Towards a spinal cord model to produce experimental protocols

A Feinberg Argonne collaboration

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Heckman Lab & Spinal Cord Research


What experimental protocol?
Would it be useful?

- Well established market for pain
  - 30,000 implants/year
  - 1.8 Billion USD
  - 50% do not work
  - No placebo studies
  - Hard to measure
- SCI Autonomic system: bladder control, blood pressure, sexual arousal, etc.
- SCI Motor system: believe to be best model as it is can be measured in animal models easily.
Background
Common Stimulation Types

Transcutaneous

Epidural

Intraspinal microstimulation

More Invasive

Less specific

Direct Electrical Stimulation (DES)

*Subdural space*

- More Invasive
- Epidural

- Intraspinal microstimulation

- Less specific

Canonical Motor Microcircuit (CMM)

*Model Choice*

- **Fundamental**: Basis for locomotion (reciprocal inhibition),
- **Understandable**: Large background of its structure (motorpools location),
- **Accessible**: Highest sensitivity to activation by DES are almost certainly the Ia axons arising in muscle spindles (large diam fiber).
- **Generalizable**: Circuit is repeated throughout the spinal cord.
Experimental Data

1. Exp1: General motor pool map with respect to location. Does this map change after full spinal cord transection?

2. Exp2: Map with respect to amplitude and frequency.
General motorpool map of the lumbar region
Methods

Feline Preparation

• Lumbar laminectomy

• **Soleus dissection**: calcaneus attached to vibration coil and transducer
Digitize Location
Protocol 1

Stimulation & Raw Data

- Measure EMG of VL, Srt, LG and MG
- Stimulation Parameter
  - 300 µA
  - 1 Hz
  - 1 ms width
- Repeat after full transection
Results
Protocol 2

Location constant but change frequency

- Stimulation Paradigm
  - Amplitude: 100, 200, 300, 400, 500 µA
  - Frequency: 10, 20, 40 Hz
  - Duration 5 s
  - Pulse Width 1 ms
Results

Time (s)
Spinal Cord Computer Modeling

1. Modeling CMM
2. Solving Maxwell Equations – Impedance Measurements
3. Scaling
Goal

Objective 1
Single CMM (8 Neurons)

Objective 2
Antagonist Pair CMM (2 x Motorpools)

Objective 3
Full Hindlimb CMM (32 x Motorpools)

Number of Equations: 172
# Neurons = 2 x (MN + RC + Ia + IaIN)

Number of Equations: 103,200
# Neurons = 2 x 300 x (MN + RC + Ia + IaIN)

Number of Equations: 3,302,400
# Neurons = 2 x 300 x 32 x (MN + RC + Ia + IaIN)
Decorrelating Actions of Renshaw Interneurons on the Firing of Spinal Motoneurons Within a Motor Nucleus: A Simulation Study

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Network weights

Example of Network Weight Distribution
MN (α) to Renshaw Cell (RC) Connection

\[ \alpha \rightarrow \text{RC} \]

\[ W_{11}, W_{12}, \ldots, W_{mn} \]

\[ d_{1n} = d_{\text{max}} \]
Model
*Simple to Complex*

- Dendrites
- Soma

**Current Motoneuron Model**

- 30 MN
- 50 Ia
- 6 Renshaw

**Actual Motoneuron**

*Synaptic control of the shape of the motoneuron pool input-output function*

Randall K. Powers\(^1\) and Charles J. Heckman\(^2\)
Scaling the model

Mouse  Rat  Cat  Human

2 mm
Spinal Cord Imaging

X-Ray microtomography (µCT). Technique provides mesoscale anatomy, of neurons, glial cells and vasculature, at an isometric resolution of ~1µm³ using large tissue samples (1-2 mm thickness).
Electromagnetic Modeling

COMSOL

7T MRI Image of Cat Lumbar Spinal Cord
Advance Photon Source (APS)
Argonne National Lab
Spinal Cord Sample
ID-32 Setup
Preliminary Image
3D Reconstruction – Dr. Kasthuri at UoC
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