Feature Selection for Learning Performance Models of Electrical Stimulation for Spinal Cord Injury

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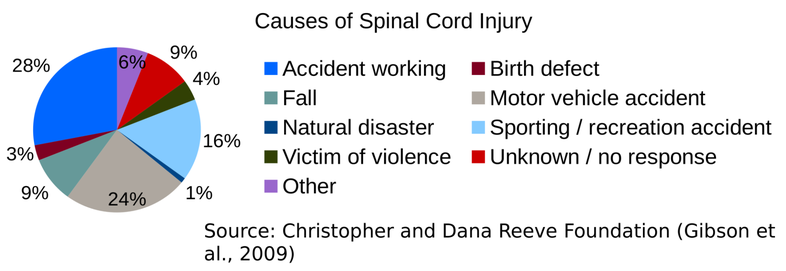
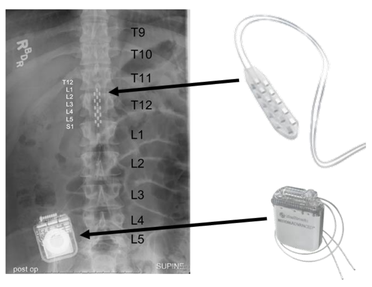
Overview and Motivation

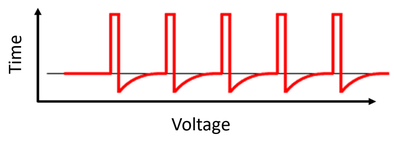
- Spinal cord injury (SCI): a disruption of communication between the brain and spinal cord levels below the injury
  - ≈ 5 million cases of severe SCI worldwide



Source: Christopher and Dana Reeve Foundation (Gibson et al., 2009)

- Electrical spinal cord stimulation allows SCI patients to stand, regain some voluntary motor control, and recover some autonomic function
- This work analyzes data from experiments with paraplegic patients, implanted with Medtronic Specify™ 5-6-5 epidural electrode arrays





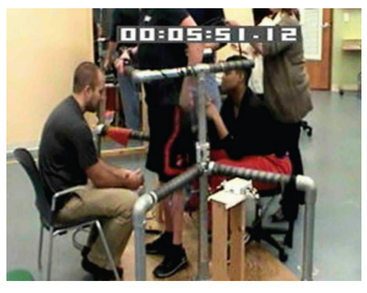
Top: Sketch of a positive-polarity stimulation waveform

Left: Patient CT-scan and enlarged implant and impulse generator

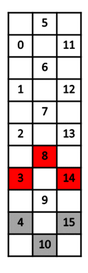
- Challenges: (1) intractably-large space of possible electrical stimuli; (2) the neural mechanisms behind the method's success remain uncertain
- Approach:
  1) Modeling the impact of electrical stimulation upon the nervous system
  2) Using simulation results to help explain the empirical performance of the stimuli in data collected from paraplegic patients
  3) Predicting the performance of untested stimulation configurations
  4) Inferring the optimal spinal cord electrical activity for the patients

Data Collection from Patients

- Data collected by Yanan Sui in collaboration with Enrico Rejc, Claudia Angeli, and Susan Harkema
- 2 paraplegic patients (ARI and ATC) tested over 2 non-consecutive weeks
- 40-60 stimuli tested per week
- CORRDUEL algorithm suggested stimuli (Sui et al., 2017)
- For each trial, physicians scored the patient's standing on a 1-10 scale

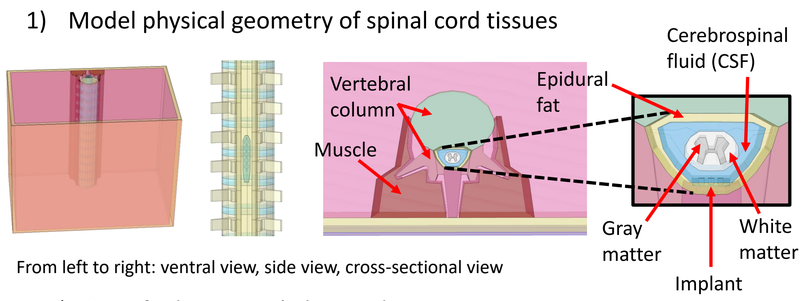


Score	Descriptions
1-2	Assisted by bungees or trainers (maximum)
3-4	Assisted by bungees or trainers (moderate)
5	Assisted by bungees or trainers (minimum)
6-7	Hip: Not assisted, back arched Knee: Not assisted, loss of extension during shifting
8-10	Hip: Not assisted, back straight Knee: Not assisted, extended during shifting



Simulations

- Electrical stimulation creates a flow of current, resulting in a voltage distribution throughout the bodily tissues surrounding the implant
- We simulate the effect of the stimulation upon the patients, following the methods of Ladenbauer (2008) and Capogrosso et al. (2013)
- Simulations are performed for all stimuli in the empirical dataset:
  1) Model physical geometry of spinal cord tissues



From left to right: ventral view, side view, cross-sectional view

  2) Specify the tissues' electrical properties
  3) Use finite element analysis to numerically solve the system of differential equations given by electromagnetics theory

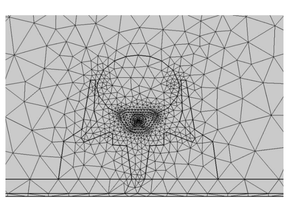
Laplace's Equation: V = voltage

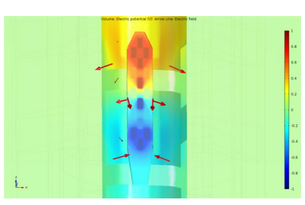
$$\nabla \cdot (\sigma \nabla V) = 0$$

σ = conductivity

Dirichlet boundary condition: $V(x) = V_0(\vec{x}),\ \vec{x} \in \Gamma_D$

Neumann boundary condition: $\vec{J}(\vec{x}) \cdot \vec{n} = (-\sigma \nabla V(\vec{x})) \cdot \vec{n} = \vec{0},\ \vec{x} \in \Gamma_N$





Left: finite element method mesh

Right: example simulation

Feature Extraction

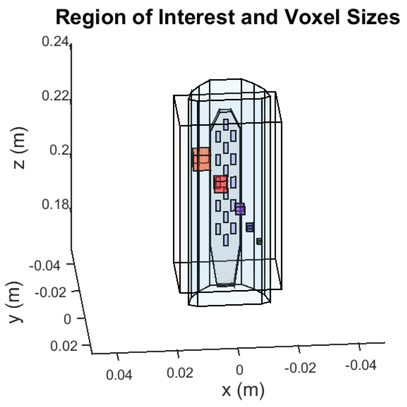
- Selected a region of interest containing the CSF and dorsal roots
- Divided the region into cubic voxels of 5 different sizes
- Calculated the following features for each voxel:

1) Voltage
2) Gradient of voltage

$$\nabla V = \left[\frac{\partial V}{\partial x} \quad \frac{\partial V}{\partial y} \quad \frac{\partial V}{\partial z}\right] = -\vec{E}$$

3) Second derivative of voltage

$$\nabla^2 V = \begin{bmatrix} \frac{\partial^2 V}{\partial x^2} & \frac{\partial^2 V}{\partial x \partial y} & \frac{\partial^2 V}{\partial x \partial z} \\ \frac{\partial^2 V}{\partial y \partial x} & \frac{\partial^2 V}{\partial y^2} & \frac{\partial^2 V}{\partial y \partial z} \\ \frac{\partial^2 V}{\partial z \partial x} & \frac{\partial^2 V}{\partial z \partial y} & \frac{\partial^2 V}{\partial z^2} \end{bmatrix}$$



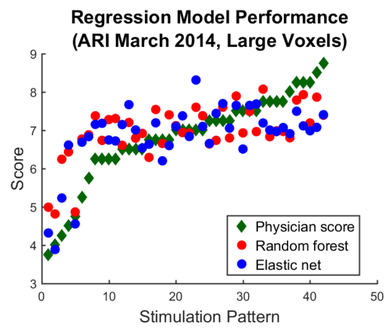
- Activating function of a neuron (Rattay, 1999) predicts the neuron's response to an extracellular electric potential

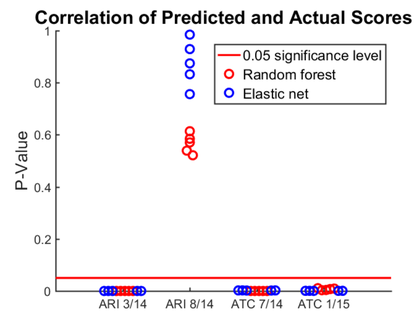
$$f(x) = \frac{d}{4\rho_a c_m} \frac{\partial^2 V_e}{\partial x^2}$$

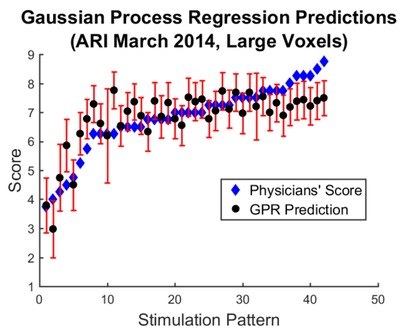
- Used 5 voxel sizes to reduce effects of arbitrary voxel partitioning

Results

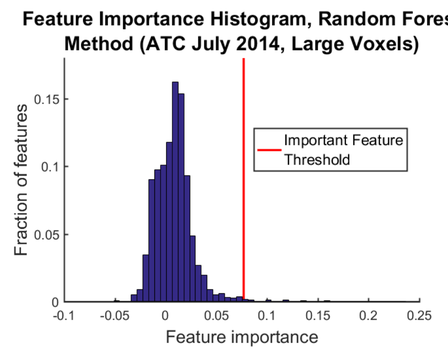
- Predicted patient responses from features via random forest, elastic net, and Gaussian process regression (GPR) models
- Modeled a distribution on the performance of stimulation patterns that were not tested in the patients, using GPR





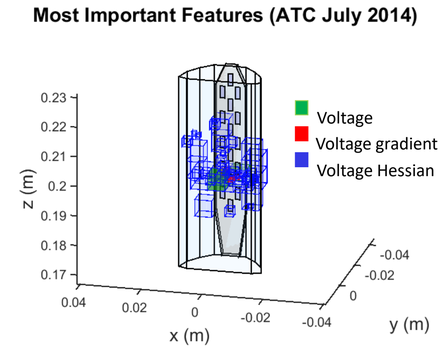


- Quantified feature importance via (1) random forest regression, (2) elastic net regression, and (3) mutual information between features and scores; strong agreement between features selected via these methods

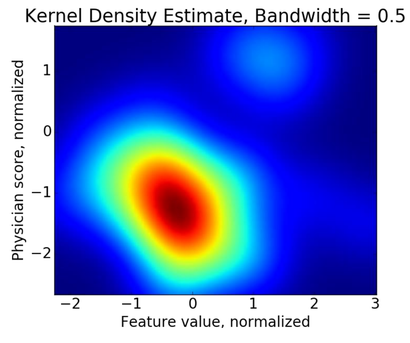


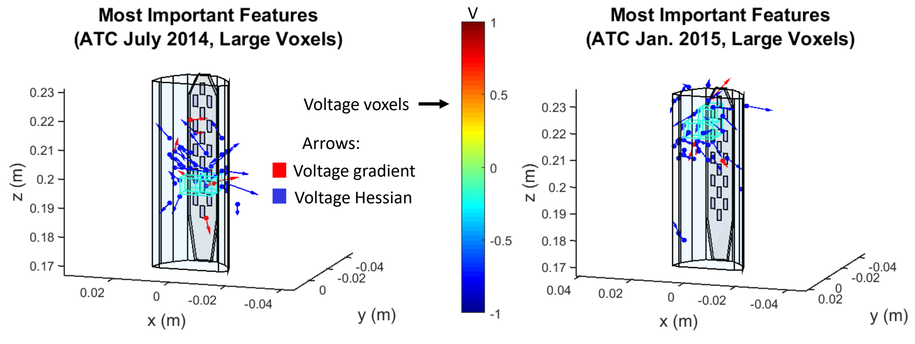
Left: Random forest permutation importance selects most informative features

Right: Voltage Hessian features are more informative than voltages and voltage gradients (p-values order 10^{-3} or lower)



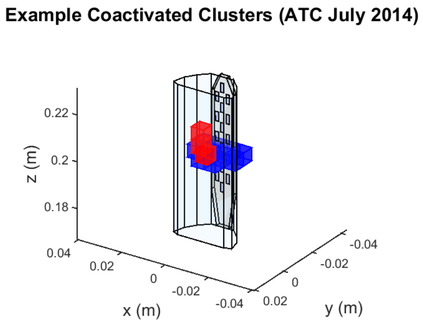
- Estimated feature values corresponding to desired patent responses using kernel density estimation
  - Evaluated $\mathbf{E}[X|Y > a]$, where X is a feature, Y is the patient response, and a is a specified threshold





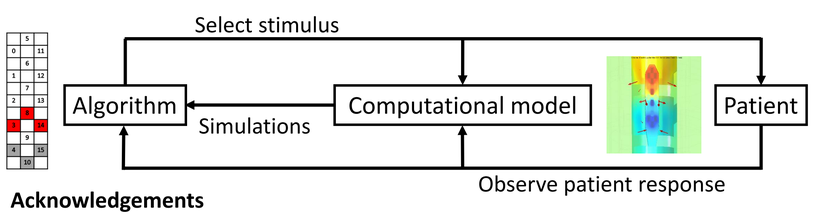
Discussion and Ongoing Work

- Can clustering the feature space help to interpret the results?
  - Performed agglomerative hierarchical clustering, using the complete linkage criterion and Pearson's correlation coefficients as the similarity measure (Candes, Fan, et al. 2016)
  - Designated *cluster representatives* to model clusters' feature values
- Finding features that are coactivated/coupled with one another
  - Looking for groups of features that are significantly more predictive of patient responses than any subset of those features
  - May indicate components of neural circuits that work together to yield better patient responses



Future Work

- Searching for optimal stimulation patterns and designing optimal arrays (electrode placement, size, shape, etc.)
- Understanding neural mechanisms underlying the stimulation's effect upon the nervous system
- Comparing the spinal cord regions identified as important via both simulations and EMG analysis



- Adjusting stimulation in real-time using measured patient responses
- Incorporating simulations into algorithms for predicting stimuli

Acknowledgements

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References

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