How to use Computational Models to Optimize Brain Stimulation

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Brief Introduction: Rationale for Computational Models

Dr. Sven Bestmann, University College London
Computational NeuroStimulation

Dr. Benjamin Hampstead, University of Michigan
Neuroimaging

Dr. Mar Cortes, Well Cornell Medical College
Physiological Mapping

slides at Neuralengr.com
How do we optimize brain stimulation?

**Who:** Subject selection
   (inclusion, exclusion)

**Where:** Targeted brain region
   (primary, secondary)

**What:** Adjunct therapies
   (training, drugs)

**When:** Timing
   (repetition)

**Why:** Mechanism driven design
   (disease etiology)
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*Individual anatomy and physiology determine response*

_Datta, Truong, Bikson et al. Inter-individual variation during transcranial Direct Current Stimulation. Front Psychiatry 2012_*
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**Where we put the electrode or coil**

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Adjunct interventions to change brain state

Bestmann and Feredoes. Combining neurostimulation and neuroimaging in cognitive neuroscience Ann N Y Acad Sci 2013
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Relative to absolute time (time of day, repetition...)  
or responsive (biomarker, symptoms...)
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  (neuromodulation)

Waveform (pulse frequency, DC...) and
intensity (supra-threshold, sub-threshold)
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From Anatomical to Functional Targeting

Network of interest (e.g. therapy, brain function)

Other networks – not targets for neuromodulation

Current flow across entire region

Preferential modulation of more active network (Activity Selective Targeting)

Bikson and Rahman, Origins of specificity during tDCS, anatomical, activity-selective, and input-bias mechanisms. Frontiers Human Neuroscience 2013
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**Functional Targeting:** Only brain regions primed by training are sensitive to stimulation

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Anatomical targeting with brain stimulation

Supra-threshold stimulation

- DBS
- Cortical stim
- TMS


Sub-threshold stimulation

- HD-tDCS
- 4x1

Stimulation primary neuromodulation target. Endogenous circuit.

Bestmann and Feredoes. Combining neurostimulation and neuroimaging in cognitive neuroscience Ann N Y Acad Sci 2013
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Focality determined by waveform
Change in outcomes with electrode/coil position ≠ focality

Bestmann and Feredoes. Combining neurostimulation and neuroimaging in cognitive neuroscience Ann N Y Acad Sci 2013
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Combination of modalities

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!!!! Large parameter space of combinations
Need to optimize + individualize brain stimulation?

• Despite the theoretical flexibility of stimulation, treatments are remarkably invariant across diverse indications (individuals)
  (number of pulses, current intensity, hardware...)

• Assume: refining brain stimulation to patient group or individual will enhance tolerability and efficacy
  We can only do better, and often need to

• Essentially every brain stimulation that developed from investigational to broadly disseminated (FDA approval) includes individualized therapy
  (DBS, TMS...)
Computational Models of Brain Stimulation

- Given the large parameter space of brain stimulation, and inevitable limits (cost, risk) of clinical treatment and trials, cannot just “try everything”

- **Computational Models of Brain Stimulation are** quantitative tools (software, protocols) that facilitate optimization.

- **Optimization**: Specific patients groups or individuals receive interventions based on unique characteristics.

- **Tools**: Software or protocols that given patient specific data, suggest treatment strategy. Evolving and iterative.

**Computational Models are informed by:**

- Models of stimulation physics and brain function (Bestmann)
- Imaging data (Hampstead)
- Physiological markers (Cortes)