Optimization of Electrode Design Parameters for Improved Preferential Activation of Small Cutaneous Nerve Fibers

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Introduction

- Several electrodes have been developed for preferential activation of small cutaneous nerve fibers for assessment of small fiber function and probing of pain pathways
- The selectivity of the electrodes is highly debated and they are limited to low-intensity stimulation
- All of the existing electrodes have been developed empirically and little investigation has been conducted into the influence of different electrode parameters
- Using computational modeling many design features may be investigated and contribute to improved electrode design

Aim

The aim of the present study was to optimize and investigate the influence of electrode parameters to enhance preferential small fibers activation.

Methods

Electrodes

- Intra-epidermal design (IE)

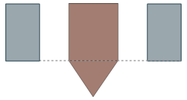


Figure 1: sketch of the intra-epidermal electrode design

- Planar concentric design (CE)

Figure 2: sketch of the planar concentric electrode design

Two step computational model

1. Finite element model of the skin and electrodes, implemented in COMSOL
   ↓ Electrical potential
2. Multicompartmental Aβ-fiber and Aδ-fiber models [1], implemented in NEURON
   ↓

Activation threshold, defined as the lowest stimulation intensity for which an action potential propagates to the end of the nerve fiber model

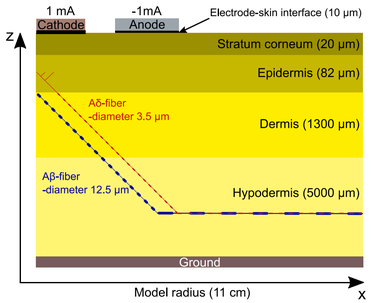


Figure 3: Sketch of the computational model

Methods (cont.)

Optimization of electrode parameters

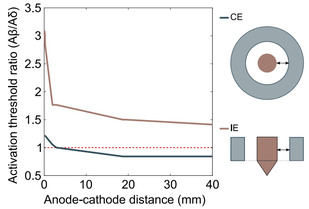
- Gradient free Nelder-Mead optimization algorithm with probabilistic restarts and fixed boundaries [2]

Table 1: Optimization bounds and original electrode dimensions

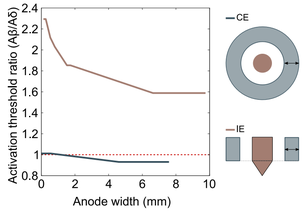
Electrode parameter	Lower bound	Upper bound	Dimension of original designs
Anode width	60 µm	1 cm	Intra-epidermal: 0.15 mm Planar concentric: 0.5 mm
Anode-cathode distance	100 µm	4 cm	Intra-epidermal: 0.5 mm Planar concentric: 2.25 mm
Cathode radius	30 µm	1 cm	Planar concentric: 0.25 mm
Needle cathode angle	26º degrees	178º degrees	Intra-epidermal: 50º degrees
Needle cathode protrusion	10 µm	30 µm, 60 µm, or 100 µm	Intra-epidermal: ~100 µm

Results

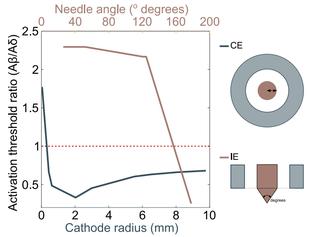
A) Activation threshold ratio for anode cathode distance



B) Activation threshold ratio for anode width



C) Activation threshold ratio for cathode dimensions



D) Activation threshold ratio for needle protrusion

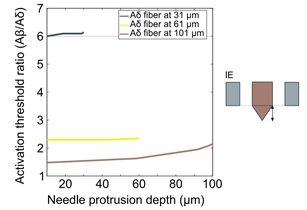


Figure 4: The activation threshold ratio between the two nerve fiber models as a function of (A) anode-cathode distance, (B) anode width, (C) cathode radius/ cathode angle, and (D) cathode protrusion. An activation threshold ratio above 1, indicates preferential small fiber activation.

Results (cont.)

- The anode width, anode-cathode distance, cathode radius and cathode angle were optimal at their respective lower bound
- The cathode protrusion was optimal a few micrometers above the Aδ-fiber termination depth
- The combination of the optimized electrode parameters increased the activation threshold ratio to a much larger extent than the optimization of individual parameters

Activation threshold ratio of the original and optimized electrode dimensions

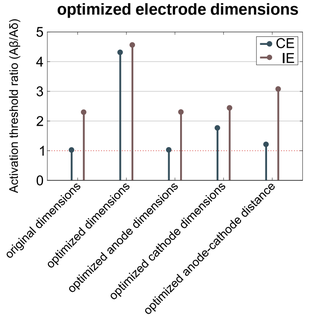


Figure 5: the activation threshold ratio for original electrode dimensions and the combined and individual optimization of the electrode parameters.

Area of selectivty for the original and optimized electrode dimensions

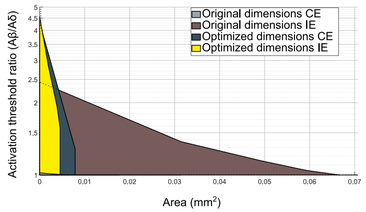


Figure 6: The area for which the original and optimized electrode dimensions display a lower activation threshold for small A-fibers than large Aβ-fibers.

Conclusions

- To enable preferential small fiber activation a small cathode is essential
- To increase preferential small fiber activation a small anode-cathode and small anode is important as it limits the current spread and decrease large fiber activation
- When using optimal electrode parameters a planar electrode may achieve similar preferential activation as an intra-epidermal electrode
- Based on the optimization a new planar electrode was designed (figure 6)

Figure 6: A new planar concentric array electrode design with 7 interconnected anode-cathode pairs. The electrode has a size of 3.8 cm x 0.99 cm. The anode width is 0.3 mm, the cathode radius 0.25 mm, and the anode-cathode distance is 0.5 mm.

References

[1] Tigerholm, J., Poulsen, A. H., Andersen, O. K., and Mørch, C. D., 2019, From Perception Threshold to Ion Channels—A Computational Study, *Biophys. J.*, **117**

[2] Luersen, M. A., Le Riche, R., and Guyon, F., 2004, A constrained, globalized, and bounded Nelder-Mead method for engineering optimization, *Struct. Multidiscip. Optim.*, **27**, 43–54.

[3] Poulsen, A. H., Tigerholm, J., Andersen, O. K. and Mørch, C. D., 2021, Increased preferential activation of small cutaneous nerve fibers by optimization of electrode design parameters. *Journal of Neural Engineering*, **18**, 016020. https://doi.org/10.1088/1741-2552/abd1e1

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