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Design Iterations on Self-Folding Neuroelectrodes

A 6-week Research Internship in the Scope of MSNE

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Abstract — Peripheral nerve interfacing offers a promising strategy for targeted neuromodulation in metabolic disorders, yet selective engagement of multiple adjacent nerves remains technically challenging. This project aimed to redesign an existing self-folding flexible cuff electrode to enable reliable multi-nerve interfacing in freely moving animals while maintaining surgical simplicity and fabrication compatibility.

An iterative, model-based development process was employed. First, the single-cuff design was expanded into a five-cuff, multi-channel electrode while preserving compatibility with the established microfabrication workflow and 16-channel connector system. Geometric refinements yielded a compact linear arrangement that maximized spatial efficiency while preserving independent nerve access. Second, an applicator-assisted implantation strategy was developed to enable stable sequential placement of low-pressure cuffs. A suturing-based temporary fixation method, implemented using a surgical 7/0 needle and integrated suturing holes, allowed reliable positioning of individual cuff electrodes on a 3D-printed five-nerve model before the activation of the self-folding mechanism. Third, three flexible tether geometries were designed and comparatively evaluated; in vivo testing in freely moving locusts demonstrated superior motion tolerance of a spiral configuration.

All investigations were qualitative and primarily conducted in vitro. The results demonstrate the conceptual feasibility of a multi-cuff self-folding electrode system and associated implantation strategy, while highlighting the need for quantitative validation and simplified surgical approaches for translational application.

1 Motivation

Peripheral nerve interfacing represents a promising therapeutic strategy for metabolic disorders such as obesity, as it enables targeted neuromodulation of pathways that regulate energy expenditure. Effective implementation of this approach requires electrodes that are mechanically compliant with soft neural tissue to minimize foreign body response and ensure long-term stability. A previously developed self-folding flexible cuff electrode addressed these requirements by reducing mechanical mismatch and simplifying surgical implantation through a suture-free design [1].

However, although the existing neuroelectrode design enables reliable interfacing with a single nerve, effective neuromodulation may require the coordinated engagement of multiple adjacent nerves to achieve sufficient functional control and therapeutic efficacy. While enlarging a single cuff to interface multiple nerves reduces spatial selectivity and controllability, implanting multiple separate cuff electrodes increases surgical complexity and adverse immune responses.

These limitations motivated the development of a multi-channel interface that integrates several cuff electrodes within a single implantable platform, thus maintaining high selectivity while reducing the implant's footprint. Building on the established self-folding concept, this project seeks to redesign the existing flexible neuroelectrode to enable reliable, multi-site interfacing in freely moving animals while preserving surgical simplicity and mechanical compatibility with neural tissue.

2 Project Scope

This research internship was guided by the following central objective:

Research Objective: Re-design an existing flexible cuff neuroelectrode to reliably interface multiple nerves in freely moving animals while maintaining relative ease of surgical implantation.

To achieve this objective, the project was structured into three interrelated components: (i) redesign of the electrode into a five-cuff, multi-channel system, (ii) development of a practical implantation strategy, and (iii) design of motion-tolerant tether geometries.

2.1 Neuroelectrode Design

The first part of the project focused on redesigning the existing self-folding cuff electrode into a multi-nerve, multi-channel interface under clearly defined engineering constraints.

Compatibility with the established microfabrication process (cf. [1]) was a primary requirement. Consequently, modifications were restricted to geometric refinements in order to preserve the existing fabrication workflow.

In addition, the redesigned layout had to remain electrically and mechanically compatible with the established 16-channel connector system to ensure seamless integration with existing hardware.

Functionally, the device was required to enable simultaneous interfacing of five distinct peripheral nerves on independent channels to ensure spatial selectivity and independent stimulation or recording capability for each targeted nerve branch.

Finally, the electrode needed to maintain mechanical robustness during handling to facilitate a practical surgical implantation and correct electrode placement.

Together, these constraints defined the framework within which the multi-nerve electrode system was developed.

2.2 Implantation Procedure

The implantation of a five-cuff construct presents considerable mechanical challenges, as each cuff is intentionally designed to exert only minimal radial pressure in order to prevent nerve damage. In a mechanically interconnected configuration, forces applied during placement of one cuff may inadvertently displace electrodes that have already been positioned.

Furthermore, the compliant nature of the electrodes makes them susceptible to twisting and deformation during implantation. This not only increases surgical complexity but also reduces procedural reproducibility.

Accordingly, a specific implantation strategy is required to ensure temporary stabilization of both the overall electrode system and the individual cuff electrodes throughout the placement process, thereby enabling reliable and successful surgery.

Within the scope of this internship, the development of such a strategy was restricted to in vitro investigations. To support this effort, a 3D-printed five-nerve model based on the peripheral nerves innervating adipose tissue in mice was designed and utilized to iteratively refine implantation techniques.

2.3 Flexible Tether

The third internship component addressed the mechanical reliability of the tether connecting the implant to the external interface. In freely moving animals, natural body movements introduce tensile, bending, and torsional strain along the tether, which can be transmitted to the electrode–nerve interface and result in compromised signal stability, altered electrode positioning, or reduced long-term functionality.

The objective of this work package was therefore to compare different tether geometries with respect to their motion tolerance and ability to accommodate animal movement while minimizing strain transmission to the electrode–nerve interface.

3 Methods

All investigations were limited to in vitro experiments and qualitative assessments. Designs and implantation concepts were evaluated using model-based approaches to assess feasibility, handling, and mechanical behavior. No quantitative biological validation was performed.

3.1 Neuroelectrode Design

The five-cuff electrode system was developed through an iterative, model-based process progressing from conceptual prototypes to fabricated constructs (cf. Figure 1).

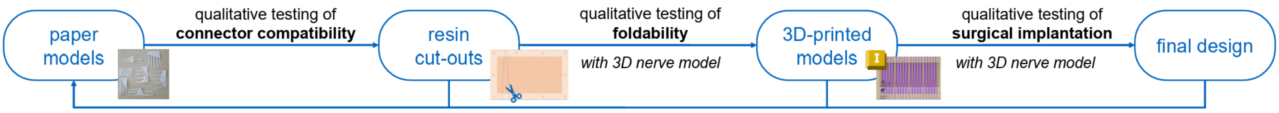

Figure 1 Iterative process of refining a multi-cuff electrode system.

Conceptual Paper Prototypes In an initial design phase, paper models (cf. Figure 2) were used to explore the spatial arrangement of five cuff electrodes relative to each other and to the existing connector. This enabled rapid assessment of how the electrodes would need to bend and orient in order to interface five adjacent nerves while maintaining connector compatibility.

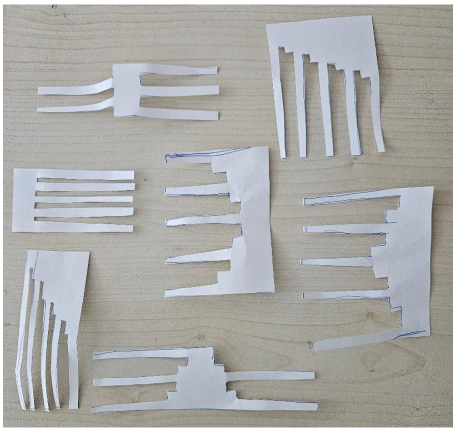

Figure 2 Selected paper prototypes of the five-cuff electrode showing different relative electrode arrangements and intermediate step features introduced to increase mobility during implantation.

It was observed that a linear arrangement of adjacent electrodes proved most practical in terms of bending behavior, orientation, and placement relative to the target nerves. Intermediate offset steps between electrodes were introduced to increase individual electrode mobility and allow for multi-directional bending with minimal strain.

Resin Sheet Cut-Outs and Model Testing Based on the paper prototypes, promising geometries were transferred to flexible resin sheets and tested on a 3D-printed five-nerve model composed of parallel 100 µm wire strands embedded in a medical resin construct (cf. Figure 3).

Testing revealed that, as the targeted nerves are largely coplanar, out-of-plane mobility was rendered unnecessary. Moreover, offsets increased the implant footprint, which could potentially induce an increased immune response in the animals. Subsequent iterations therefore eliminated these geometric step features in favor of a more compact linear layout.

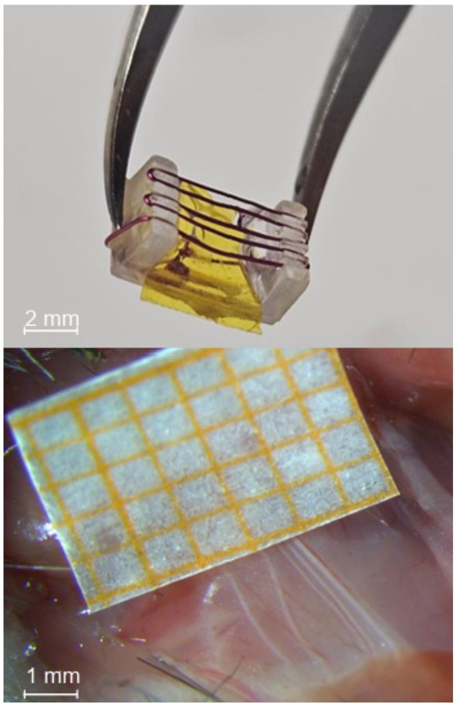

Figure 3 Top: 3D-printed nerve model consisting of five parallel 100 µm wire strands embedded in a medical resin construct. Bottom: Anatomical peripheral nerves innervating adipose tissue in mice, serving as the geometric reference for the fabricated model.

CAD Refinement and Fabrication Refined designs were implemented in *Autodesk Inventor* – allowing a greater control over individual design features than previous prototypes –, fabricated following [1], and tested on the above mentioned nerve model. Design iterations focused on electrode spacing, cuff dimensions, and geometrical distribution of folding regions to ensure reliable self-folding and ease of simulated implantation; whether individual designs were discarded or further explored was informed by their handling behaviour, practical feasibility, mechanical stability, and spatial efficiency.

3.2 Implantation Procedure

Implantation strategies were tested on the same 3D model and a similar iterative approach as the neuroelectrode design. Different approaches to temporarily stabilize both individual electrodes and the whole implant were assessed based on the achieved mechanical stability, surgical feasibility, and their ability to be removed fully after the activation of the electrodes' folding process.

Concept Development Following extensive brainstorming, a sliding support structure was identified as the most practical solution. The device holds the electrode system in a stable, open configuration, enabling precise positioning beneath the target nerves through simple "sliding". Each cuff is looped around its respective nerve from below and temporarily secured to small hook structures. Fixation to the hooks was implemented using a shoelace-inspired string mechanism. Once all five cuffs are in place, the self-folding mechanism is activated by hydration, after which the temporary fixation is released and removed.

However, when further developing this concept, two major challenges emerged: the design of suitable hook structures and the attachment of the delicate electrodes to these hooks.

Hook Integration Challenge Attempts to integrate hooks directly into the electrode during 3d-printing or form them using adhesives were unsuccessful due to fabrication incompatibility and insufficient adhesion. A separate applicator device was therefore designed to (i) stabilize the electrode array, (ii) provide temporary hook structures, and (iii) be removable after folding.
Multiple applicator designs were developed in *Autodesk Inventor*, with iterative refinement of geometry, scale, and structural features. Printing time and material usage were minimized while ensuring sufficient mechanical stability.

Electrode Attachment Challenge Due to the small dimensions and mechanical fragility of the electrodes, achieving stable attachment to the hook structures without causing damage proved challenging. A shoelace-inspired fixation strategy was therefore developed, in which the electrodes were attached indirectly rather than directly to the hooks. Using a needle–thread combination, each electrode was first secured to a common thread. The thread was then looped around the hooks, positioning the electrodes appropriately. Repeating this process for all electrodes created a crisscross pattern, allowing simultaneous stabilization of the entire system. This configuration ensured reliable temporary fixation while enabling rapid release by simply pulling the thread.

Various combinations of household threads and needles were initially evaluated. Several iterations were required to identify suitable materials and dimensions before transitioning to surgical round needles of appropriate size to ensure controlled handling and minimize damage to the electrode substrate.

To accommodate this fixation method, the electrode design was further refined. Dedicated suturing holes were incorporated into the layout to permit controlled attachment without inducing tearing or mechanical failure during stitching. As with the overall development process, the positioning and dimensions of these features were iteratively optimized through repeated testing on the 3D nerve model.

3.3 Flexible Tether

Conceptual paper models were initially used to brainstorm tether geometries that could reduce strain transmission during animal movement. Based on qualitative assessment of bending behavior and strain distribution, three principal tether geometries were selected for further investigation: (i) a short tether incorporating a single bend, (ii) a longer tether with a bend region, and (iii) a spiral-shaped tether (cf. Figure 4). The bent geometries were intended to introduce a compliant section that allows multi-planar deflection while reducing direct tensile loading on the electrode interface. The spiral configuration was expected to further enhance flexibility by distributing strain along a curved path, thereby increasing overall motion tolerance.

Layouts were implemented in *KiCad* and fabricated as flexible PCBs. Motion tolerance was qualitatively assessed using freely moving locusts implanted with a single cuff electrode. Geometries were compared based on flexibility, handling robustness, and visible strain transmission to the implant interface.

4 Results

The following results summarize the final design states and outcomes of the three project components. As all investigations were conducted in vitro and evaluated qualitatively, emphasis is placed on design feasibility,

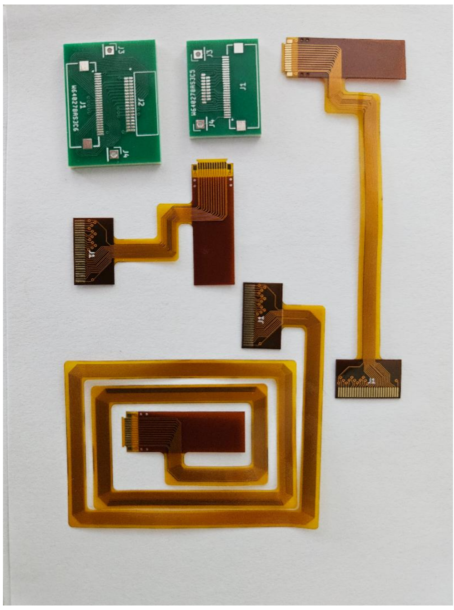

Figure 4 Printed flexible PCBs and FPC connectors developed for the motion system.

mechanical behavior, and practical handling characteristics rather than quantitative performance metrics.

4.1 Neuroelectrode Design

The final implant design consists of five linearly arranged self-folding cuff electrodes (cf. Figure 5). The predefined design criteria were fulfilled as follows.

Compatibility with the Established Fabrication Process No modifications to the fabrication workflow were required; only the geometry of the printed layout was adapted, ensuring full process compatibility.

Compatibility with the 16-Channel Connector Each cuff incorporates three electrode channels, resulting in a total of 15 channels. This configuration ensures seamless electrical and mechanical integration with the established 16-channel connector system.

Simultaneous Multi-Nerve Interfacing Each cuff provides three electrically independent channels, enabling spatially selective stimulation or recording for each targeted nerve branch without cross-interference between electrodes.

Mechanical Robustness During Surgery To support the implantation strategy developed in parallel, dedicated suture holes were integrated into each cuff structure. This modification emerged from iterative refinement of the surgical procedure and enables temporary fixation without compromising structural integrity.

Minimized Implant Footprint The final design places the cuffs directly adjacent to one another, optimizing spatial efficiency and minimizing potential tissue burden while preserving independent mechanical compliance. The offset positioning of electrode bodies relative to the feedline routing further improved space management and reduced interference between adjacent cuffs during placement.

Overall, the final geometry fulfills the defined requirements for multi-channel interfacing, fabrication compatibility, connector integration, and surgical practicality.

4.2 Implantation Procedure

The final implantation concept successfully addressed the primary mechanical and handling challenges identified during development by using a dedicated applicator system providing temporary mechanical stabilization (cf. Figure 7).

Final Applicator Design The finalized applicator (cf. Figure 7) consists of a rigid support structure into which the multi-cuff electrode is slid. This configuration stabilizes the otherwise flexible and curl-prone electrode substrate, preventing uncontrolled rolling or deformation during handling. Integrated sewing hooks and a dedicated knotting hook provide temporary fixation points during the electrode placement procedure, decoupling handling forces from the nerve–electrode interface, and enabling reliable stepwise placement.

Suturing Strategy and Needle Selection A surgical 7/0 round needle provided an effective balance between compatibility with the delicate electrodes and practical handling. This needle size was sufficiently small to pass through the electrodes' suturing holes without damaging the electrode material, yet large enough to allow controlled and practical handling during the procedure.

Additionally, during experimentation, it became evident that the suturing thread required a defined fixation point to maintain stable tension throughout implantation. This observation led to the integration of a dedicated knotting hook within the applicator design. The thread could be temporarily fastened at this location during placement of the individual cuffs, ensur-

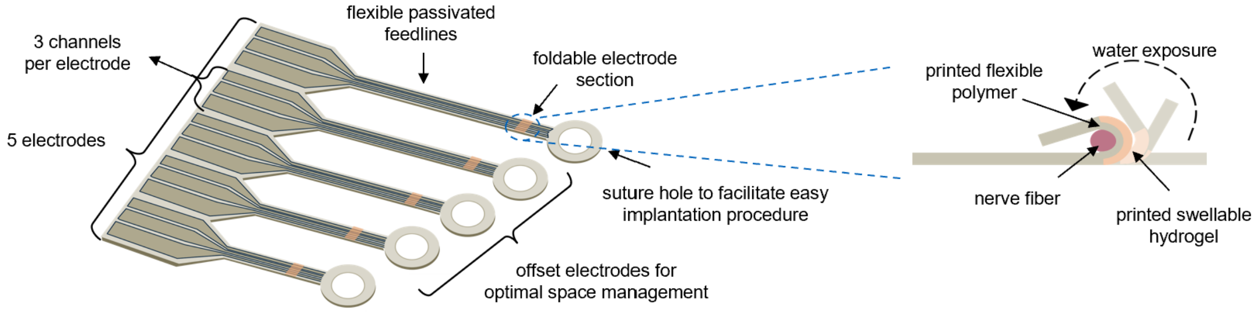

Figure 5 Illustration of the final 5-cuff flexible self-folding electrode system.

ing consistent stabilization. After successful implantation and activation of the self-folding mechanism, the thread was detached from the knotting hook and completely removed.

Functional Validation on the Nerve Model

Using the finalized applicator and suturing method, all five cuff electrodes could be positioned correctly and reproducibly on the 3D-printed five-nerve model (cf. Figure 6). The electrodes remained stably fixed throughout sequential placement. Once proper alignment was achieved, the self-folding mechanism was activated via water exposure. After folding, the temporary sutures were released and the applicator removed, leaving the cuffs securely wrapped around their respective nerve analogues.

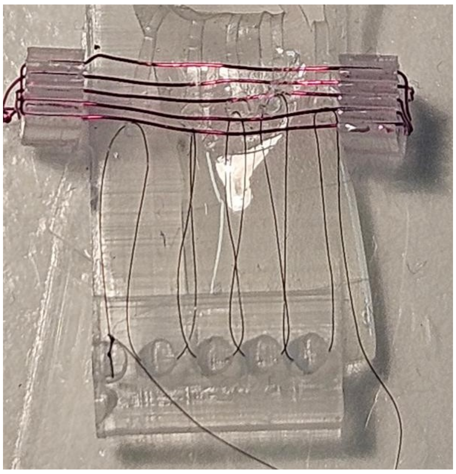

Figure 6 Multi-cuff electrode mounted in the applicator and temporarily secured using sutures attached to the sewing and knotting hooks prior to activation of the self-folding mechanism.

Overall, the final implantation procedure overcame the initial instability challenges and enabled reliable, stepwise placement of the multi-cuff system while preserving the low-pressure nerve interface principle.

4.3 Flexible Tether

Comparison of three tether geometries – short with bend, long with bend, and spiral – revealed clear differences in motion tolerance.

The short tether with a single bend provided limited compliance. Although the bend introduced a defined flexural region, movement of the animal resulted in visible tension. Extending the bend improved strain distribution but did not fully eliminate localized stress under directional pulling.

The spiral geometry exhibited superior mechanical decoupling by distributing tensile, bending, and torsional loads along its curved structure. During in vivo testing in freely moving locusts, the spiral tether accommodated natural locomotion without visible strain transmission to the electrode interface.

These observations indicate that distributed geometric compliance is more effective than localized bend regions for minimizing mechanical loading in tethered neuromodulation setups.

5 Discussion and Outlook

This project demonstrates the conceptual feasibility of a multi-cuff, self-folding peripheral nerve interface together with a corresponding implantation strategy and motion-tolerant tether design. Through an iterative, model-based development process, key mechanical and surgical challenges were identified and addressed.

The final multi-cuff electrode design fulfilled the defined criteria of multi-channel interfacing, connector compatibility, and preservation of the established fabrication workflow. Likewise, the applicator-assisted implantation strategy successfully enabled sequential and stable placement of all five cuffs in a controlled model environment. For tethering, the spiral geometry emerged as the most mechanically compliant con-

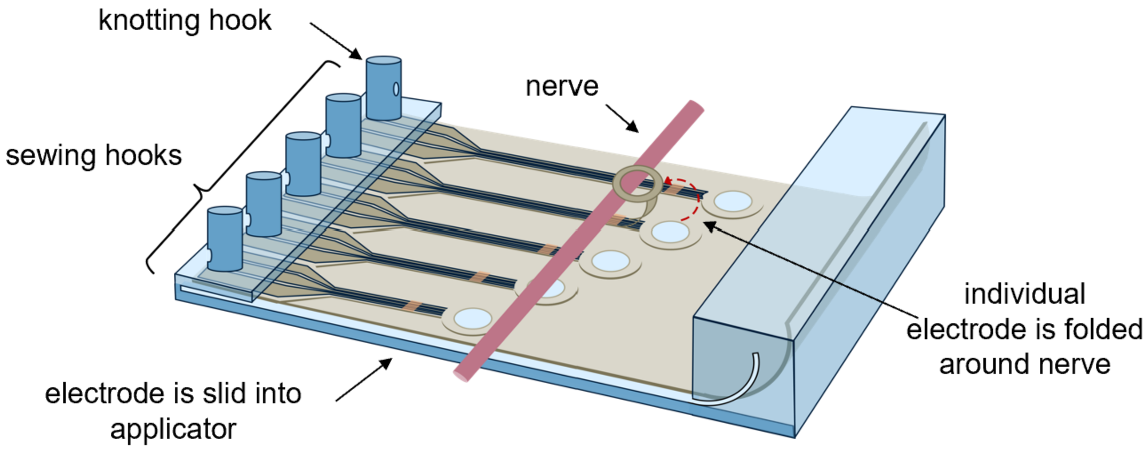

Figure 7 Illustration of the final applicator design used for guiding and securing individual cuff electrodes during the implantation procedure.

figuration under dynamic conditions, highlighting the importance of distributed strain-relief structures for experiments in freely moving animals.

Despite these promising outcomes, several limitations must be acknowledged.

First, all investigations were qualitative in nature. No quantitative mechanical characterization, force measurements, or electrical performance analyses were conducted. As a result, conclusions regarding mechanical stability and motion tolerance are based on observational assessment rather than numerical validation.

Second, the electrode systems evaluated during development were not fully fabricated with complete feedline integration in all iterative stages; prototypes were simplified geometrical representations used for mechanical testing and implantation assessment. Consequently, full-system integration effects were not comprehensively examined.

Third, the evaluation of the multi-cuff system was limited to in vitro testing using a 3D-printed nerve model. No in vivo implantation of the five-cuff construct was performed. Therefore, biological responses, long-term stability, and physiological performance remain unaddressed.

Finally, although the developed implantation procedure proved effective in the in vitro model setting, its current implementation is not readily transferable to in vivo applications. Even under controlled laboratory conditions, the procedure was relatively lengthy and technically demanding, which limits its practical applicability. The reliance on temporary suturing and a dedicated external applicator system increases procedural complexity and may pose significant constraints in a real surgical environment.

These considerations indicate that, for translational use, the implantation strategy would require substantial simplification. Alternative approaches to multi-cuff implantation – or potentially alternative strategies to individual cuff electrodes altogether – may need to be explored for future translational development.

Declaration

Declaration of Generative AI and AI-assisted technologies
ChatGPT (OpenAI, February 2026 version) was used to assist with text condensation and formulation. The first author reviewed and edited the content and takes full responsibility for the publication.

References

[1] L. Hiendlmeier, F. Zurita, J. Vogel, F. Del Duca, G. Al Boustani, H. Peng, I. Kopic, M. Nikić, T. F. Teshima, and B. Wolfrum. 4d-printed soft and stretchable self-folding cuff electrodes for small-nerve interfacing. *Advanced Materials*, 35:2210206, 2023.

Appendix

All relevant files have been made publicly available in the following GitHub repository: https://github.com/SaraETaube/Design-Iterations-on-Self-Folding-Neuroelectrodes.git.