Mathematical Modeling of Neural and Behavioral Response in Deep Brain Stimulation

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Promise

...a complete bench-to-bedside approach in the Deep Brain Stimulation (DBS) treatment of Parkinsons disease
Promise

...a complete bench-to-bedside approach in the Deep Brain Stimulation (DBS) treatment of Parkinson's disease

Result

...far from a complete one, but definitely bench-to-bedside approach in the DBS treatment of Parkinson's disease
Contributors outside IT

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**Biomedical Center:**
- Hanna Pettersson, Organismal Biology
- Emma Arvidsson, Neuroscience

**Uppsala University Hospital:**
- Dag Nyholm, Neurology
- Elena Jiltsova, Neurosurgery
- Markus Fahlström, Radiology

**Medtronic Bakken Research Center:**
- Mattias Åström
Contributors from IT

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Systems and Control:
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- Kristiaan Pelckmans
- Rubén Cubo
- Helena Andersson, Master student

Scientific Computing:
- Stefan Engblom
- Pavol Bauer
Contents

• What is Deep Brain Stimulation?
• What does IT in DBS?
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• What does the University Hospital in DBS?
• The SPARC DBS Project: Results
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• Plans for the future
What is Deep Brain Stimulation?

- DBS is an established treatment in various neurological diseases.
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  - Parkinsons Disease
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  - epilepsy

DBS makes use of implanted electrodes. Electrical stimuli are delivered to a target in the brain. The mechanism of DBS is unknown. Only alleviates symptoms. Produces side effects.
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DBS is used in the treatment of various neurological diseases. It only alleviates symptoms and produces side effects.
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Play
What does IT in DBS?
Stimuli optimization in DBS

Simulation of electric field distribution in the brain

Figure: Electric field distribution surrounding a target area.

Figure: Non-convex field distributions for compensation of an offline contact (left) and heavy anisotropy (right)
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  - Maximize the target coverage

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- Minimize the spill beyond the target

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- No direct connection to neurons of the brain. See ongoing activities.
What does Neuro in DBS? Connecting DBS stimuli to behavior

- Optogenetics

Figure: Optical brain stimulation (left) and animal installation (right)

Figure: Behavioral response
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  - Neurons genetically sensitized to light

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- **Control** of behavior through stimuli

**Figure:** Behavioral response
Behavioral modeling

**Aim:** To understand how DBS influences motor behavior

**Goal:** Quantify behavioral output in response to neural stimulation

- Animal experiments:
Behavioral modeling

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  - Behavior classification from video data
  - Behavior quantification
Behavioral modeling
Mouse Behaviors

- Standing still in a corner
- Moving in a corner
- Standing still along a wall
- Moving along a wall
- Crossing in the middle

**Figure:** Behavioral patterns in position data
Optogenetical stimulation of

- **Dopamine** – pleasure system of the brain
- **Glutamate** – the precursor for GABA, the brain’s main inhibitory neurotransmitter
Figure: Input and output data of the DBS model predicting therapeutical effect
Individualization of the DBS model

**Aim:** To make the DBS model *patient-specific*

**Goal:** Use the information pre-operative and post-operative MRI

- **Neurosurgery:**
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    - Cerebrospinal fluid
  - DBS lead position calculation
  - Electrical field calculation in non-homogeneous media
Figure: Patient case: An isolevel of electrical field produced by the lead covering the target area of STN
Clinical evaluation the DBS model
Infinity DBS platform from St Jude

- iPod/iPad programming
- Bluetooth communication
- Upgradable software
- Impedance monitoring
- Stabilized stimulation current
Clinical evaluation the DBS model
Segmented electrode from St Jude

Figure: Infinity lead from St Jude

- Eight contacts
- Asymmetric (directional) stimulation
- First ET patient in Uppsala in May 2016
- One more ET patient and a PD patient in May 2016
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- the stimulated volume
- the Zona Incerta
- the Ruber (the Red Nucleus)
- STN

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Figure: Patient case: Essential tremor, isolevel of 150 V/m
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Based on a neural model by from firing to electrical field (Engblom and Bauer)

**Figure**: DBS pulse in time
Modeling DBS stimulation of STN neuron
Space- and time-dependent PDE

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- Master thesis of Helena Andersson
A short list

- Two journal papers, 2015-2016
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- Best Paper Award from International Conference on Smart Portable, Wearable, Implantable and Disability-oriented Devices and Systems, Brussels, Belgium, 2015.
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- Proposal to VR Medical Engineering with Strand and Nyholm
Plans for the future

- A paper on DBS model individualization
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