

Patient-specific modeling

Tool development & applications to niSCS

Conor Keogh

Oxford Neural Interfacing

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

- 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 to model

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

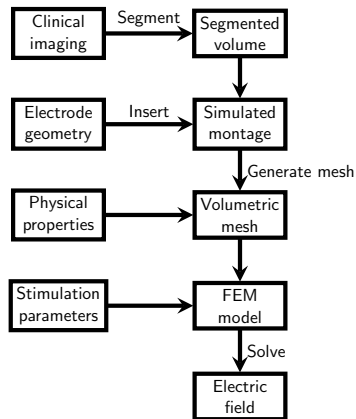


Figure: Flowchart of implemented method.

Image segmentation

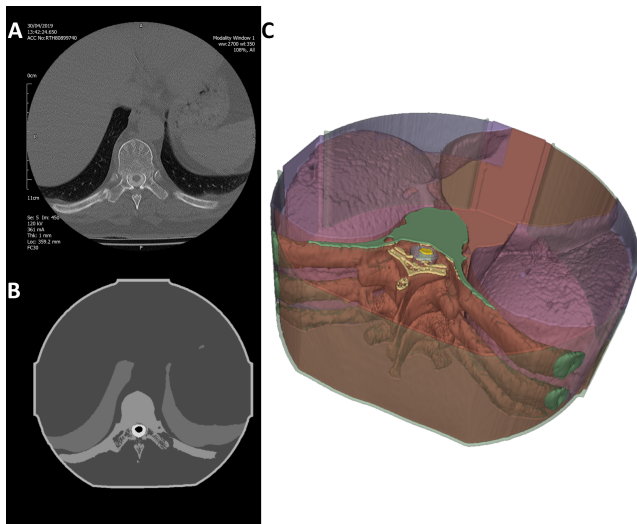


Figure: Image derived model

Electrodes & meshing

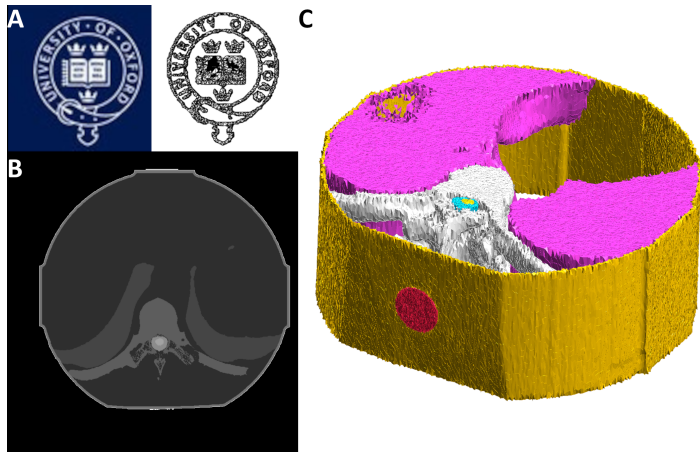


Figure: Mesh from imaging

Solving models

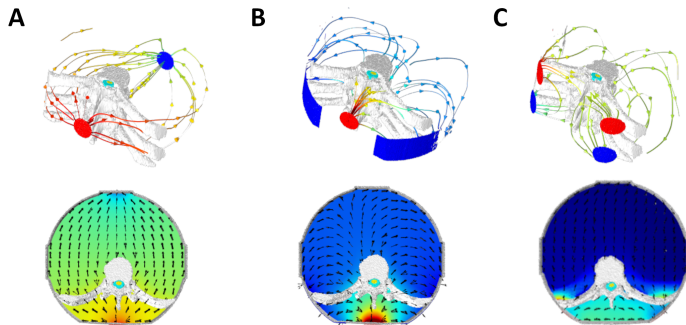


Figure: Results: $V(x, y, z)$ & \vec{E}

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

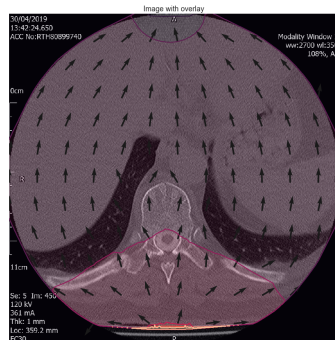


Figure: Axial slice with overlay

Activating function

- Electric field produced by stimulation experienced by neurons that pass through it
- We aim to create an electric field that influences neural activity in useful ways
- We need to link the external field to neural activity to make useful models
- Approximations exist: activating function!
 - ▶ The external electric field drives a transmembrane current
 - ▶ This current results in membrane potential changes & (hopefully) action potential initiation
 - ▶ This inward current is related to the rate of change of the external field
 - ▶ Where there is more current flow into a point than out of it, this drives current into the cell
- There are challenges to generalising this to 3D, realistic fields
 - ▶ But we can do it now!
 - ▶ Can compute AF for any given orientation in 3D space to predict activation

A generalised activating function

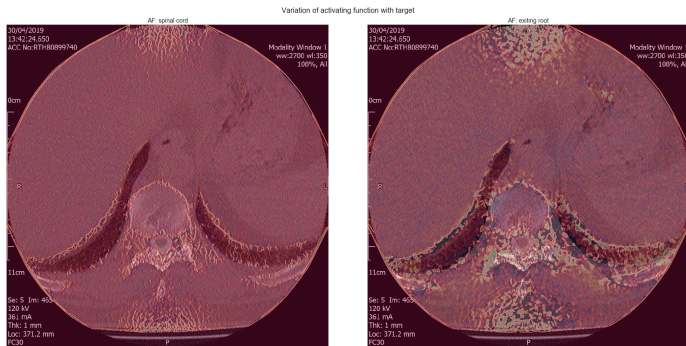


Figure: Activation function, spinal cord vs. spinal root

Axon models

- AF still an approximation
- Full biophysical model: most physiologically accurate
- Need to "place" axon in model space
 - ▶ Method developed: axon model with explicit mapping to 3D model
 - ▶ Requires "trajectory" to map to in 3D
 - ▶ ... but we can also compute that!

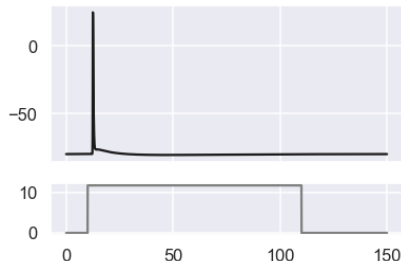


Figure: Action potential generation by simulated stimulation

Axon trajectories

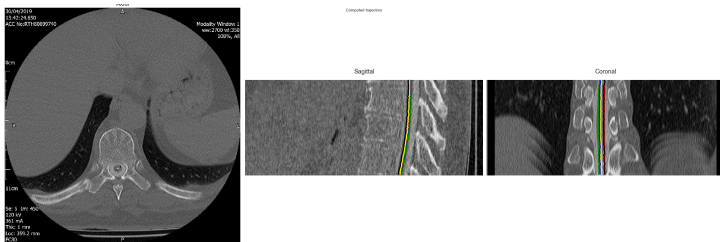


Figure: Example axon trajectories

Abstraction

- Useful methods: anatomically & physiologically realistic models
- Entirely patient-specific
- Can simulate electrode placement & effects of stimulation
- Complex to implement!
 - ▶ Methods generalised & packaged
 - ▶ Can get patient-specific models direct from clinical imaging
 - ▶ Can create computational models & 3D printed models for validation

- Graphical interface
- Allows easy model specification
- No knowledge of underlying implementation necessary
- Specify image volume, electrode geometry & stimulation parameters
- Automatically creates & solves model
- More complex biophysics & extended functions being added to GUI...

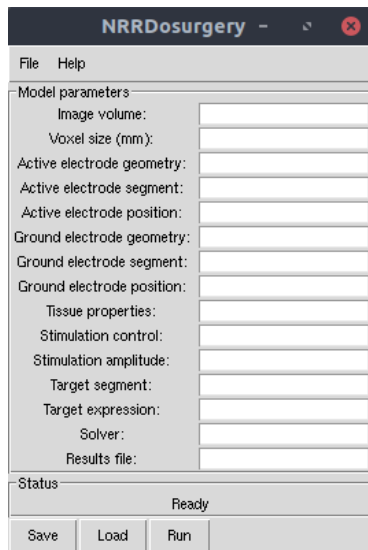
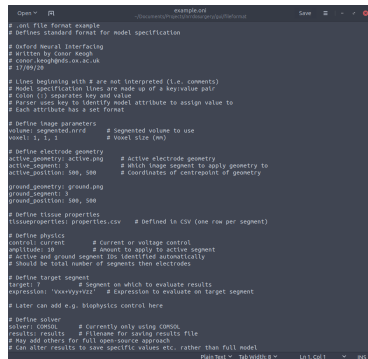


Figure: Graphical interface

Data format

- Standard file format
- Allows reproducibility & easy model specification
- Can directly write to model files
- Directly maps to data structures
- Can use direct programming interface to generate automatically
- Allows algorithmic model iteration! Optimisation of parameters, etc...



```
# .vml file format example
# Defines standard format for model specification

# Oxford Neural Interfacing
# Written by Conor Keogh
# conor.keogh@ox.ac.uk
# 17/09/20

# Lines beginning with # are not interpreted (i.e. comments)
# Model specification lines are made up of a key:value pair
# colon (:) separates key and value
# Parser uses key to identify model attribute to assign value to
# Each attribute has a set format

# Define image parameters
volume: segmented.nii.gz # Segmented volume to use
voxel: 1, 1, 1 # Voxel size (mm)

# Define electrode geometry
active_geometry: active.png # Active electrode geometry
active_segment: 3 # Switch image segment to apply geometry to
active_position: 500, 500 # Coordinates of centropoint of geometry

ground_geometry: ground.png
ground_segment: 3
ground_position: 500, 500

# Define tissue properties
tissueproperties: properties.csv # Defined in CSV (one row per segment)

# Define physics
control: current # Current or voltage control
amplitude: 50 # Amount to apply to active segment
# Active and ground segment IDs identified automatically
# Should be total number of segments then electrodes

# Define target segment
target: 7 # Segment on which to evaluate results
expression: 'xxxxxyyzzz' # Expression to evaluate on target segment
# Later can add e.g. biophysics control here

# Define solver
solver: COMSOL # Currently only using COMSOL
results: results # Filename for saving results file
# May add others for full open-source approach
# Can alter results to save specific values etc. rather than full model
```

Figure: File specification

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

DC stimulation

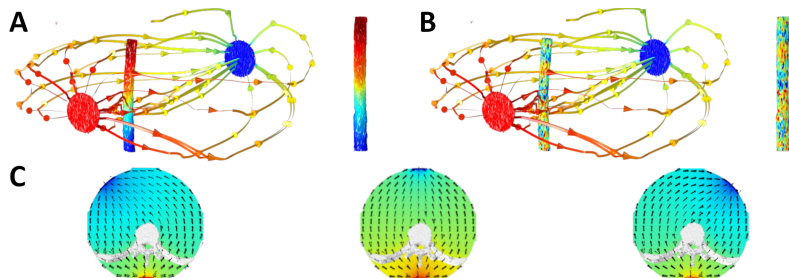


Figure: DC stimulation

DC stimulation

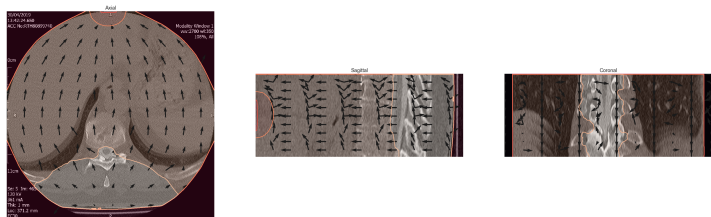


Figure: V & \vec{E} , DC stimulation

DC stimulation

Variation of activating function with target

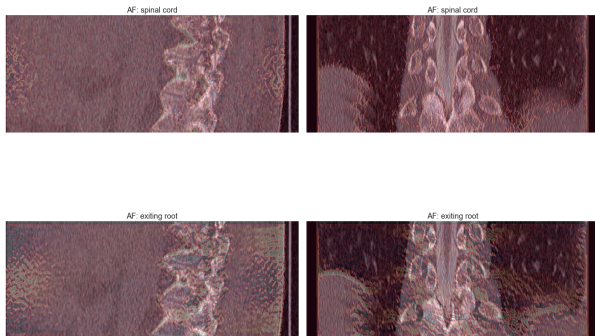
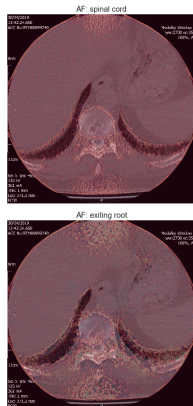
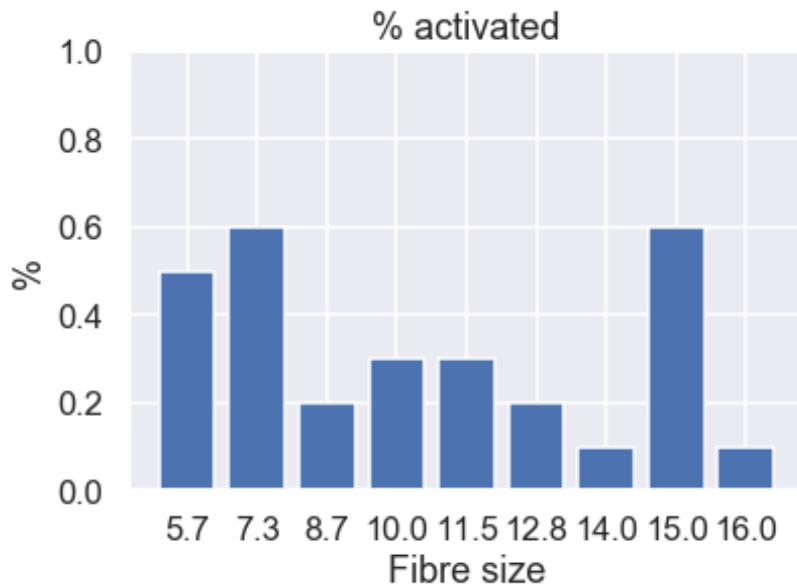


Figure: Activating function, DC stimulation

DC stimulation



DC stimulation

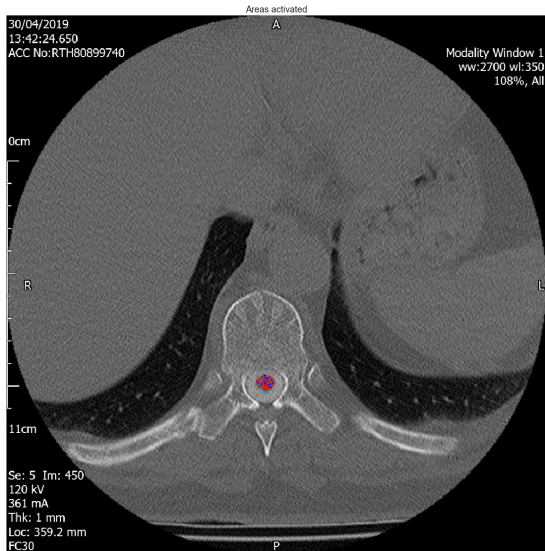


Figure: Distribution of activated vs. unactivated trajectories

Interferential stimulation

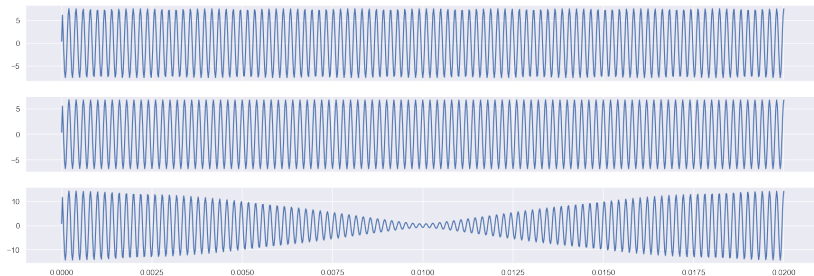


Figure: Time series of V: interferential stimulation

Interferential stimulation

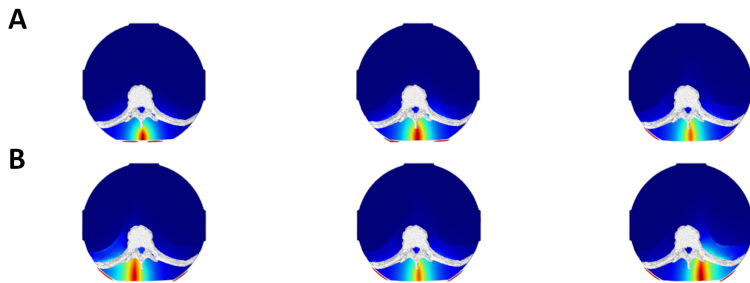


Figure: Interferential: steering

Interferential stimulation

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

- niSCS 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