

# MODELLING THE ACTIVATION OF NEURONAL POPULATIONS DURING DEEP BRAIN STIMULATION

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**Abstract** - Deep brain stimulation (DBS) has become an increasingly used clinical therapy for several neurological conditions. However, it is currently impossible to directly measure the distribution of the stimulus in the patient's brain surrounding the implanted electrode, and as a result computational models in the form of finite element models coupled to axon cable models for predicting the volume of tissue activated have proved useful for visualizing stimulation effects. The use of such unconnected axon models, however, relies on the debatable assumption that the excitation of efferent fibres is the functional effect of DBS. We propose that quantifying the volume of tissue activated using anatomically accurate neuronal models as an alternative can provide further clues about the mechanism of DBS.

## I. INTRODUCTION

Deep brain stimulation involves the surgical insertion of an electrical pacemaker into a target region of the patient's brain, causing local changes in the activity of the surrounding neurons. It is a reversible neuromodulatory technique, widely used at present to treat movement disorders. This study focuses in DBS for the treatment of Parkinson's disease. []

High frequency stimulation of the subthalamic nucleus (STN) has been proven to offer therapeutic effects by reducing tremor and associated involuntary contractions in PD subjects []. The few animal electrophysiology studies at a cellular level propose that high frequency DBS contributes to silencing of neuronal activity in the STN [], and this reduction in bursting modes associated with pathological activity contributes to the improved symptoms.

However, inhibition of axonal efferent fibers has not been observed [], and while STN neurons are inhibited, axons fire in a 1:1 frequency with the stimulus.

## II. METHODS

We used results from a finite element electric field model [ref Nada papers] which provided the extracellular potential as a stimulus for a range of multicompartment models, starting with myelinated axons [5] and

followed by the subthalamic projection neurons of increasing complexity [6].

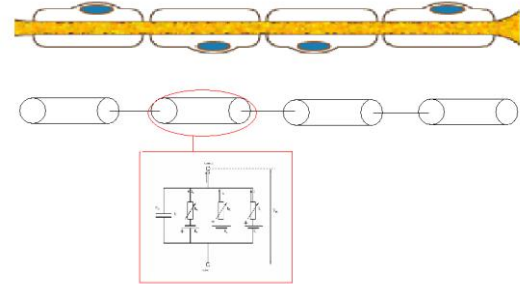
Multicompartment models of neurons were created utilising the NEURON simulation environment [2].

### A. Multicompartment model of a mammalian axon

Axons have been found to be the most excitable elements during DBS, and several studies have simplified neurons to consider only the axonal elements [4].

For the first part of the study, a model of an axon with 21 compartments was created [5] and 100 of these axons were placed in a configuration similar to the one shown below (Figure 1B). [6]

A



B

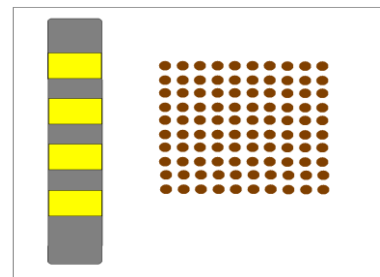


Figure 1: A An illustration of an axon and a simplified multicompartment equivalent. Each section is modelled as a set of cylinders. Each cylinder contains linear and non linear conductances that define the properties of the neuron model at that particular point .

B A representation of 100 axons in a 10x10 mesh placed perpendicular to the DBS stimulation electrode (left)

### B. Multicompartment model of a subthalamic projection neuron

The subthalamic nucleus (STN) is the region of the brain most commonly stimulated during treatment of PD[1]. The arrangement (figure 1B) was also mimicked in the case of a population of 100 STN projection neurons and observed dynamic behaviour was approximated and included in the models. Details about STN cell behaviour are not yet well understood [8].

## III. RESULTS AND DISCUSSION

Both models were implemented in the arrangement shown above, and the volume of tissue activated was qualitatively observed. The contour plots below represent the number of action potentials fired by the neurons as a function of distance from the stimulating electrode.

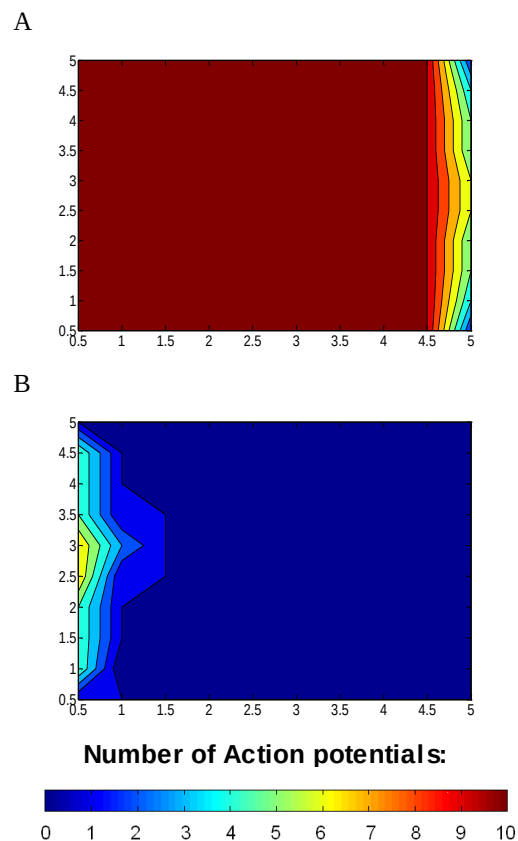


Figure 2 Contour plots to illustrate the number of action potentials fired by 100 neuronal elements after high frequency stimulation for 100ms (The stimulus obtained from finite element model). The horizontal and vertical axes represent the distance (mm) from the stimulation electrode.

A. Action potentials fired by 100 axons

B. Action potentials fired by 100 subthalamic neurons.

The results show that under the same stimulation conditions (1V, xHz), axonal elements produce action potentials up to 5mm away from the electrode, and thus, are more excitable than subthalamic projection neurons.

In the case of STN neurons, we can see that at distances greater than 1.5mm from the electrode the model neurons do not fire at all. None of the STN neurons fired at the stimulus frequency.

This may support the hypothesis that the therapeutic action of DBS appears as a result of neuronal inhibition of the target region. More studies are needed to develop the complex STN projection neuron morphology further.

## IV. CONCLUSION

In agreement with previous work [1], the prediction of the VTA using cable models of unconnected axons and defining activation as generating action potentials in a 1:1 ratio with the stimulus frequency, provides a convenient way of comparing stimulation parameters. However, the responses of the subthalamic projection neurons, with more complex morphologies and membrane dynamics provide more detailed information about the possible mechanisms underlying the observed improvement in patients' symptoms.

Further work on the subthalamic models will include the addition of synaptic conductances and the inclusion of more complex dendritic morphologies and ion channel dynamics.

## REFERENCES

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TABLE I  
TYPE SIZES AND APPEARANCE

| Place of text                | Type sizes and appearance |               |              |
|------------------------------|---------------------------|---------------|--------------|
| Title                        | 12 pts                    | <b>Bold</b>   | All capitals |
| Authors' Names               | 11 pts                    |               |              |
| Affiliation, Address, e-mail | 9 pts                     |               |              |
| Main Text                    | 10 pts                    |               |              |
| Subheadings                  | 10 pts                    | <i>italic</i> |              |
| Equations                    | 8 pts                     |               |              |
| Abstract                     | 8 pts                     | <b>Bold</b>   |              |
| Section Titles               | 10 pts                    |               | All          |
| Figure Captions              | capitals                  |               |              |
| Table Captions               | 8 pts                     |               |              |
| Tables                       | 8 pts                     |               | All          |
| References                   | capitals                  |               |              |
|                              | 8 pts                     |               |              |
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