Mixed Integer Linear Programming for Active Contact Selection in Deep Brain Stimulation

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Abstract: Deep brain stimulation (DBS) programming is a complex, manual process aimed at maximizing therapeutic effects while minimizing side effects. This study investigates mathematical optimization for DBS using functional subdivisions of the subthalamic nucleus (STN) to define a desired activation profile. A Mixed Integer Linear Programming (MILP) framework is introduced, allowing for dissimilar current distribution across active contacts.

1. INTRODUCTION

Deep Brain Stimulation (DBS) is an established treatment for neurological and psychiatric conditions such as Parkinson's Disease (PD), where electrical pulses are delivered to targeted brain regions via implanted leads. The goal of DBS programming is to optimize symptom relief while minimizing side effects by selecting suitable stimulation parameters. Despite advancements in DBS technology, the process remains largely manual and time-consuming, relying heavily on trial-and-error and subjective assessments. To address these limitations, patient-specific computational modeling and image-guided tools have emerged as promising aids in streamlining DBS programming. The growing complexity of modern DBS leads—with up to 16 contacts—further underscores the need for automated, optimization-based approaches.

DBS programming can be formulated as a mathematical optimization problem aimed at achieving a desired activation profile. This includes maximizing activation within the target region while avoiding activation of surrounding structures associated with side effects. Here, a Mixed Integer Linear Programming (MILP) framework, previously used in general brain stimulation contexts, is adapted to DBS programming, allowing dissimilar current distributions across a set of active contacts.

2. METHODOLOGY

2.1 Patient Cohort

This study includes a cohort of ten PD patients treated at Uppsala University Hospital [1]. Nine of these patients received bilateral DBS, resulting in a total of 19 implanted leads. All patients were implanted with state-of-the-art, eight-contact directional leads. In all cases, the intended surgical target was the subthalamic nucleus (STN). The lead designs along with the contact labels used in this paper are illustrated in Fig. 1a and Fig. 1b.

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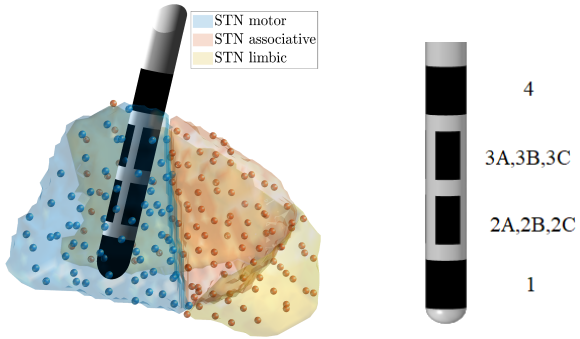

Fig. 1. (a) An eight-contact Boston Scientific Vercise Cartesia™ Directional lead relative to the functional subdivisions of the STN Ewert et al. (2018) along with target (blue) and constraint (orange) points. The original set of points were downsampled using a voxel filter with a voxel length of 0.95 mm. (b) The Abbot's Medical Infinity™ Directional lead with the contact nomenclature used in this study.

2.2 Mathematical Modeling

In DBS modeling, a common and practical approach to estimate the volume of tissue activated (VTA) involves identifying regions where the electric field norm E exceeds a given threshold, E_{th}. A point k is considered activated (or excited), if $E_k \geq E_{\text{th}}$. DBS programming is formalized as a procedure seeking activation in a set of target points Ω_{t}, while avoiding activation in a set of constraint points Ω_{c}.

The spread of the electric field in neural tissue surrounding the DBS lead is simulated using a Finite Element Method (FEM) model. A static approximation of the electric field is computed by solving the following partial differential equation (PDE) that describes the distribution of the electric potential u in three dimensions

$$\nabla \cdot (\sigma \nabla u) = 0, \tag{1}$$

where σ denotes conductivity.

For a DBS lead with N contacts, (1) is solved N times, each time applying a unit stimulus of 1 mA to a single contact while all others contacts remain inactive. For a set of points Ω with N_Ω locations relevant to the problem-

setup, the electric field norm E_{kp} for a unit stimulus applied to contact p at each location $k = 1, \ldots, N_\Omega$ is interpolated to construct the transfer matrix defined as

$$\mathbf{T} = \begin{bmatrix} E_{11} & E_{12} & E_{13} & \ldots & E_{1N} \\ E_{21} & E_{22} & E_{23} & \ldots & E_{2N} \\ \vdots & \vdots & \vdots & & \vdots \\ E_{N_\Omega 1} & E_{N_\Omega 2} & E_{N_\Omega 3} & \ldots & E_{N_\Omega N} \end{bmatrix}. \quad (2)$$

The linearity of electrical model (1) allows scaling the unit stimulus solution to any desired current amplitude. When multiple contacts belonging to the set $p = 1, ..., N$ are simultaneously active, the cumulative electric field norm can be computed by superimposing individual solutions. This is expressed as

$$\mathbf{y} = \mathbf{T}\mathbf{u}, \quad (3)$$

where $\mathbf{u} = [u_1, ..., u_N]$ is the vector of current amplitudes applied to each contact, and $\mathbf{y}$ is the resulting electric field norm at all relevant locations.

Switching a contact from inactive to active alters the boundary conditions in (1), making exact superposition of individual fields strictly speaking incorrect. Specifically, the superimposed solutions include the influence of induced currents at other contacts, which should not be present when a contact is actively stimulating. As a result, neglecting the effect of induced currents is expected to slightly overestimate the electric field norm, in particular near the DBS lead.

2.3 Mixed Integer Linear Programming

A general approach to solving electrical stimulation problems using MILP was introduced in Abouelseoud et al. (2018). In this work, the formulation was adapted to the context of DBS by using VTA, rather than induced currents, to quantify stimulation effects. Additionally, since only unipolar stimulation is considered, constraints on the reference electrode (anode) or the inclusion of negative current amplitudes become redundant. Under these considerations, the MILP formulation can be rewritten as

$$\begin{aligned} \mathbf{u}^* = \arg\min_{\mathbf{u},\mathbf{d}} \quad & \left(\frac{1}{N_\mathrm{t}} \sum_{i=1}^{N_\mathrm{t}} d_i + \frac{1}{N_\mathrm{c}} \sum_{j=1}^{N_\mathrm{c}} d_j \right), \\ \text{s.t.} \quad & \mathbf{T_i u} + L d_i \geq E_{\mathrm{th,t}}, \quad \forall i \in \Omega_\mathrm{t}, \\ & \mathbf{T_j u} - L d_j \leq E_{\mathrm{th,c}}, \quad \forall j \in \Omega_\mathrm{c}, \\ & d_i, d_j \in \{0, 1\}, \end{aligned} \quad (4)$$

where d_i and d_j are binary dummy variables and L is a larger number that allows for the relaxation of the constraint at a given target or constraint point. To allow for sufficient constraint relaxation, L should be chosen significantly larger than $E_{\mathrm{th,t}}$, but too large L may result in computational inefficiency. A solution derived from (4) directly allows to determine the number of targets points and constraint points that are activated and therefore either fulfill or violate the optimization objective.

3. RESULTS

The optimized current distributions computed with the MILP approach are given in Fig. 2. Notably, the MILP approach suggests zero amplitude in both leads of Patient 10. This is likely explainable by the poor lead placement relative to the atlas-based subdivisions of the STN in this patient.

Fig. 3 presents the runtimes for solving the MILP algorithm, for different voxel filter sizes. Larger voxel filter sizes imply smaller number of both target and constraint points, i.e. N_t and N_c.

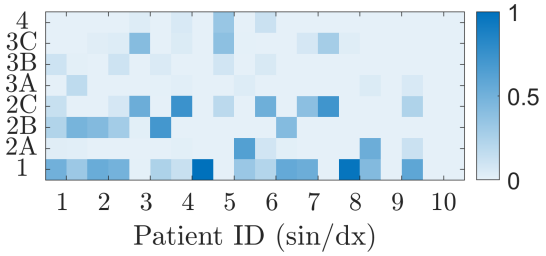

Fig. 2. Optimized current distributions across all eight contacts computed from the MILP approach given in (4). The values range from zero (light blue) to one (dark blue), representing the proportion of the total applied current allocated to each contact.

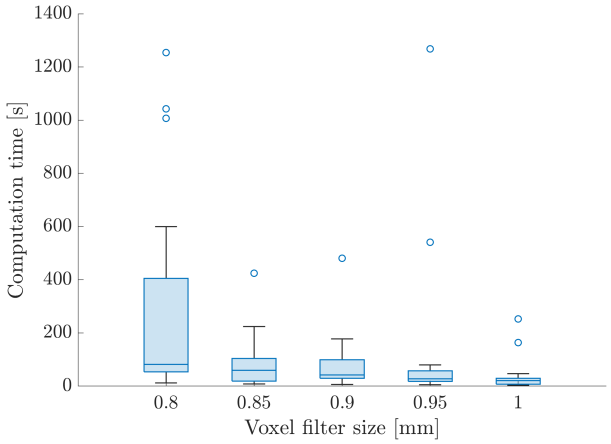

Fig. 3. Runtimes to solve the MILP formulation for different voxel filter sizes. Runtimes for MILP exceeded the time limit of 1500 s in three cases at 0.8 mm and in one case at 0.85 mm.

4. DISCUSSION

The results show that MILP can be used used in automated DBS programming, including dissimilar current distribution across active contacts. As the number of target and constraint points increases, the computational complexity of the MILP problem increases. Additionally, the optimization results rely heavily on the selected target and constraint regions. Choosing atlas-based subdivisions of the STN may be overly simplistic. In reality, therapeutic DBS likely modulates not only local structures but also connected white matter tracts. Therefore, future work should focus on comparing quantified patient response of the suggested configurations with clinically active settings to further assess target and constraint structures and improve the utility of the optimization models.

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