

# Synaptic wiring motifs in posterior parietal cortex support decision-making

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Boston Children's Hospital / Harvard Medical School

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# Behavioral Choices

← from UCLA Meyer and Renee Luskin Conference C...  
to Institute for Pure and Applied Mathematics, 46...

## UCLA Meyer and Renee Luskin Conference Center

425 Westwood Plaza, Los Angeles, CA 90095

↑ Head northeast on Westwood Plaza

30 ft

↖ Slight left toward Portola Plaza

98 ft

↖ Turn left toward Portola Plaza

Take the stairs

75 ft

↗ Turn right toward Portola Plaza

75 ft

↗ Turn right toward Portola Plaza

30 ft

↖ Turn left toward Portola Plaza

Take the stairs

328 ft

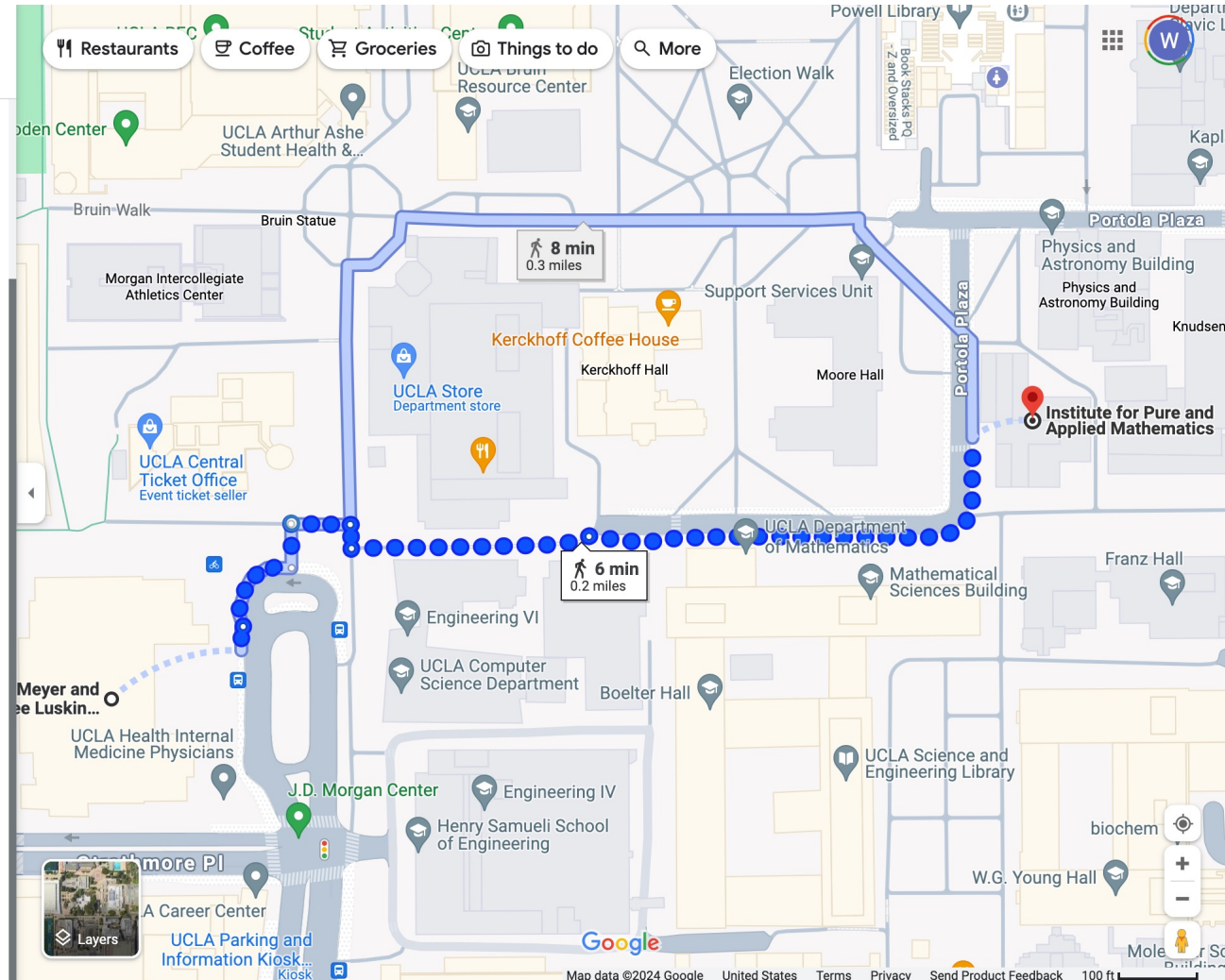
↗ Continue onto Portola Plaza

Destination will be on the right

0.1 mi

## Institute for Pure and Applied Mathematics

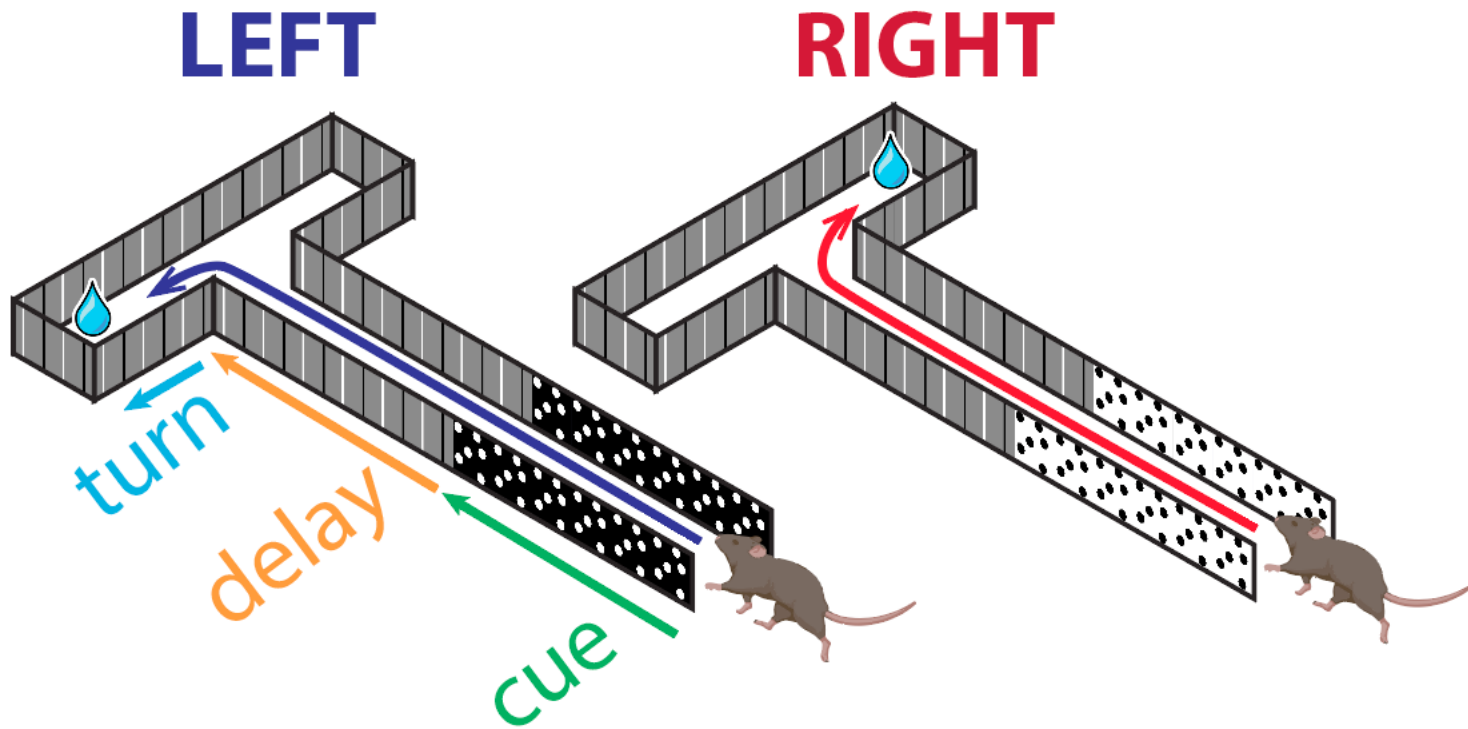
460 Portola Plaza, Los Angeles, CA 90095



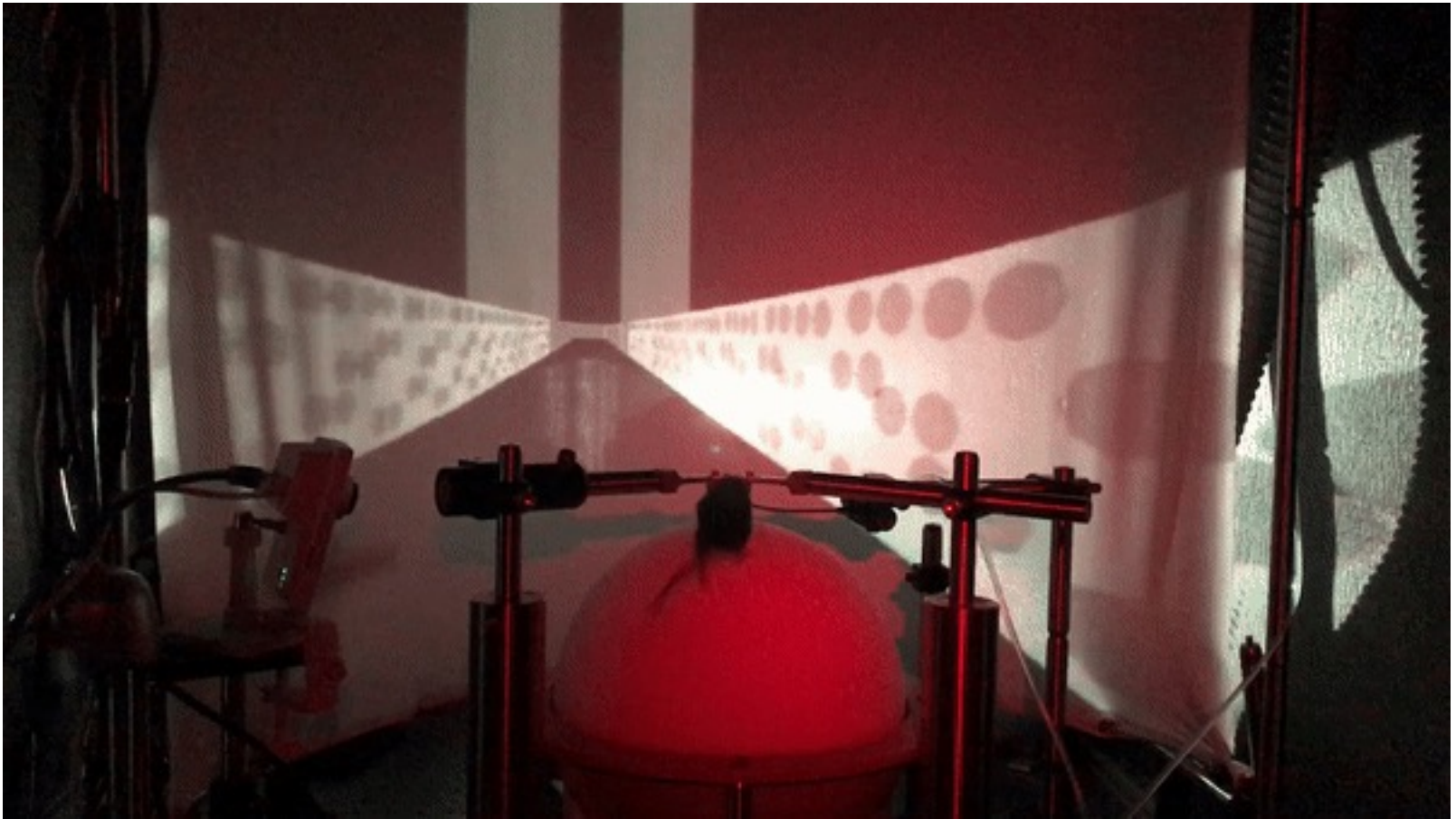
# Forced Choice Memory Task



Chris Harvey

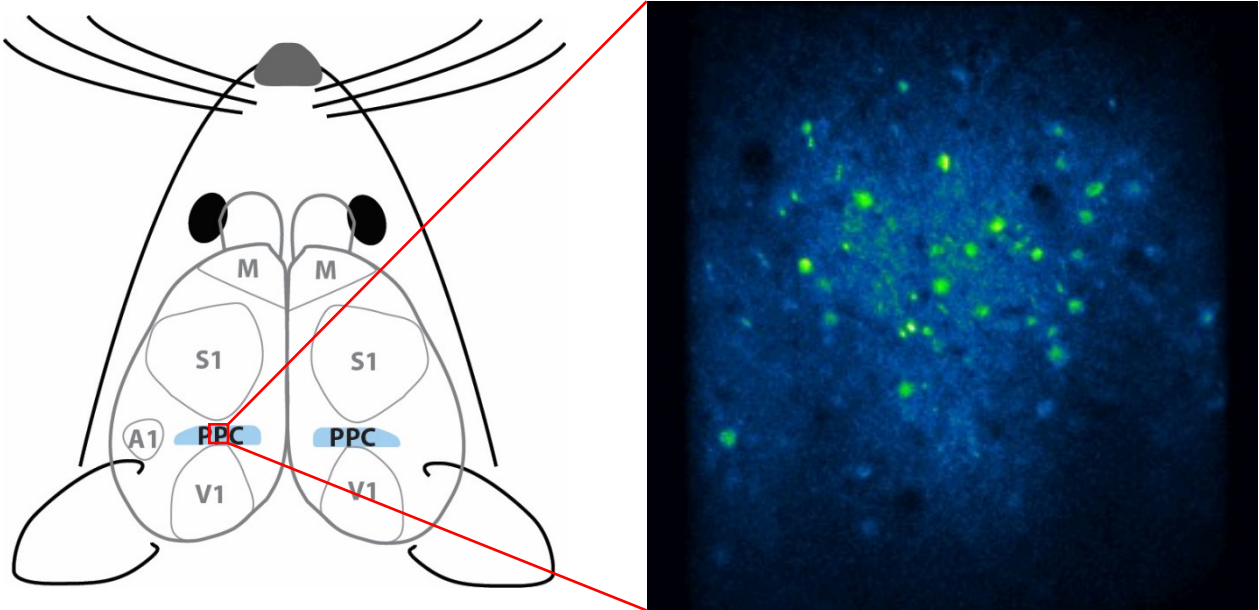


# Forced Choice Memory Task





# Posterior Parietal Cortex (PPC)

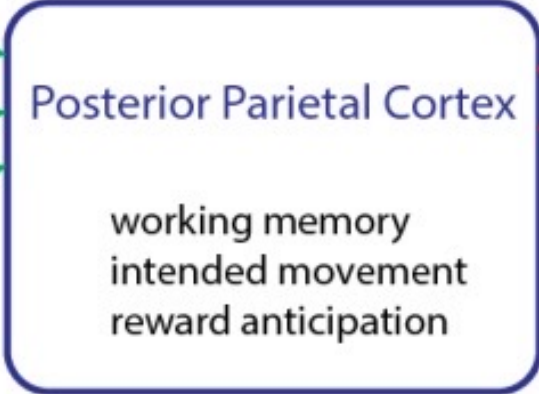


Somatosensory Cortex

Visual Cortex

Auditory Cortex

sensory perception

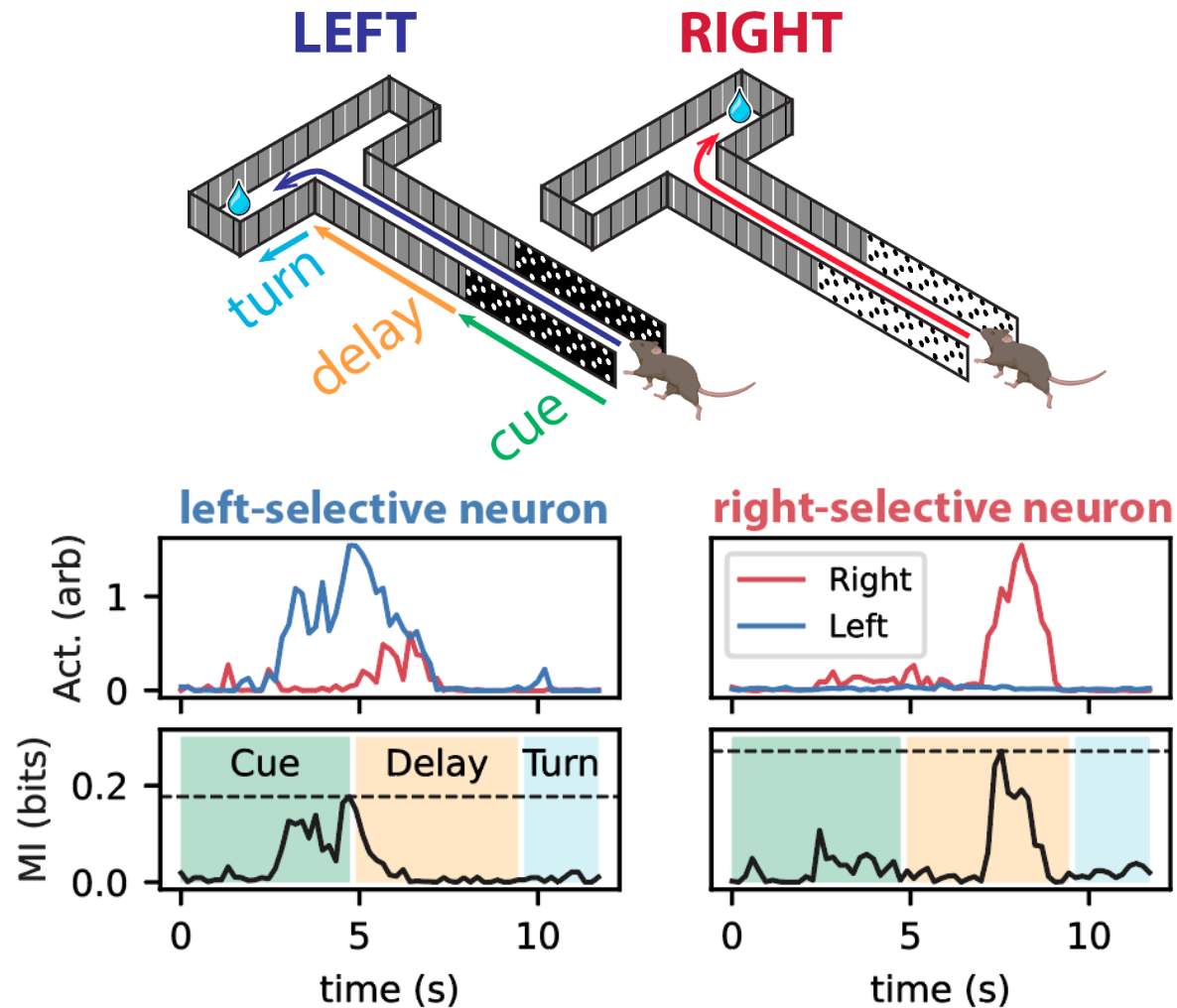


Anterior Cingulate Cortex

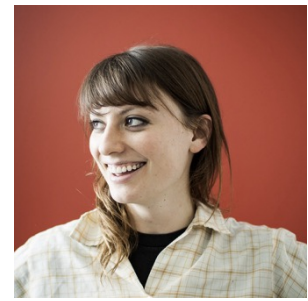
Orbital Frontal Cortex

navigational choice

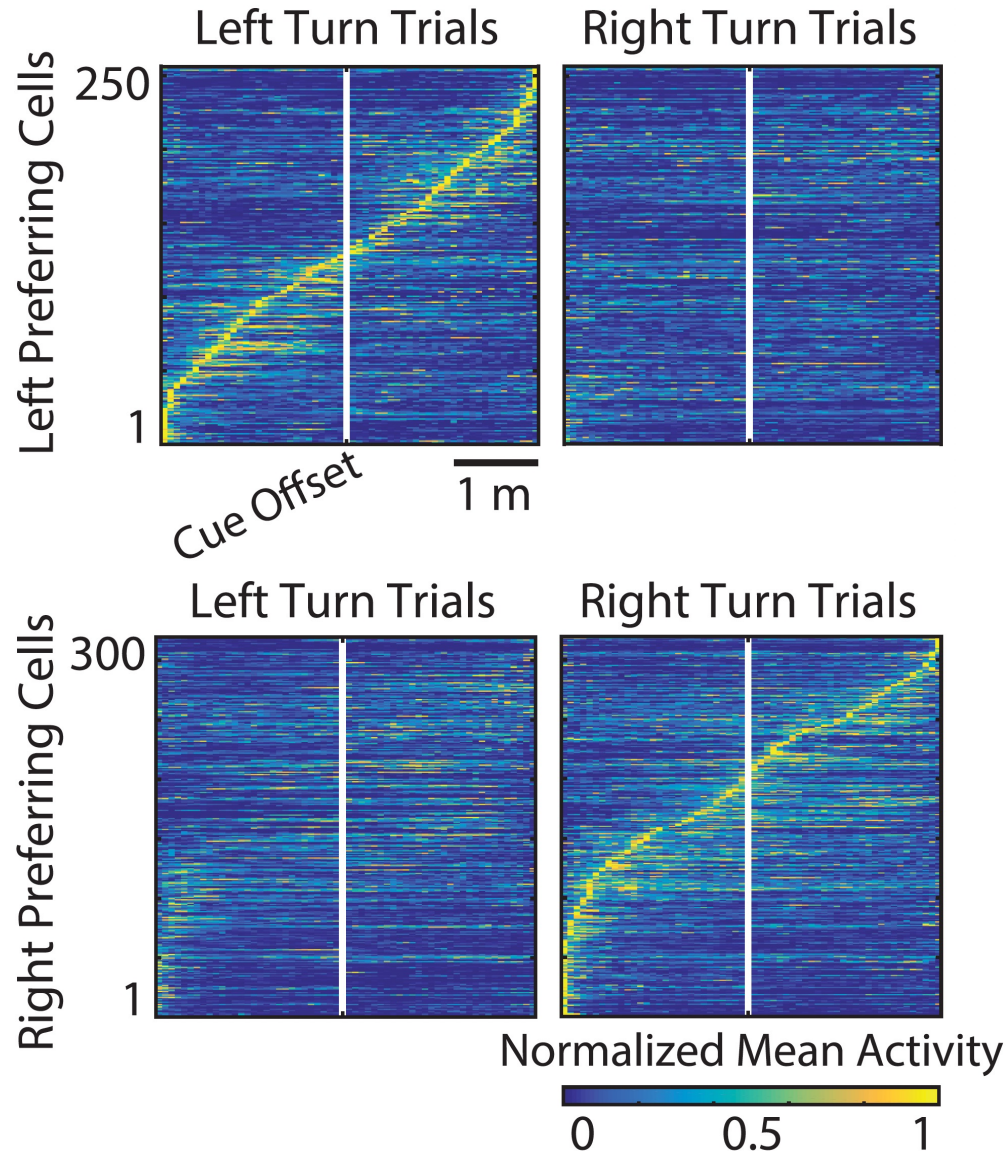
# Trial-Type Selective Cells in PPC



# Activity Sequences in PPC



Laura Driscoll

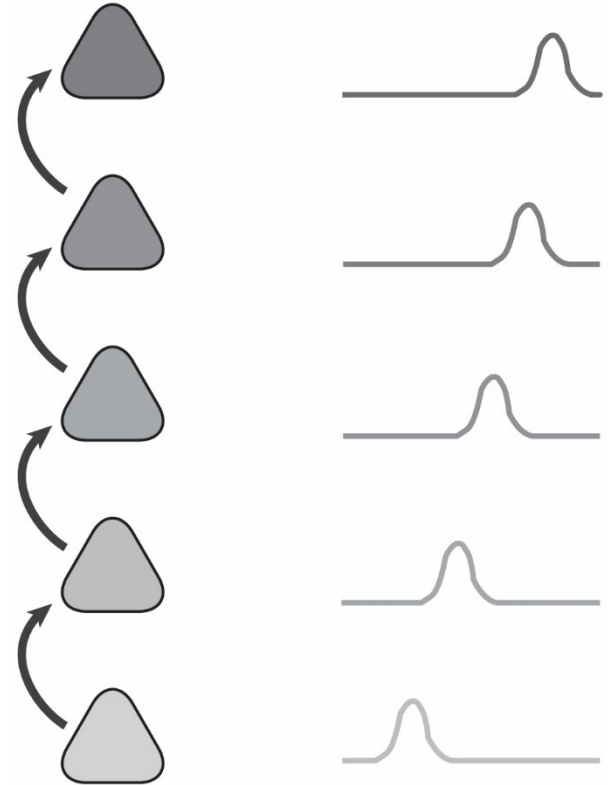


# Roadmap

- How is circuit connectivity organized to support perceptually guided decision-making?
- “Functional connectomics”
- An opponent inhibition motif amplifies selective inputs, improving trial-type encoding
- *Individuality*

# How might connectivity enable dynamics?

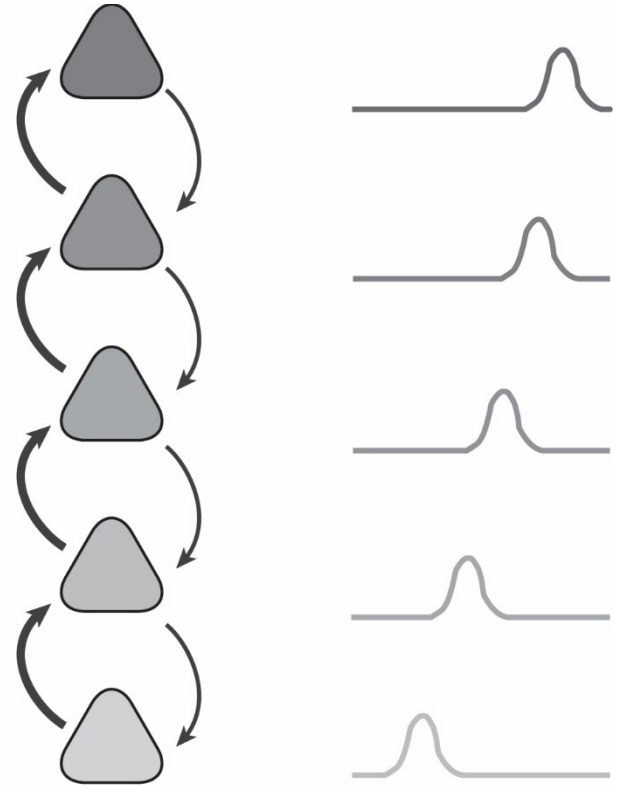
## 1. Synaptic chain motif





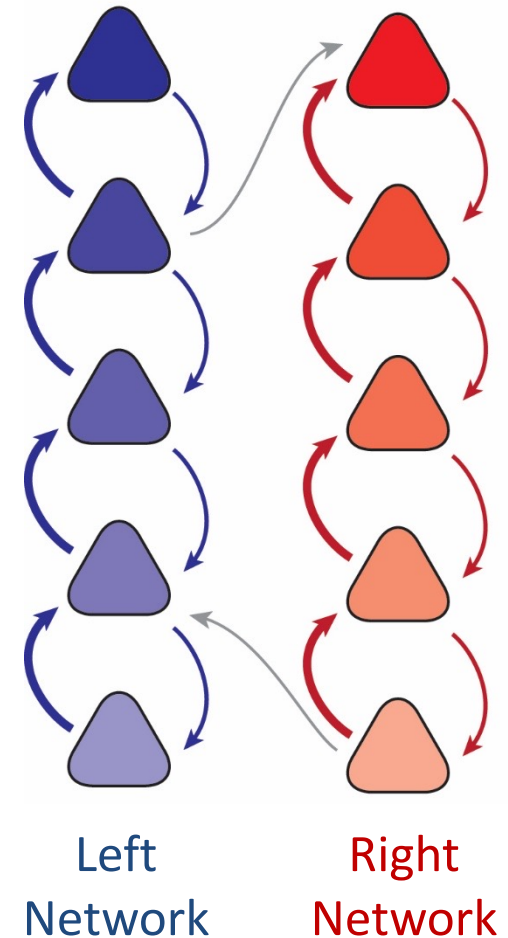
# How might connectivity enable dynamics?

1. Synaptic chain motif
2. Recurrent connectivity



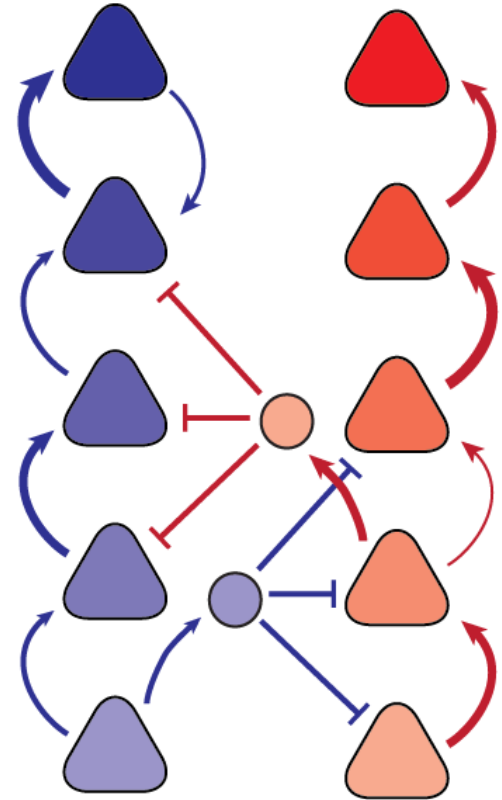
# How might connectivity enable dynamics?

1. Synaptic chain motif
2. Recurrent connectivity
3. Choice-specific subnetworks



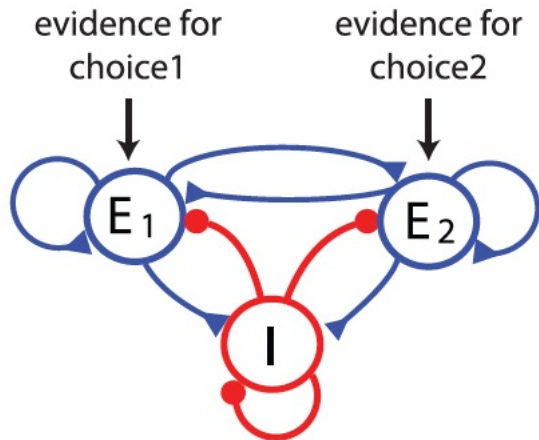
# How might connectivity enable dynamics?

1. Synaptic chain motif
2. Recurrent connectivity
3. Choice-specific subnetworks
4. Selective inhibition suppressing opposing subnetworks



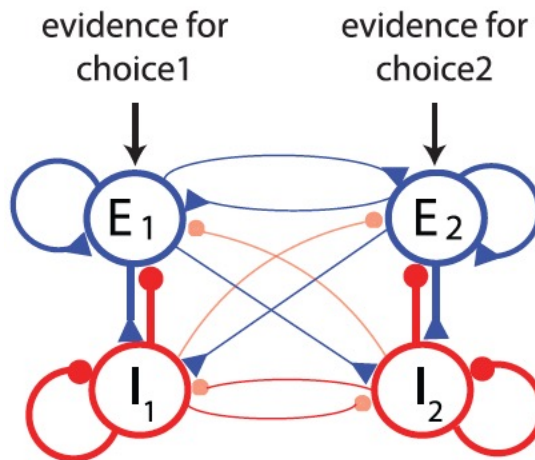
# How is Inhibition Wired?

**Non-selective**



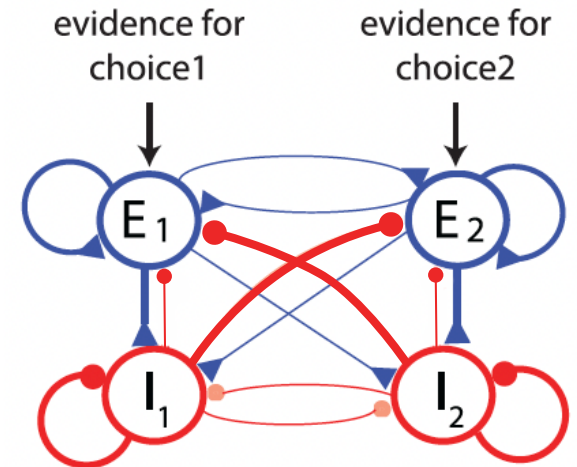
Amari and Arbib, 1977  
Shadlen et al., 1996  
Maas, 2000  
Wang, 2002

**Signal-selective**



Najafi, et al., 2020  
Roach, et al., 2022

**Signal-selective**



?

Bock, et al., 2011  
Hofer, et al., 2011  
Fino and Yuste, 2011  
Packer and Yuste, 2011

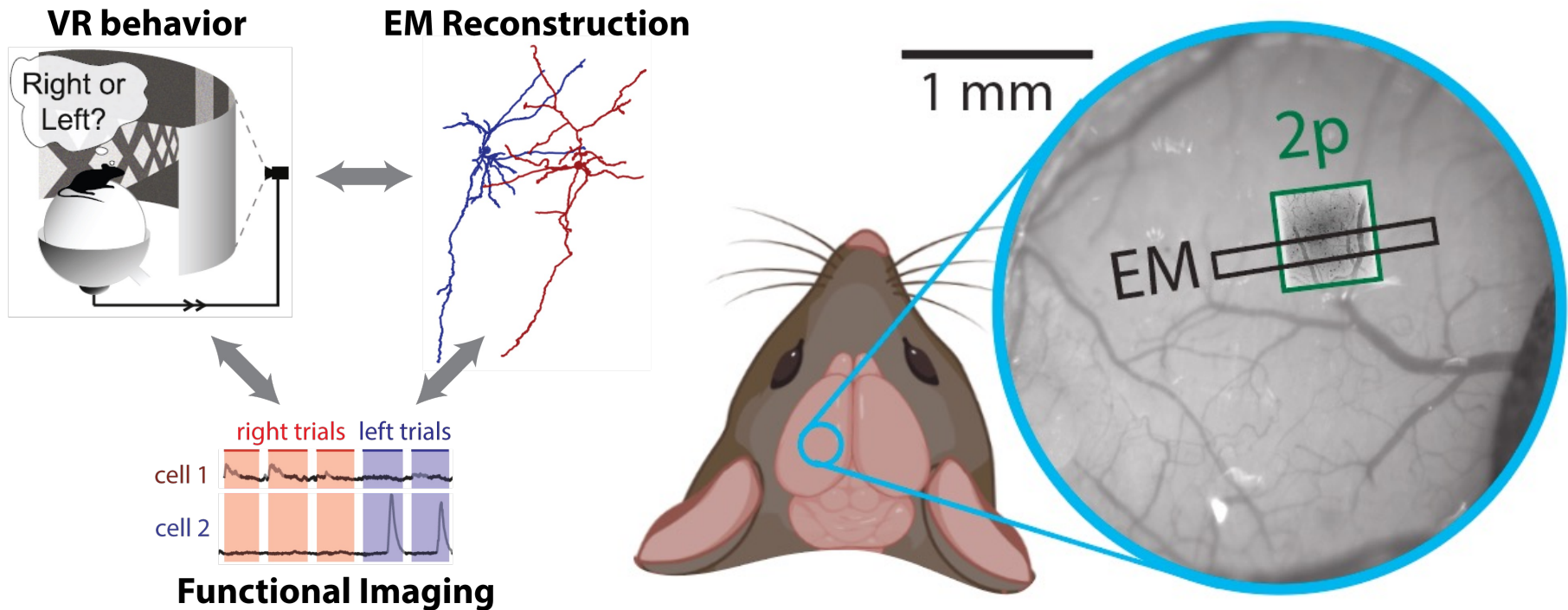
# How can we test these hypotheses?

Needs:

- Population activity during behavior
- Ensemble wiring diagrams



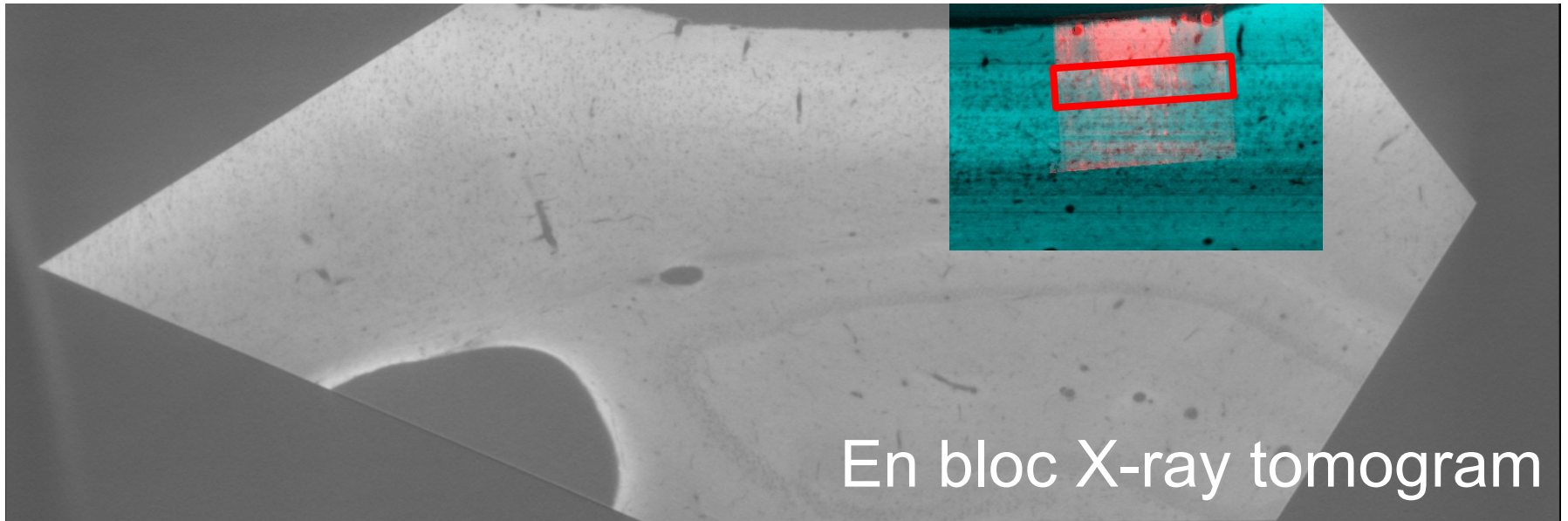
# Functional Connectomics



Combine behavior, neuronal activity, and neuronal connectivity for the same circuit

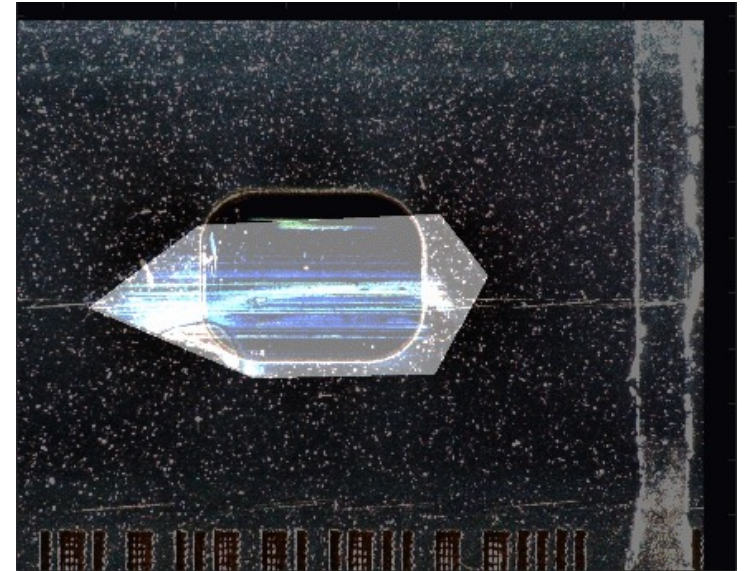
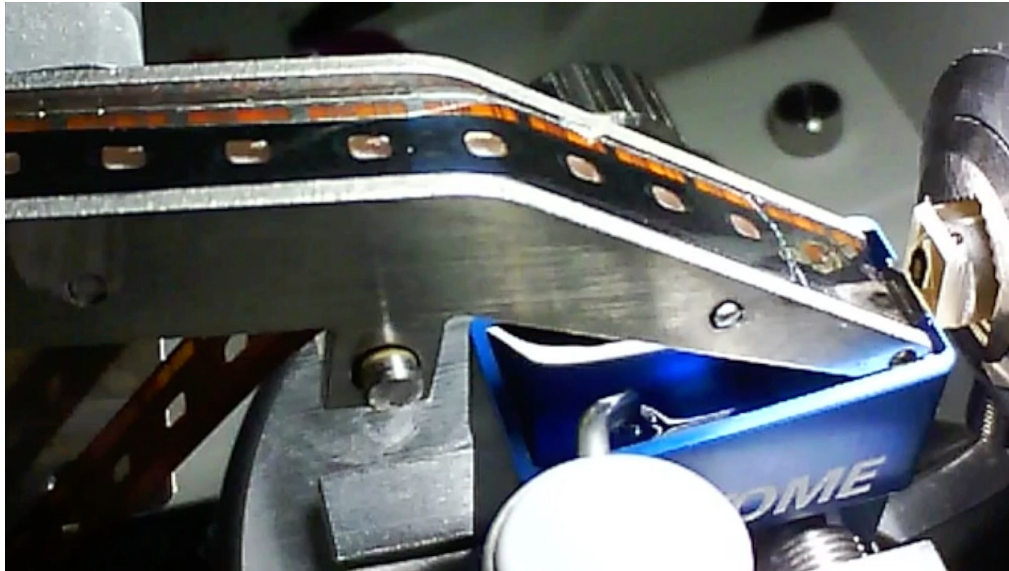
# *In Vivo* to X-ray Correspondence

Functionally imaged volume  
EM imaging region of interest



Sectioned block:	2.5 x 1.5 x 0.2 mm
<i>In vivo</i> imaging volume:	0.5 x 0.1 x 0.5 mm
TEM volume:	1.2 x 0.8 x 0.2 mm

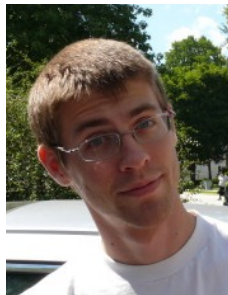
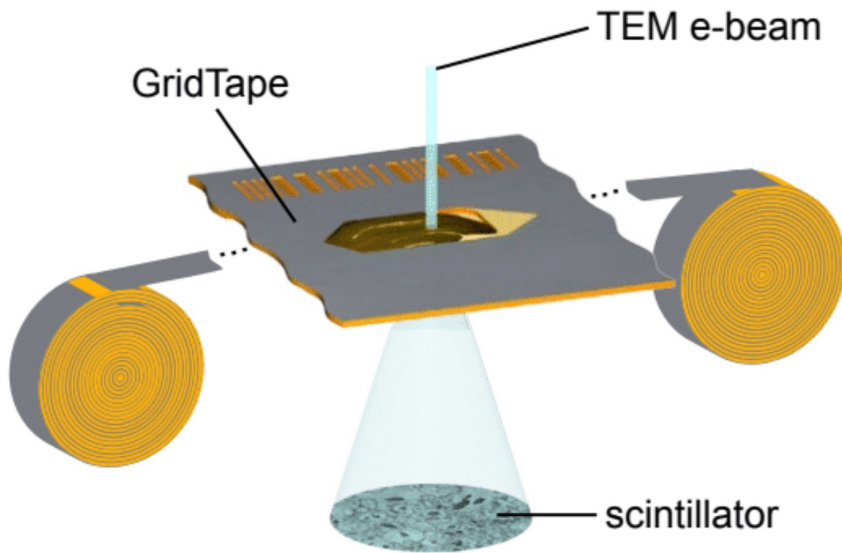
# Tape System for High-Throughput TEM



2500 sections  
100 um thickness  
14 hr pickup time  
98.6% on-target



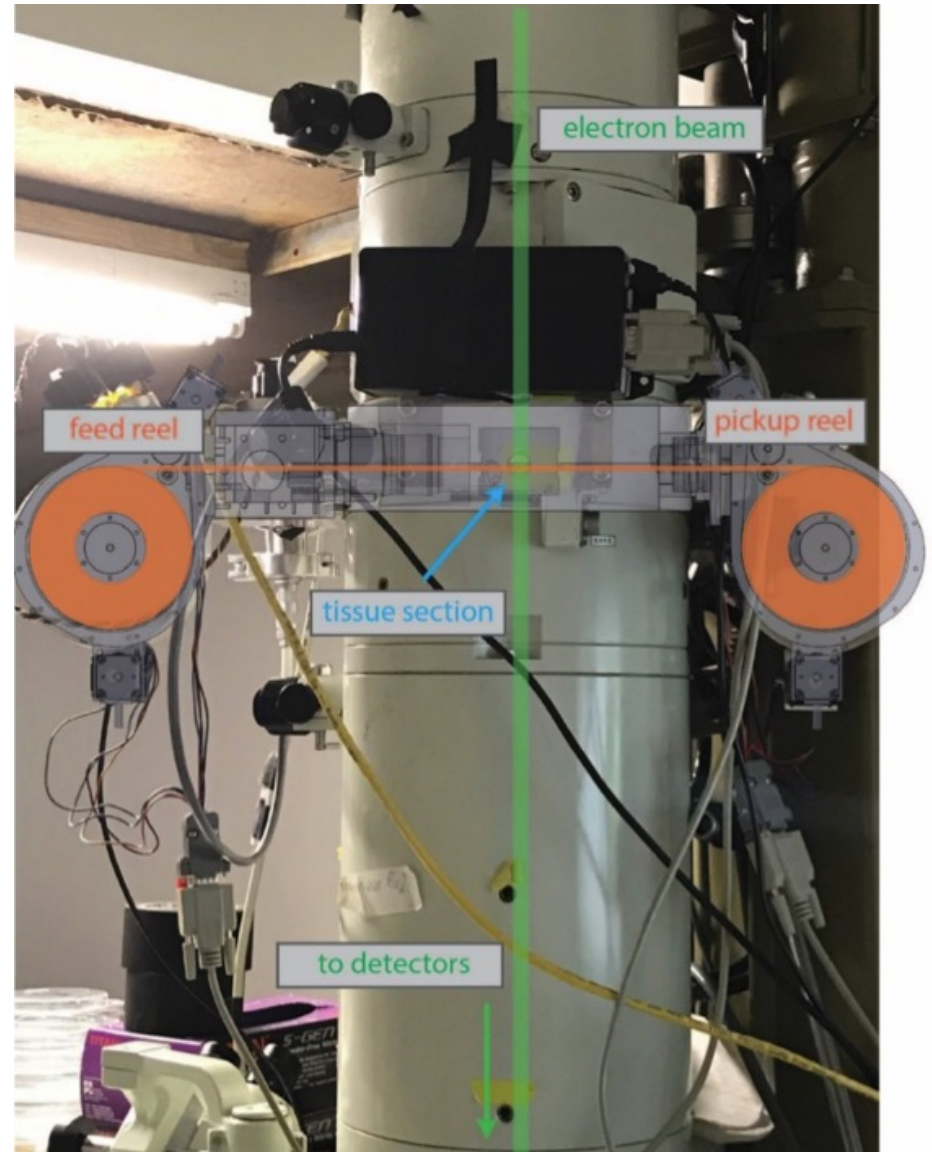
# Tape System for High-Throughput TEM



Brett Graham



David Hildebrand

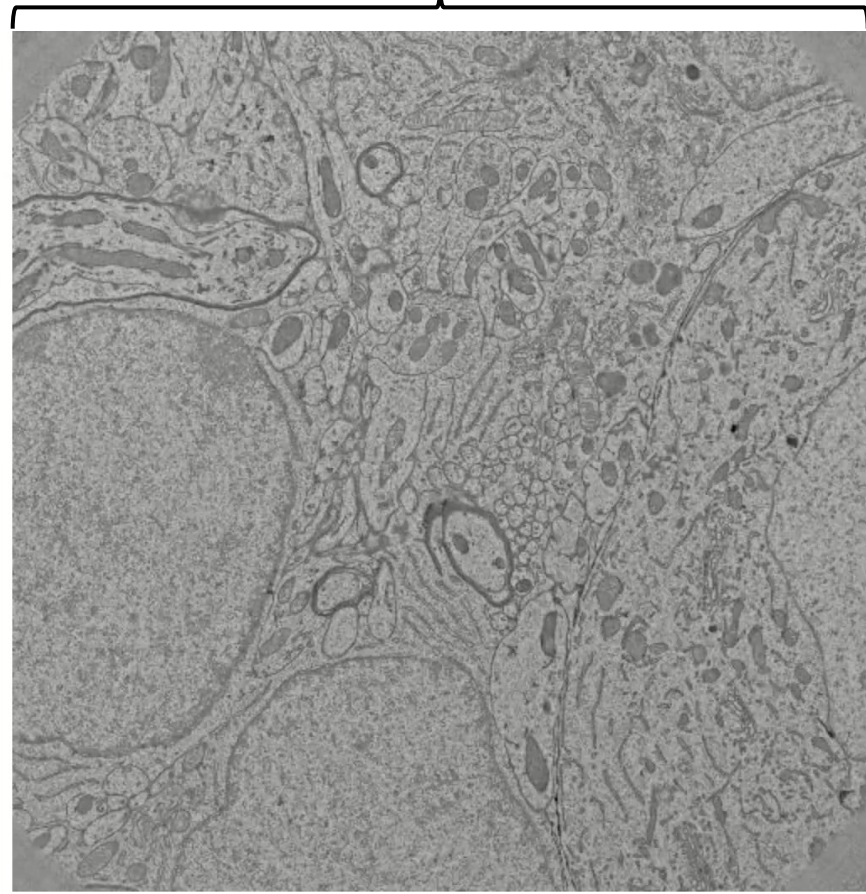


# Tape System for High-Throughput TEM

~750 $\mu$ m

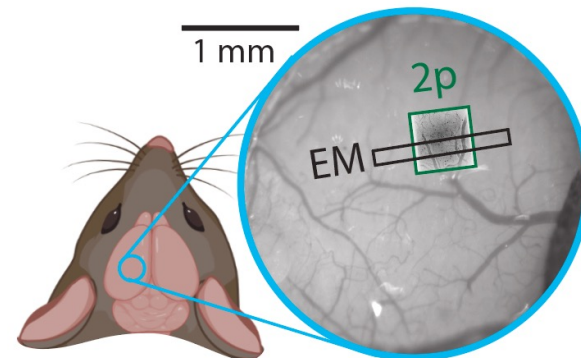
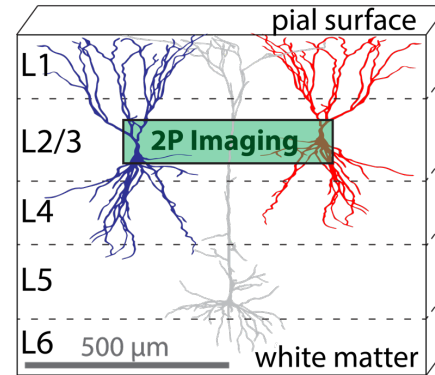
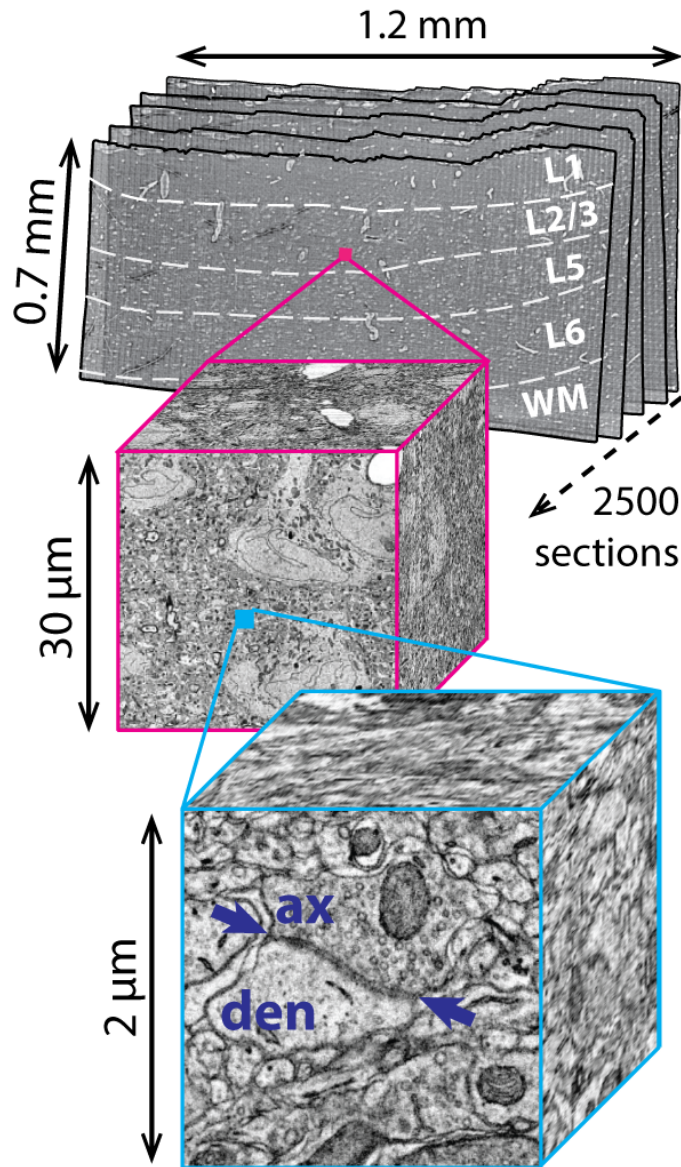


16 $\mu$ m

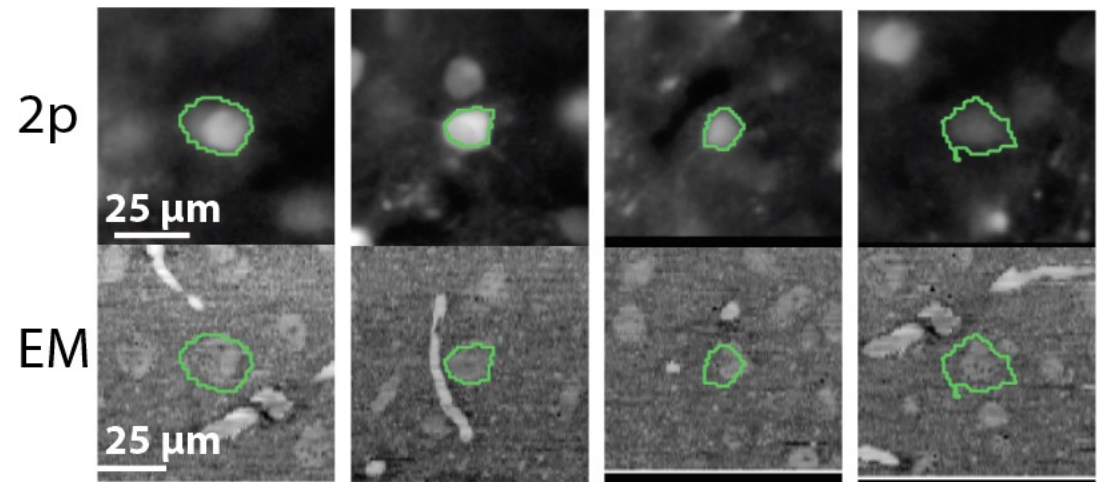
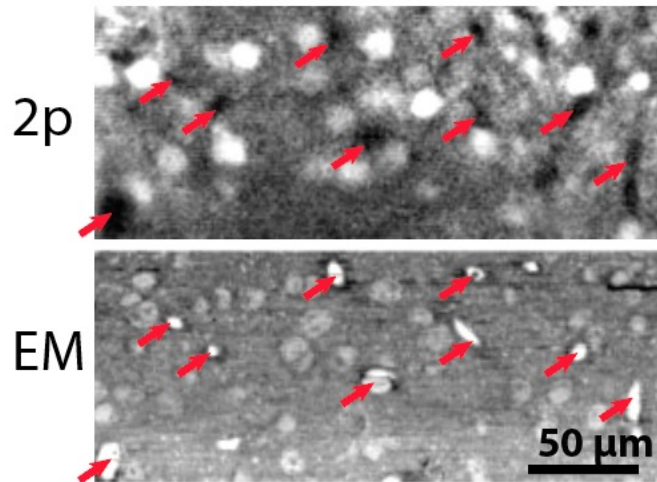


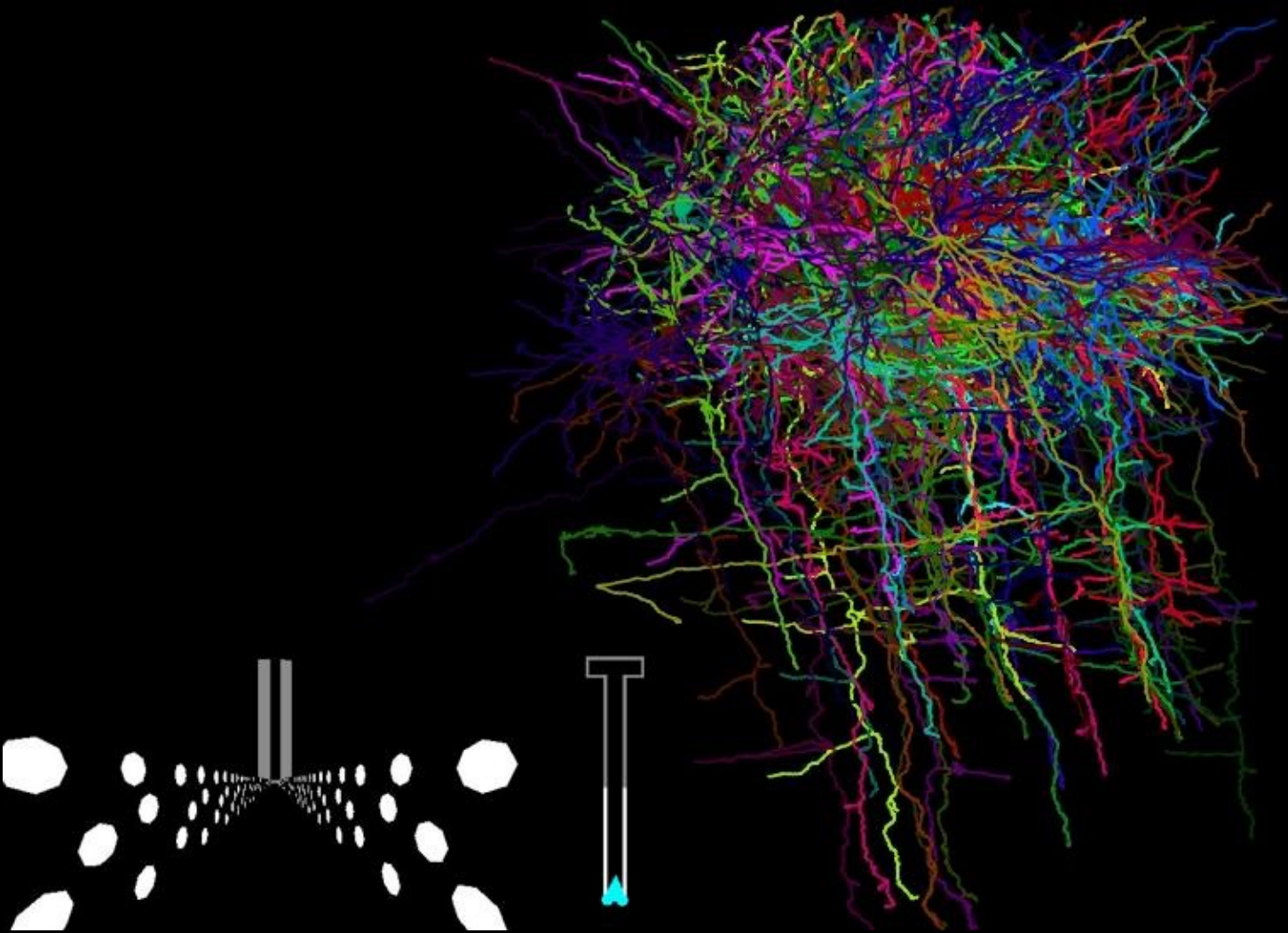


# PPC EM Dataset



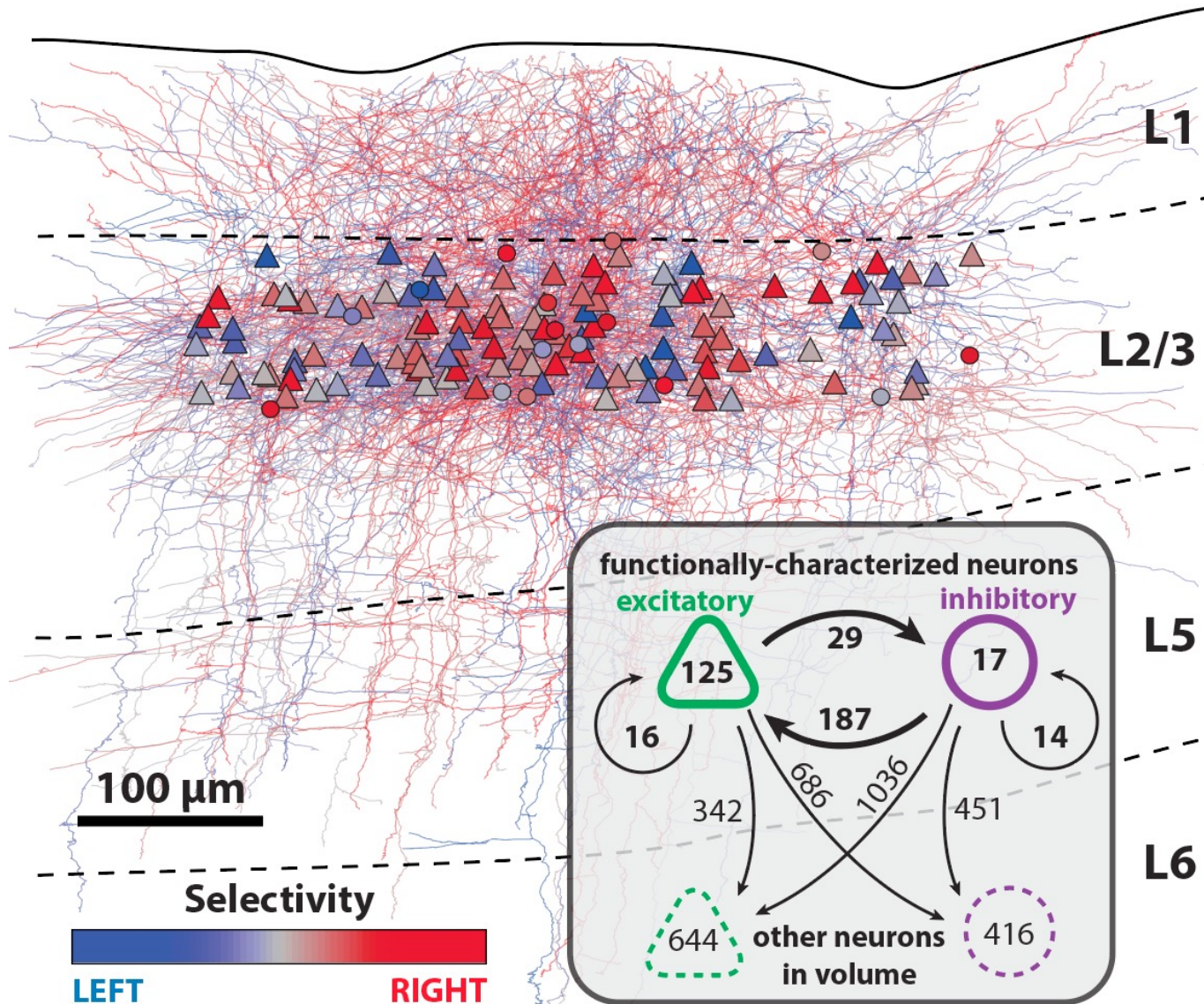
# *In Vivo* and EM correspondence



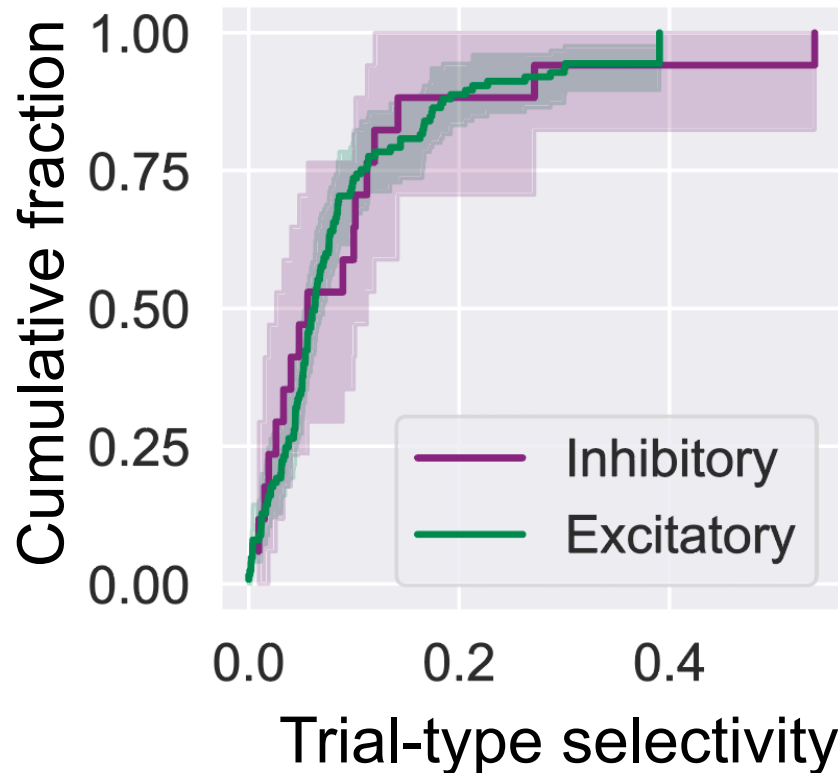




# Reconstruction of a Functionally Characterized Circuit in PPC



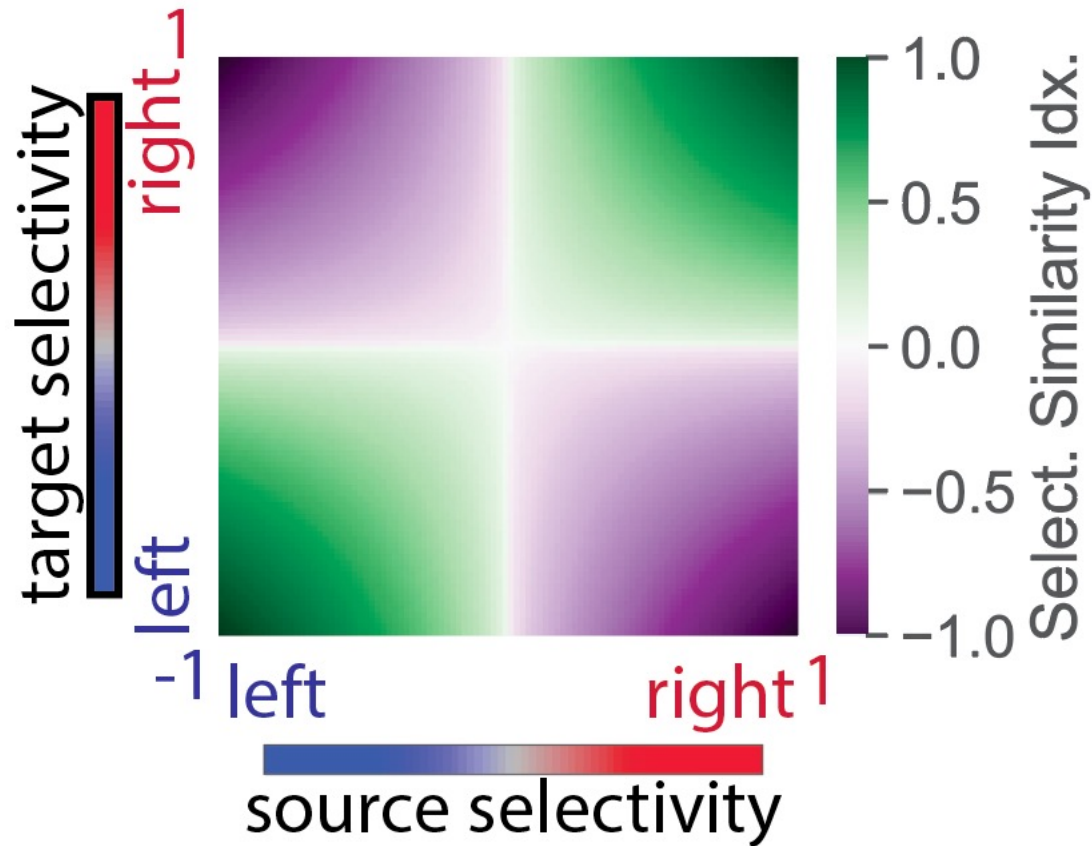
# Interneurons are Selective for Trial-Type in PPC



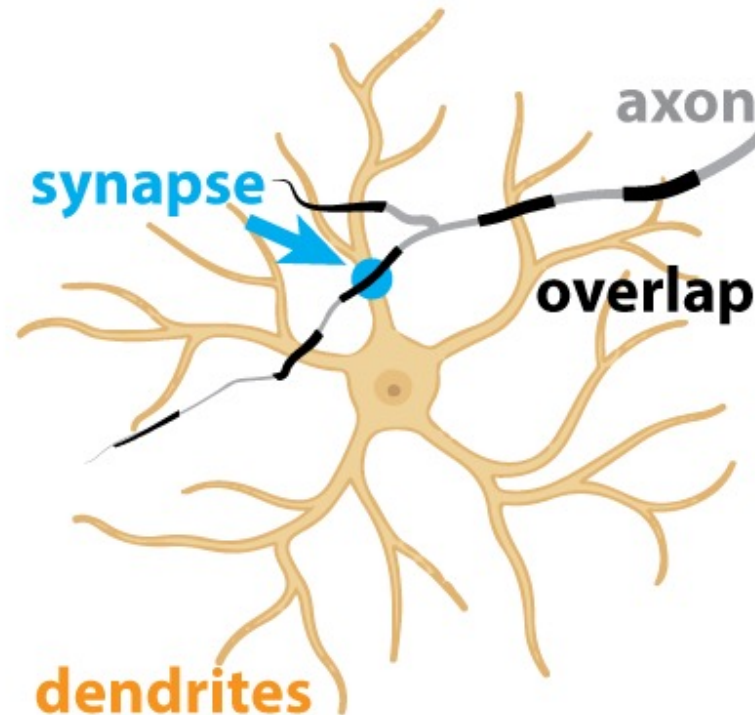
Pyramidal and non-pyramidal cells have indistinguishable levels of choice selectivity in PPC.



# Functional Similarity



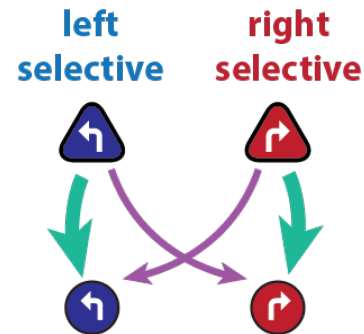
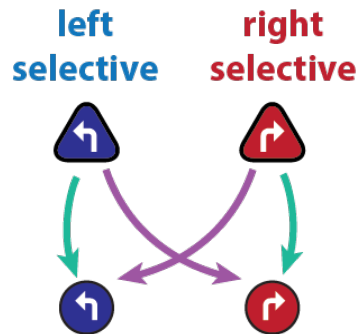
# Synapse Frequency



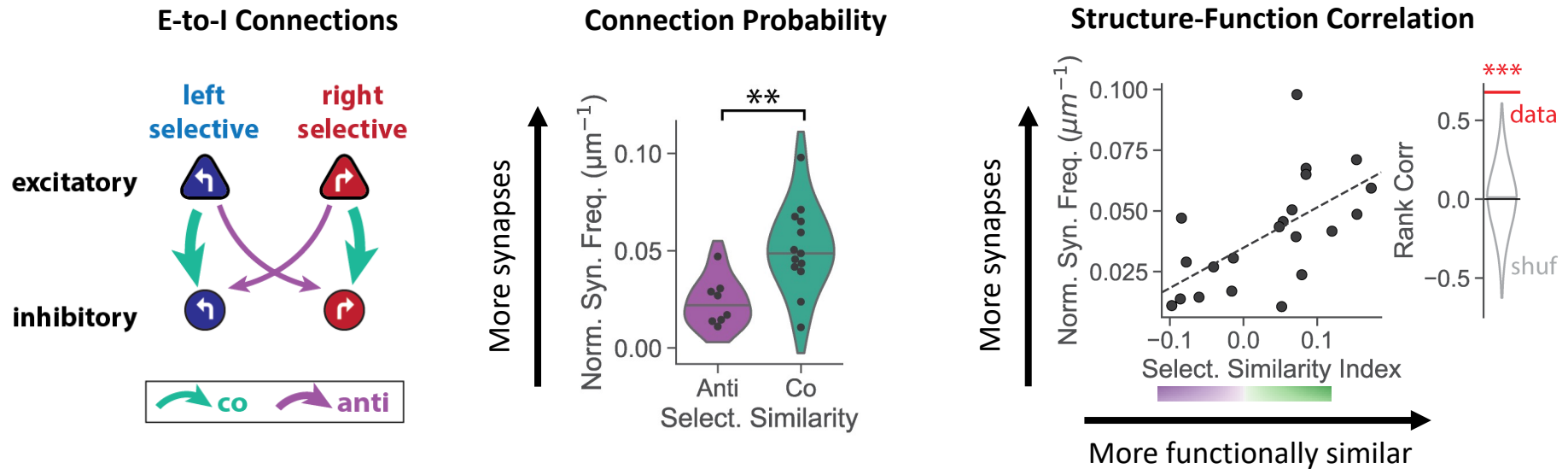
**dendrites**

$$\text{Norm. Syn. Freq.} = \frac{\# \text{ synapses}}{\text{overlap}}$$

# Are excitatory outputs to inhibitory neurons functionally selective?

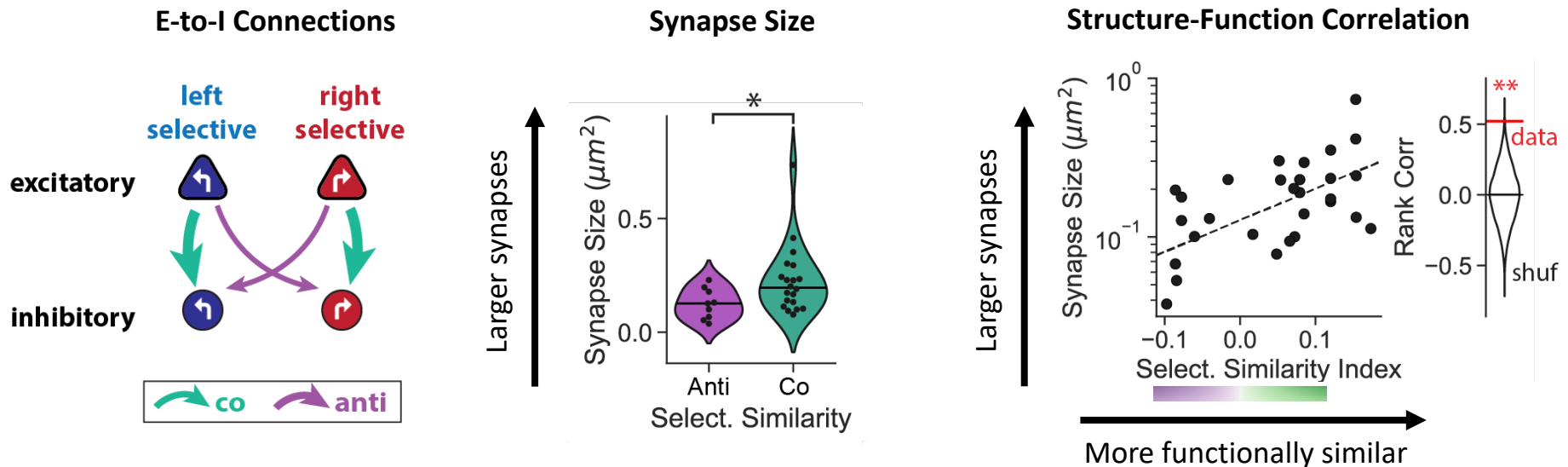


# E-to-I Connectivity is Co-Selective



Pyramidal cells synapse onto interneurons with more similar choice selectivity.

# E-to-I Synapse Size is Co-Selective

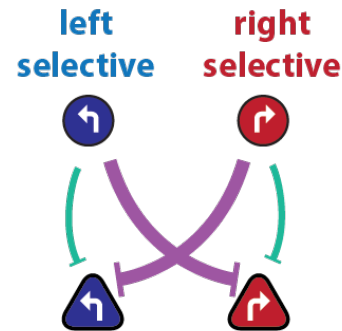
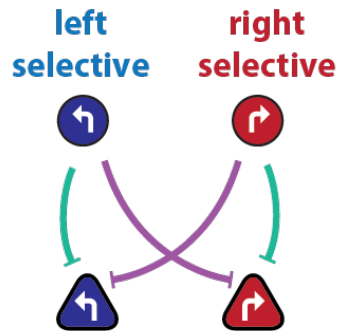


Pyramidal cells synapse onto similarly selective interneurons with larger (stronger\*) synapses.

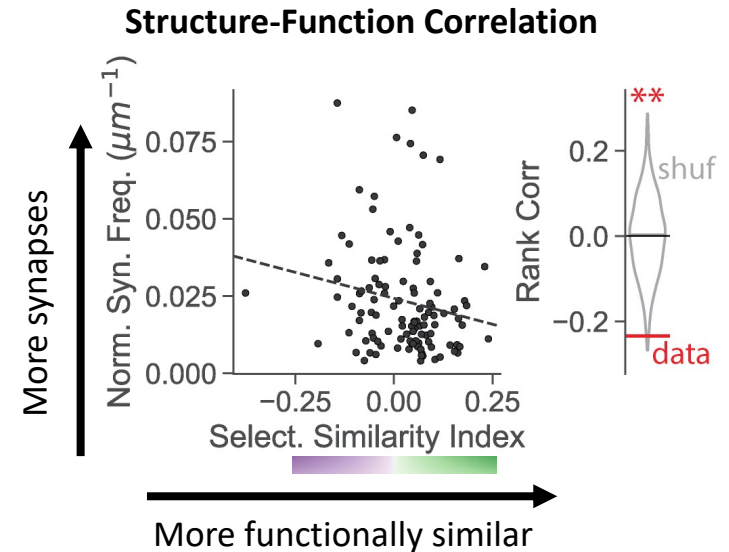
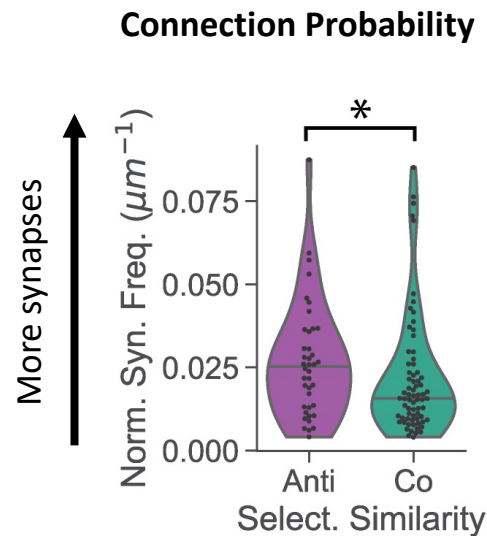
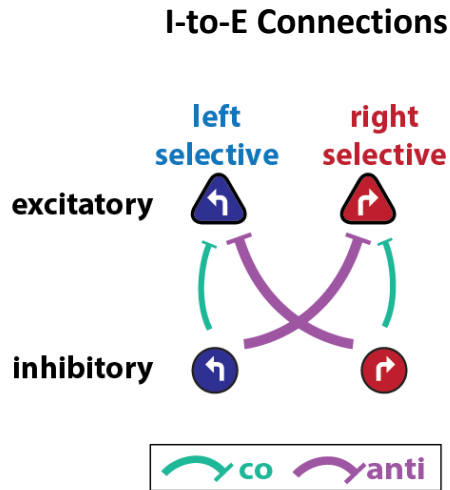
\* Holler, et al., *Nature* (2021)  
Kuan, Bondanelli, et al., *Nature* (In Press)



# Are inhibitory outputs to excitatory neurons functionally selective?



# I-to-E Connectivity is Anti-Selective



Interneurons synapse onto pyramidal cells with more opposing choice selectivity.

How do artificial neural networks  
trained to exhibit PPC dynamics  
compare?

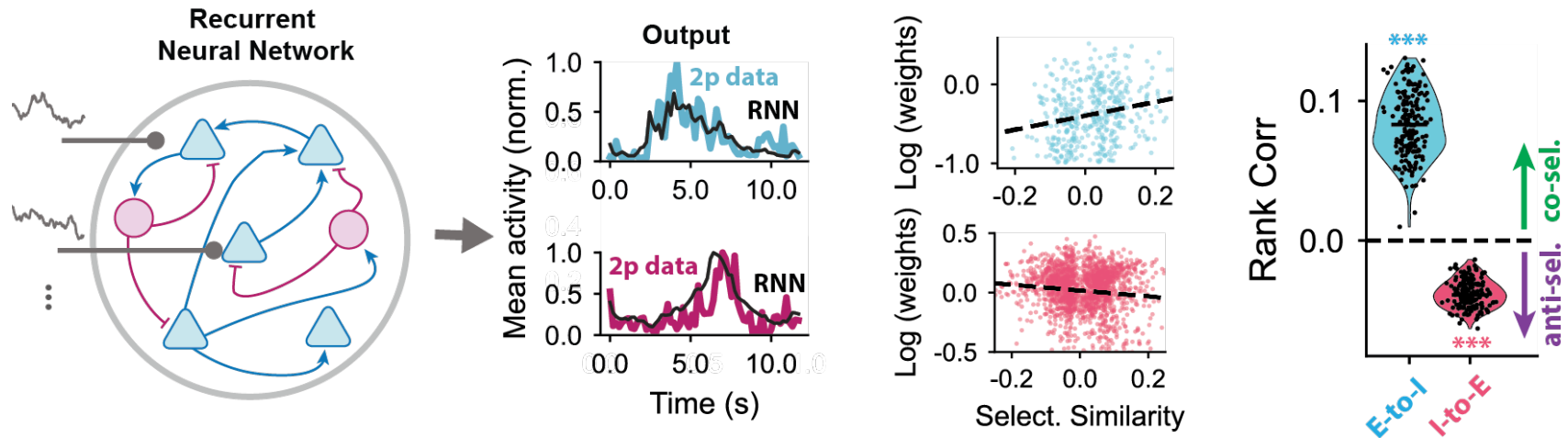
# RNN Connection Weights



Giulio Bondanelli



Stefano Panzeri

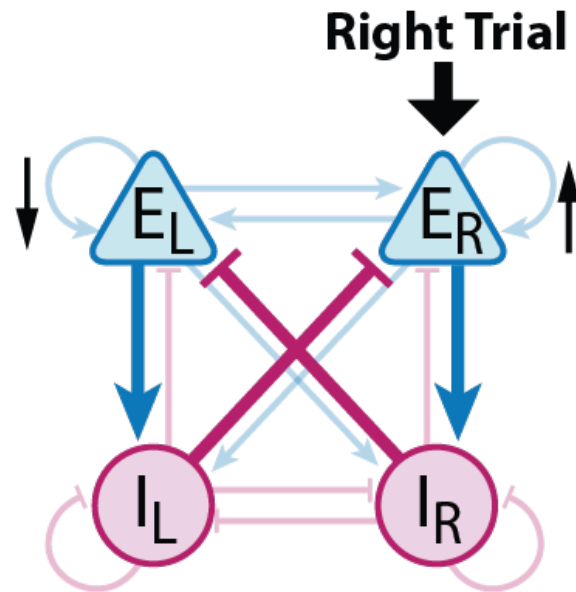


Recurrent neural networks reproducing measured dynamics have opponent inhibitory connectivity.

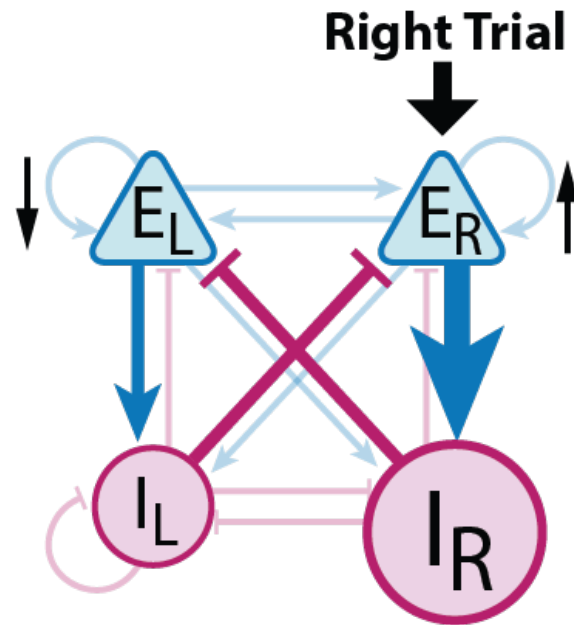
How does opponent inhibition  
impact PPC function?



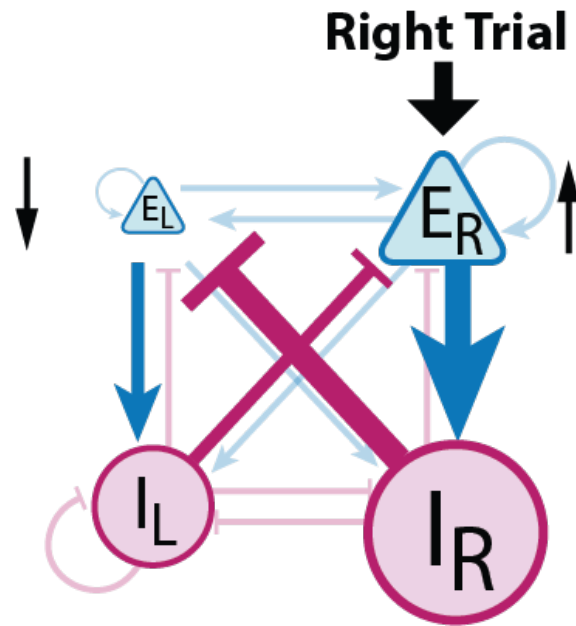
# Competitive Amplification



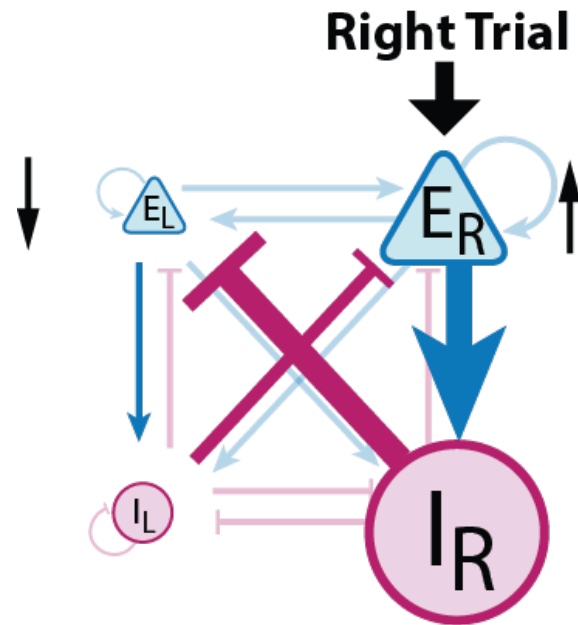
# Competitive Amplification



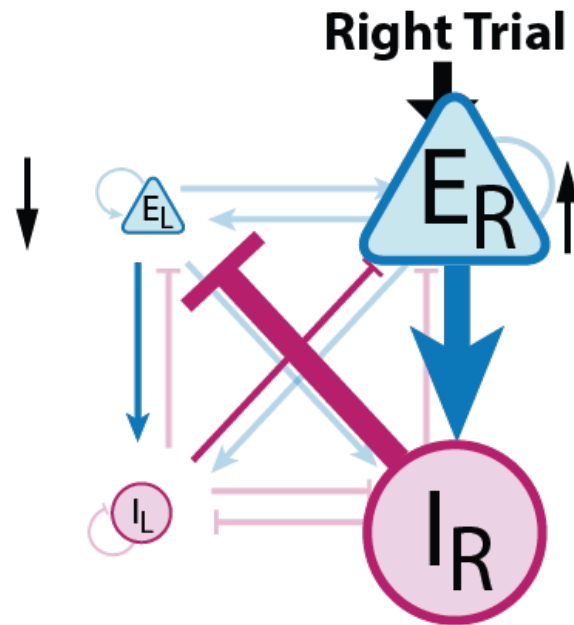
# Competitive Amplification



# Competitive Amplification

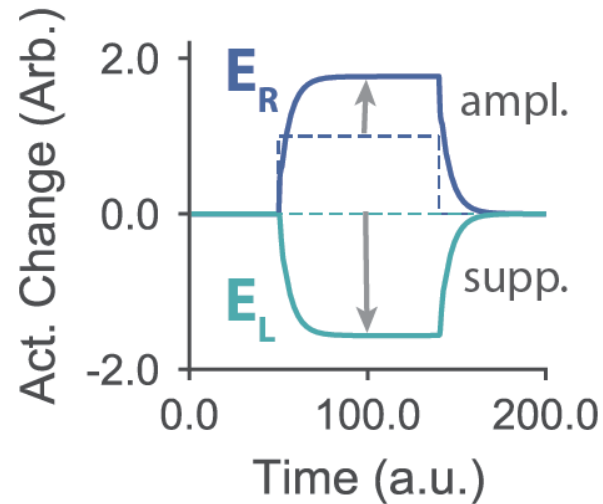
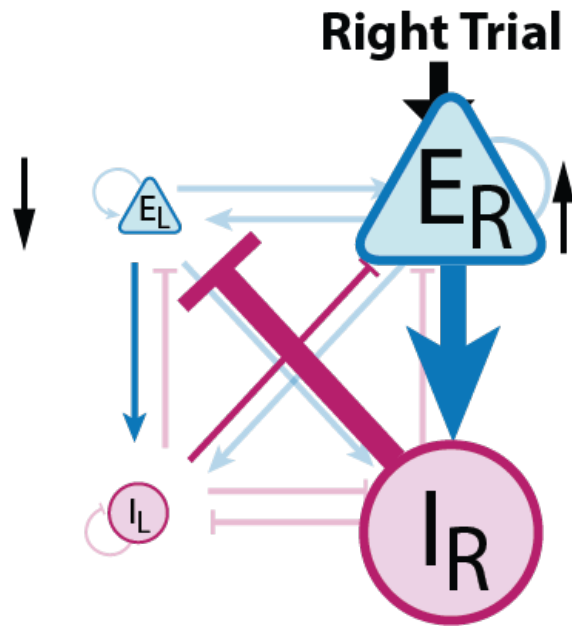


# Competitive Amplification

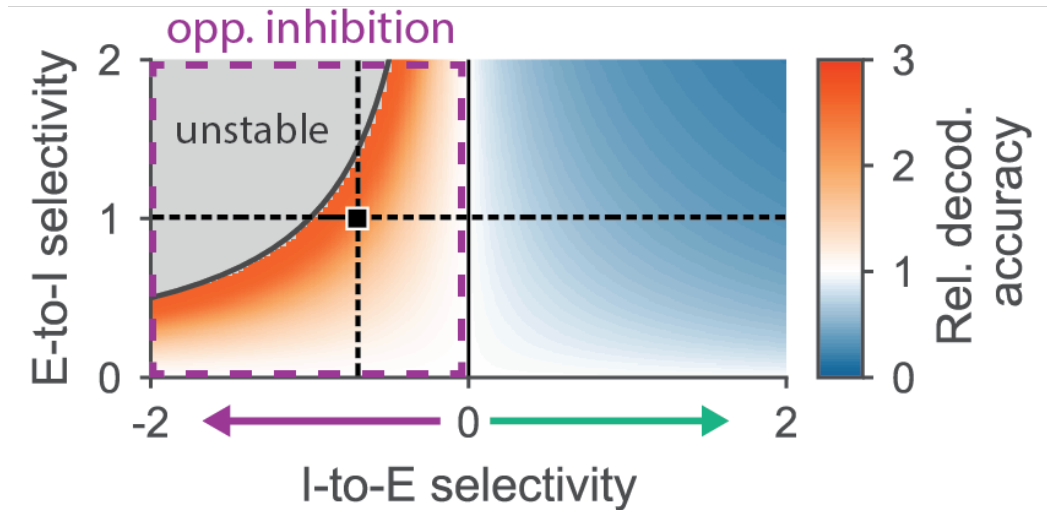
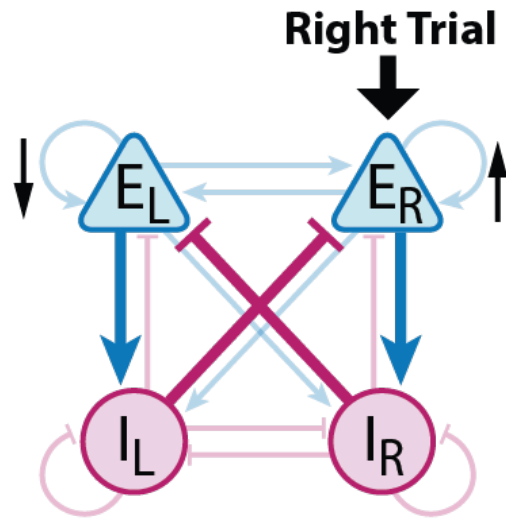




# Competitive Amplification

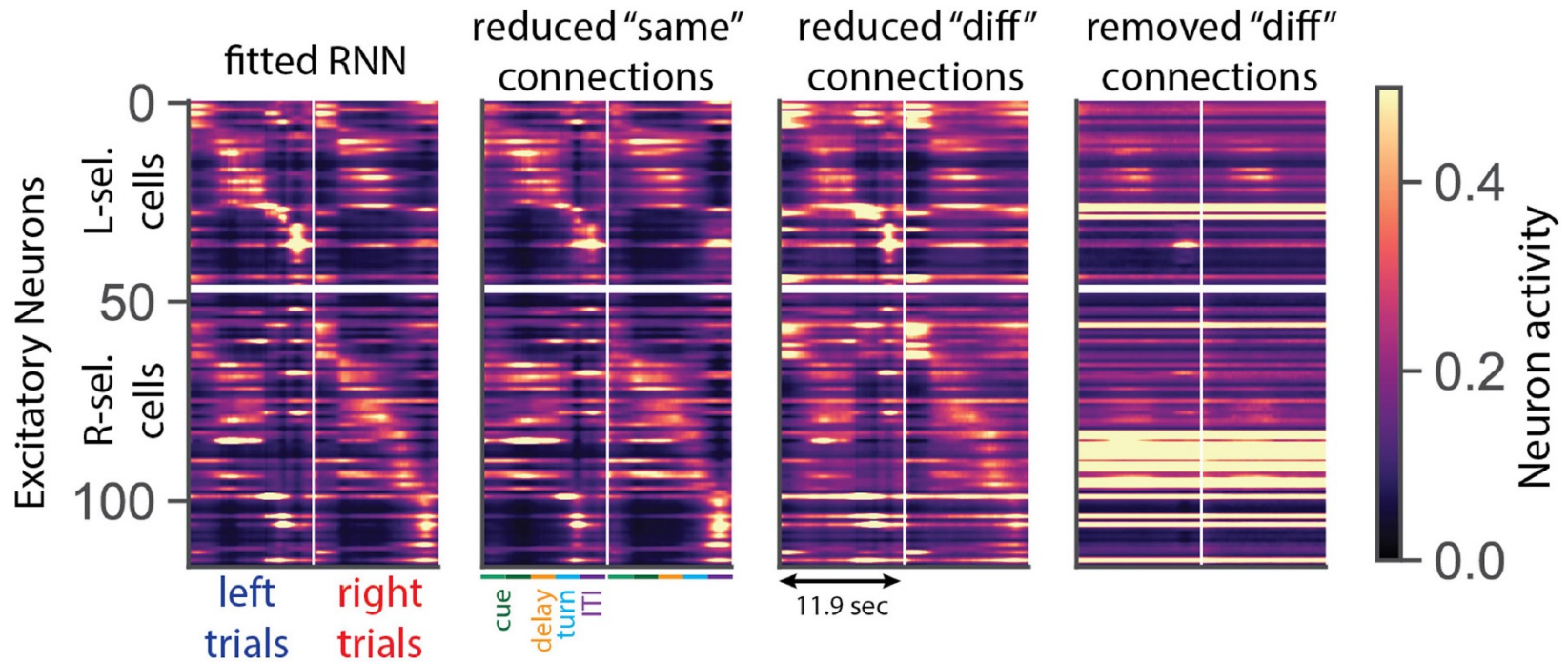


# Competitive Amplification



Opponent inhibition amplifies selective inputs and improves encoding of trial-type information.

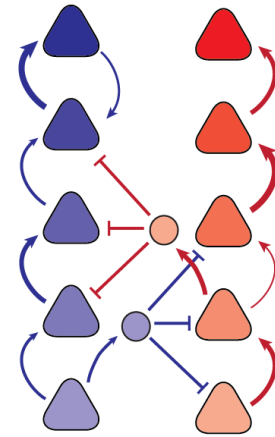
# Opponent Inhibition Generates Temporal Windows for Sequential Activity



# Summary

Opponent inhibition in PPC supports decision-making

- E-to-I connectivity is co-selective
- I-to-E connectivity is anti-selective
- Opponent inhibitory circuit motifs support selective amplification and improve trial-type decoding
- Opponent inhibitory circuit motifs contribute to choice-specific sequential activity



# Acknowledgements



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## LEE LAB

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## COLLABORATORS

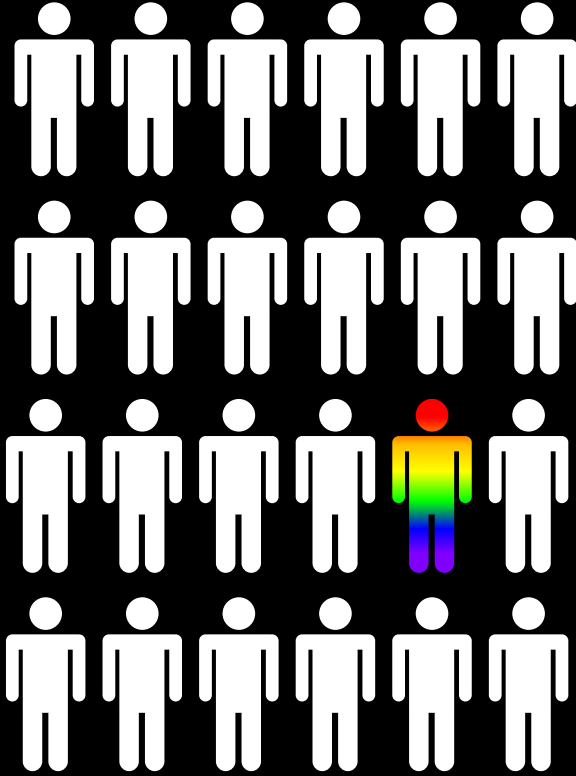
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Laura Driscoll (HMS)  
Dan Wilson (HMS)  
  
Sefano Panzeri (IIT)



## FUNDING & SUPPORT

NIMH  
NINDS  
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Genise Goldenson Award  
Stanley and Theodora Feldberg Fund

# Individual variability





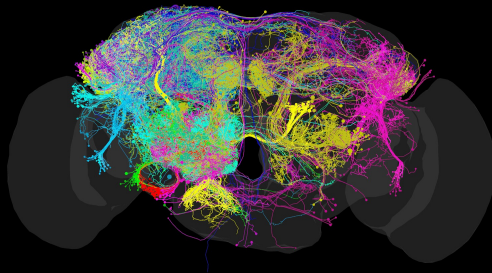
How do variations in brain wiring and connectivity underlie differences in network function and behavior?

# Individuality

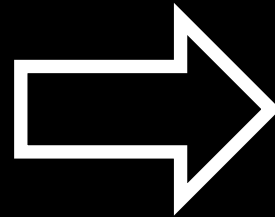


Ben de Bivort  
(Harvard)

How to test connectivity patterns underlying individual behavioral variability?



Connectome



Behavior

Combine behavioral quantification with EM connectomics

# Individuality



Ryan Maloney  
(Harvard)

Choose stable, individualized behaviors

number of right turns: 0

number of left turns: 0

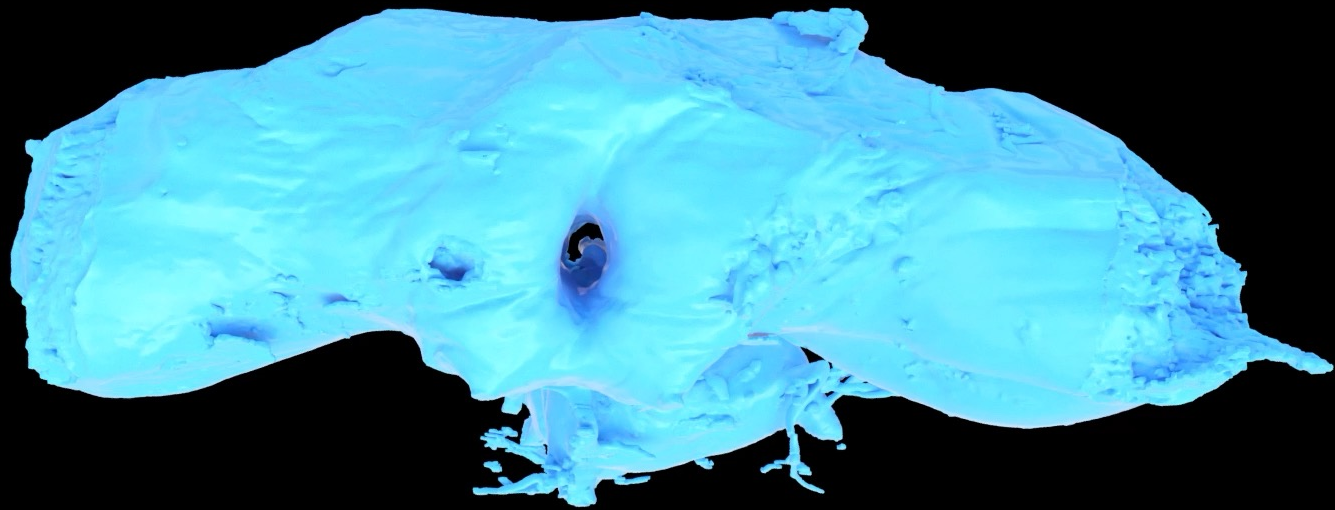


3x real speed

Locomotor handedness

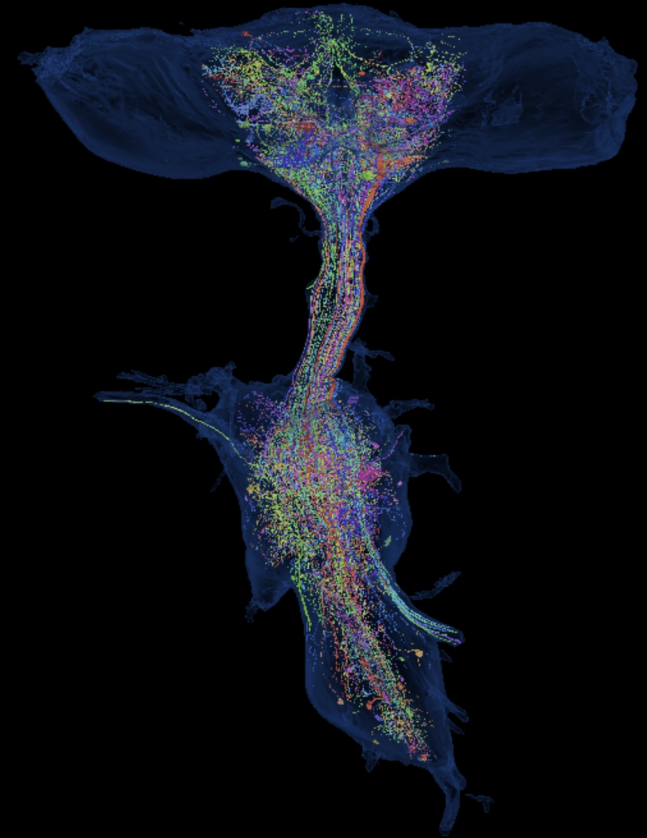
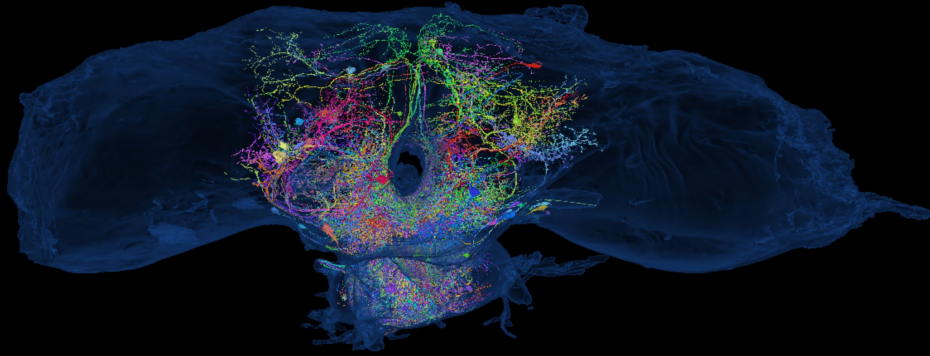
Buchanan et al. 2015  
Skutt-Kakaria et al. 2019





The BANC: Brain And Nerve Cord

# The BANC (Brain and Nerve Cord)





# Individuality

“Lefty”



71% left turns

“Righty”



70% right turns

Thanks!

