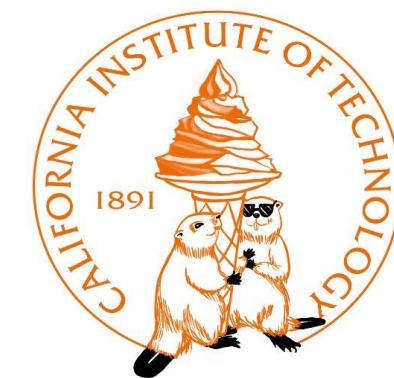
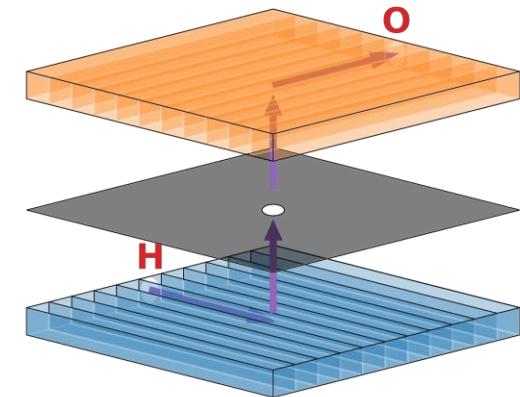


Cognition with and without Cortex:

Implications from Mouse Navigation in a Novel Reconfigurable Maze

Nov. 14th, 2024, Harvard Medical School, RL and the Brain Seminar

Jieyu Zheng, PhD Candidate in Neurobiology, **Meister Lab**, California Institute of Technology



8.7×10^6



1



What makes human intelligence special?

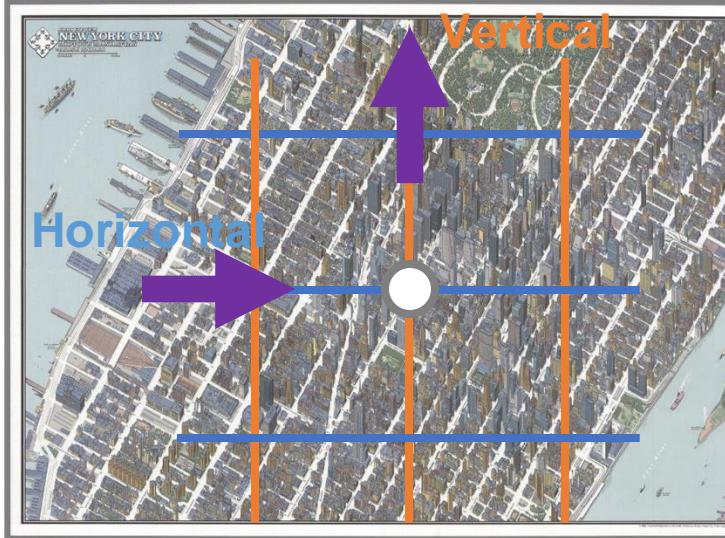
Behavior

- The cognitive differences: of degree or of kind?
- **Complex and rapid cognitive processes in mice**

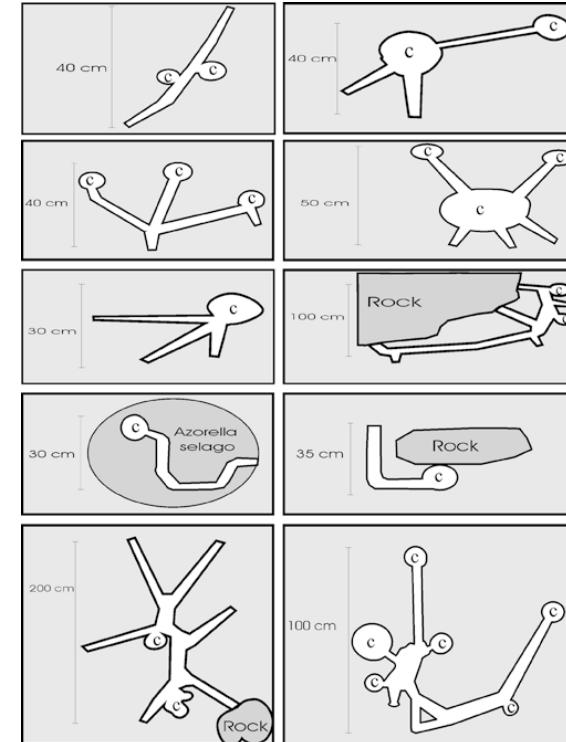
Neuroscience

- What brain structures cause these differences?
- **The role of cortex in mouse cognition**

A Navigation Task for Mouse cognition

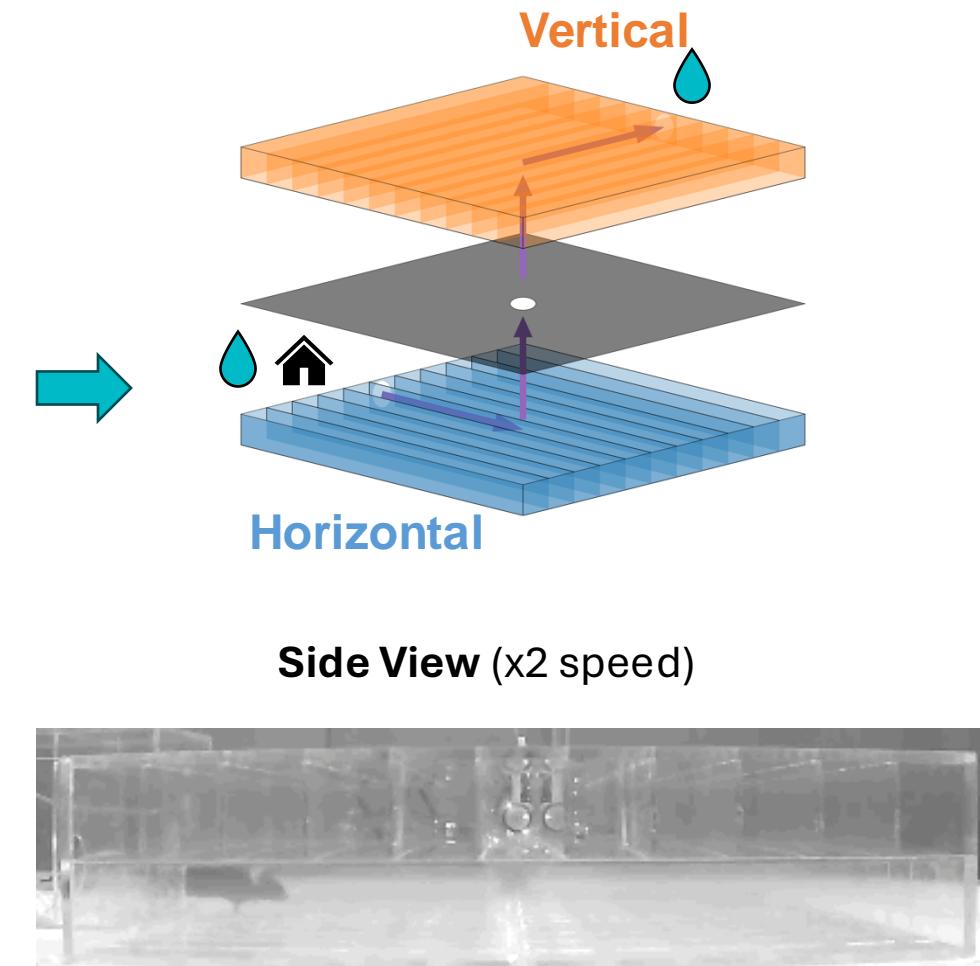


David Rumsey

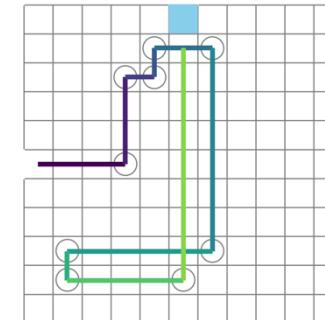
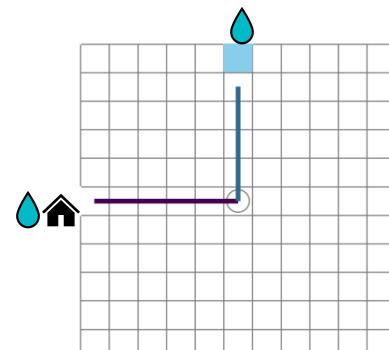
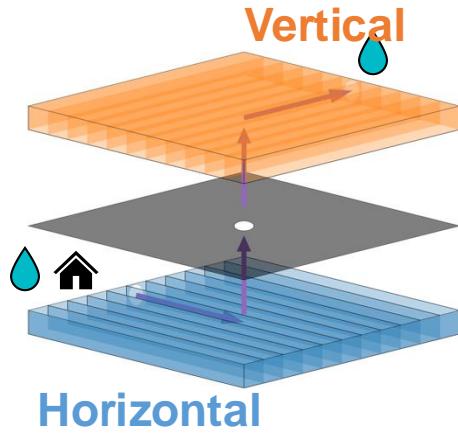


Avenant, 2002

The Manhattan Maze

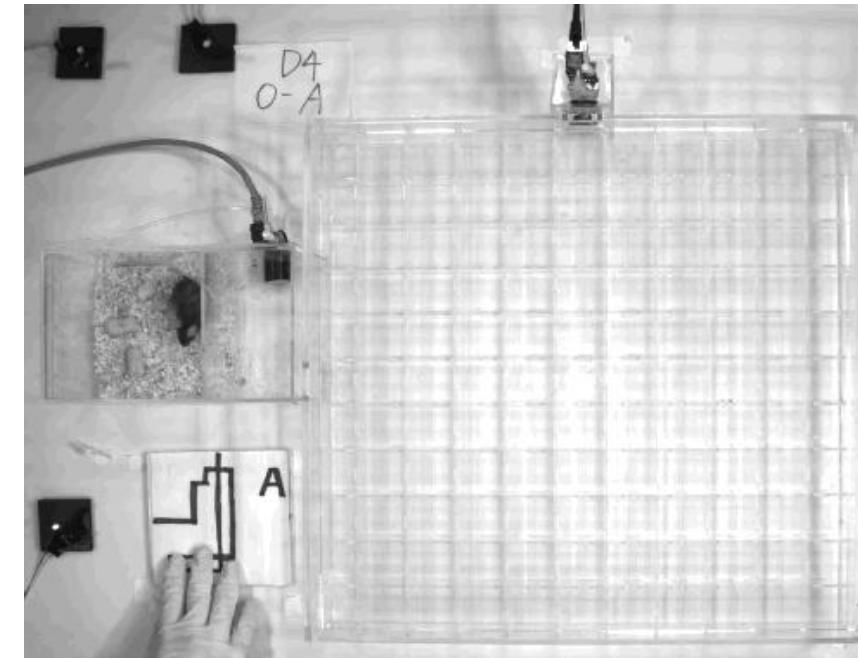
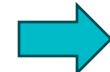
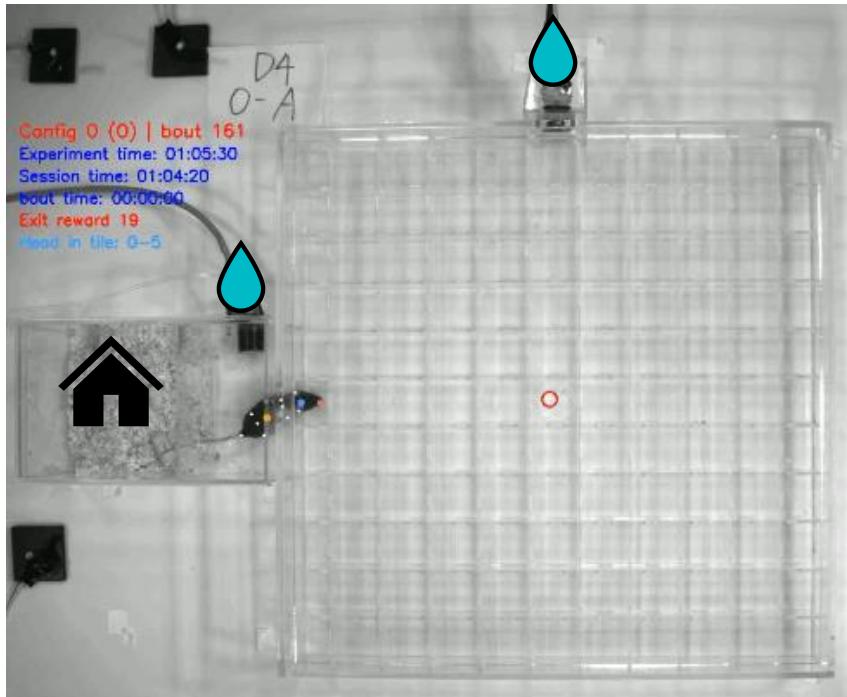


Easy and drastic task switch



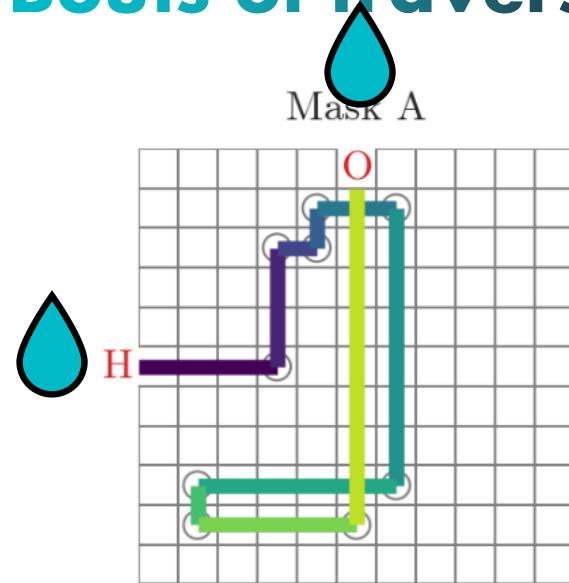
1-hole Mask O

9-hole Mask A

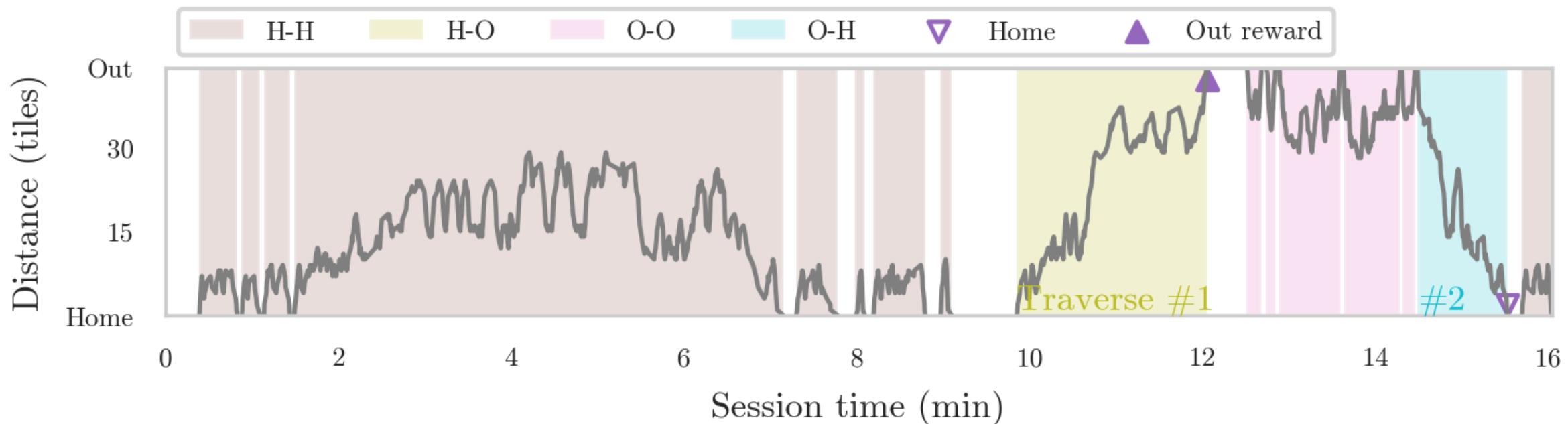


Easy Reconfiguration

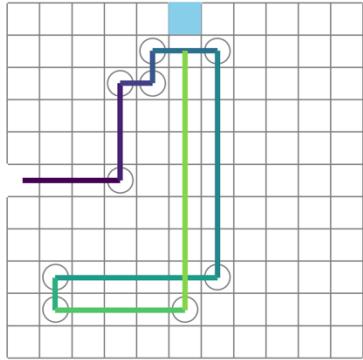
Bouts of traverses



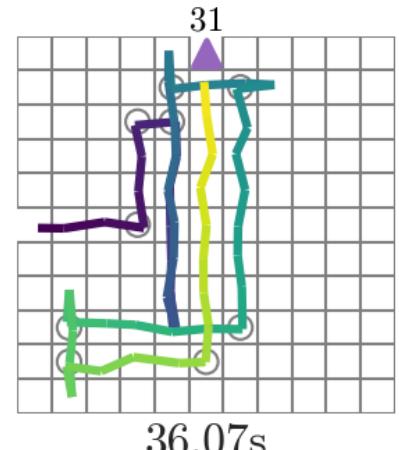
- Bout defined by start and endpoint
 - **H – Home**
 - **O – Out**
- Bouts in session: H-Hs → H-O → O-Os → O-H → H-Hs ...
- **Traverses:** H-O (outbound) and O-H (homebound)



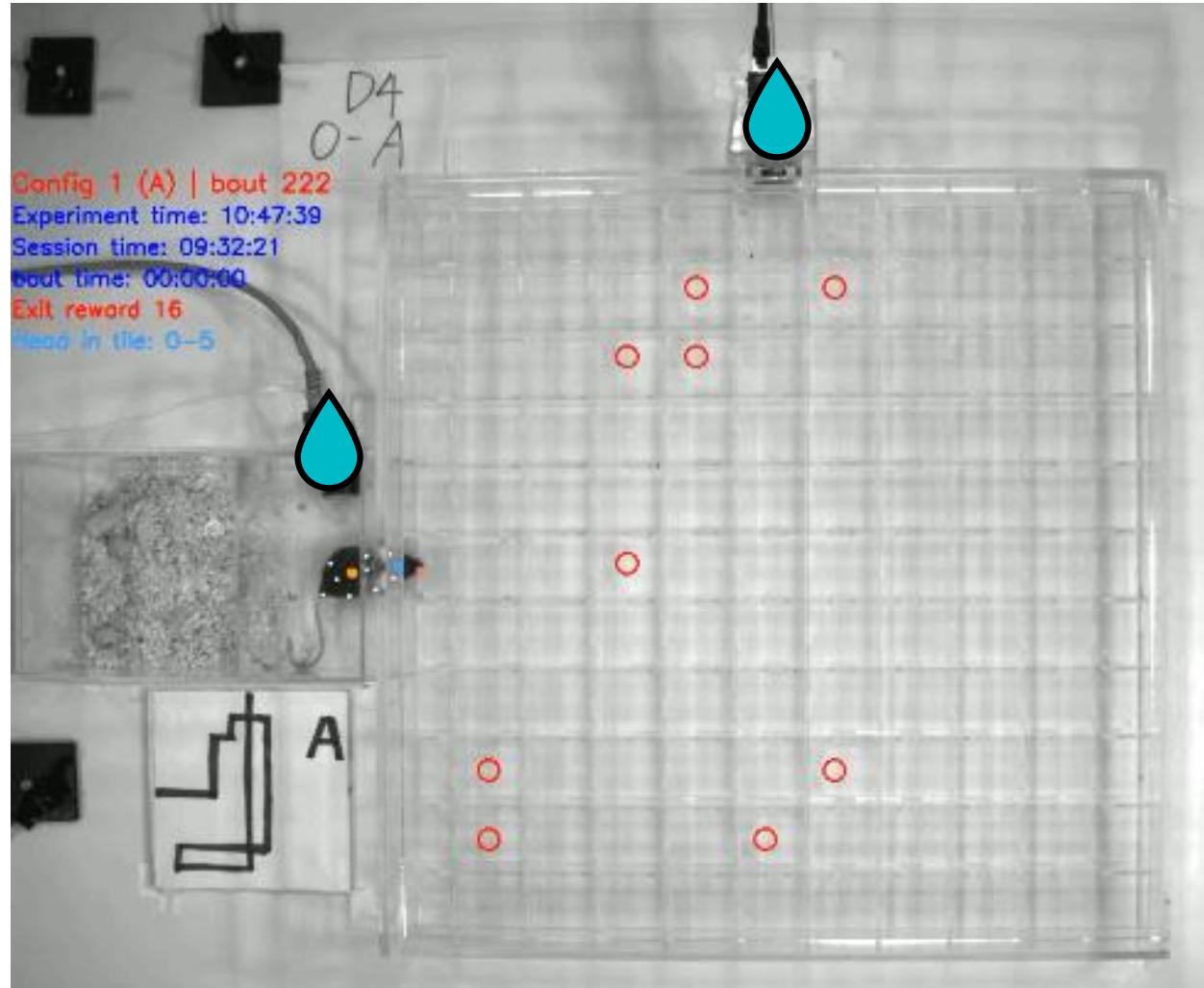
Rapid learning of a 9-hole mask



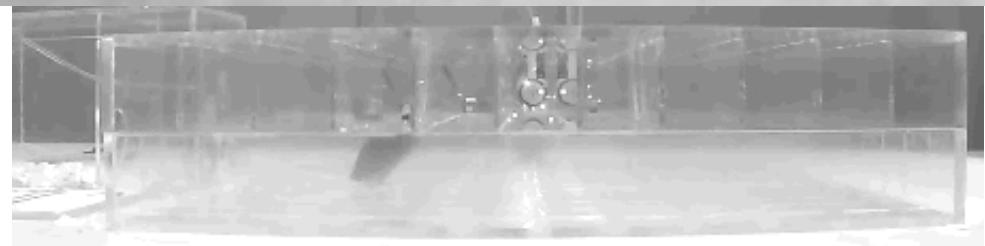
Optimal solution



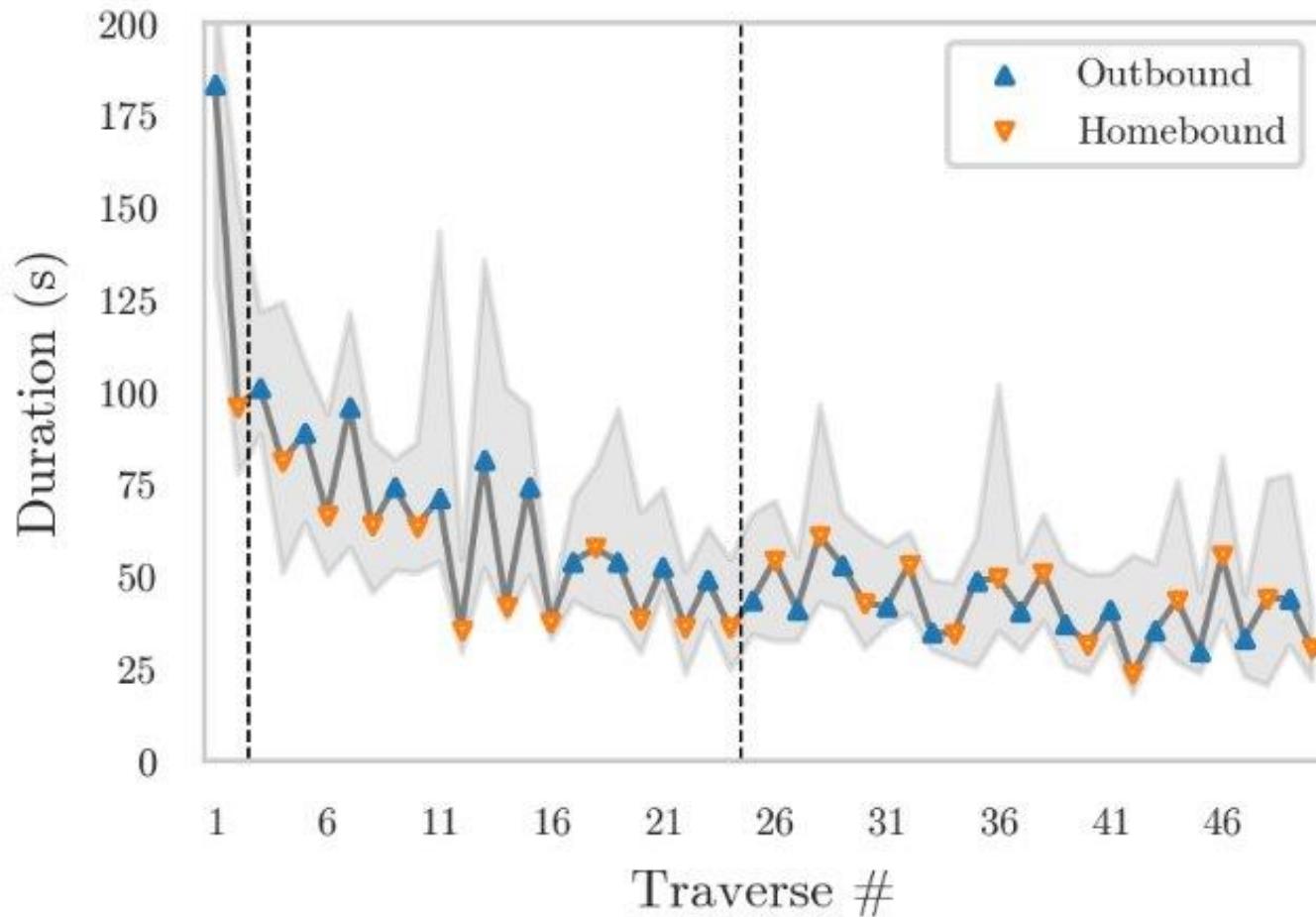
Mouse Trajectory



Side view



Day 1: Rapid learning in Mask A

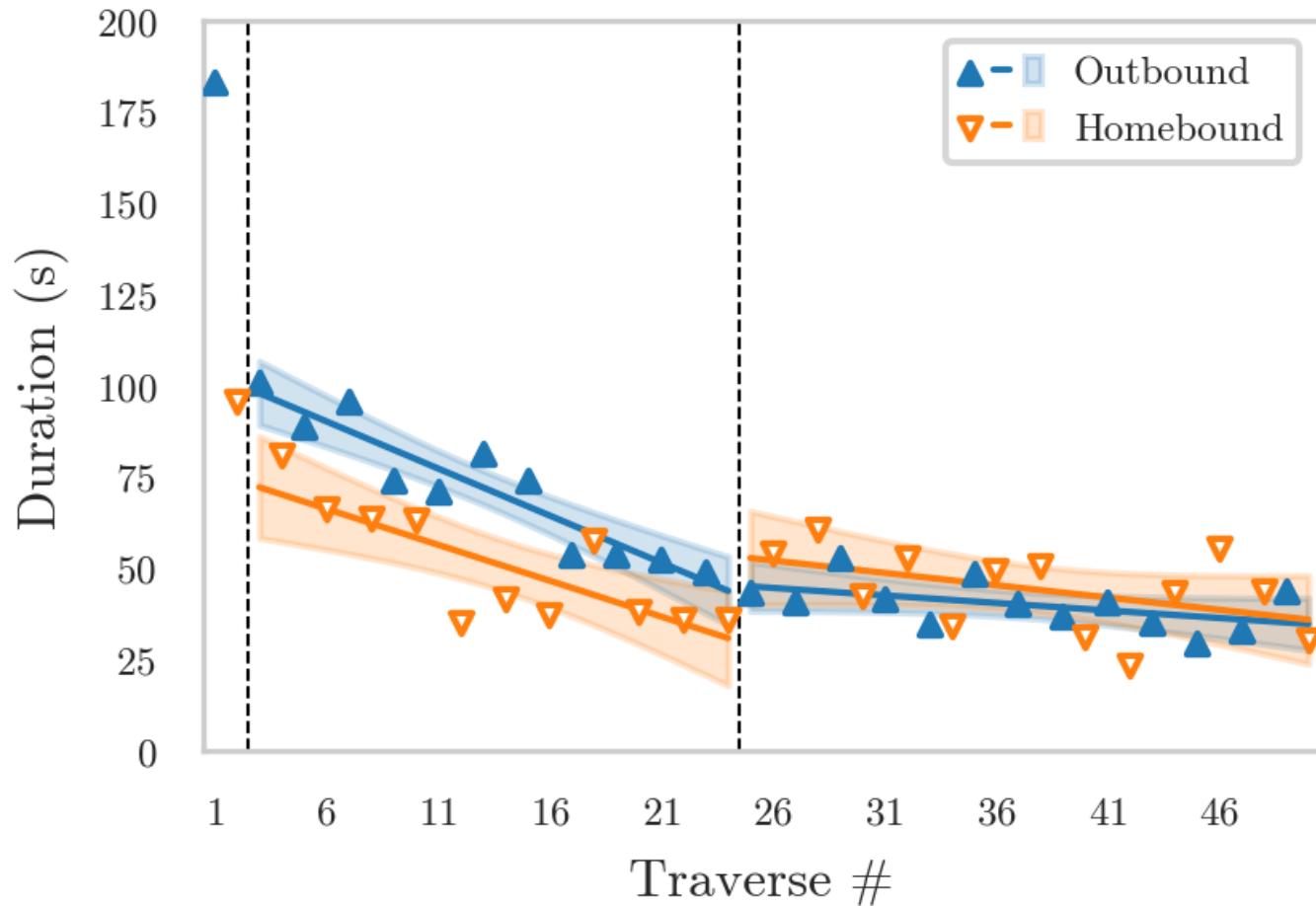


1. Phase 1: 2x improvement by the first homebound traverse

N=15,
median & IQR

(Traverse: A trip from one port to the other)

Day 1: Rapid learning in Mask A

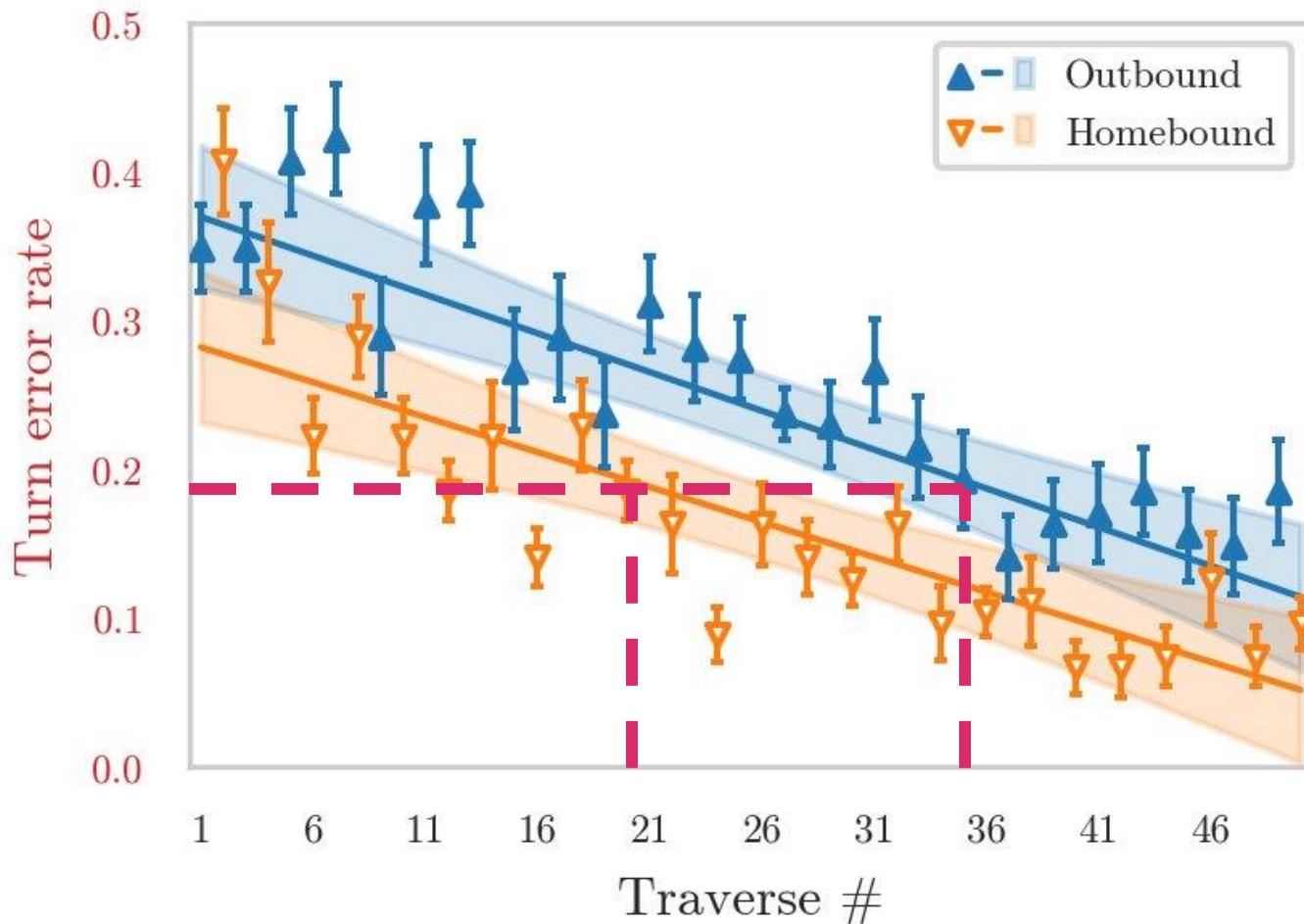


N=15, linear fits of median &
95% confidence Interval

2. Asymmetry in Phase 1
and 2:

Homebound traverses are
shorter

Day 1: Rapid learning in Mask A



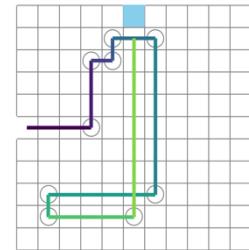
N=15, mean±se.

$$\text{Turn error rate: } 1 - \frac{N_{\text{correct first turns}}}{9}$$

Mice improved their turn decisions over time,

Reaching 80% correct after 10-15 roundtrips.

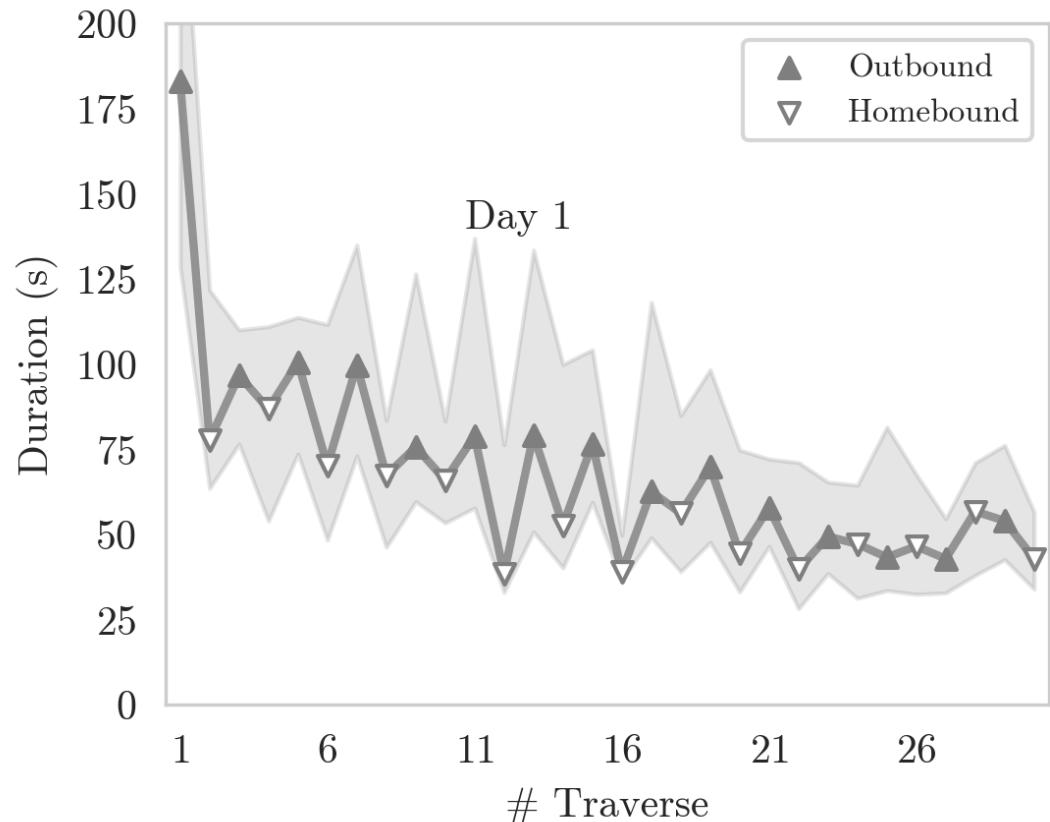
Day2 : Multiple masks



Day 1 Mask A

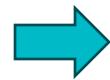


Day 2

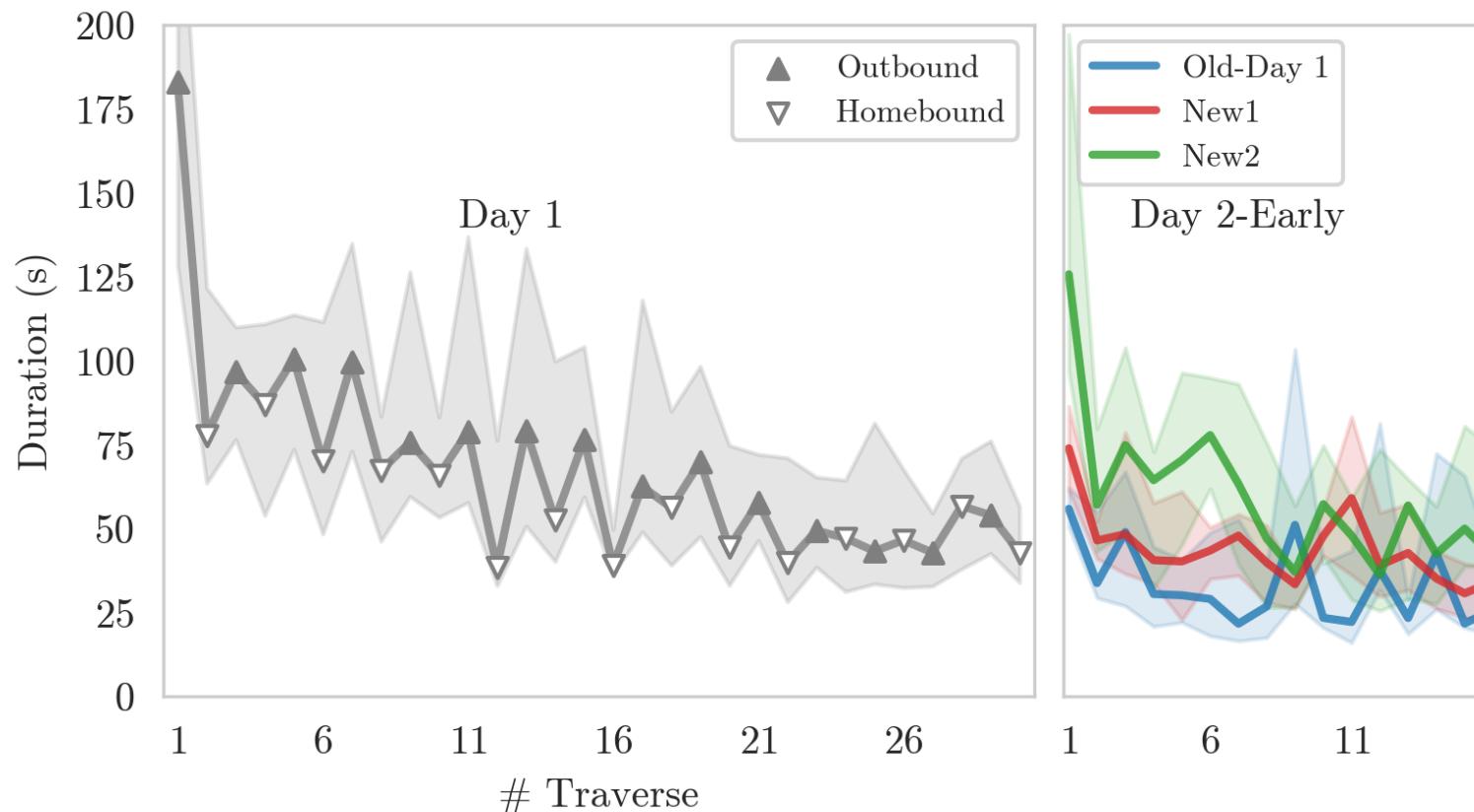
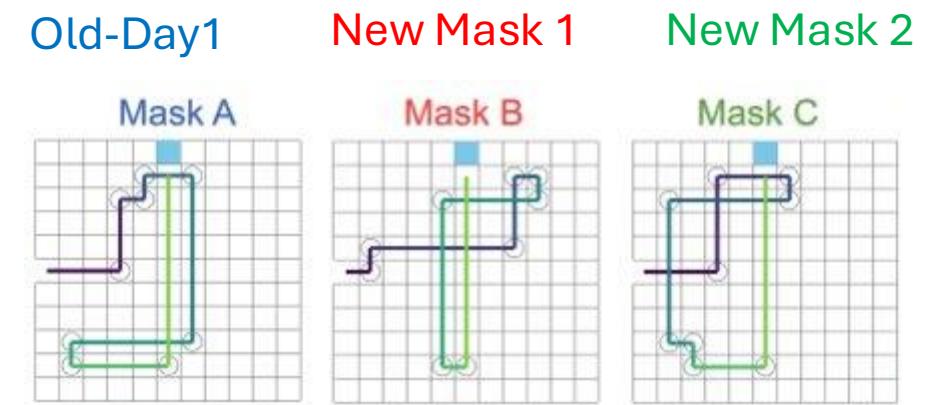


→ Overnight memory

Day2 : Three masks introduced



Day 2

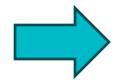


Generalization
& Continual learning

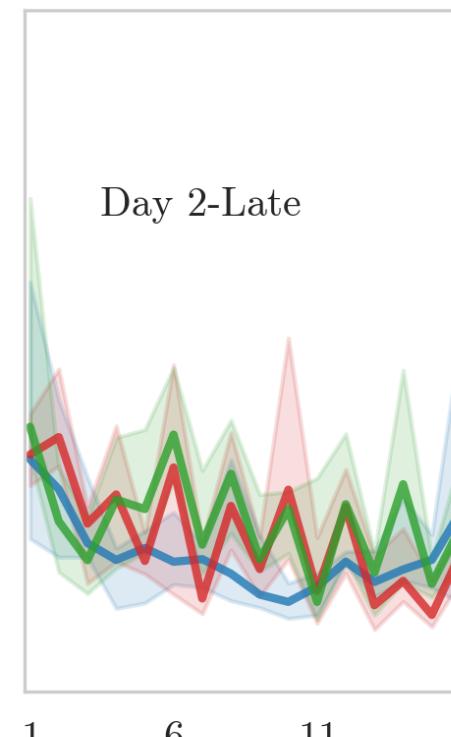
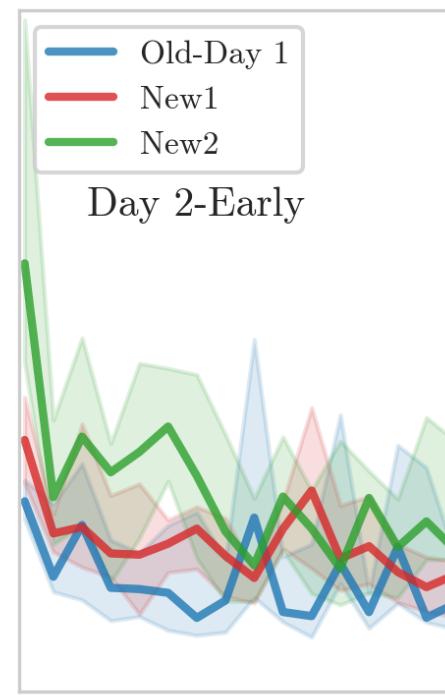
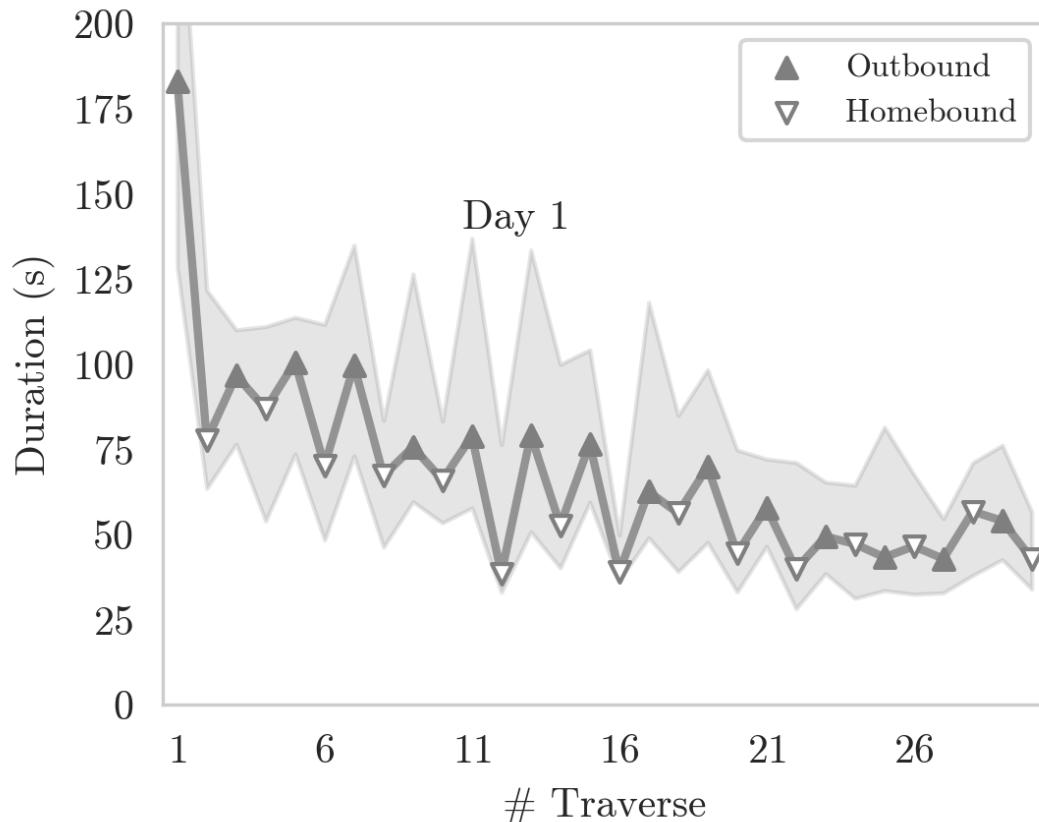
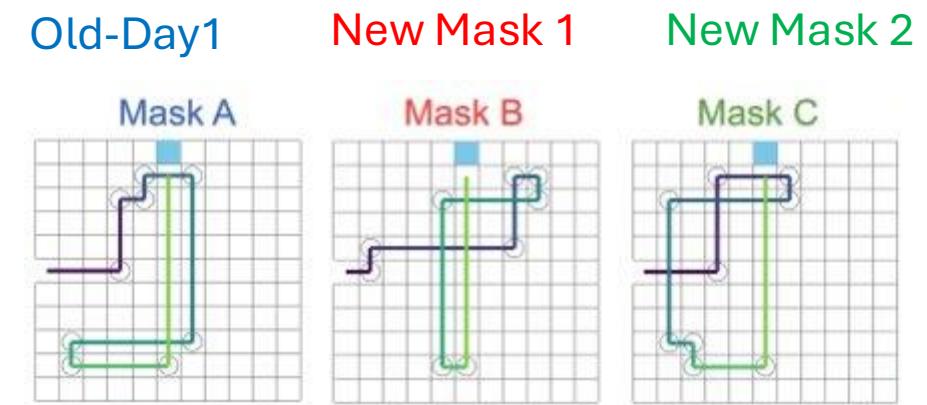
Day2 Late: saturated performance



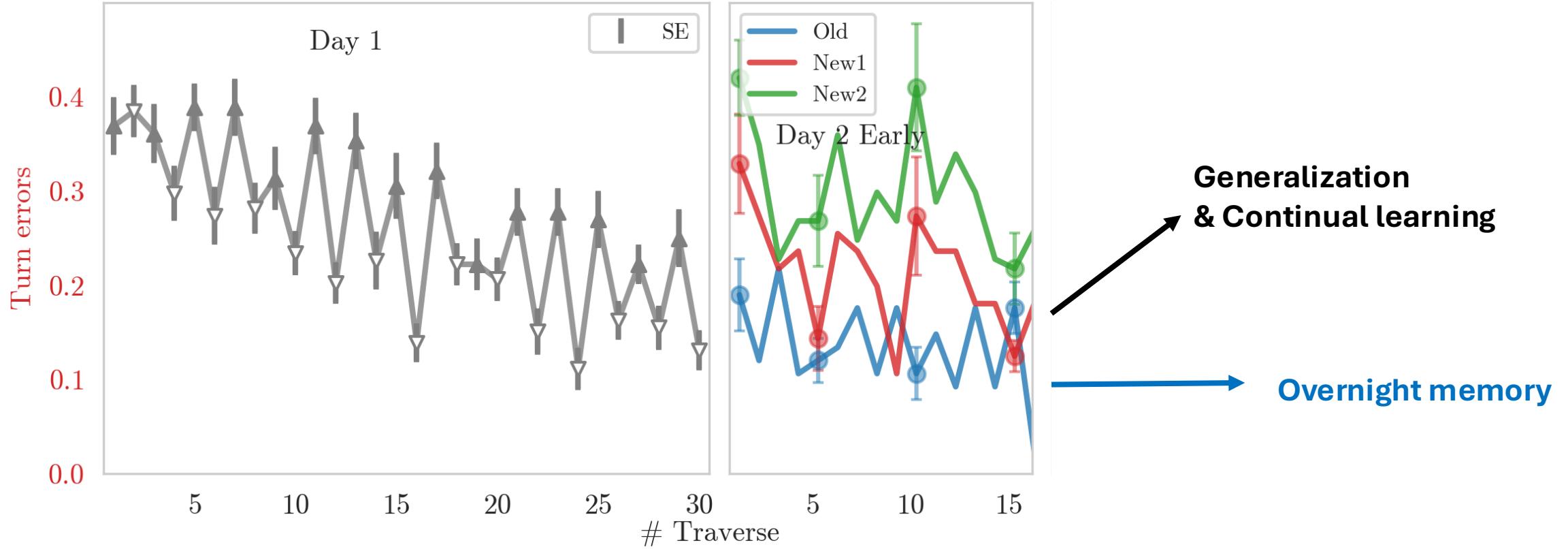
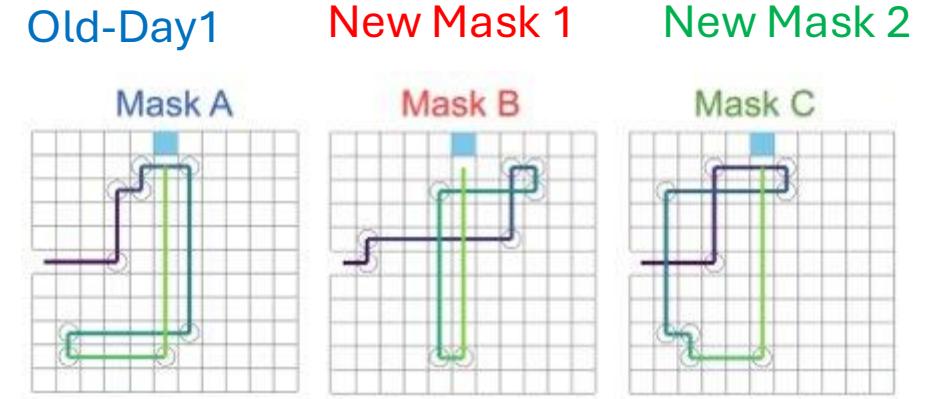
Day 1 Mask A



Day 2

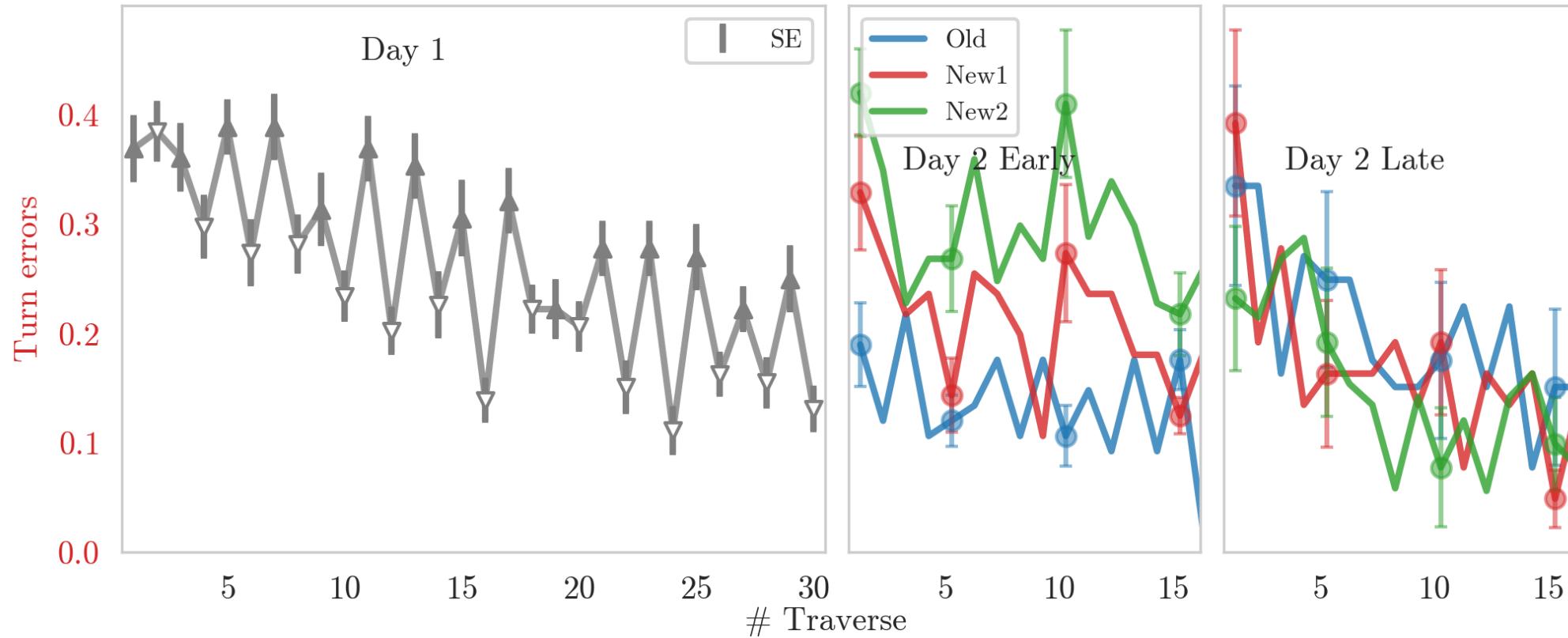
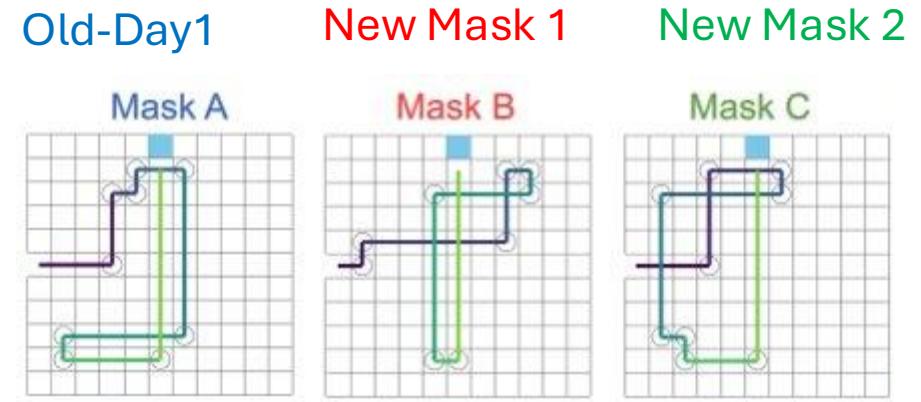


Turn error rates: memory and generalization

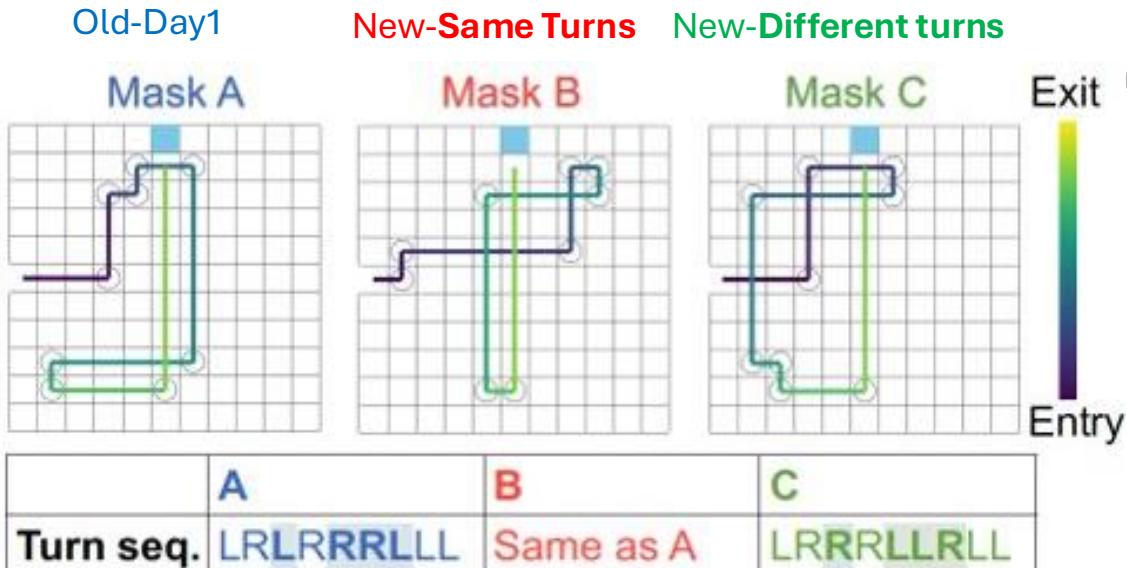


Rapid learning
Long-term memory
Cognitive flexibility
Generalization

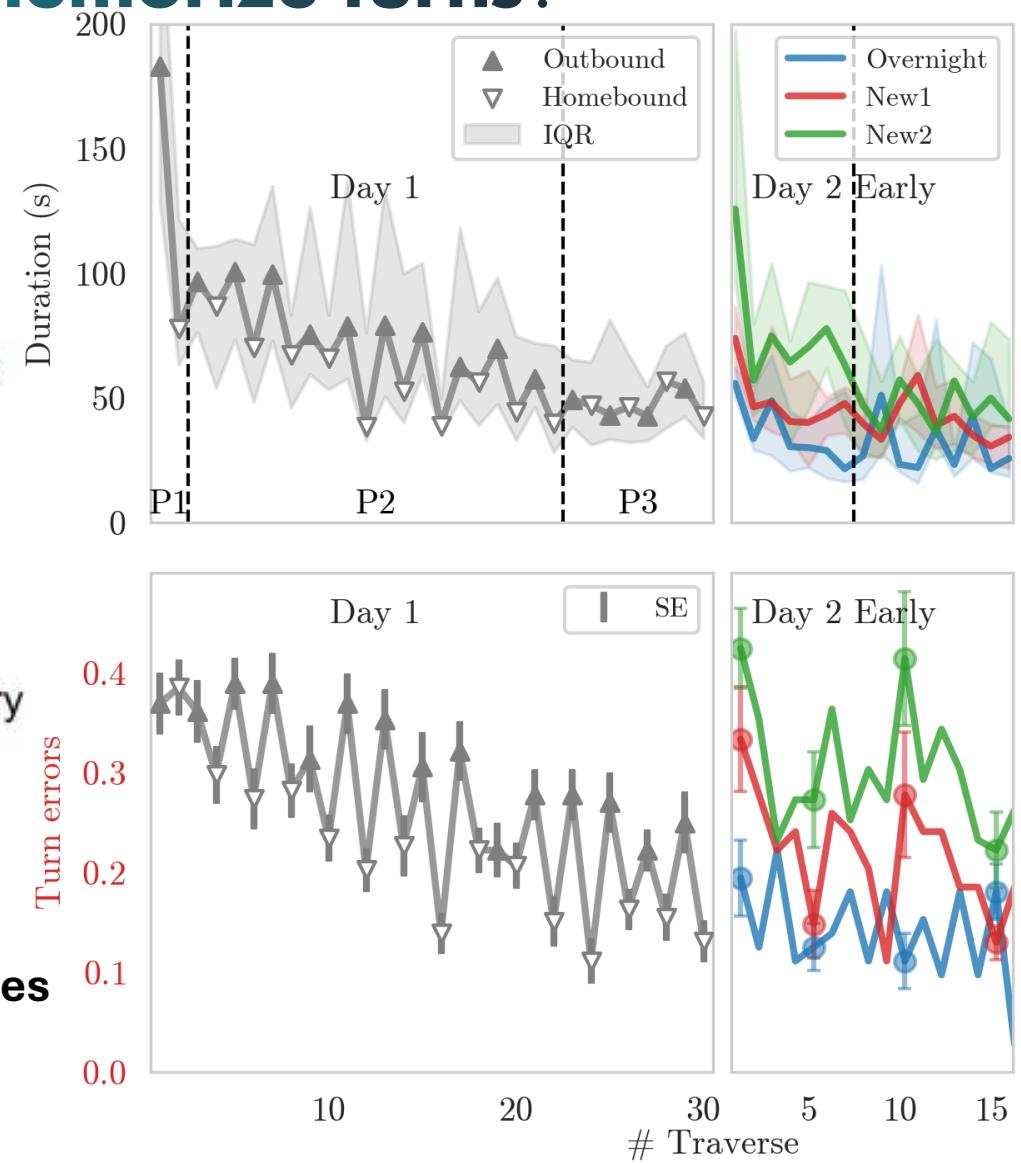
In 2 days!



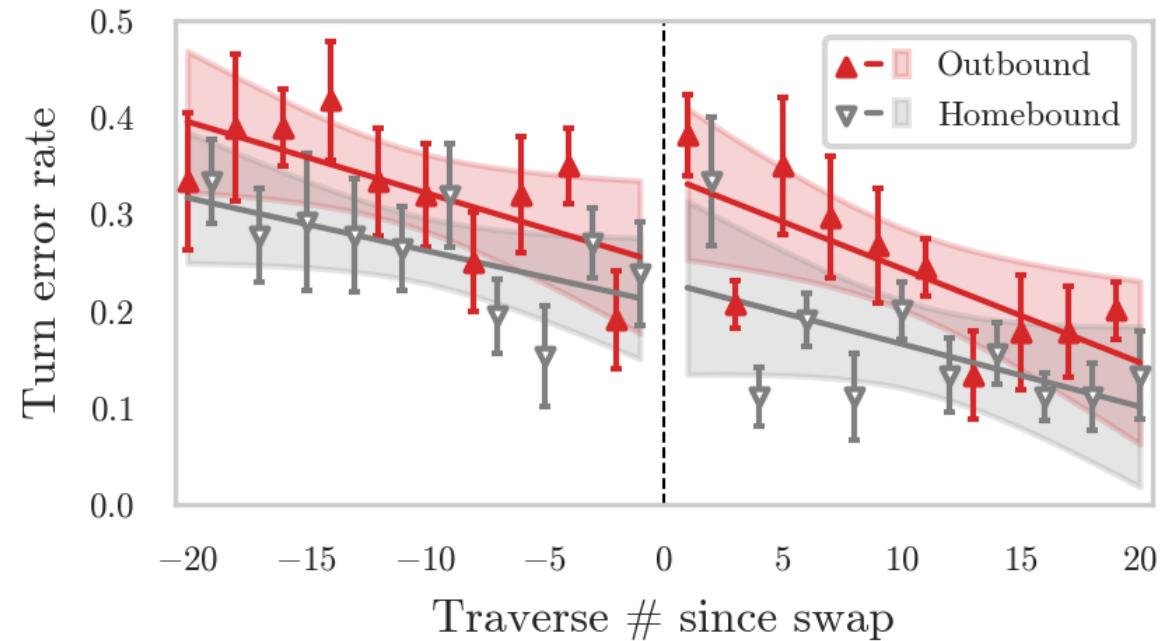
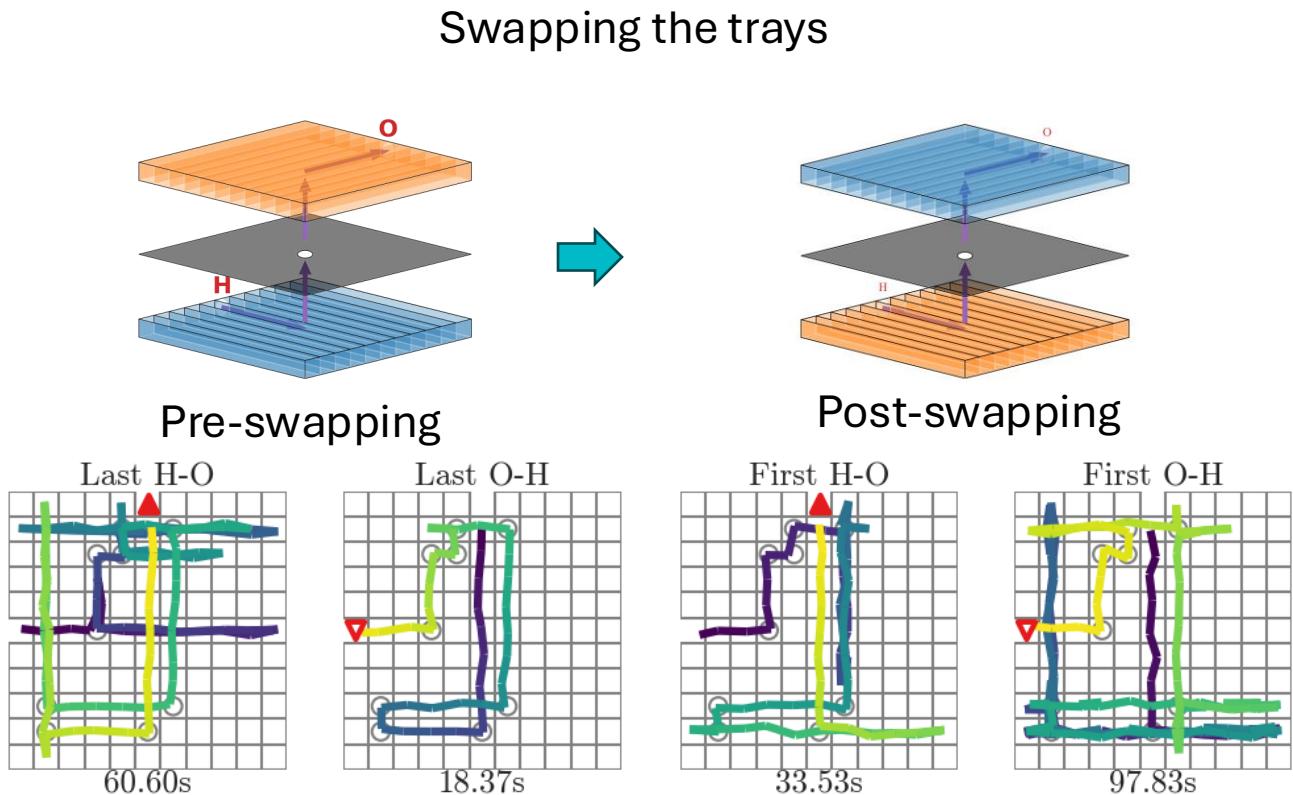
Sequence learning: did mice memorize turns?



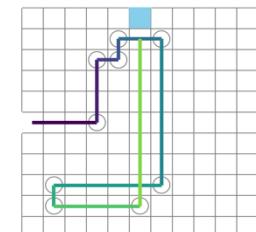
Learning was not facilitated by same turn sequences



Olfactory cues in Mask A



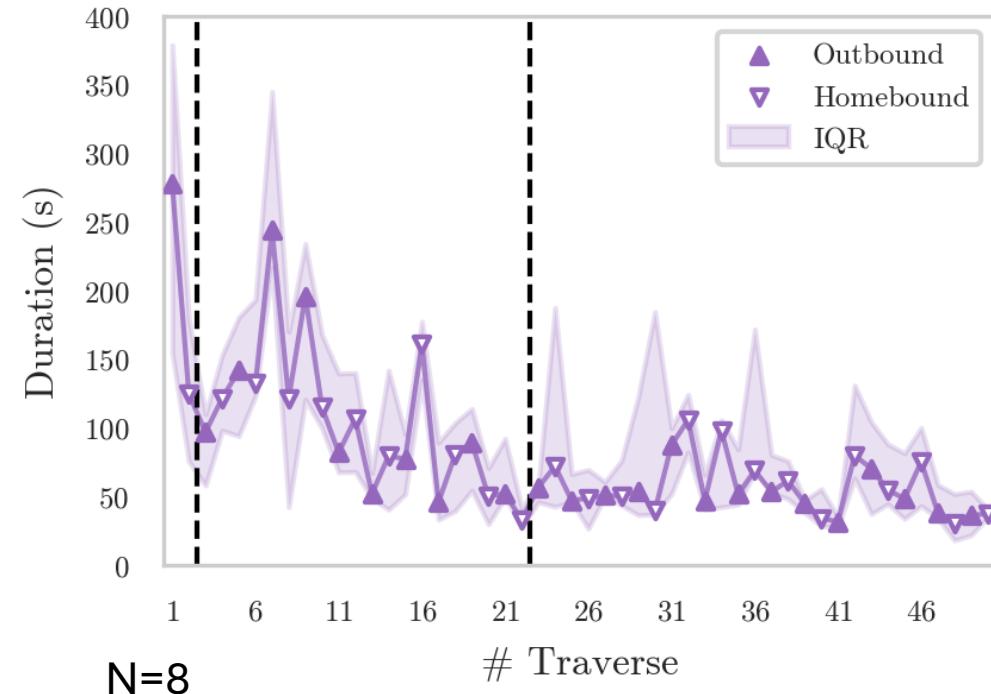
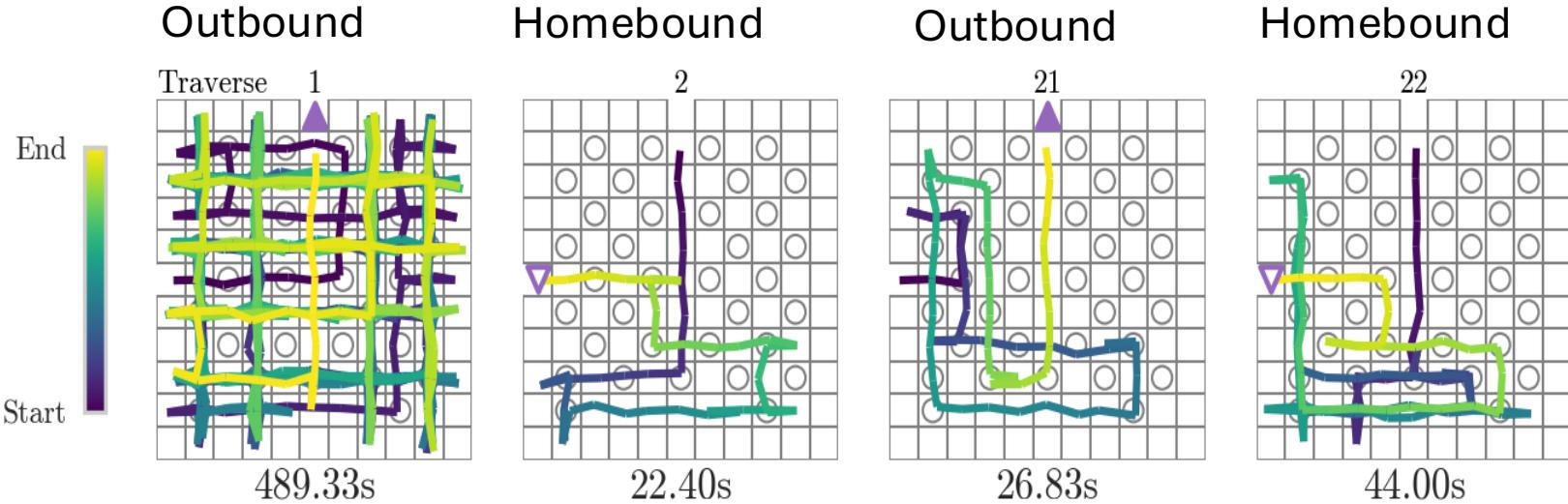
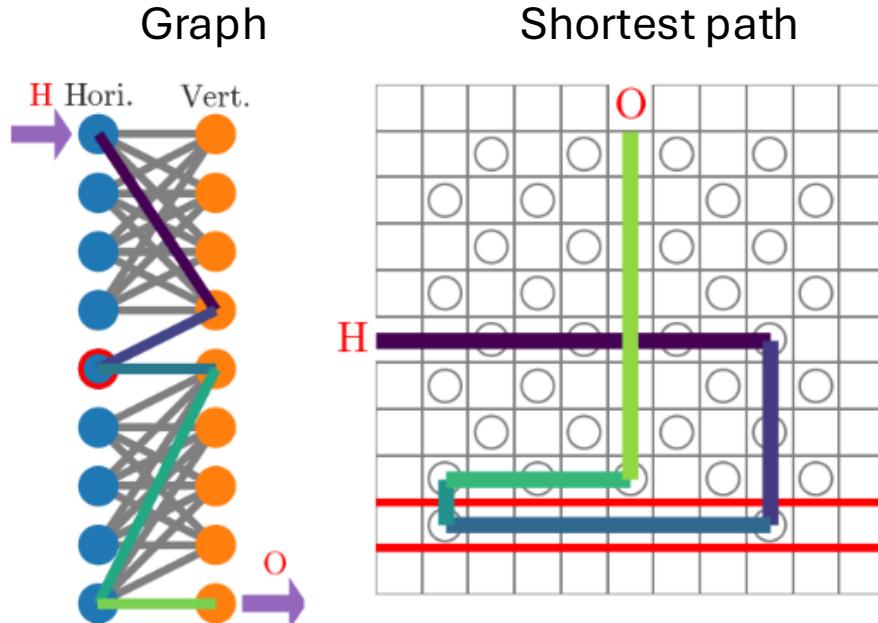
N=8, mean \pm se; Linear fits with 95% confidence intervals



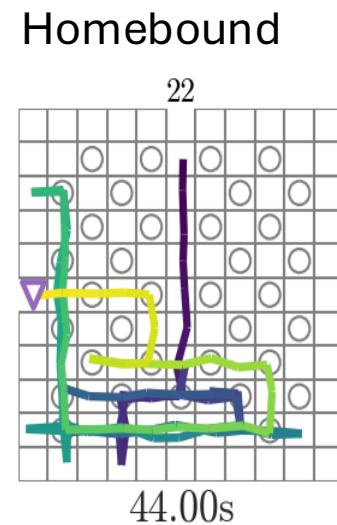
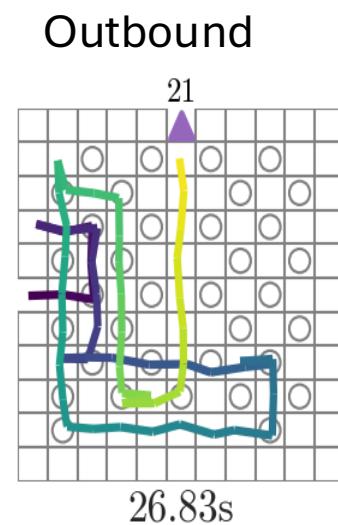
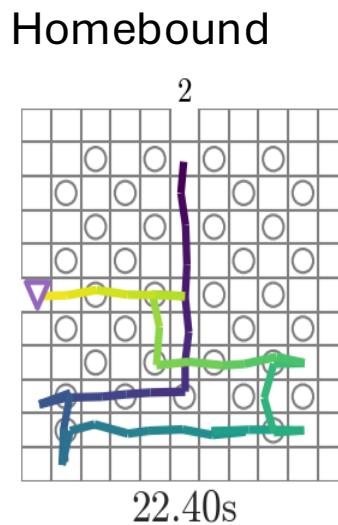
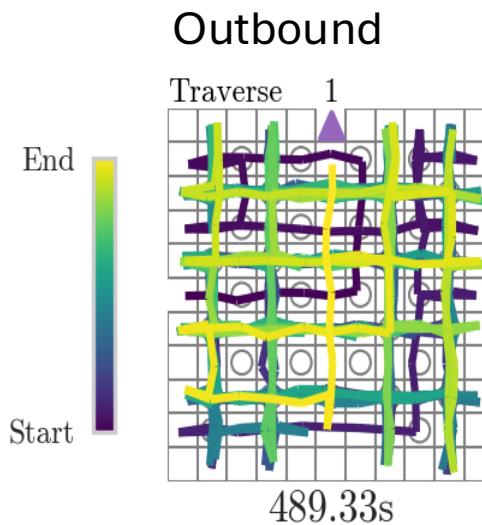
Optimal solution

Flexible routing in a complex Mask

Two all-to-all connected areas with a bottleneck
 - Many loops
 - Redundant paths



Evaluate route similarity in the maze

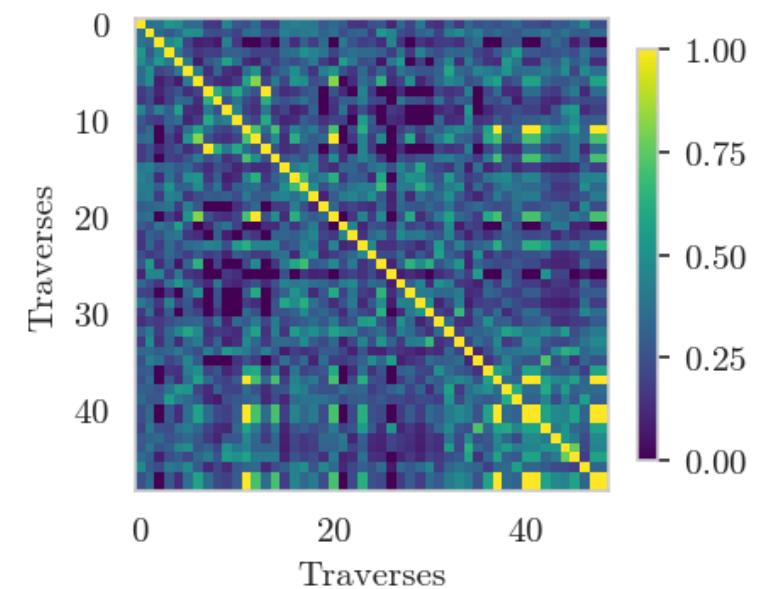


Vectors of hole visit frequency: [0, 0, 1, 3, ...]

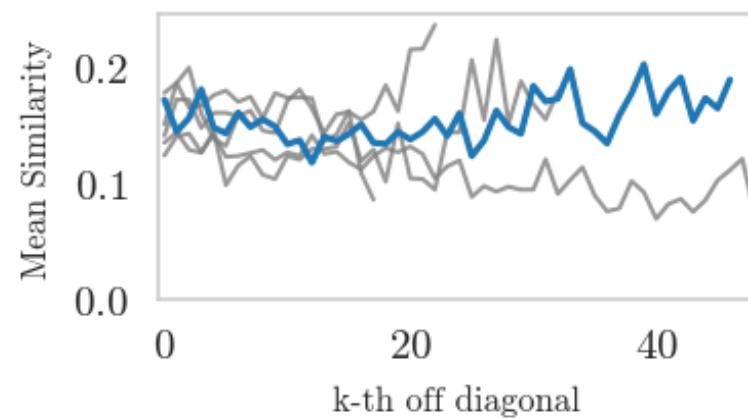
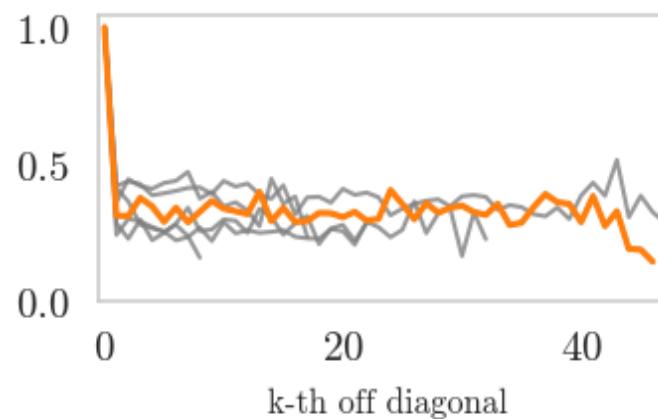
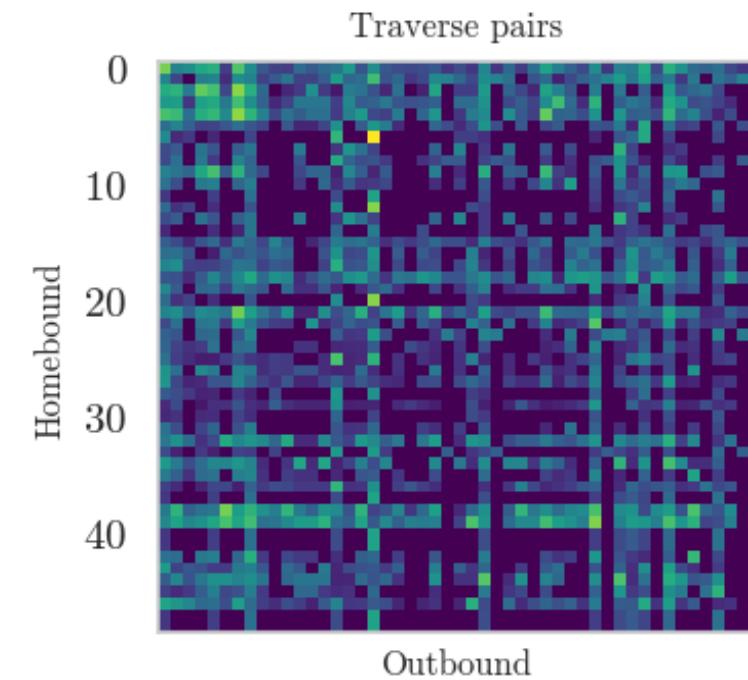
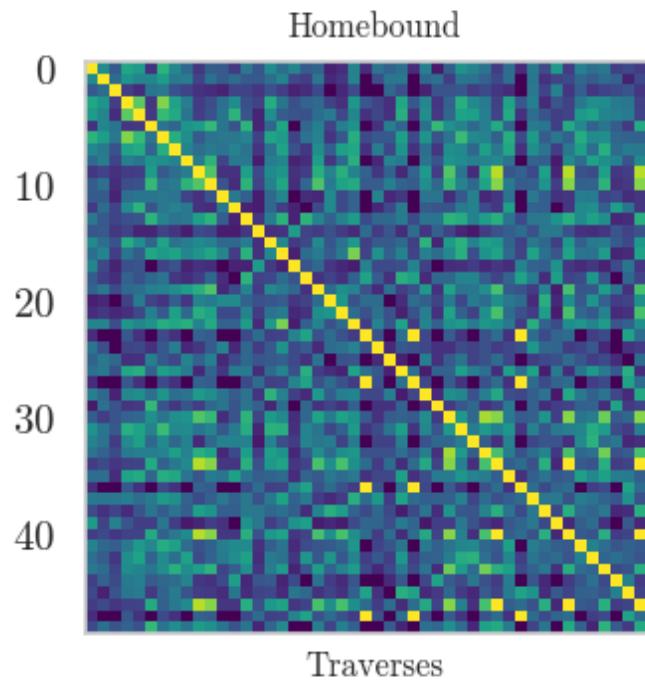
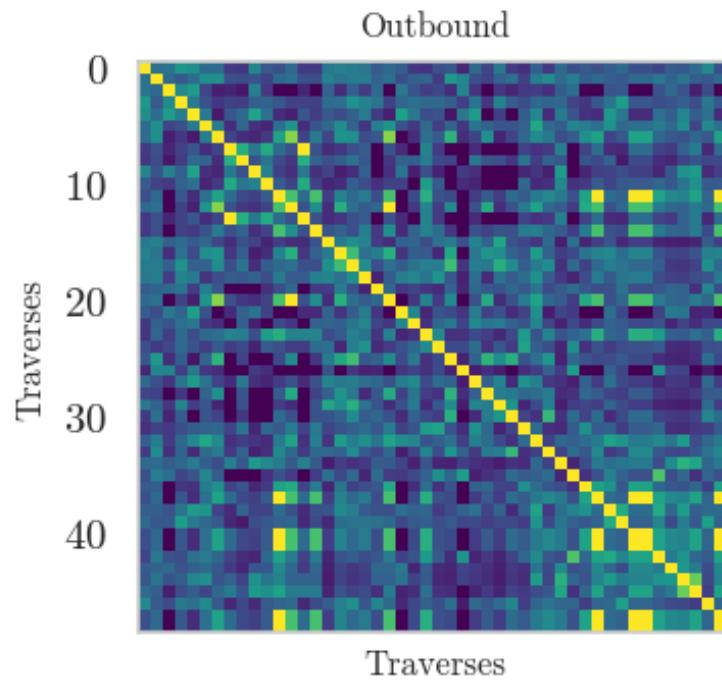


Similarity between vectors:

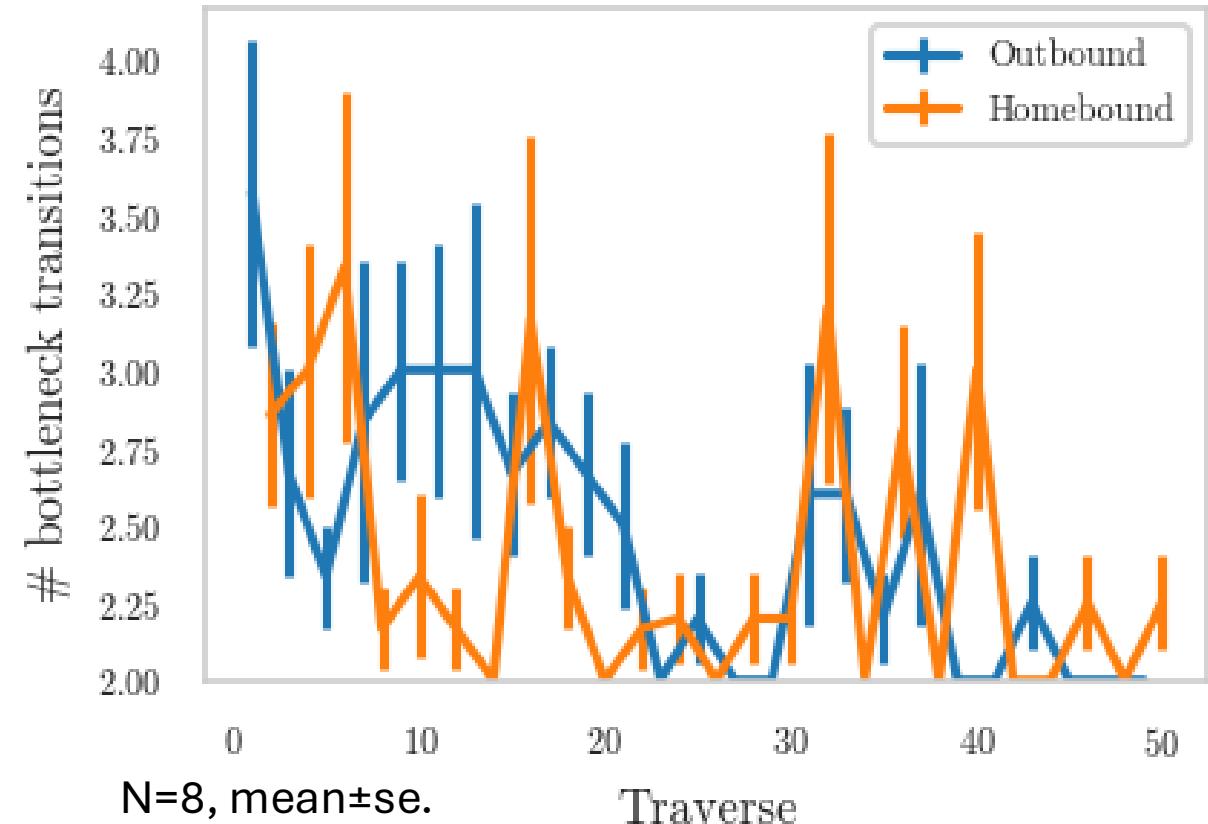
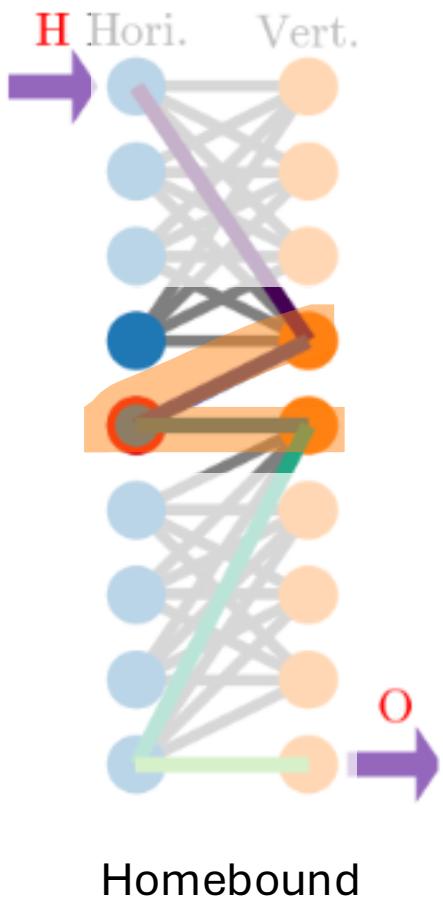
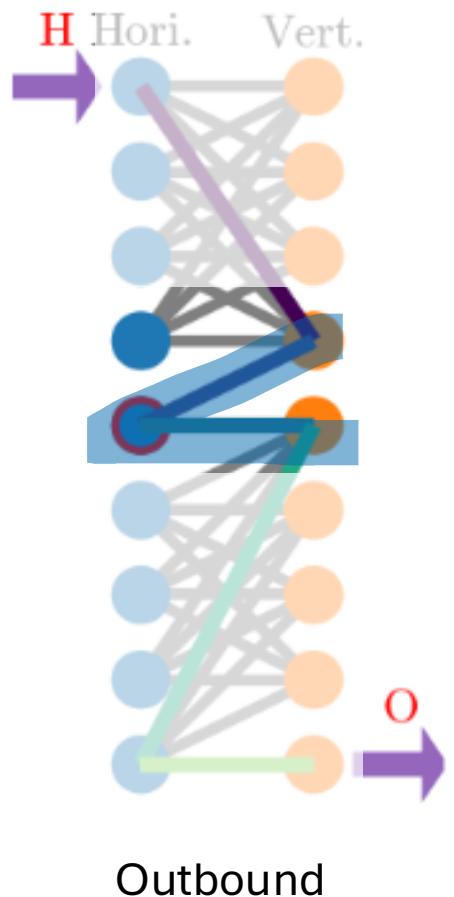
$$\text{Cosine Similarity} = \frac{\mathbf{A} \cdot \mathbf{B}}{\|\mathbf{A}\| \|\mathbf{B}\|}$$



Flexible routing in Mask D



Learning about the bottleneck:



Summary

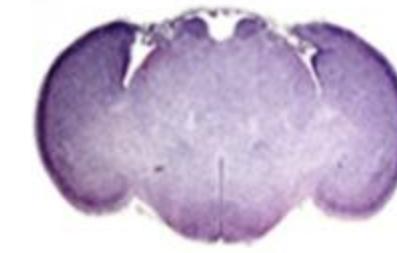
- **Rapid learning** (two types of maps):
 - First homing: **2x difference**
 - Optimal performance: **5x difference**
- **Overnight memory** in early Day 2:
 - **Same** performance as Day 1
- **Generalization** in 2 days:
 - Accelerated learning of new masks
 - Not reliant on turn sequences or olfactory cues
- **Learning a complex map:**
 - Flexible routing in redundant regions

The role of cortex

Structural Mutant: Emx1-Cre⁺ x Pals 1 flox/flox, born **without neocortex or hippocampus**



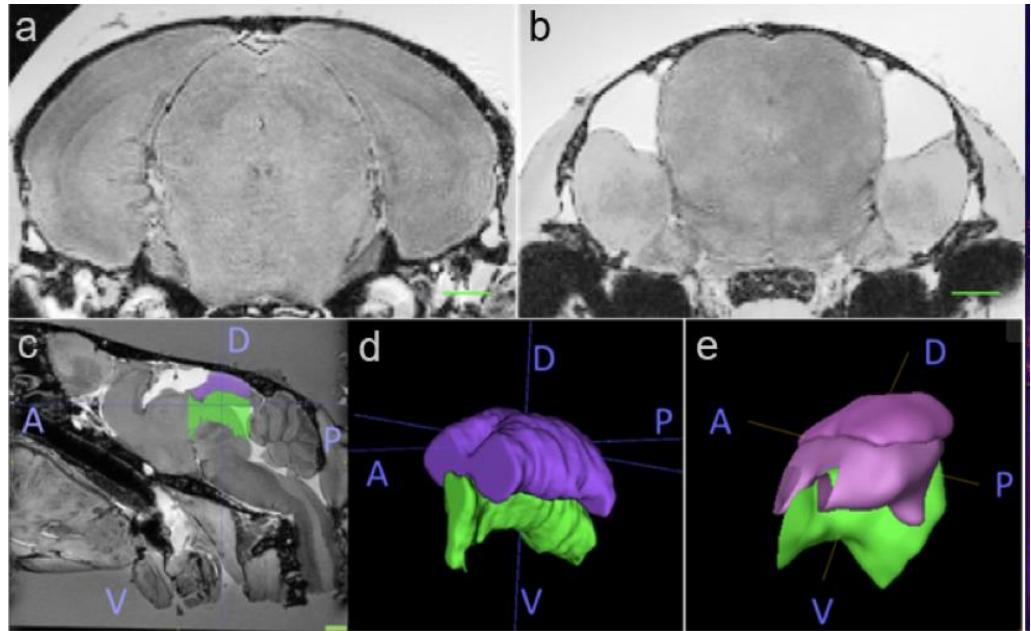
C57BL/6J Wildtype



Emx1-Cre⁺ x Pals1 flox/flox

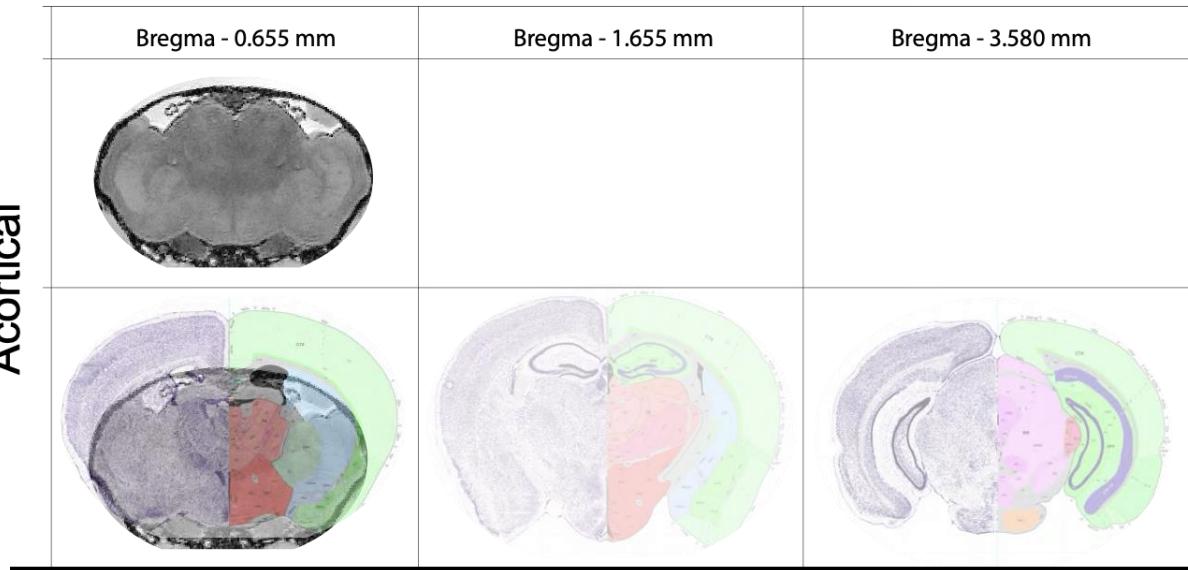
Kim et Walsh, 2010

The acortical brain



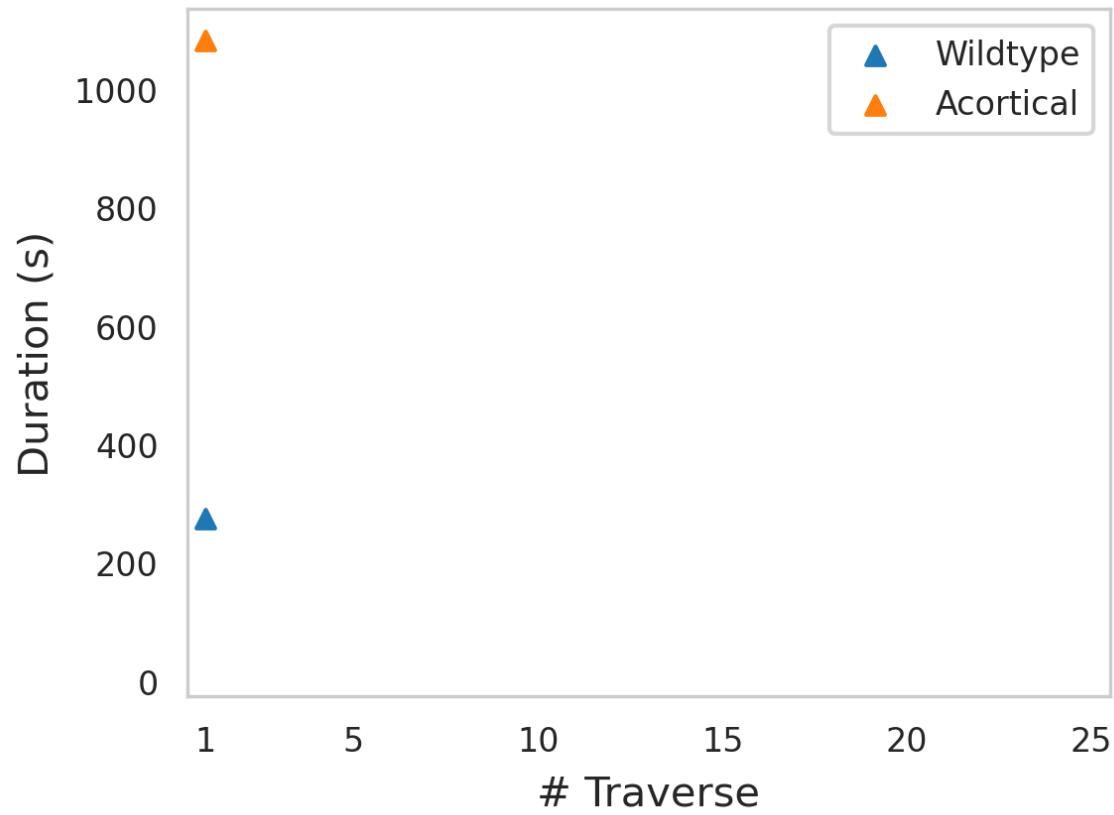
Turan 2021, MRI scan of the brains

- Dorsal cortex all gone: no primary visual cortex
- Has vision through superior colliculus (Turan 2021)
- No hippocampus, but has piriform cortex
- Subcortical structures did not expand to the cavity

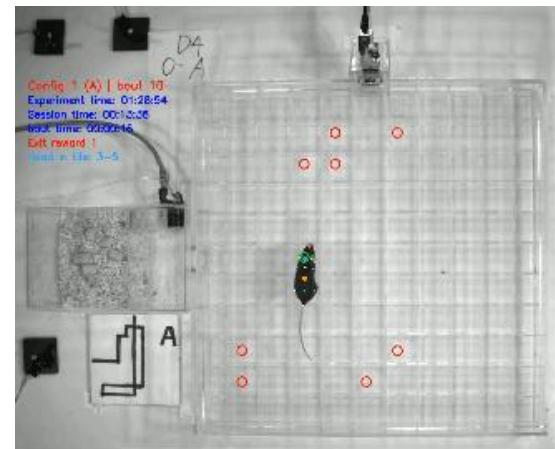


Acortical mouse took 3x time to solve the first mask

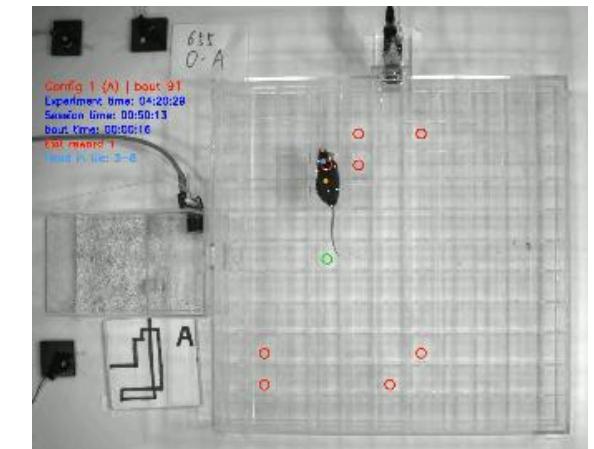
First reward



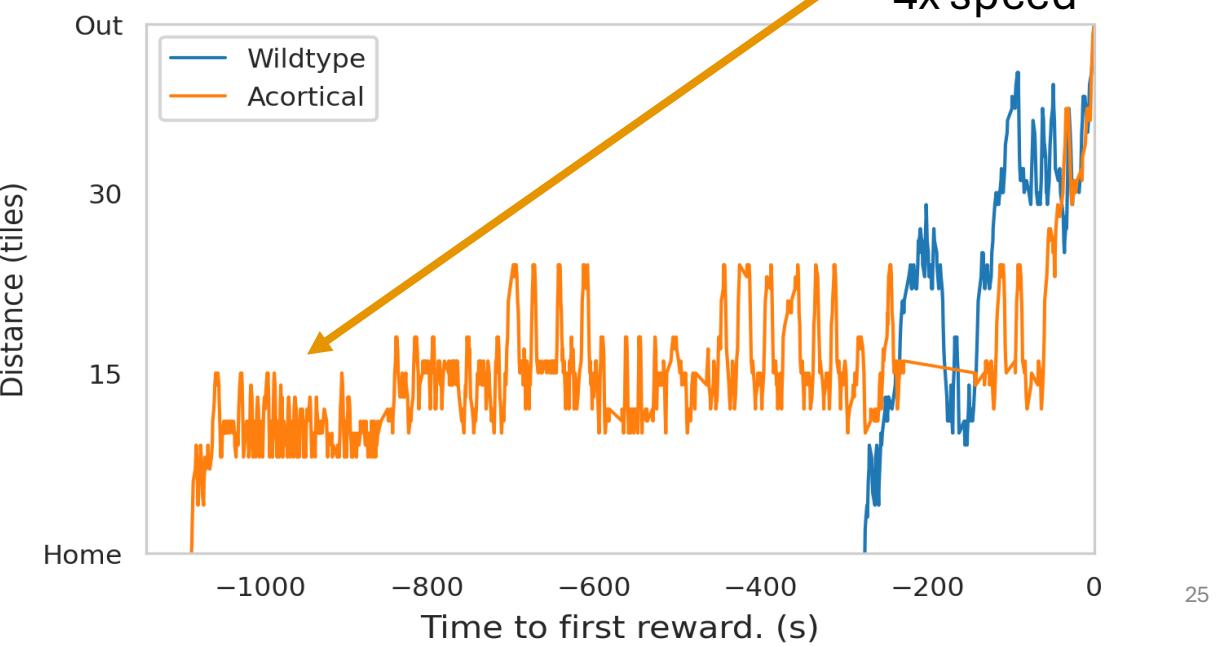
Wildtype



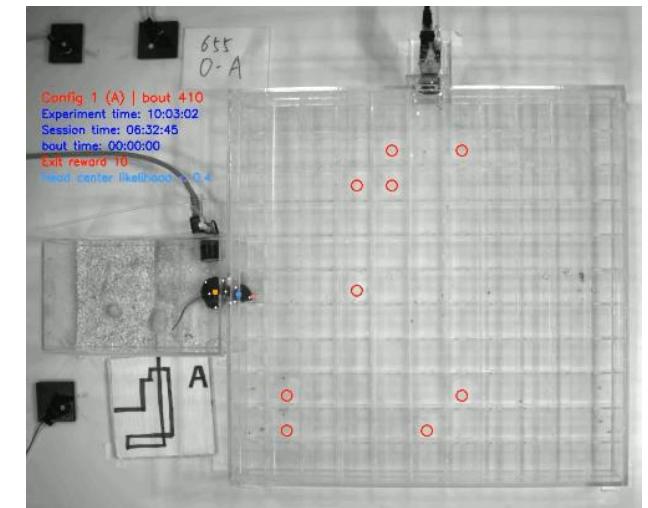
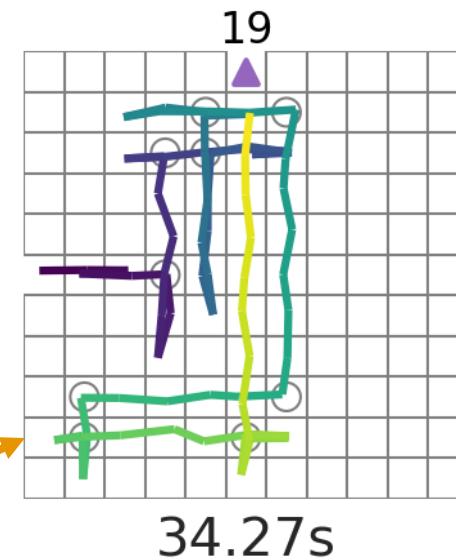
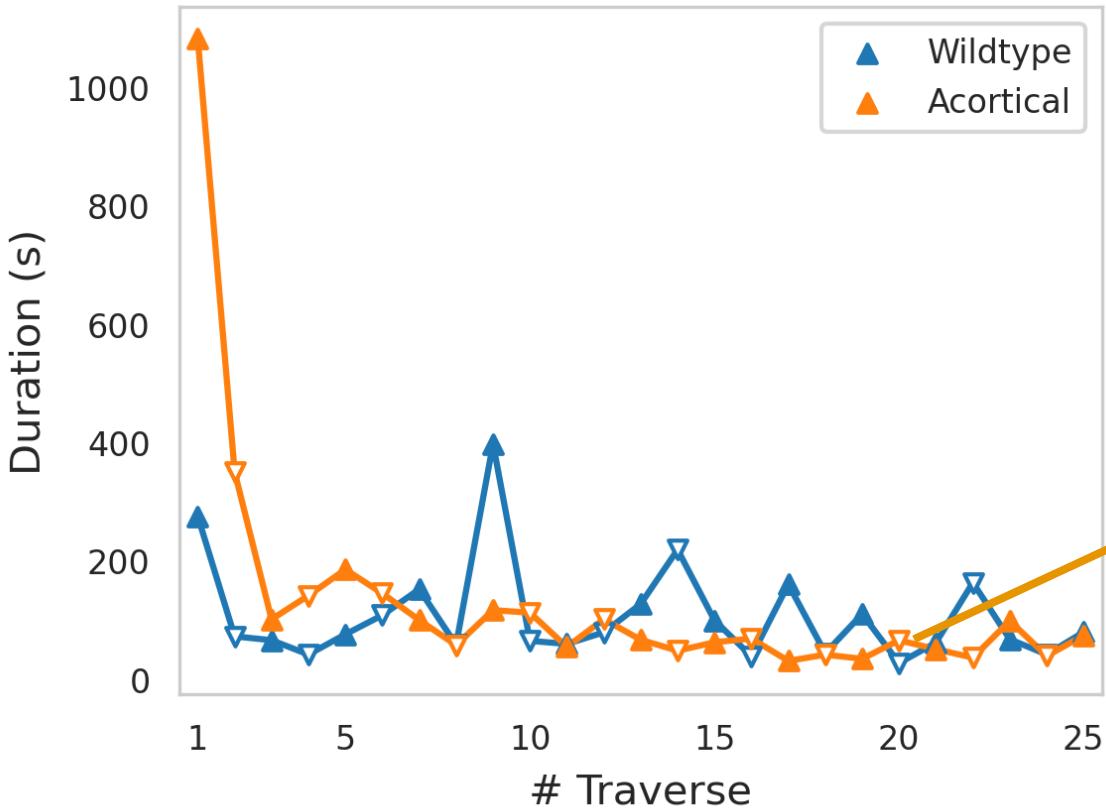
Acortical



4x speed

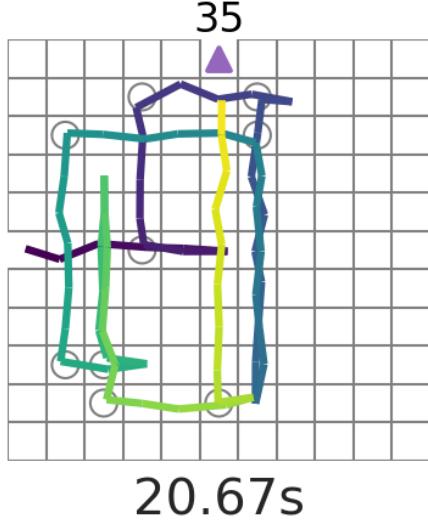


Acortical mouse learning the first mask



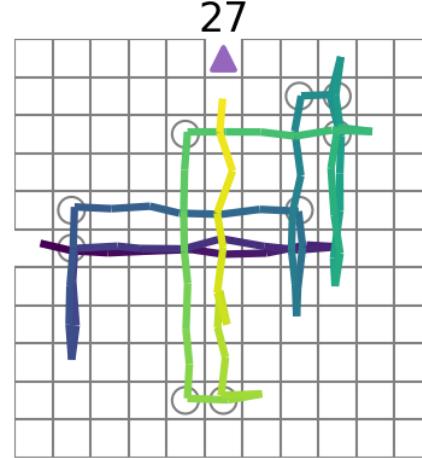
Learning multiple masks

New Mask 1



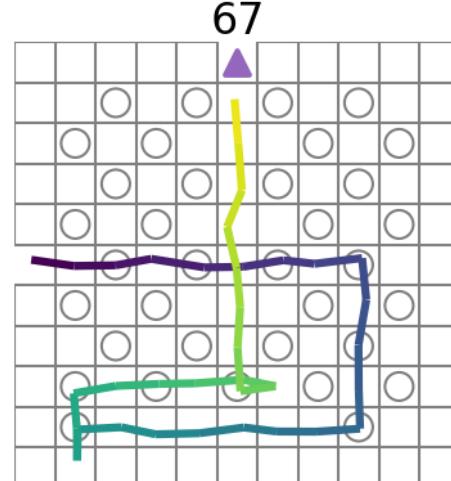
20.67s

New Mask 2



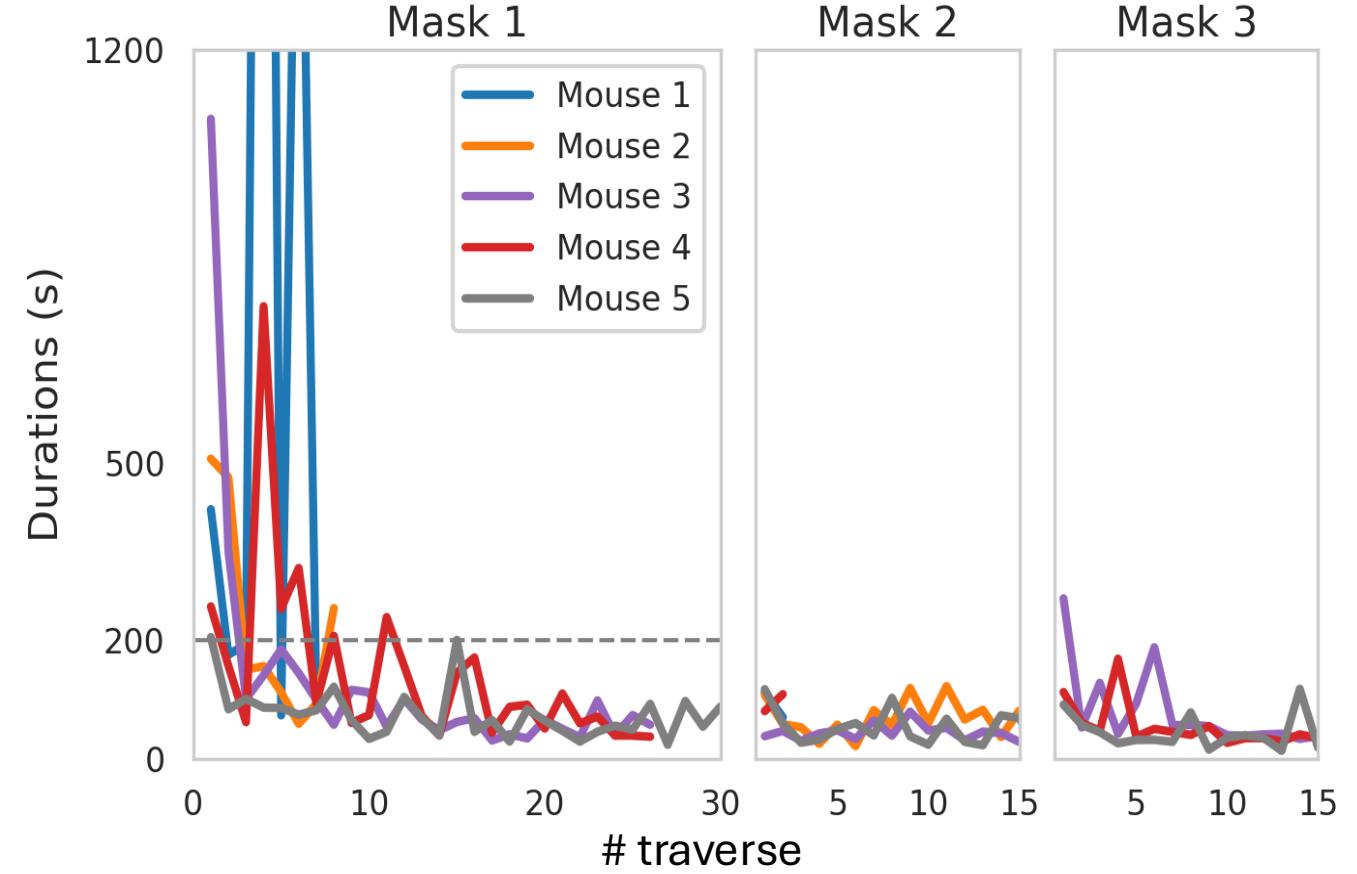
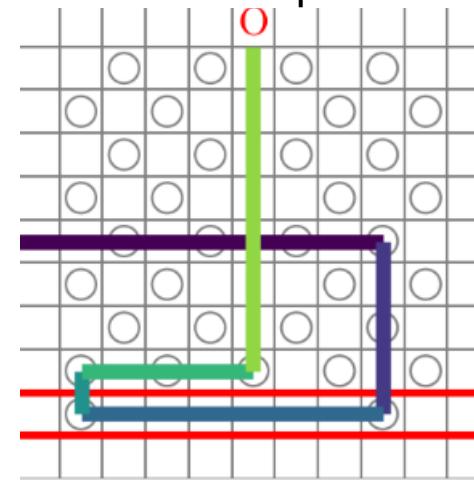
34.17s

Complex Mask

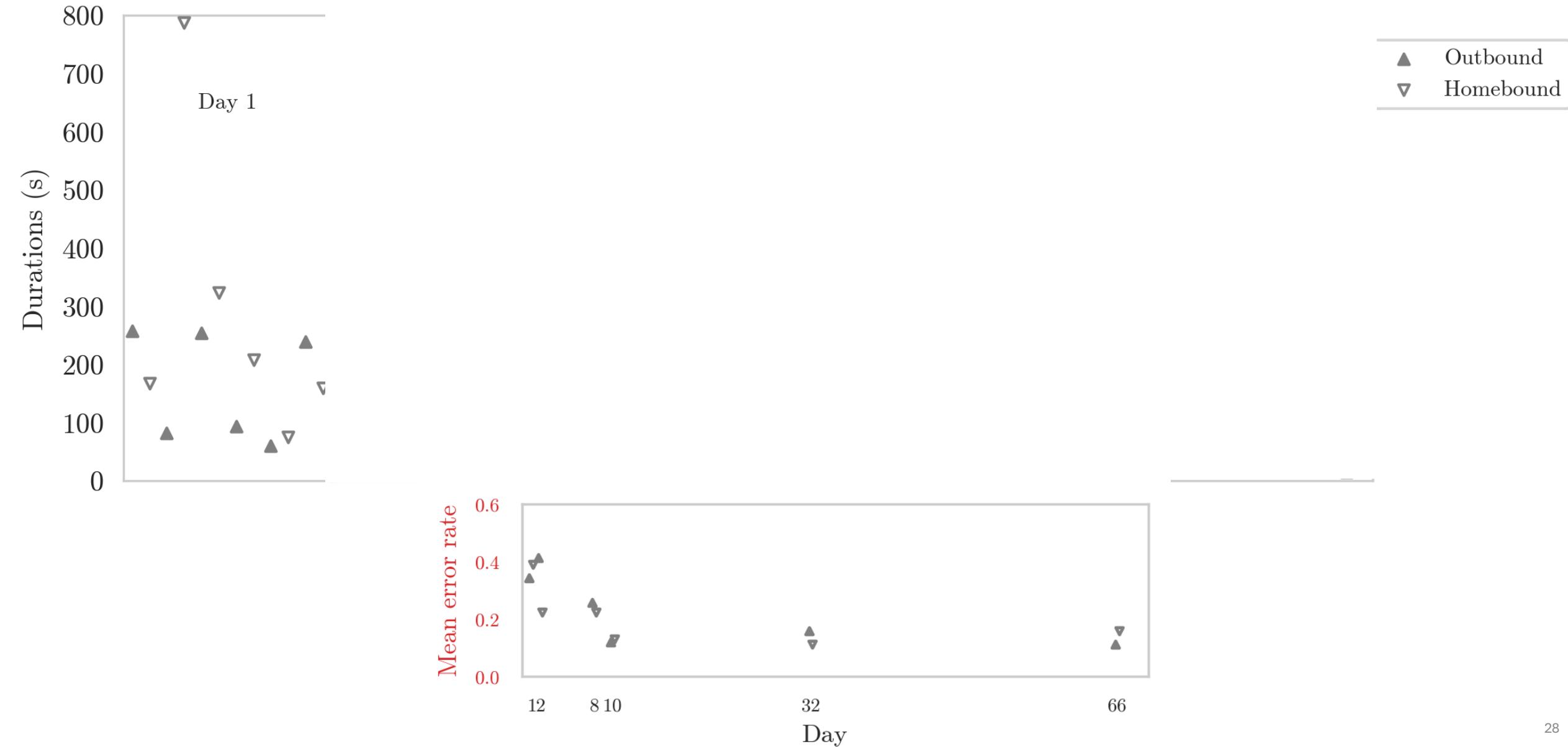


9.77s

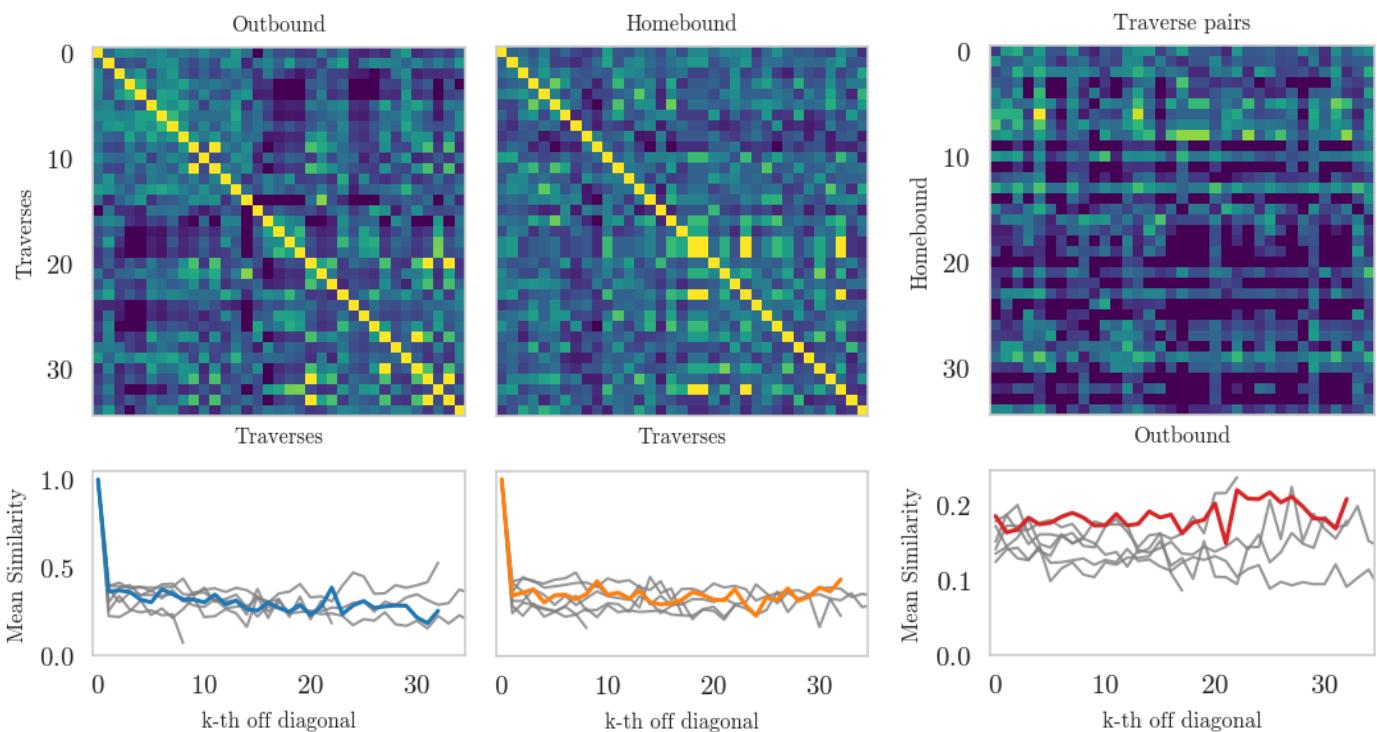
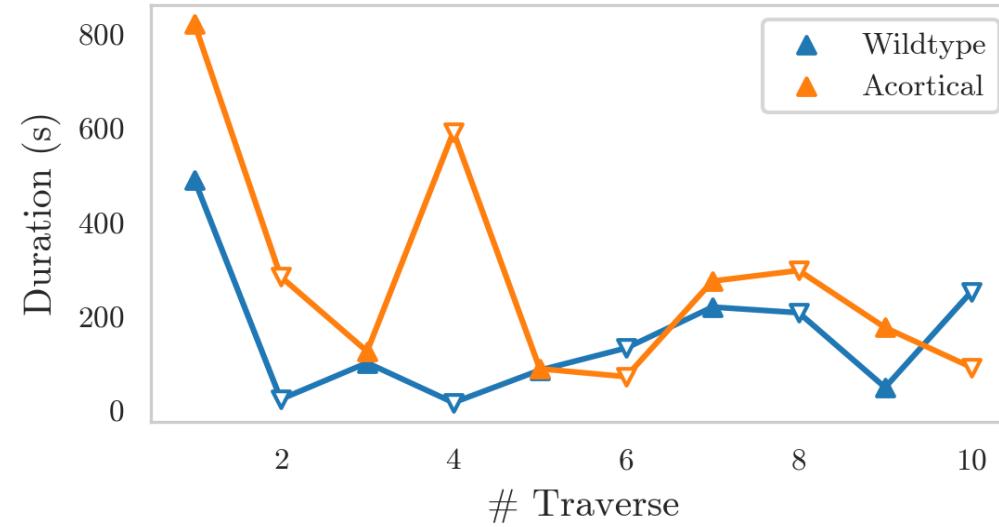
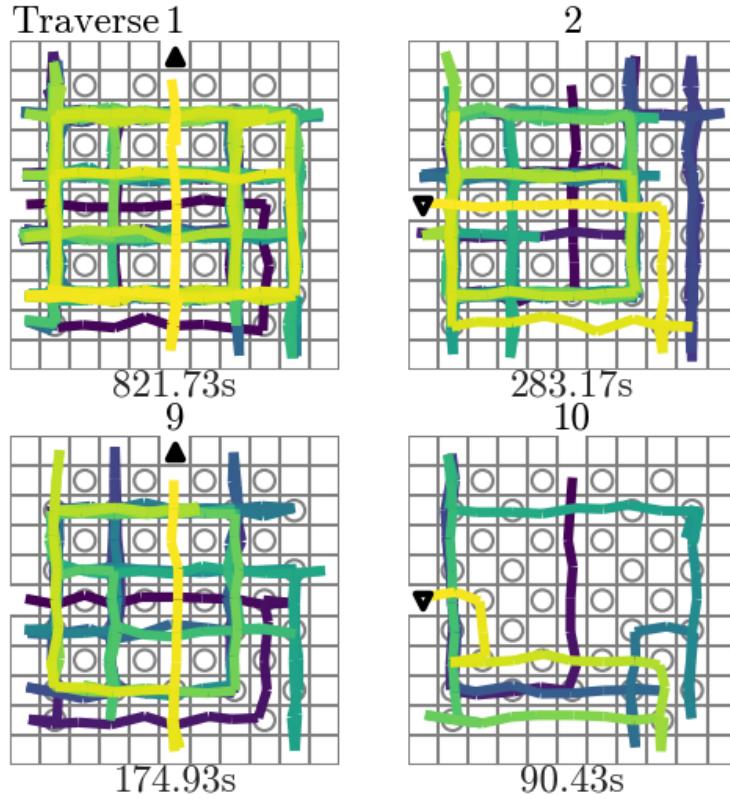
Shortest path



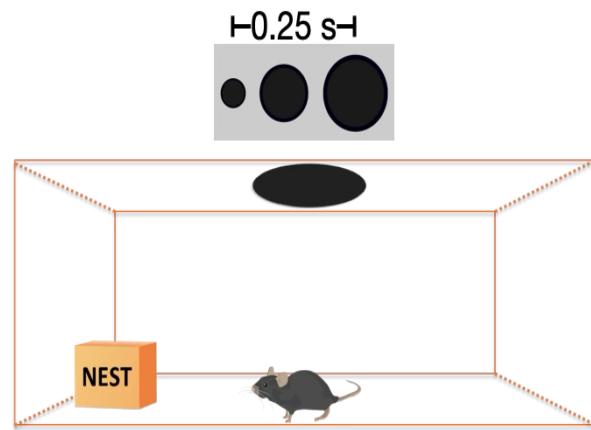
Long-term memory in an acortical mouse



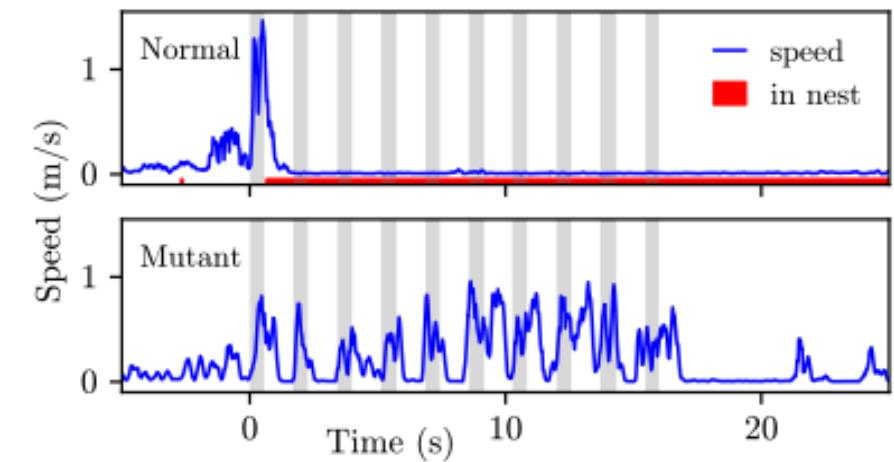
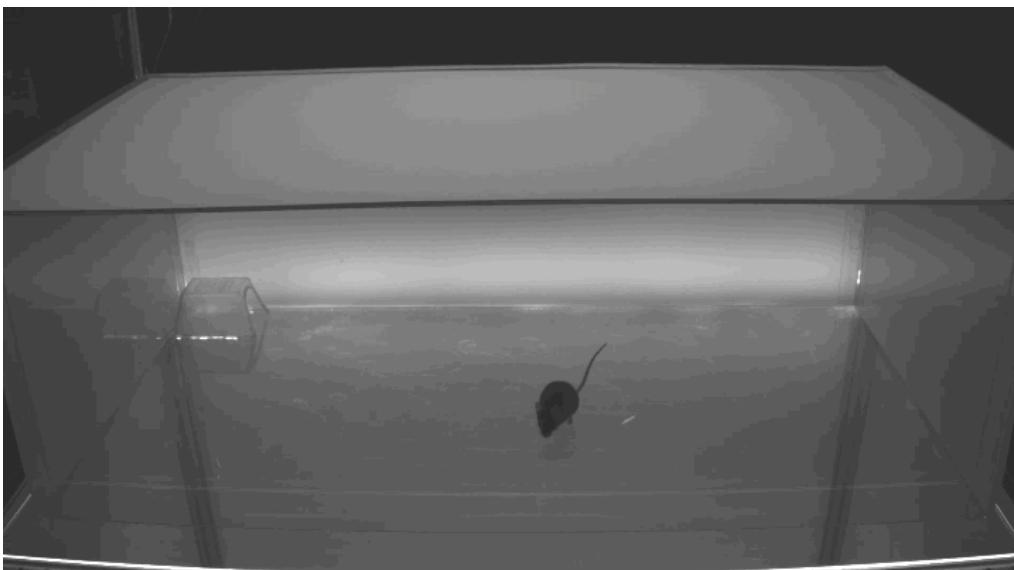
Flexible routing in Mask D



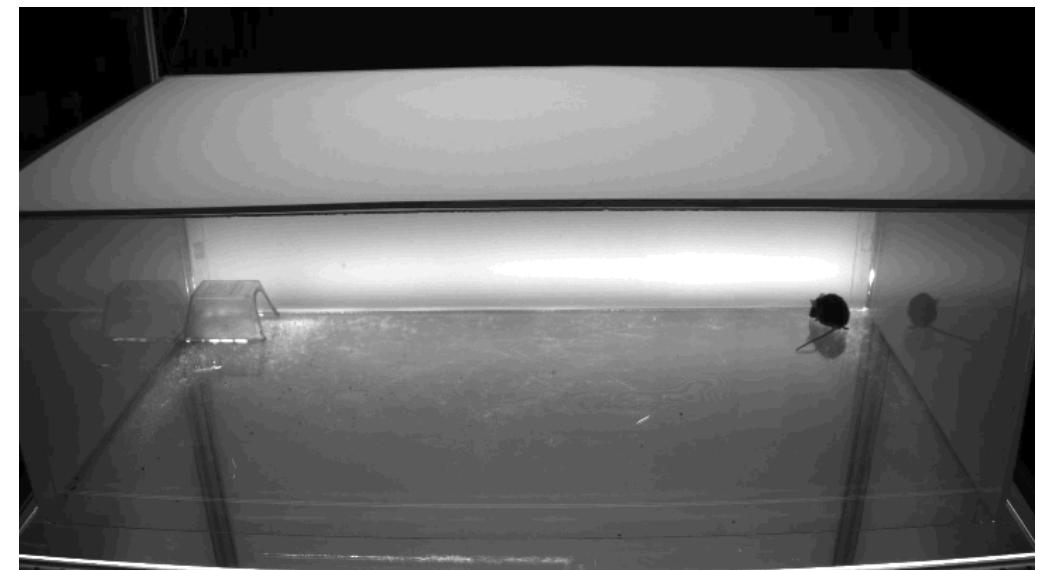
A lethal deficit of acortical mice



Wildtype

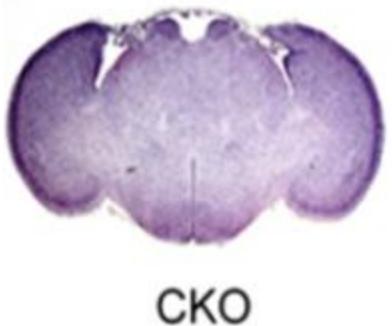


Acortical



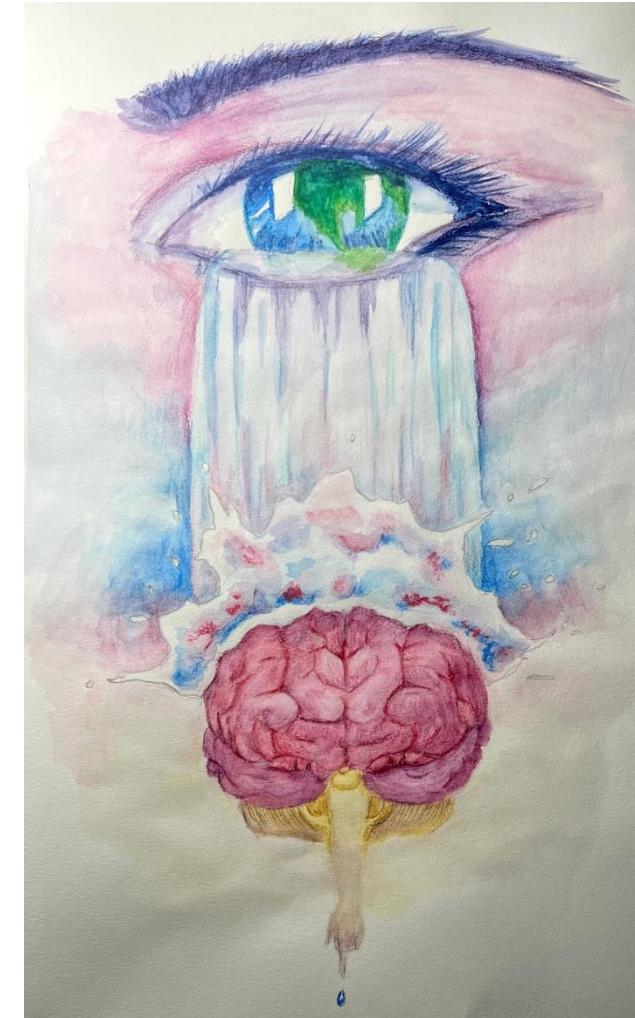
Summary

- **Acortical mice:**
 - **Preserves the ability of**
 - Few-shot learning
 - Generalization
 - Long-term memory
 - Flexible routing
- **Deficit:**
 - **3x** longer first traverse with inefficient exploration
 - Running to shelter from looming stimuli



Conclusions from the study

- Rapid learning, long-term memory and generalization with and without cortex
- Importance of naturalistic learning tasks
- Can we infer human cortex functions from mouse cortex findings?
- So, what is the role of cortex?
 - Zheng, & Meister. (2024). *The unbearable slowness of being*. arXiv:2408.10234



Art by Jieyu Zheng, 2021

Acknowledgement

- The Manhattan Maze:
 - **Markus Meister, Pietro Perona**
 - **Rogério Guimarães**
 - Jen Hu, Anwesha Das
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 - Yingxi Jin
 - Zeyu Jing
 - Leo Li
 - Dan Pollak
 - Jiang Wu



Markus Meister



Pietro Perona



Rogério
Guimarães



Zeynep Turan



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FOUNDATION

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