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by Sanaul Haque

Optimizing Electrode Interspacing in Cuff-Based Brain–Computer Interfaces: Effects on Stimulation Thresholds and Selectivity in Computational Models of Vagus Nerve Stimulation

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Research Topic: Advancing Electrode Design for Therapeutic BCIs

Research Aims

This project aims to bridge the gap between computational modeling and clinical translation by providing design recommendations that can be directly applied in the fabrication of next-generation neuromodulation devices. By focusing on reproducibility and open data, the study will ensure that its findings can be validated, extended, and applied by other researchers and engineers worldwide. (1) Quantitatively evaluate how inter-electrode spacing in cuff-based arrays affects stimulation thresholds in finite-element simulations of the cervical vagus nerve. (2) Measure the impact of spacing on selectivity (target vs. off-target fiber recruitment) and identify spacing ranges that optimize the trade-off between low threshold and high selectivity. (3) Produce reproducible design heuristics and datasets to inform future cuff electrode design for spinal cord injury (SCI) applications.

Research Questions

1. How does inter-electrode spacing influence stimulation threshold current in cuff electrodes as predicted by finite-element models?

2. To what extent does spacing affect selectivity of vagus nerve activation in computational simulations?

3. Which spacing configurations produce the best balance of low threshold, high selectivity, and realistic energy requirements for practical BCI devices?

Introduction & Historical Context

Brain–computer interfaces (BCIs) have evolved from basic electroencephalography (EEG) prototypes to clinically used neuromodulation systems. Cuff electrodes occupy an important niche between non-invasive surface electrodes and fully invasive intraneural interfaces, offering safer peripheral nerve access while enabling stimulation and recording with improved spatial resolution. Despite material and signal-processing advances, inconsistent stimulation thresholds and poor selectivity remain persistent obstacles to reliable BCI deployment and effective therapies for conditions such as spinal cord injury (SCI) [4], [5]. Historical progress in electrode design demonstrates that geometry and placement materially affect neural activation, yet inter-electrode spacing—a parameter readily modifiable in array fabrication—has not been systematically explored for cuff-based vagus nerve stimulation (VNS) in a way that provides direct, reproducible design guidance.

The vagus nerve is a particularly important target because of its role in autonomic regulation, inflammation control, and neuroplasticity. Optimizing stimulation efficiency in this nerve could have far-reaching implications not only for SCI rehabilitation but also for conditions such as epilepsy, depression, and cardiovascular disorders. Thus, the significance of this study extends beyond a single application, potentially influencing the broader field of neuromodulation.

Current Conversation (Key Evidence)

Recent work confirms that electrode geometry modifies threshold behavior and activation patterns. Yang et al. demonstrated that cuff parameters can "substantially influence the threshold current" under MR conditions, indicating geometry strongly shapes stimulation efficiency [1]. Ravagli et al. employed cuff arrays combined with electrical impedance tomography (EIT) to achieve organ-specific selectivity, showing arrangement and contact placement alter target recruitment [2]. Cardiac pacing research reports that electrode spacing lowers capture thresholds while maintaining safety margins, suggesting spacing is a generalizable lever for optimizing stimulation [3]. Parallel research highlights persistent signal acquisition challenges and the complementary roles of hardware design and algorithmic processing in improving BCI performance [4]–[7]. Literature on electrode misplacement in ECG systems further underscores that small configuration changes can produce large signal deviations [8]. Despite these advances, no published study has isolated inter-electrode spacing as the primary variable for cuff VNS and charted its effect on thresholds and selectivity across a systematic parameter sweep—leaving a practical design gap. This evidence suggests that electrode spacing is not merely a secondary design detail but a potentially decisive factor in determining whether neuromodulation therapies succeed or fail. By systematically mapping this parameter, the proposed study will provide clarity where current literature remains fragmented.

Problem Statement & Research Gap

The central problem is lack of empirical, reproducible guidance on how inter-electrode contact spacing in cuff arrays affects stimulation thresholds and selectivity for VNS. Existing studies document geometry or array design effects and demonstrate general correlations with threshold and selectivity [1]–[3], but do not present a systematic, parameterized mapping of spacing vs. outcome for cuff electrodes targeting the vagus nerve. This gap limits informed engineering decisions for implantable/semi-invasive BCIs and impedes progress toward energy-efficient, selective neuromodulation for SCI and related clinical uses. Without such guidance, device manufacturers risk producing electrodes that are either inefficient (requiring excessive current and energy) or unsafe (activating unintended fibers). This project addresses that engineering bottleneck, focusing on one unexplored variable of electrode interspacing and its implications.

Hypothesis: Closer inter-electrode spacing (sub-millimeter to ~1 mm) will reduce predicted stimulation thresholds but may reduce spatial selectivity; an optimal spacing range exists that minimizes threshold while preserving acceptable selectivity for therapeutic purposes.

Methodology and Study Design

A computational experimental study using finite-element modeling (FEM) and axon activation proxies will be conducted to quantify the relationship between electrode interspacing and neural activation metrics in cuff-based BCI.

Model Construction

- Geometry: 3D model of the cervical vagus nerve (nominal outer diameter = 3 mm) with multi-fascicular internal structure (3 representative fascicles). Surrounding tissue layers (epineurium, perineurium, saline/tissue) modeled per published conductivity values [1], [2], [5].

- Electrode: Semi-flexible cuff with multiple ring/contact segments. Contact arc width fixed at 1.0 mm for primary sweep; contact spacing varied as the independent variable.

- Spacing Grid (primary sweep): 0.5, 1.0, 1.5, 2.0, 3.0, and 4.0 mm center-to-center values. Secondary finer sweep around promising ranges (0.2–0.7 mm) will be performed if simulations indicate steep gradients in outcomes.

- Stimulation Waveform: Biphasic rectangular pulses; pulse widths tested: 100 µs and 300 µs. Amplitude swept to determine threshold.

Activation & Metrics

Activation proxy: Activating-function approximation and published axon threshold models (e.g., McIntyre-type relationships) will be used to estimate fiber activation from extracellular potentials [1], [2].

- Dependent variables:

  • Threshold current (I_thresh): minimum current amplitude required to recruit a defined percentage (e.g., 10%) of target fascicle fibers.

  • Activation volume (V_act): tissue volume where activation condition is met (mm^3).

  • Selectivity Index (SI): ratio of target-fascicle activation to off-target activation (dimensionless).

  • Energy per pulse (Joules): amplitude × pulse width × duty assumptions.

These metrics were chosen because they directly reflect both engineering efficiency (thresholds, energy) and clinical relevance (selectivity, activation volume

Sensitivity, Validation, and Computational Analysis

To ensure the robustness and credibility of the results, the study will integrate sensitivity testing, validation procedures, and rigorous computational analysis into a unified framework. For each electrode spacing condition, Monte Carlo simulations (N = 10) will be conducted by randomly varying nerve diameter (±10%), tissue conductivities (±10%), and electrode-to-nerve gap (0.1–1.0 mm). This approach will generate confidence intervals around the predicted outcomes and test the stability of the findings across realistic biological variability. Model verification will be performed by reproducing one published scenario—such as threshold or field distributions reported by Yang et al.—to confirm solver accuracy and parameterization. In addition, if laboratory access permits, an optional benchtop phantom experiment using an agarose/saline model with an embedded conductor will be carried out to qualitatively validate field distributions for selected spacing cases.

The computational workflow will rely on COMSOL Multiphysics as the primary FEM platform, with FEniCS or other open-source alternatives as backups. Post-processing and analysis will be conducted in Python using NumPy, Pandas, and Matplotlib. Adaptive meshing will be applied near electrode contacts, and a quasi-static electromagnetic solver will be employed, with mesh refinement tests ensuring numerical convergence. Statistical analysis will include ANOVA and regression to evaluate the effects of spacing on threshold current (I_thresh) and selectivity index (SI), with effect sizes and 95% confidence intervals reported. Finally, Pareto analysis will be used to visualize the trade-offs between low stimulation thresholds and high selectivity, providing a clear framework for identifying optimal electrode spacing configurations.

Timeline (12 Weeks)

- Weeks 1–2: Finalize literature synthesis, select modeling parameters, arrange software access and mentor support.
- Weeks 3–4: Build baseline nerve/cuff model; run verification cases reproducing published results.
- Weeks 5–7: Execute primary spacing parameter sweep (batch simulation runs).
- Weeks 8–9: Conduct Monte Carlo sensitivity analyses and secondary fine sweeps.
- Weeks 10–11: Data analysis, plots, and preparation of design heuristics (spacing recommendations).
- Week 12: Finalize written report, figures, reproducibility package (code, CSVs), and submission materials.

Feasibility, Resources & Ethics

This project is highly feasible within the proposed 12-week timeframe because it relies on established computational modeling techniques rather than resource-intensive or ethically complex in-vivo experiments. By using finite-element modeling (FEM), the study eliminates the need for human or animal subjects, ensuring that the work can be conducted entirely with accessible digital tools. The required resources are realistic for a high school–level research environment: access to FEM software through a school or university license, a workstation with at least 16 GB of RAM, and a Python environment for data analysis. Mentor oversight from faculty experienced in biomedical modeling will provide technical guidance and ensure methodological rigor. To further strengthen the study, optional access to a basic laboratory setup—such as a function generator and oscilloscope—would allow for phantom validation experiments using agarose or saline models, providing a tangible bridge between simulation and physical reality.

Expected Outcomes & Deliverables

The study is expected to generate a comprehensive quantitative mapping of electrode spacing against stimulation thresholds and selectivity, complete with confidence intervals to establish statistical reliability. These findings will be illustrated through a series of figures, including threshold-versus-spacing curves, activation volume heatmaps, and selectivity index trade-off plots, providing clear visual insights into the relationships uncovered. From this analysis, a concise set of design heuristics will be developed, offering practical recommendations for optimal spacing ranges in cuff electrodes targeting vagus nerve applications. To ensure transparency and reproducibility, the project will also produce a suite of deliverables—including simulation input files, Python analysis notebooks, CSV datasets, and a final written report—suitable for both peer review and conference submission.

Limitations & Risk Mitigation

- Model limitations: FEM models approximate biological complexity: fiber heterogeneity, encapsulation, and chronic tissue responses are not fully captured. Conclusions will focus on relative differences rather than absolute in-vivo thresholds.

- Mitigations: Use sensitivity analyses and validation against published data to increase confidence. Clearly state assumptions and recommend in-vivo validation as follow-up work.

Concluding Significance & Contribution

This project fills a demonstrable gap in BCI engineering by isolating inter-electrode spacing as a design variable for cuff-based VNS and quantifying its impact on thresholds and selectivity. The results will produce actionable design guidance that may reduce energy demands, improve safety, and elevate the therapeutic precision of neuromodulation devices—particularly those intended to support SCI rehabilitation. The reproducible dataset and open analysis pipeline will provide a practical resource for subsequent bench and in-vivo studies, bridging gaps in BCI technology, helping patients with paralysis, and advancements in real-world clinical innovations.

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