Non-invasive spinal cord stimulation

Technique development & initial tests

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Outline

SCS

- Well established in pain management
- Emerging applications: including rehabilitation
- Limitations wrt access, risk, reintervention, etc.

niSCS

- Noninvasive option would overcome many issues
- Removes interventional risk, reintervention, etc.
- Far greater access
  - Non-invasive trialing
  - Non-invasive rehabilitation options

Question

- Unclear if niSCS feasible
  - Some reports: limited methodology, vague outcomes
  - Some modeling: very simplistic, unconvincing metrics
- Answer required detailed, accurate models
  - Individual anatomy influences E-field
  - Precise models would allow individualised targeting
  - Potential applications to other areas

Image $\mapsto V(x, y, z)$

- Derive detailed patient-specific models from clinical imaging
- Image $\mapsto$ FEM $\mapsto V(x, y, z)$
- Technique discussed in detail previously
  - Map in electrodes
  - Form mesh
  - Apply physics
  - Solve for V

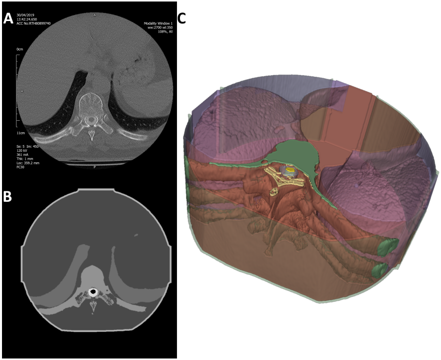


Figure: Image derived model

What to do with V?

- Can solve for field in complex patient-specific anatomy
- But what next?
  - Unintuitive visualisation
  - Metrics divorced from physiology

Visualisation

- $f : (x, y, z) \rightarrow V$
- Interpolate slices, etc.
- Visualise results as overlay
- Extends to any metric

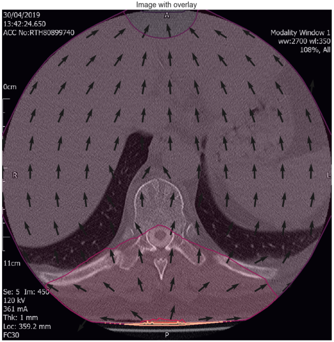


Figure: Axial slice with overlay

Activating function

- Classically $\frac{\partial^2 V}{\partial n^2}$, where n is the long axis of the axon
  - Based on cable equation: 1D axon in space
  - External field acts as "source" where $-\frac{\partial E_n}{\partial n} > 0$
- Generalisation to 3D: $V(n) \rightarrow V(x, y, z)$
  - Second derivative of scalar field: $\nabla^2 V$ as approximation?
  - $\nabla^2 V = \nabla \cdot \nabla V$, i.e. $-div(\vec{E})$
  - Retains interpretation as external field $\rightarrow$ local source
  - But invariant to direction - loses influence of axon orientation
- Need directional measure of activation for arbitrary direction
  - $\nabla V = (\frac{\partial V}{\partial x}, \frac{\partial V}{\partial y}, \frac{\partial V}{\partial z})$
  - Can get true activation by differentiating along basis vectors
  - But need any direction!

A generalised activating function

- $J(\nabla V) = H(V)$: full matrix of all second derivative information
- $H = \begin{bmatrix} \frac{\partial^2 V}{\partial x^2} & \frac{\partial^2 V}{\partial x \partial y} & \frac{\partial^2 V}{\partial x \partial z} \\ \frac{\partial^2 V}{\partial y \partial x} & \frac{\partial^2 V}{\partial y^2} & \frac{\partial^2 V}{\partial y \partial z} \\ \frac{\partial^2 V}{\partial z \partial x} & \frac{\partial^2 V}{\partial z \partial y} & \frac{\partial^2 V}{\partial z^2} \end{bmatrix}$
- $R = \begin{bmatrix} \cos\alpha\cos\beta & \cos\alpha\sin\beta\sin\gamma - \sin\alpha\cos\gamma & \cos\alpha\sin\beta\cos\gamma + \sin\alpha\sin\gamma \\ \sin\alpha\cos\beta & \sin\alpha\sin\beta\sin\gamma + \cos\alpha\cos\gamma & \sin\alpha\sin\beta\cos\gamma - \cos\alpha\sin\gamma \\ -\sin\beta & \cos\beta\sin\gamma & \cos\beta\cos\gamma \end{bmatrix}$
- $H' = R_n H R_n^T$ - Rotate basis vectors to desired trajectory
- $(H')_{11} = \frac{\partial^2 V}{\partial n^2}$: activation for any arbitrary orientation

A generalised activating function

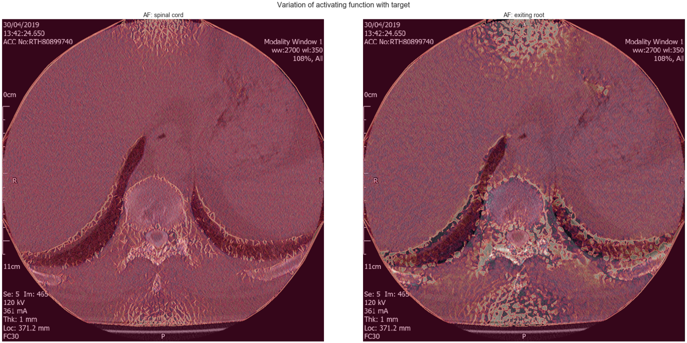


Figure: Activation function, spinal cord vs. spinal root

Axon models

- AF still an approximation
- Full biophysical model: most physiologically accurate
- Need to "place" axon in model space

Linking axon models

- Get trajectory
  - Random seed
  - Follow trajectory
  - Get length
  - Get $f : d \rightarrow (x, y, z)$
- Define axon model
  - Set fibre size
  - Segment length
  - Unit length
  - Unit number
  - Unit distances
- Link V to axon
  - $d_a \mapsto pos_a$
  - $pos_a \mapsto V_a$
  - Set $V_{ext}^a = V_a$
  - Run simulation

Axon models

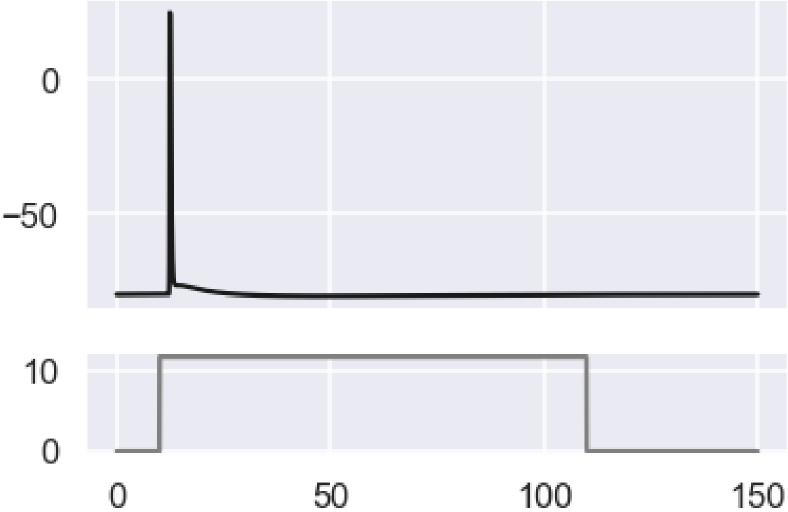


Figure: Action potential generation by simulated stimulation

ONI axon model

- ONI axon model
  - MRG-style myelinated model (NODE, MYSA, FLUT, STIN)
  - Maps automatically to 3D model space
  - Allows easy application of simulation results to axon models
- Can repeat arbitrary times: distribution of fibre types, randomly placed in target

Axon trajectories

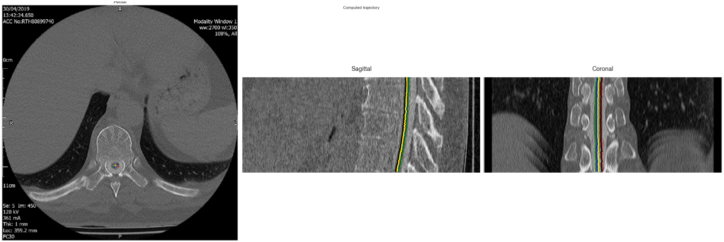


Figure: Example axon trajectories

Applications

- Lots of fancy methods: need to do something with them...
- Does noninvasive spinal cord stimulation do anything?
  - Simple: 3.2cm diameter round electrode over T11, 30mA DC
  - Interferential: 2 pairs of electrodes lateral to midline; 1kHz & 1.02kHz, 30mA peak

Applications

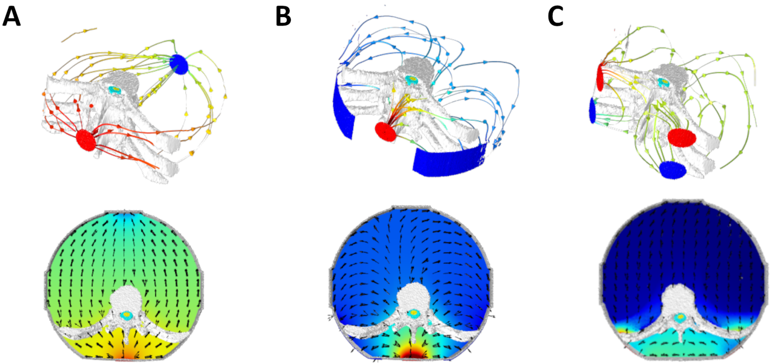


Figure: Electrode montages

DC stimulation

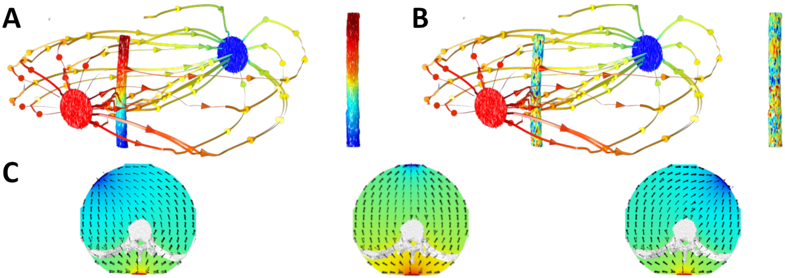


Figure: DC stimulation

DC stimulation

Figure: V & $\vec{E}$, DC stimulation

DC stimulation

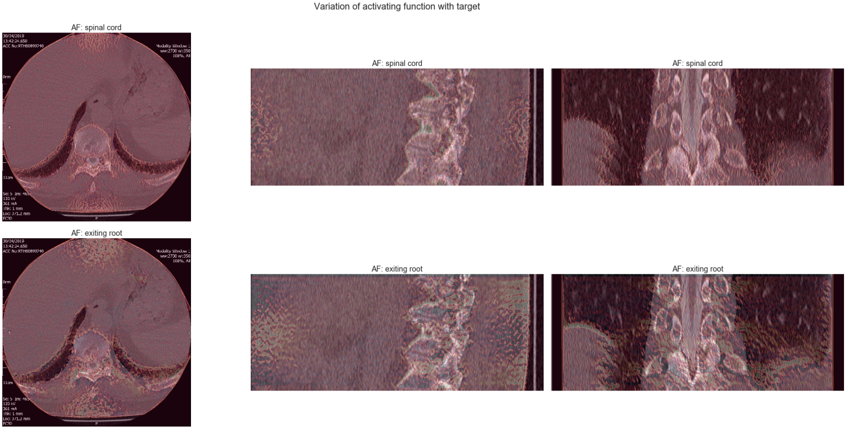
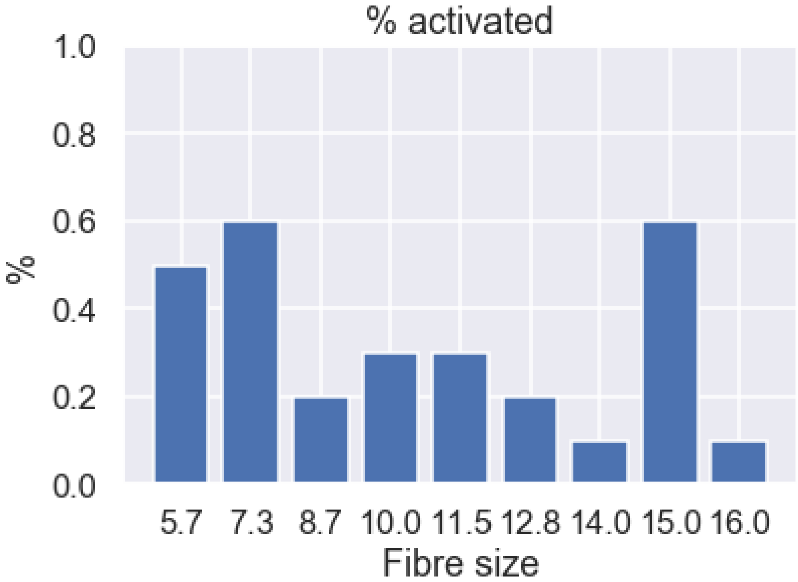


Figure: Activating function, DC stimulation

DC stimulation



DC stimulation

Areas activated

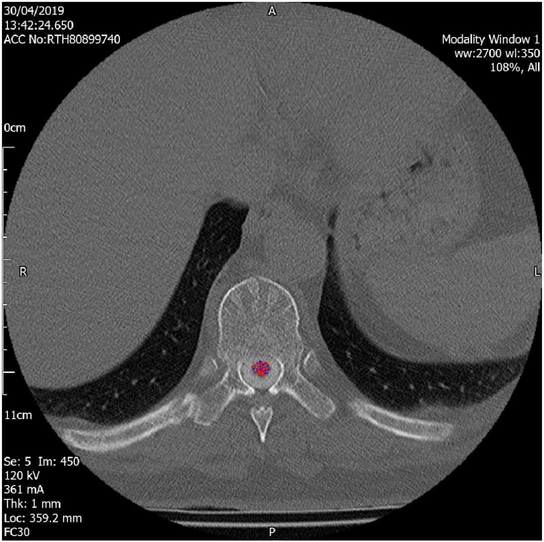


Figure: Distribution of activated vs. unactivated trajectories

Interferential stimulation

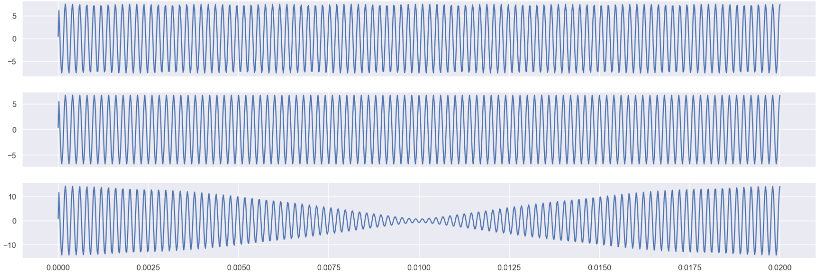


Figure: Time series of V: interferential stimulation

Interferential stimulation

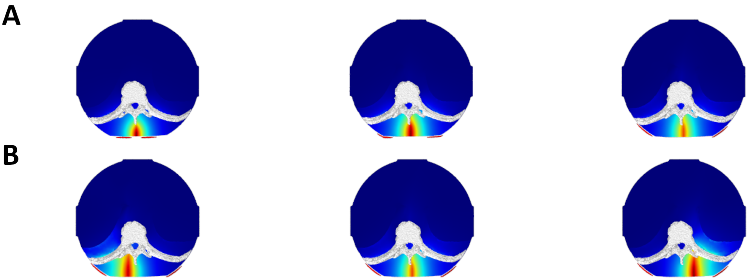


Figure: Interferential: steering

Interferential stimulation

- Activation metrics for interferential in progress
- RAM limited - need to be a bit more clever...

niSCS

- niSCS seems possible
- Generates activation on highly accurate models
- Mechanism needs more modeling: ?spinal roots
- Interferential seems promising: can steer
- Needs more work: ?target areas of cord with steering

Analysis tools

- Tools developed useful
- Provide generalisable way to produce models from imaging
- Simple (to use) methods to get activating function in 3D, link axon models, etc.
- Other application areas...

Next steps

- Validation: printed structures
- Optimisation: maximise activation
- Interface: fit tools into single tool
- Applications: ?priorities