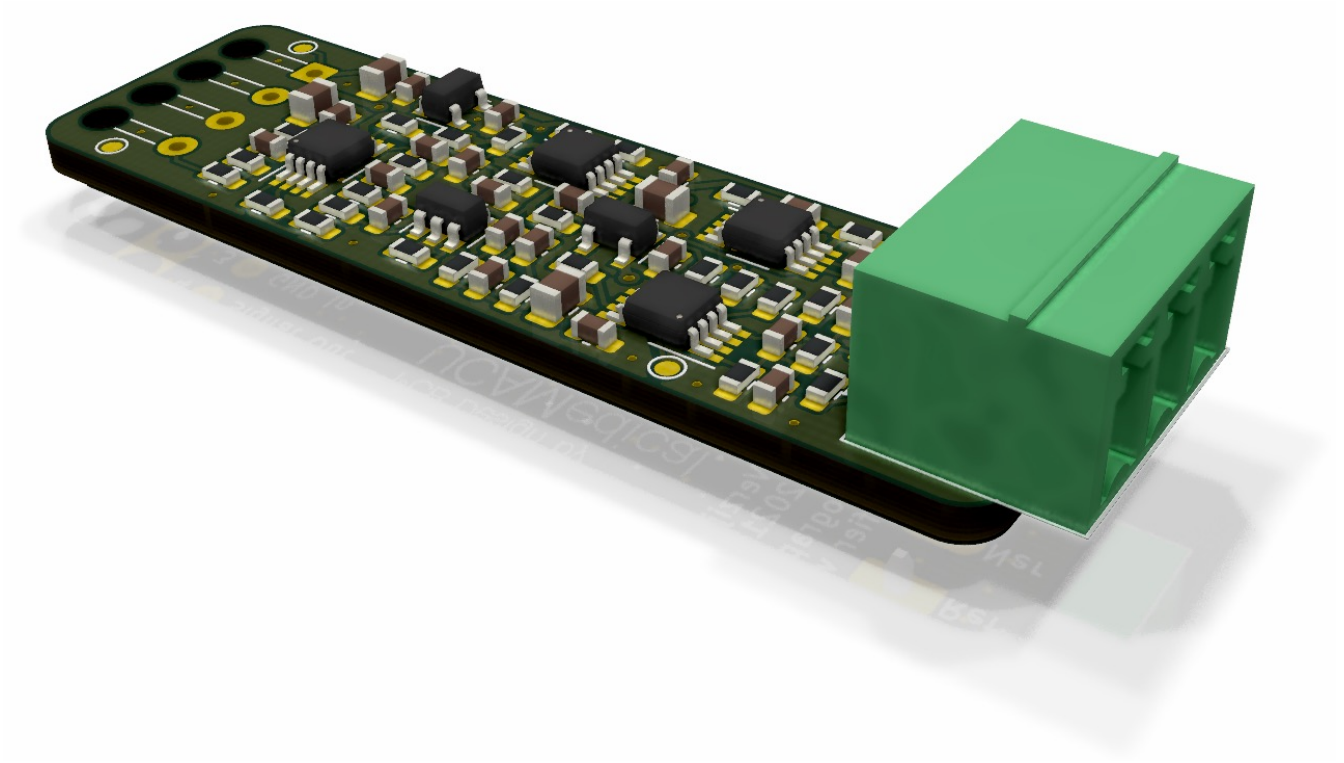

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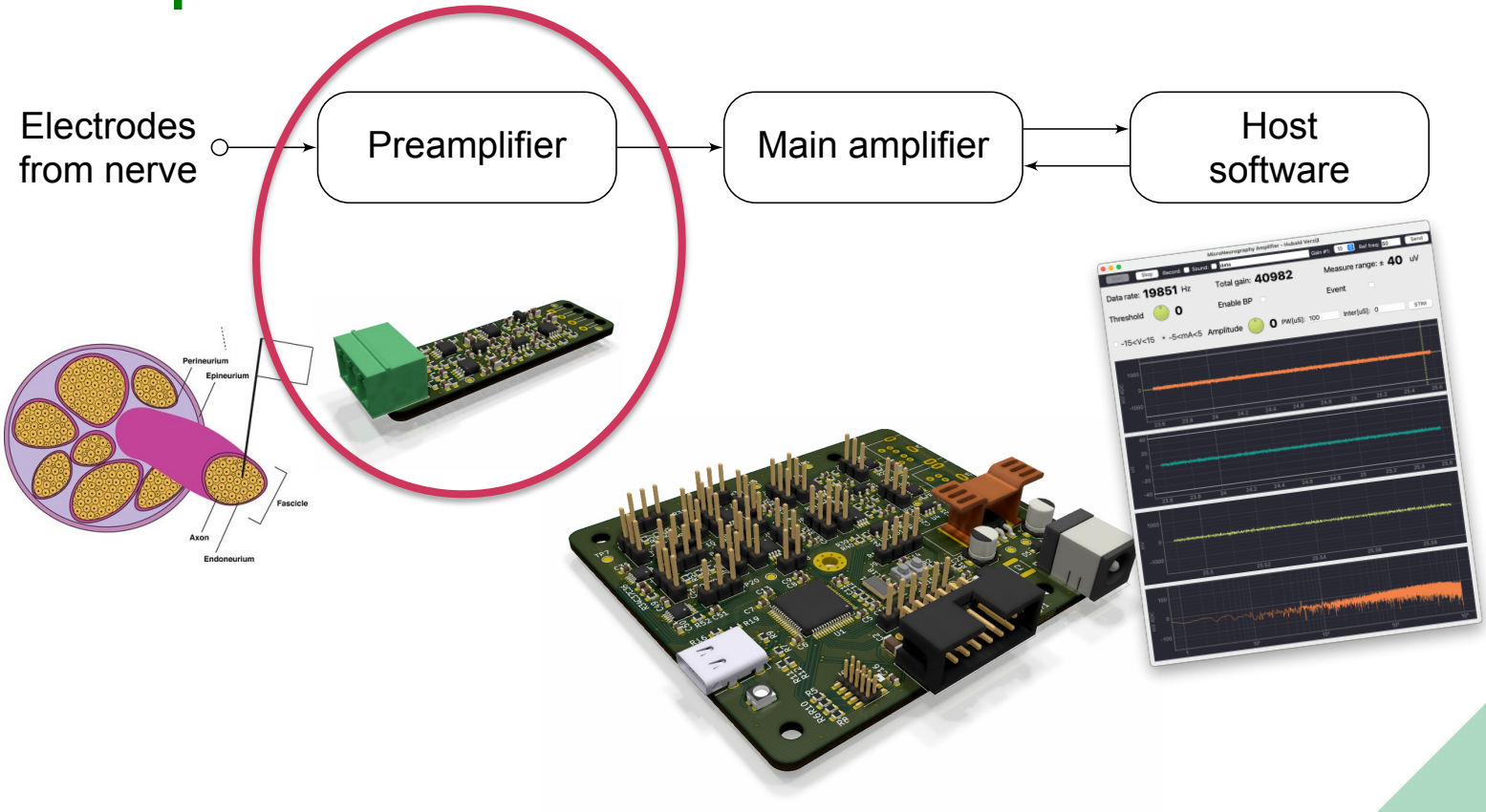
Proposed hardware



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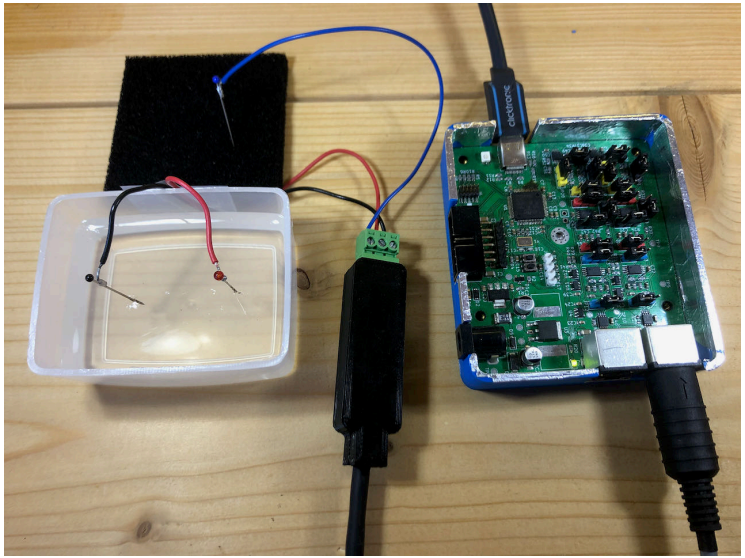
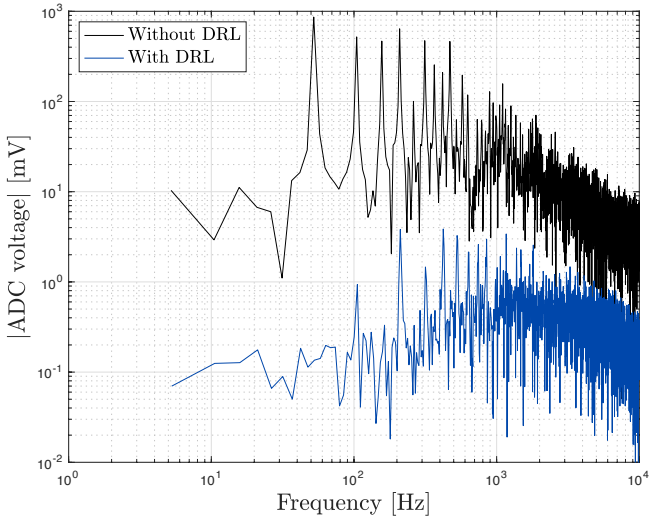
Preamplifier | Validation





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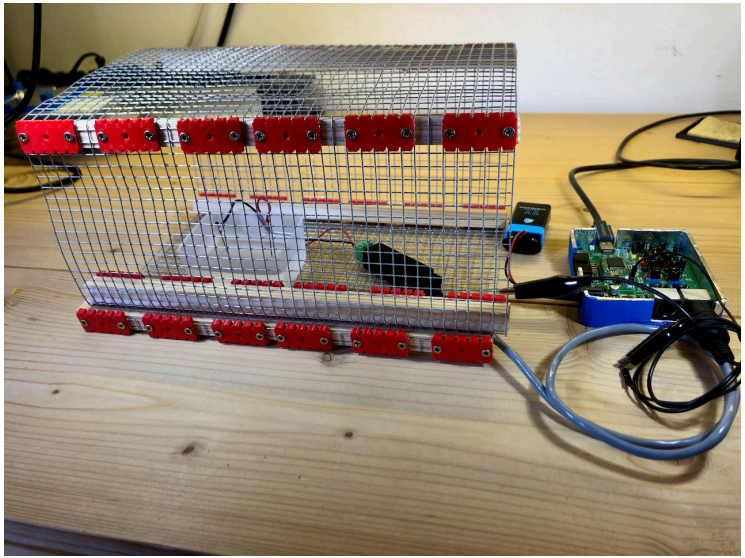

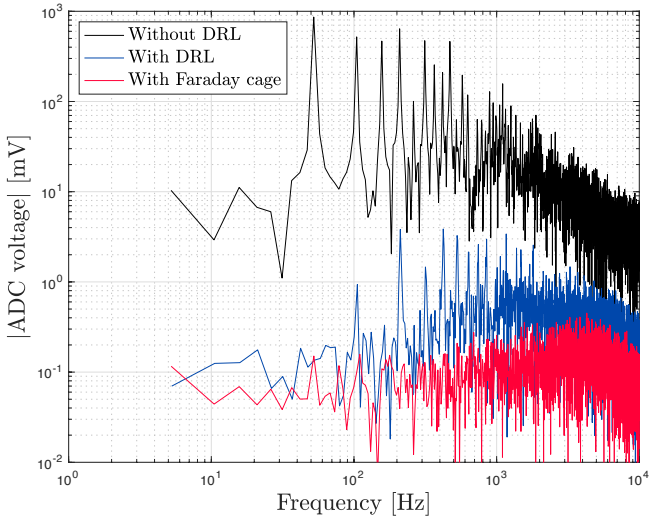

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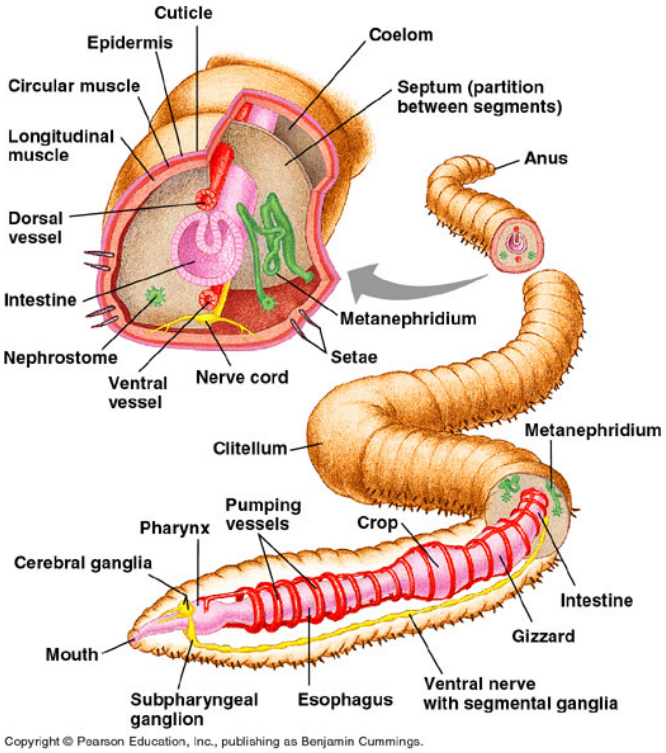
Validation | *In-vivo*



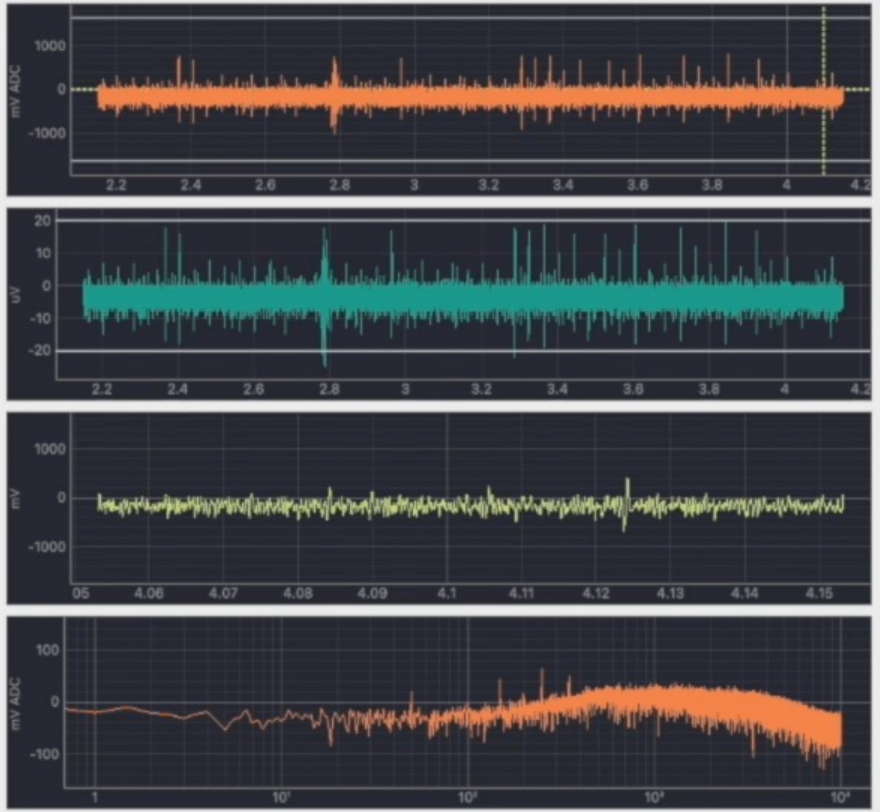
MicroNeurography Amplifier - Hubald Verzijl

Start | Stop | Record: | Sound: | data | Gain #1: 20 | Ref freq: 50 | Send

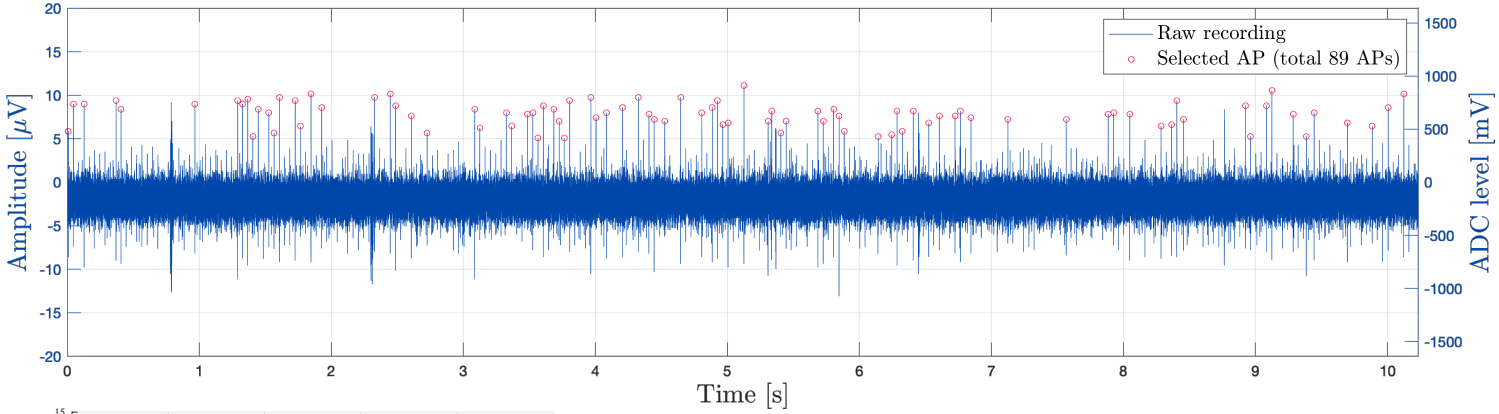
Data rate: 0 Hz | Total gain: 81965 | Measure range: ± 20 uV

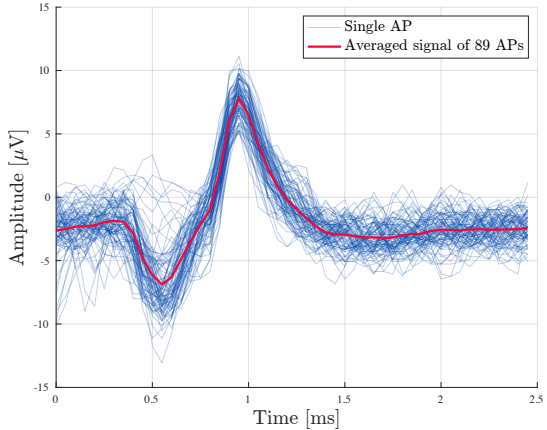
Threshold 0 | Enable BP | Event

-15<V<15 • -5<mA<5 | Amplitude 0 | PW[uS]: 100 | Inter[uS]: 0 | STIM



Validation | *In-vivo*





Warning: *next slide contains pictures of animal surgery!*

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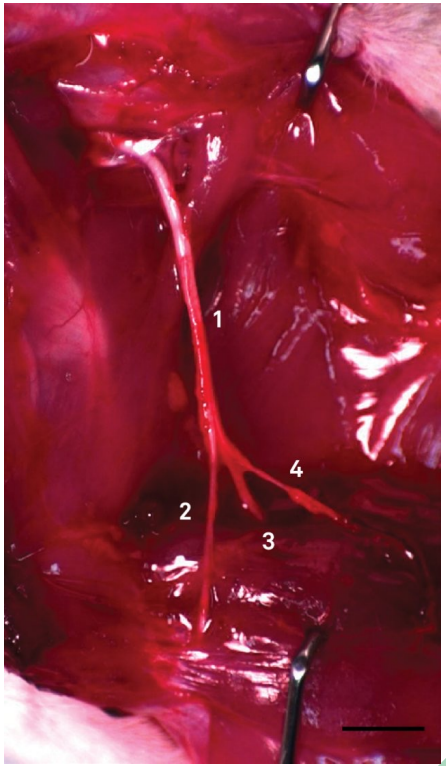
Validation | *In-vivo*



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Validation | *In-vivo*

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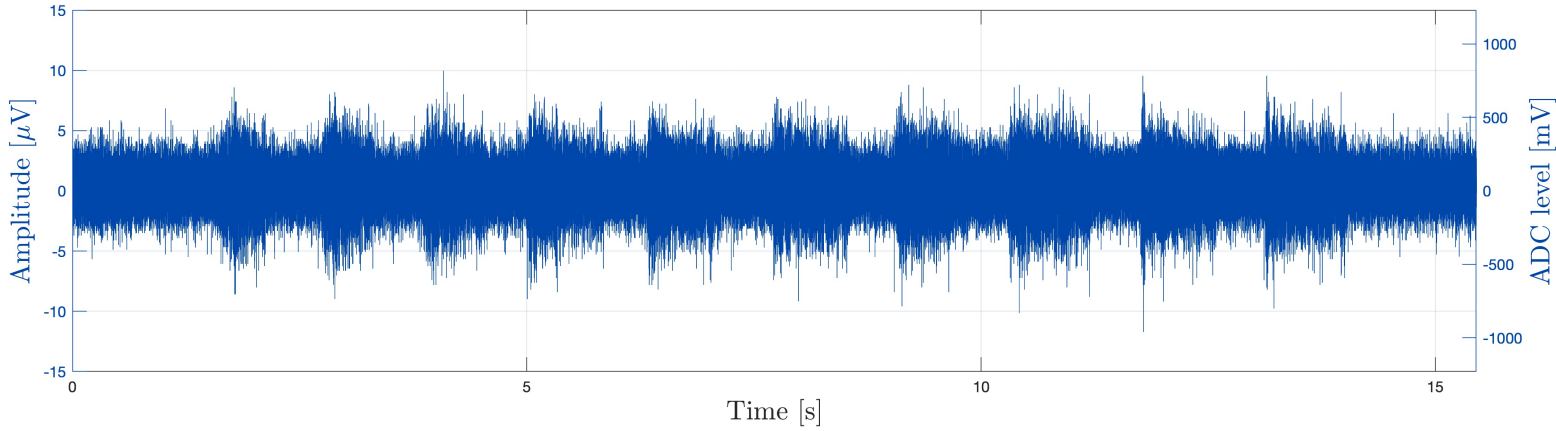

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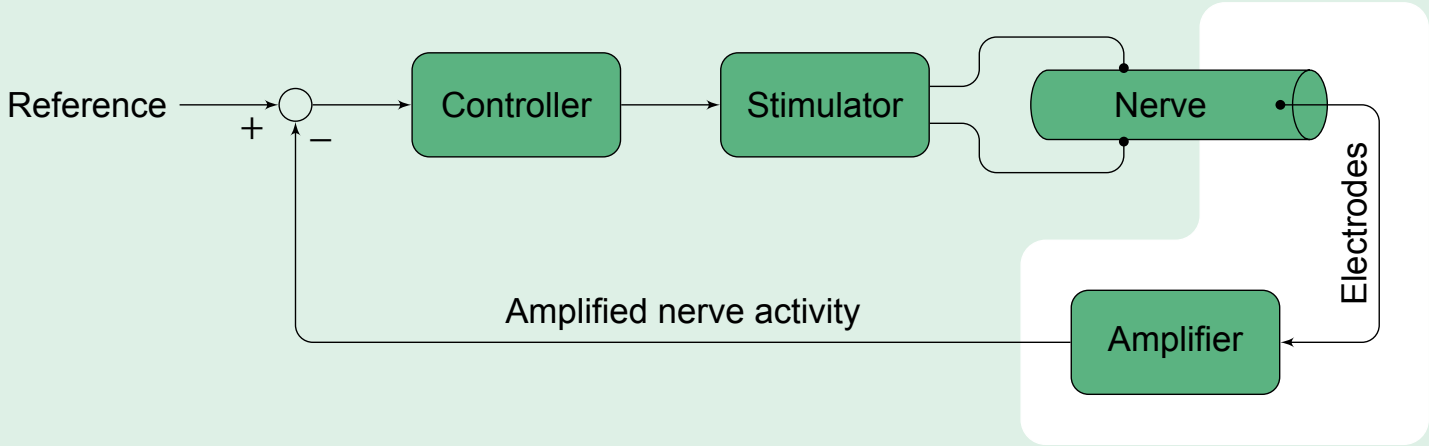
Part 2



Design of an **extended signal amplifier** for **microneurography**

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Neuropathic pain
Our strategy
Part 1
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To practice
Nerve activity
Field distribution
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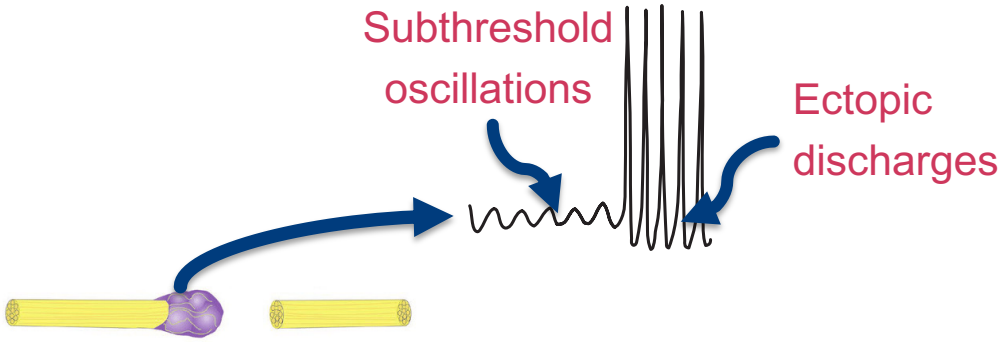
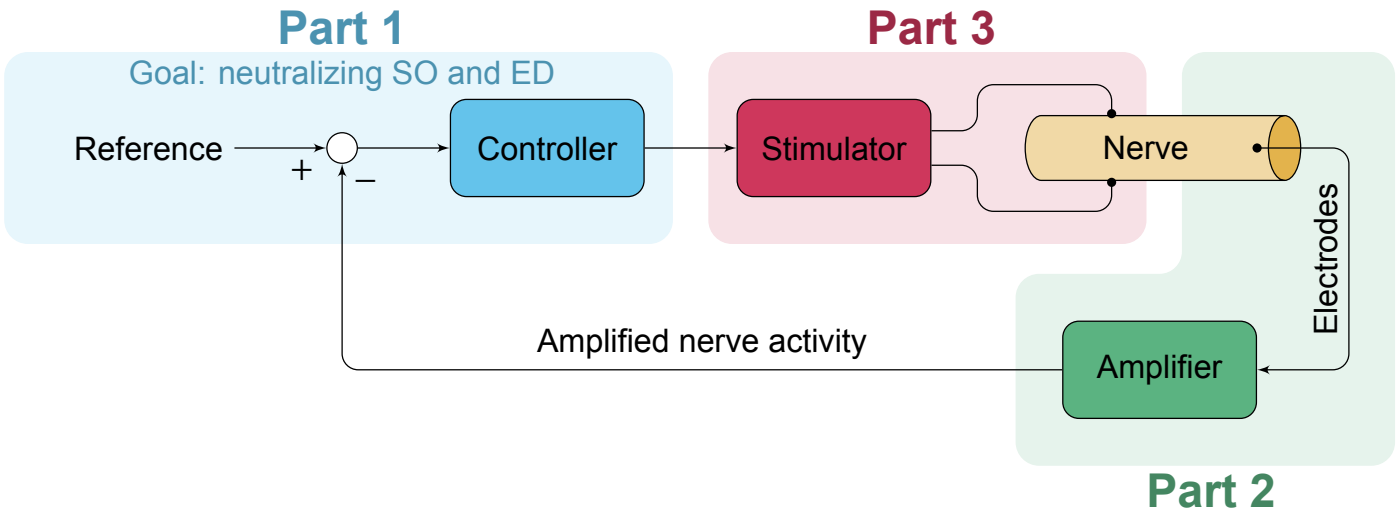
Summary

Discussion





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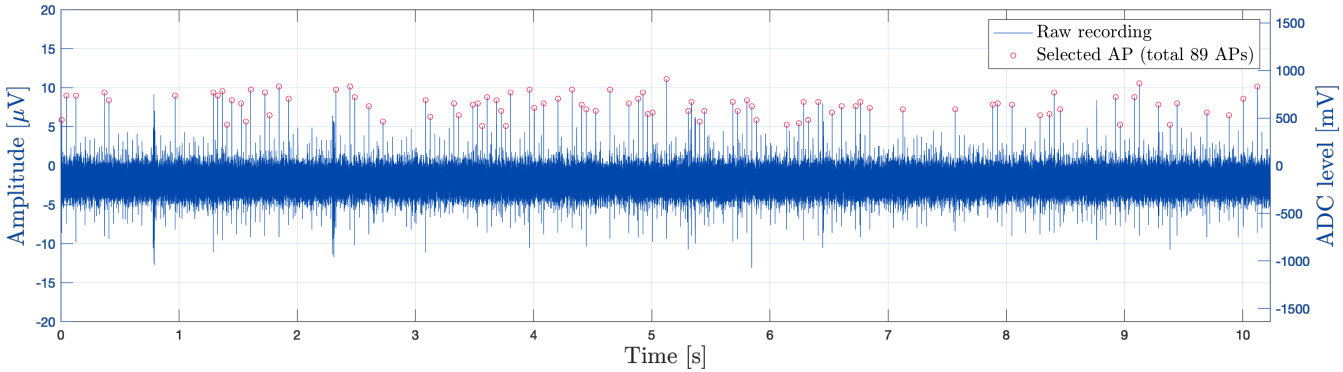
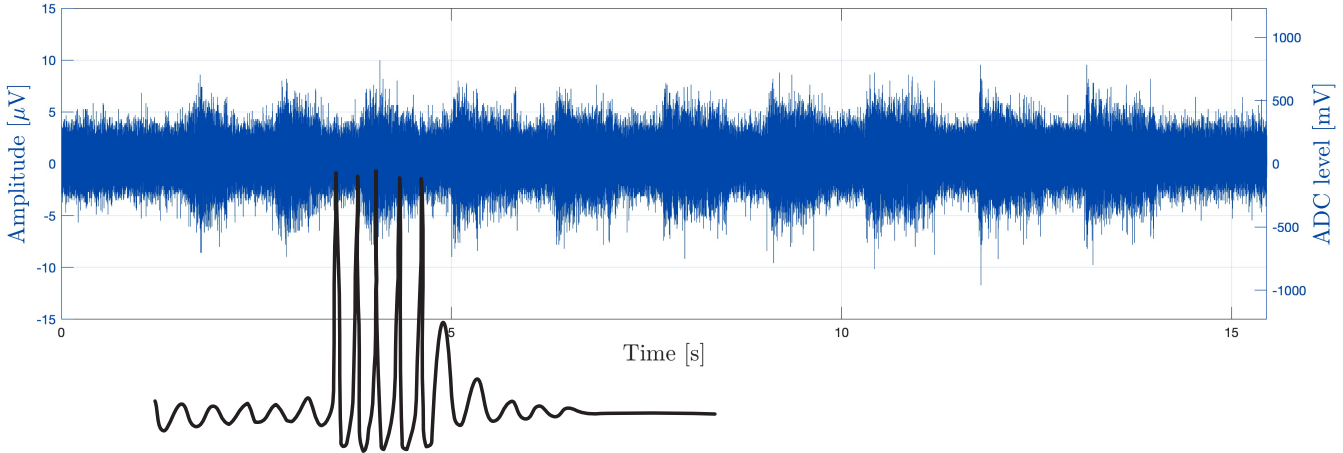
Single-unit versus multi-unit





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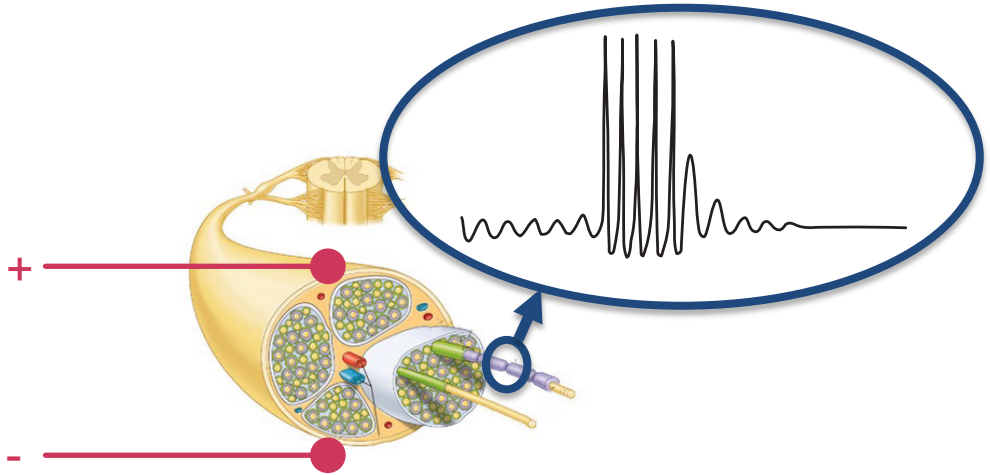
Electric field distribution



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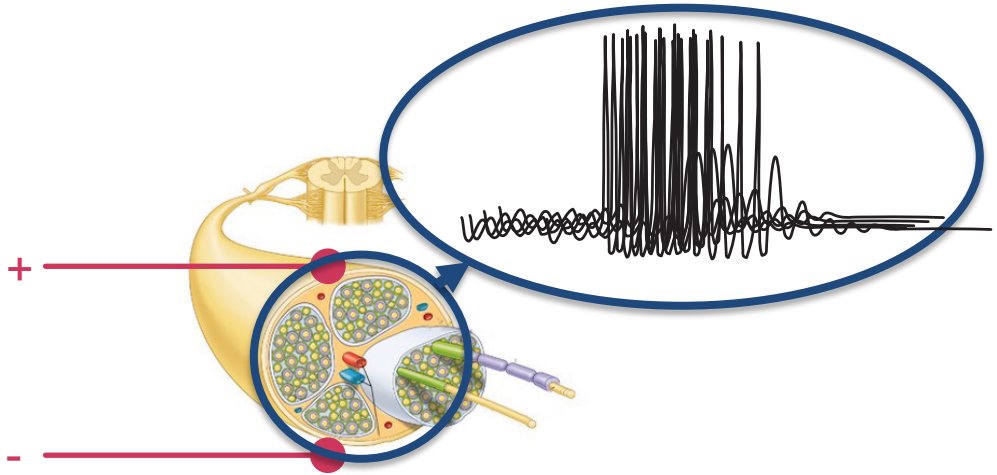

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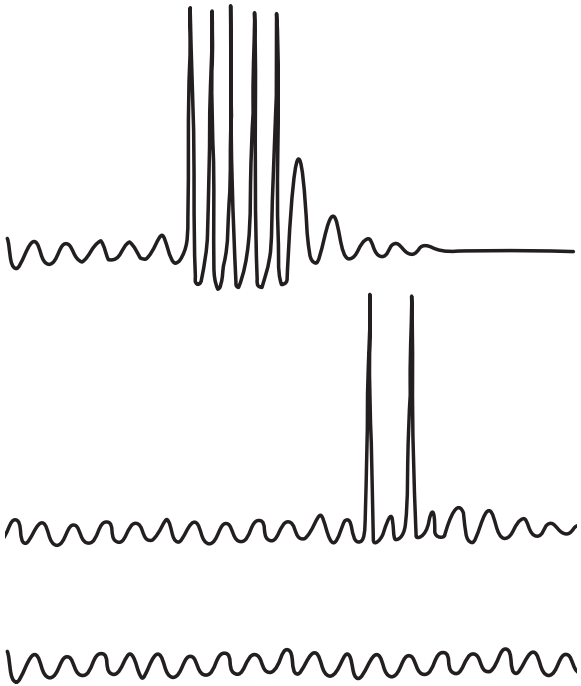
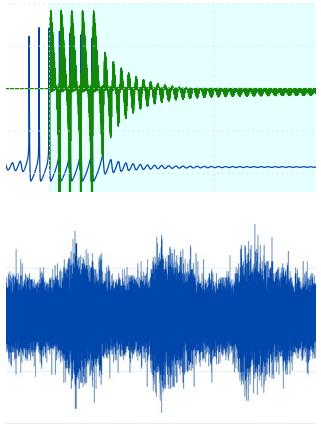
Working hypotheses



Summary

- Stimulus can be found that neutralizes SO and ED *in-silico*[1]
- Full functional and *in-vivo* tested microneurography amplifier
- Ready to go from theory to practice!



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[1] **Submitted to Journal of Neural Engineering:**

U.C.A.M. Verzijl, M.J.A. Malessy, S.G.A. van Neerven, W.A. Serdijn, K. Kolovou-Kouri, V. Giagka, and S. Pequito (2021). *"Mitigating neuropathic pain at the neuron level through electrical neurostimulation: a model predictive control approach with fractional-dynamicy proxy".*