Connectomics + Dynamics = Nervous System -> Behavior

Eli Shlizerman
Washington Research Foundation Assistant Professor
University of Washington,
AMATH & ECE

http://faculty.washington.edu/shlizee
Twitter: @shlizee
Outline

1. **Static** Connectome

2. **Dynamic** Connectome

3. **Functional** Connectome

4. Connectome -> **Behavior**
Introduction-Outline

1. **Static Connectome**
   What is the *connectome*?  How to analyze the *connectome*?

2. **Dynamic Connectome**
   What the *connectome* is *good for*?  How to *model dynamics*?

3. **Functional Connectome**
   What is *function*?  How to infer functional pathways *in the *connectome*?

4. **Connectome -> Behavior**
   How does the *connectome* *dictate* behavior?
Outline

1. **Static Connectome**
   - What is the *connectome*?
   - How to analyze the *connectome*?

2. **Dynamic Connectome**
   - What the *connectome* is *good for*?
   - How to model dynamics?

3. **Functional Connectome**
   - How to *define* function?
   - Functional pathways in the *connectome*?

4. **Connectome -> Behavior**
   - How does the *connectome* *dictate* behavior?
Q. How does the connectome dictate behavior?
Add More Layers – Bio-Mechanics

Whole Integration of Biomechanics and Neural Dynamics

https://shlizee.github.io/CelegansWholeIntegration/

Kim, Santos, Alkema, Shlizerman, *bioRxiv*, in review 2019
Whole Body Model Locomotion – Wave Force

Forward Integration

Inverse Integration

Nervous System

Map to Muscles

Biomechanical Model

Neural Stimuli

Wave Force

Wave Initiation ON

Wave Force Forward and Backward Locomotion
Are these movements simple responses?

Nonlinear Response!
Underlying Neural Dynamics

Wave Force

Neural Dynamics Induced By External Force

A

FORWARD

BACKWARD

ALL NEURONS

Voltage

0  8  16

time (sec)

B

FORWARD

BACKWARD

TURN

MOTOR

Voltage

time (sec)

C

Coeff 3

Coeff 2

Coeff 1

-10  -45  45

TURN  FWD  BWD

0  8  16

time (sec)
Whole Body Model Locomotion – Neural Stim

Neural Stimulus Initiated Forward and Backward Locomotion
Are these movements typical?

Comparison with Eigenworms
Neural Impulses during locomotion

Avoidance
Neural Impulses during locomotion

“A worm in a box”
Neural impulses during locomotion

Excitation-Inhibition Balance

Huang et al., Elife 2019
Neural impulses during locomotion

Excitation-Inhibition Balance

![Graph showing neural impulses during locomotion with excitatory and inhibitory signals. The graph displays velocity normalized against time, with different lines representing wild and AVA ablative conditions.]
Neural Impulses during Locomotion

Asymmetric Stimulus

Posture related stimulus
Ablation (Back to Connectomics)

![Graphs showing velocity (normalized) for different conditions (Wild, DD-, VD-, GABA-, VD/DD+/GABA-)](image)

**Gentle Touch Response**

- Posterior (PLM)
  - AVB- AVA-
  - AVA- AVE-
  - AVE- AVD-
  - AVD- AVD/AVE-
  - PVC-LUA-

**Harsh Touch Response**

- Posterior (PVD, PDE)
  - Wild
  - PVC-
  - DVA-
  - PVC-DVA-

**Locomotion**

- Start: D
- Muscle Activity: Body Trajectory
- Time (sec)
- Bias (Deg/s)
  - Wild
  - DD-
  - VD-
  - GABA-VD/DD/RME
  - GABA-DD
  - GABA-VG
  - GABA-VD/DD
  - GABA+VD/DD

Head Tail
gentle touch region (PLM)
Ablation of groups of neurons

**Gentle Touch Response**

- Posterior (PLM)
- Anterior (ALM, AVM)

**Harsh Touch Response**

- Posterior (PVD, PDE)
- Anterior (FLP, ADE, BDU, SDQR)

**Locomotion**

- Body Trajectory
- Muscle Activity
- Bias

**Validation**
**Recapitulation**
**Prediction**
Ablation Search (Back to Connectomics)
Behavioral Circuits

Olfactory Circuit

Synaptic link

AWC

AIY

AIB

AIZ

SMB

RME

Asymmetric Stimulus

Stimulus ON

Stimulus OFF

Stimulus ON

Stimulus OFF

Head Offset Angle

Degrees

C

D

V

D

20

V

0

20

D

150

0

150

D

0

20

V

-150

SMBD

SMBD

SMBV

SMBV

AWC

AIB

AWC

AIY

AIB

AIY

AIB

AIB

AIB

AIB

AIB

AIZ

AIZ

AIY

AIY

AWC

AWC

AWC

AWC

AIY

AIY

AIY

AIY

AWC

AWC

AWC

AWC

AIY

AIY

AIY

AIY

SMB

SMB

SMB

SMB

RME

RME

RME

RME
Stimulation Flow

A

AIZ Stimulus

<table>
<thead>
<tr>
<th>Ablated</th>
<th>Turn Angle (V)</th>
<th>Turn Angle (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>53°</td>
<td>-31°</td>
</tr>
<tr>
<td>AWC</td>
<td>52°</td>
<td>-30°</td>
</tr>
<tr>
<td>AIY</td>
<td>52°</td>
<td>-28°</td>
</tr>
<tr>
<td>AIB</td>
<td>45°</td>
<td>-26°</td>
</tr>
<tr>
<td>AIZR</td>
<td>40°</td>
<td>-13°</td>
</tr>
<tr>
<td>AIZL</td>
<td>36°</td>
<td>39°</td>
</tr>
<tr>
<td>SMB</td>
<td>57°</td>
<td>-10°</td>
</tr>
<tr>
<td>RME</td>
<td>48°</td>
<td>-3°</td>
</tr>
</tbody>
</table>

From ALL interneurons

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Turn Angle (V)</th>
<th>Turn Angle (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIAL</td>
<td>32°</td>
<td>2°</td>
</tr>
<tr>
<td>RIS</td>
<td>56°</td>
<td>-41°</td>
</tr>
<tr>
<td>AVKR</td>
<td>57°</td>
<td>-20°</td>
</tr>
</tbody>
</table>
Conditional Ablation (Stimulation Flow)

**AWC+AIY Stimulus**

<table>
<thead>
<tr>
<th>Ablated</th>
<th>Turn Angle (V)</th>
<th>Turn Angle (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>26°</td>
<td>-25°</td>
</tr>
<tr>
<td>AWC</td>
<td>16°</td>
<td>-31°</td>
</tr>
<tr>
<td>AIYR</td>
<td>9°</td>
<td>2°</td>
</tr>
<tr>
<td>AIYL</td>
<td>3°</td>
<td>26°</td>
</tr>
<tr>
<td>AIB</td>
<td>19°</td>
<td>-32°</td>
</tr>
<tr>
<td>AIZ</td>
<td>24°</td>
<td>-25°</td>
</tr>
<tr>
<td>SMB</td>
<td>13°</td>
<td>-2°</td>
</tr>
<tr>
<td>RME</td>
<td>50°</td>
<td>15°</td>
</tr>
</tbody>
</table>

From ALL interneurons | AIZ Ablated

<table>
<thead>
<tr>
<th></th>
<th>AVAR</th>
<th>AVEL</th>
<th>AVER</th>
<th>AIAR</th>
<th>RIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVAR</td>
<td>-7°</td>
<td>-28°</td>
<td>26°</td>
<td>-1°</td>
<td>40°</td>
</tr>
<tr>
<td>AVEL</td>
<td>26°</td>
<td>1°</td>
<td>63°</td>
<td>-12°</td>
<td></td>
</tr>
<tr>
<td>AVER</td>
<td>23°</td>
<td>-12°</td>
<td>40°</td>
<td>-42°</td>
<td></td>
</tr>
<tr>
<td>AIAR</td>
<td>23°</td>
<td>-12°</td>
<td>40°</td>
<td>-42°</td>
<td></td>
</tr>
<tr>
<td>RIS</td>
<td>40°</td>
<td>-42°</td>
<td>26°</td>
<td>1°</td>
<td></td>
</tr>
</tbody>
</table>

From ALL neighbors | AIZ Ablated

<table>
<thead>
<tr>
<th></th>
<th>RIML</th>
<th>RIMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIML</td>
<td>20°</td>
<td>1°</td>
</tr>
<tr>
<td>RIMR</td>
<td>3°</td>
<td>-7°</td>
</tr>
</tbody>
</table>
Ablation Survey
Inference of behavioral circuits

**From ALL interneurons | AIZ Ablated**

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Angle 1</th>
<th>Angle 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVAR</td>
<td>-7°</td>
<td>-28°</td>
</tr>
<tr>
<td>AVEL</td>
<td>26°</td>
<td>1°</td>
</tr>
<tr>
<td>AVER</td>
<td>63°</td>
<td>-1°</td>
</tr>
<tr>
<td>AIAR</td>
<td>23°</td>
<td>-12°</td>
</tr>
<tr>
<td>RIS</td>
<td>40°</td>
<td>-42°</td>
</tr>
</tbody>
</table>

**From ALL neighbors | AIZ Ablated**

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Angle 1</th>
<th>Angle 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIML</td>
<td>20°</td>
<td>1°</td>
</tr>
<tr>
<td>RIMR</td>
<td>3°</td>
<td>-7°</td>
</tr>
</tbody>
</table>
Is the model accurate enough?

- Search for model failures in prediction

- Head Offset Angle

- Degrees

- AWC AIB AWC AIB AWC AIB AIY AIY AIB AIB AIY AIY SMB SMB SMB SMB SMB SMBV SMBV

- Starting point

- Dorsal Asymmetric

- Stim into AIY
Model Refinement

Configuration

Connectome

Movement Trajectory

(Dorsal Asymmetric Stim into AWC)

Base

GluCl

(AWC → AIA, AIY)

Dorsal asymmetrical stimuli (AWC)

with GLUCL (AWC -> AIY, AIA)

Negative Neuropeptides into AIY, AIA

Starting point

Dorsal Asymmetric Stim into AIY
Model Refinement

Configuration

Connectome

Movement Trajectory

Dorsal asymmetrical stimuli (AWC) with GLUCL (AWC -> AY, AIY)
Negative Neuropeptides into AY, AIY

(AWC à AIA, AIY)

(AWC à AIA, AIY)

(Dorsal Asymmetric Stim into AWC)

Starting point

Dorsal Asymmetric Stim into AIY

(AIA, AIB, AY)

(AIA, AIB, AY)
Spontaneous Behavior/Stochastic behavior

“Can of worms”
Stochastic Behavioral Circuits

From ALL interneurons | AIZ Ablated

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Turn Angle (V)</th>
<th>Turn Angle (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWC</td>
<td>(-53^\circ)</td>
<td>(-31^\circ)</td>
</tr>
<tr>
<td>AIY</td>
<td>(-52^\circ)</td>
<td>(-28^\circ)</td>
</tr>
<tr>
<td>AIB</td>
<td>(-45^\circ)</td>
<td>(-26^\circ)</td>
</tr>
<tr>
<td>AIZR</td>
<td>(-40^\circ)</td>
<td>(-13^\circ)</td>
</tr>
<tr>
<td>AIZL</td>
<td>(-36^\circ)</td>
<td>(-39^\circ)</td>
</tr>
<tr>
<td>SMB</td>
<td>(-57^\circ)</td>
<td>(-10^\circ)</td>
</tr>
<tr>
<td>RME</td>
<td>(-48^\circ)</td>
<td>(-3^\circ)</td>
</tr>
</tbody>
</table>

From ALL neighbors | AIZ Ablated

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Turn Angle (V)</th>
<th>Turn Angle (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIAL</td>
<td>(-32^\circ)</td>
<td>(-2^\circ)</td>
</tr>
<tr>
<td>RIS</td>
<td>(-56^\circ)</td>
<td>(-41^\circ)</td>
</tr>
<tr>
<td>AVKR</td>
<td>(-57^\circ)</td>
<td>(-20^\circ)</td>
</tr>
<tr>
<td>AVAR</td>
<td>(-7^\circ)</td>
<td>(-28^\circ)</td>
</tr>
<tr>
<td>AVEL</td>
<td>(-26^\circ)</td>
<td>(1^\circ)</td>
</tr>
<tr>
<td>AVER</td>
<td>(-63^\circ)</td>
<td>(-1^\circ)</td>
</tr>
<tr>
<td>AIAR</td>
<td>(-23^\circ)</td>
<td>(-12^\circ)</td>
</tr>
<tr>
<td>RIML</td>
<td>(-20^\circ)</td>
<td>(1^\circ)</td>
</tr>
<tr>
<td>RIMR</td>
<td>(-3^\circ)</td>
<td>(-7^\circ)</td>
</tr>
<tr>
<td>RIS</td>
<td>(-40^\circ)</td>
<td>(-42^\circ)</td>
</tr>
<tr>
<td>RIM</td>
<td>(20^\circ)</td>
<td>(1^\circ)</td>
</tr>
<tr>
<td>RIML</td>
<td>(20^\circ)</td>
<td>(1^\circ)</td>
</tr>
<tr>
<td>RIMR</td>
<td>(3^\circ)</td>
<td>(-7^\circ)</td>
</tr>
</tbody>
</table>