Virtual Reality to study neural basis of behavior

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Anna Henzi

VR to study neural basis of behavior

Cell 2017

Visuomotor Coupling Shapes the Functional Development of Mouse Visual Cortex

Nature, 2017

Virtual reality for freely moving animals

John R Stowers[1,2], Maximilian Hofbauer[1–4], Renaud Bastien[5,6], Johannes Griessner[1], Peter Higgins[1], Sarfarazhussain Farooqui[3,4,7], Ruth M Fischer[3], Karin Nowikovsky[7], Wulf Haubensak[1], Iain D Couzin[5,6], Kristin Tessmar-Raible[3,4] & Andrew D Straw[1,8]

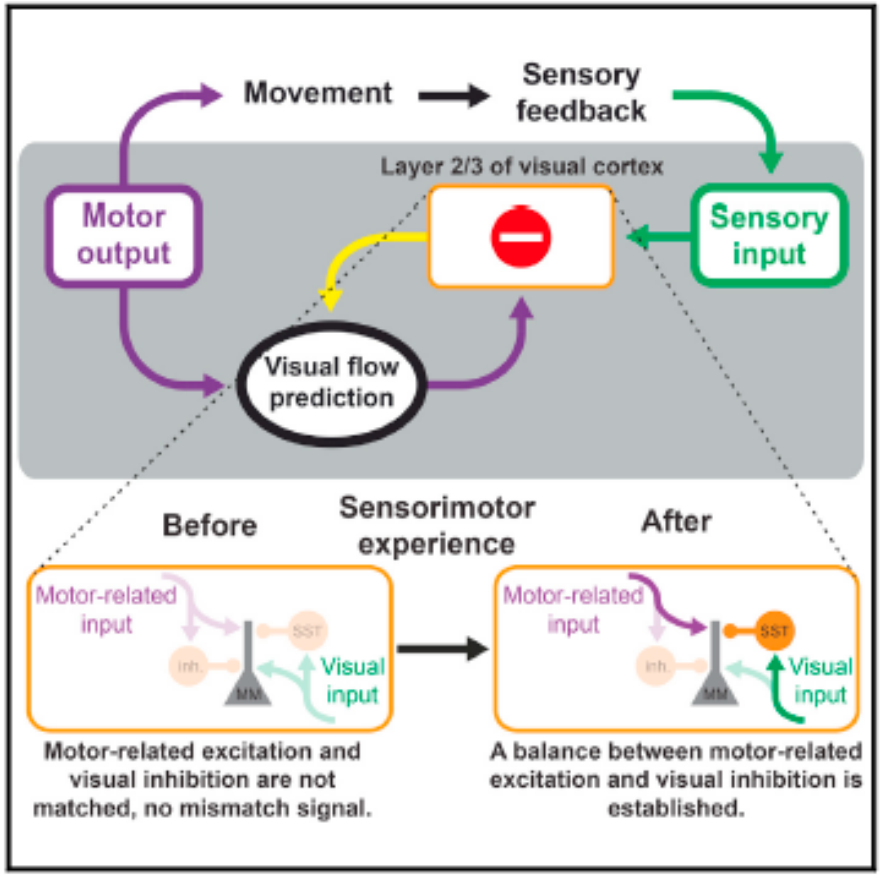
- Closed-loop manipulations of environment
- Overcome limitations of physical arenas
- Head fixation impedes normal behaviour, distorts vestibular inputs

Paulk et al. 2015
Cushman, 2013

Cell

Visuomotor Coupling Shapes the Functional Development of Mouse Visual Cortex

Graphical Abstract



Authors

Alexander Attinger, Bo Wang, Georg B. Keller

Correspondence

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In Brief

The coupling of sensory and motor experience during development shapes visual perception by tuning a cortical circuit that compares inhibitory visual input and excitatory motor input and is able to detect mismatches between actual and expected sensory experience.

Background

- Sensorimotor coupling necessary for development of sensory-guided behavior

- Response of visual cortex V1
  - motor-related signals
  - Predictive coding

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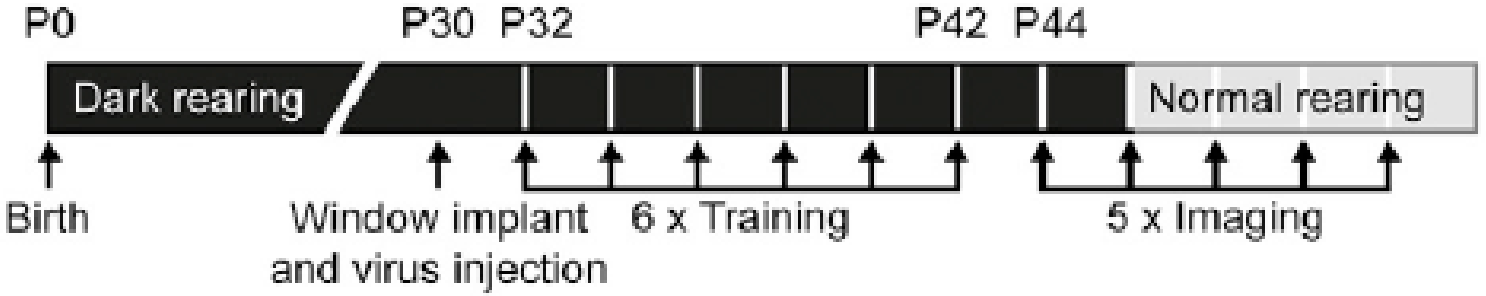
Methods

- Mice dark-reared and trained in VR system

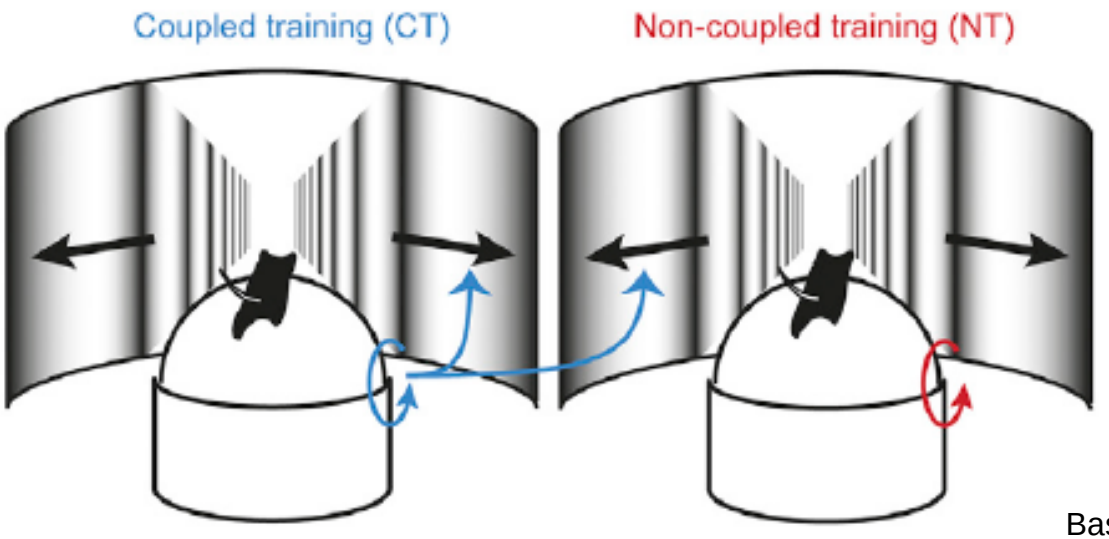


Methods

- Mice trained in VR system

Training sessions
Coupled (CT)
Non-coupled (NT)

Imaging
Closed loop session
Open loop session



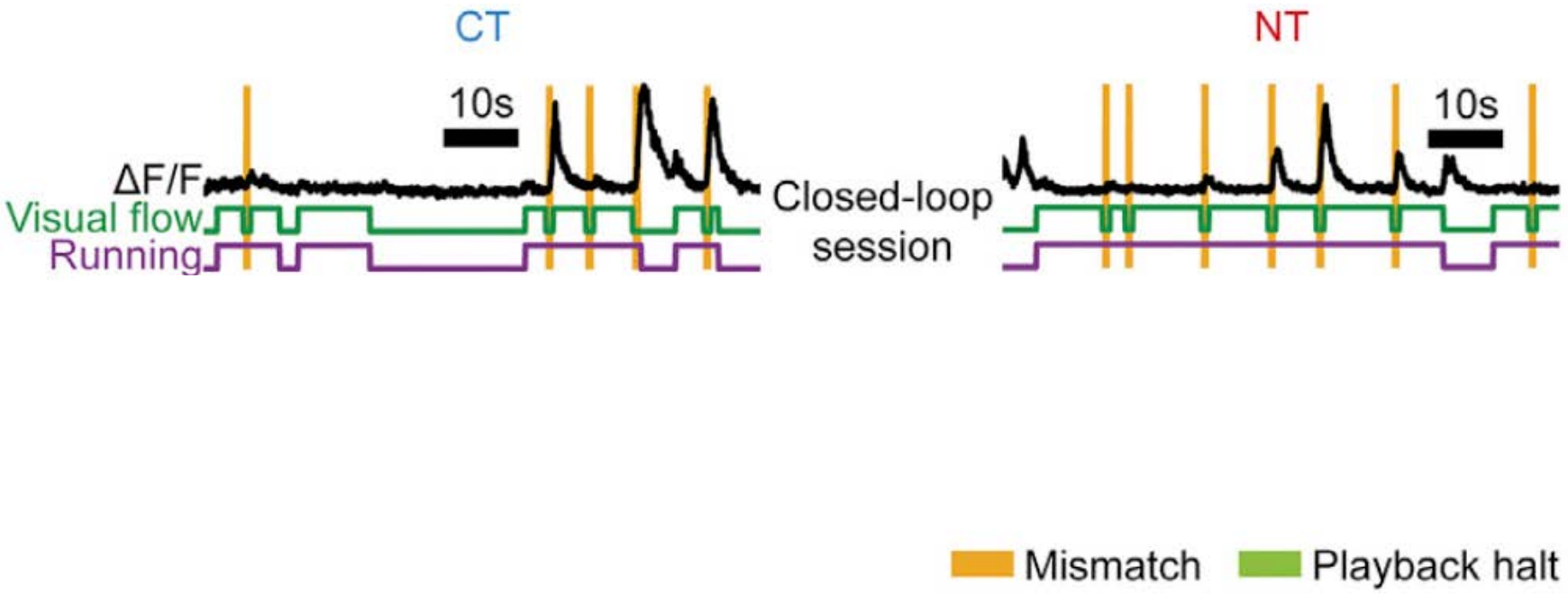
Basic setup: Hölscher 2005

Methods

- Imaging sessions (closed + open loop)
- Measure neuronal activity in V1 layer 2/3
  - 2 photon-imaging of GCaMP5/6f
  - Only excitatory neurons (total 2’259 neurons)

Results

- Sign. fraction of **excitatory neurons responds to mismatch in CT** mice (38.3% compared to 20% in NT mice)



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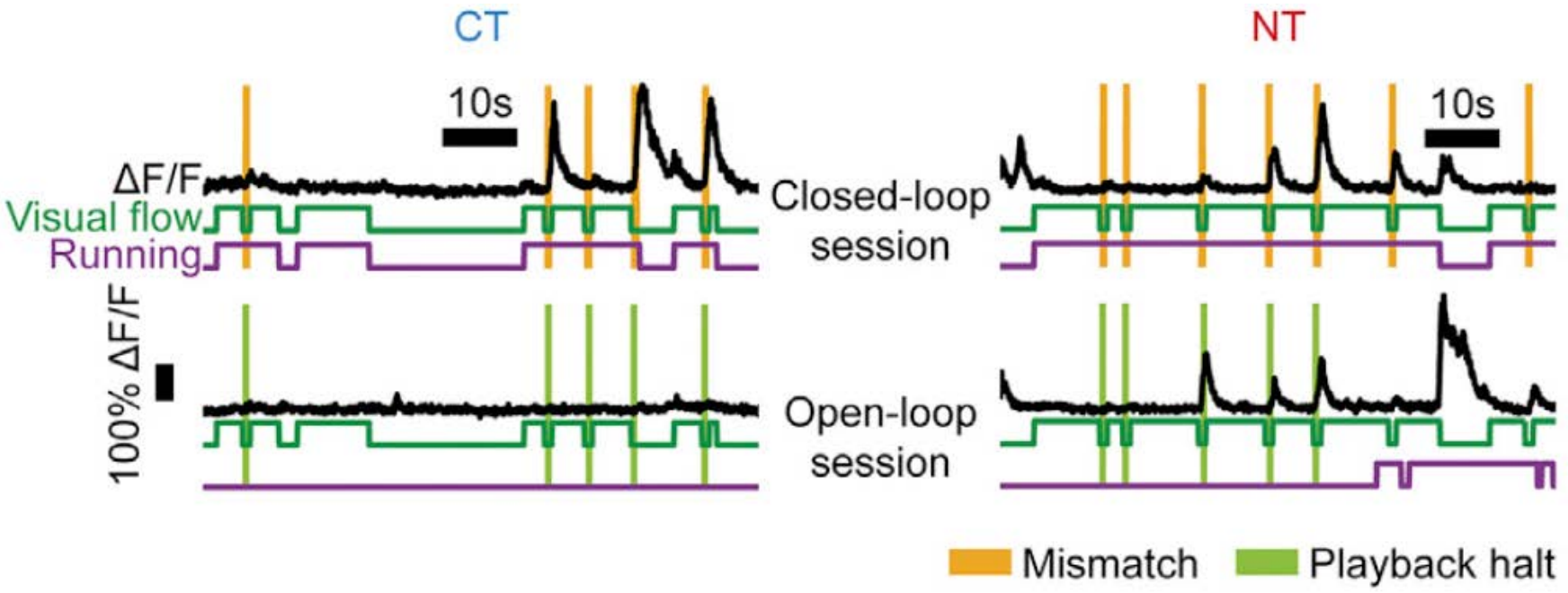
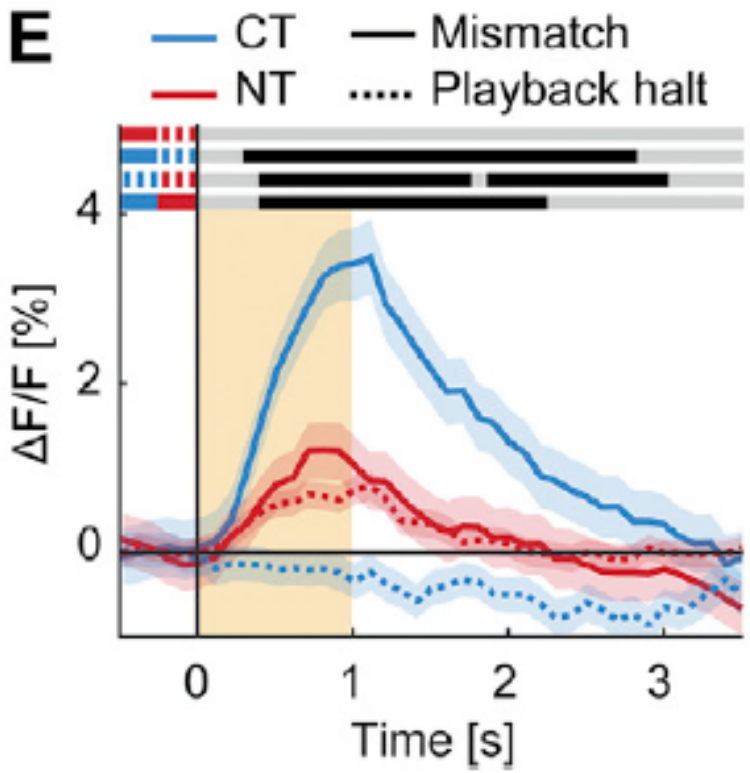
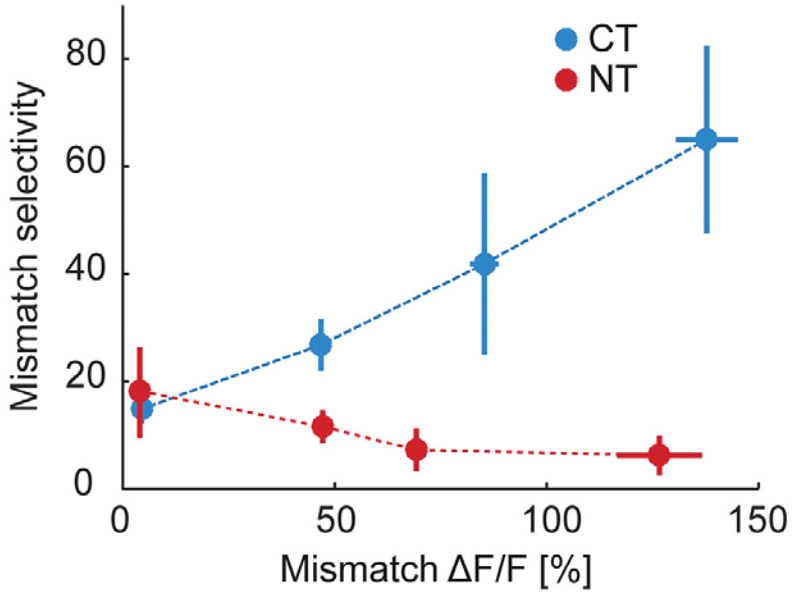


Results

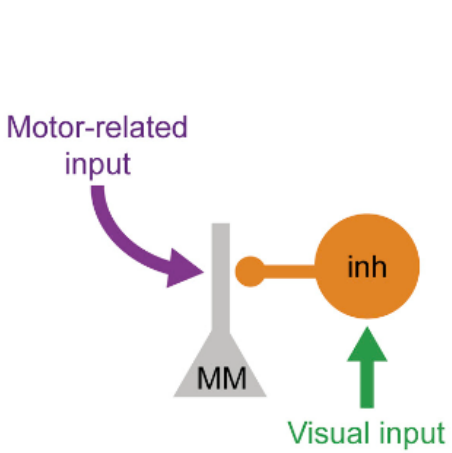
- Population response





Mismatch response

- Difference between excitatory prediction and inhibitory visual input?



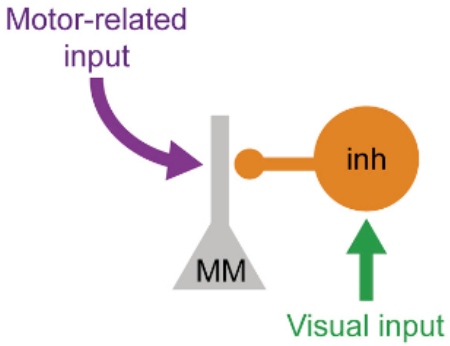
  - Inputs balanced when predictions match visual experience
  - Mismatch: ↓ visual inhibition > activation of neuron by excitatory motor-related input
  - Correlation of activity with visual flow and running speed

Mismatch response

Correlation of activity with visual flow and running speed in open loop sessions:

CT mice

A



Mismatch response

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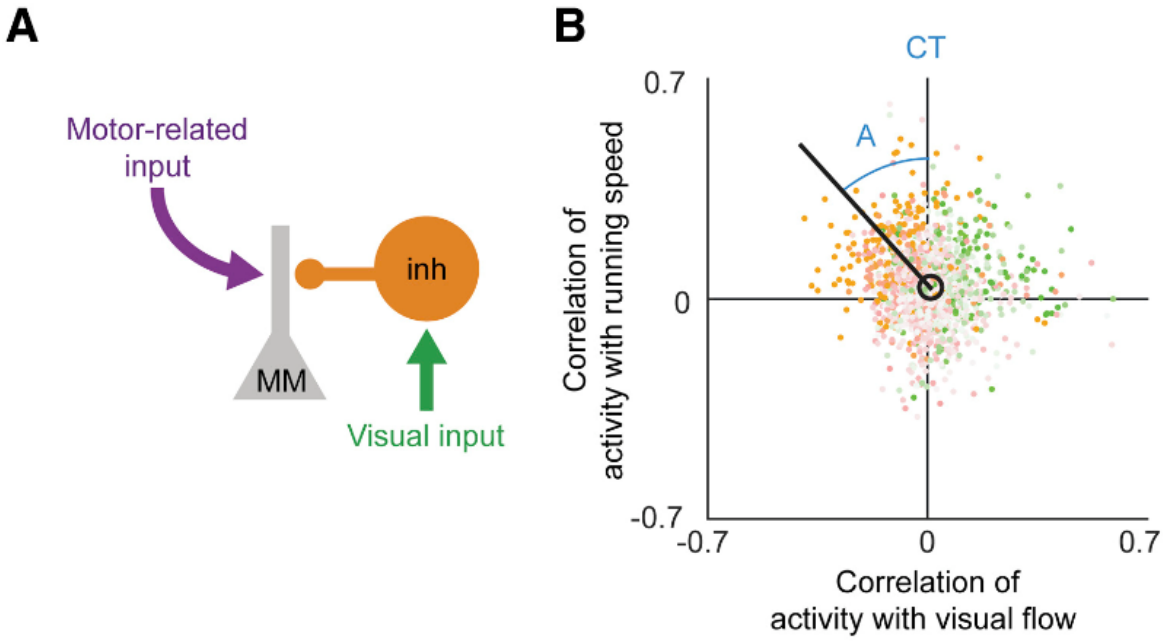
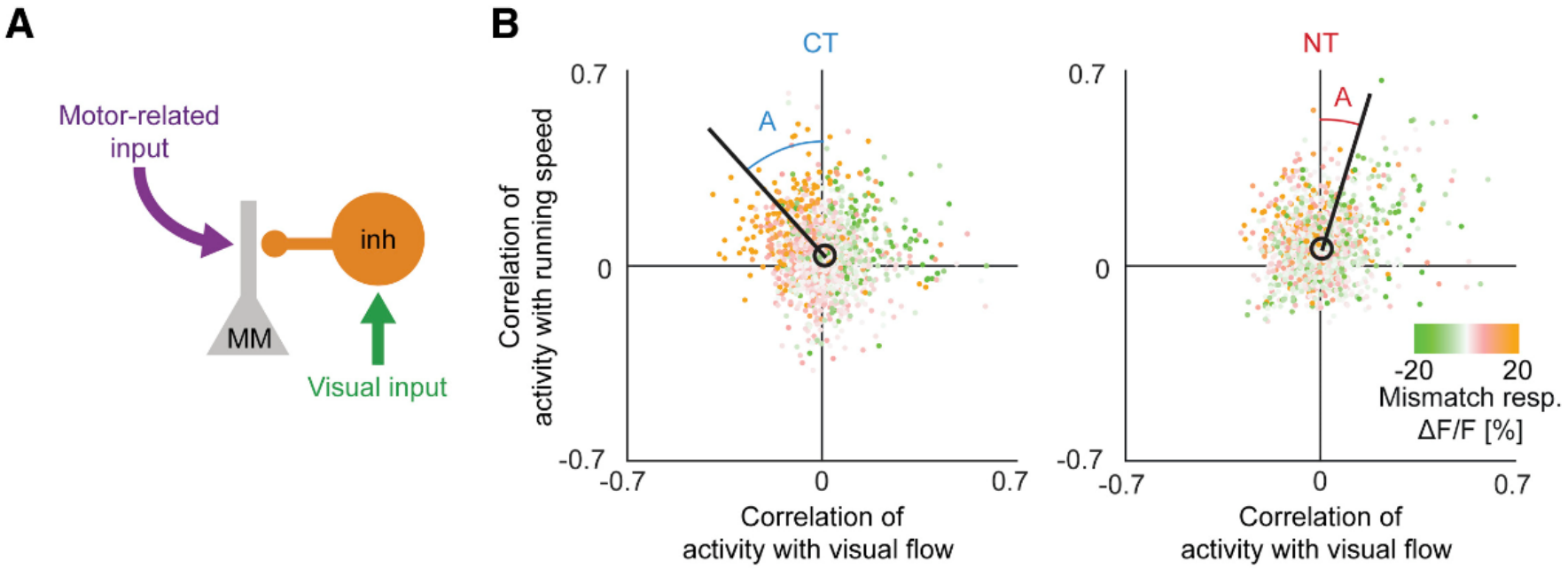


Mismatch response

Correlation of activity with visual flow and running speed:

- CT mice NT mice



Mismatch response

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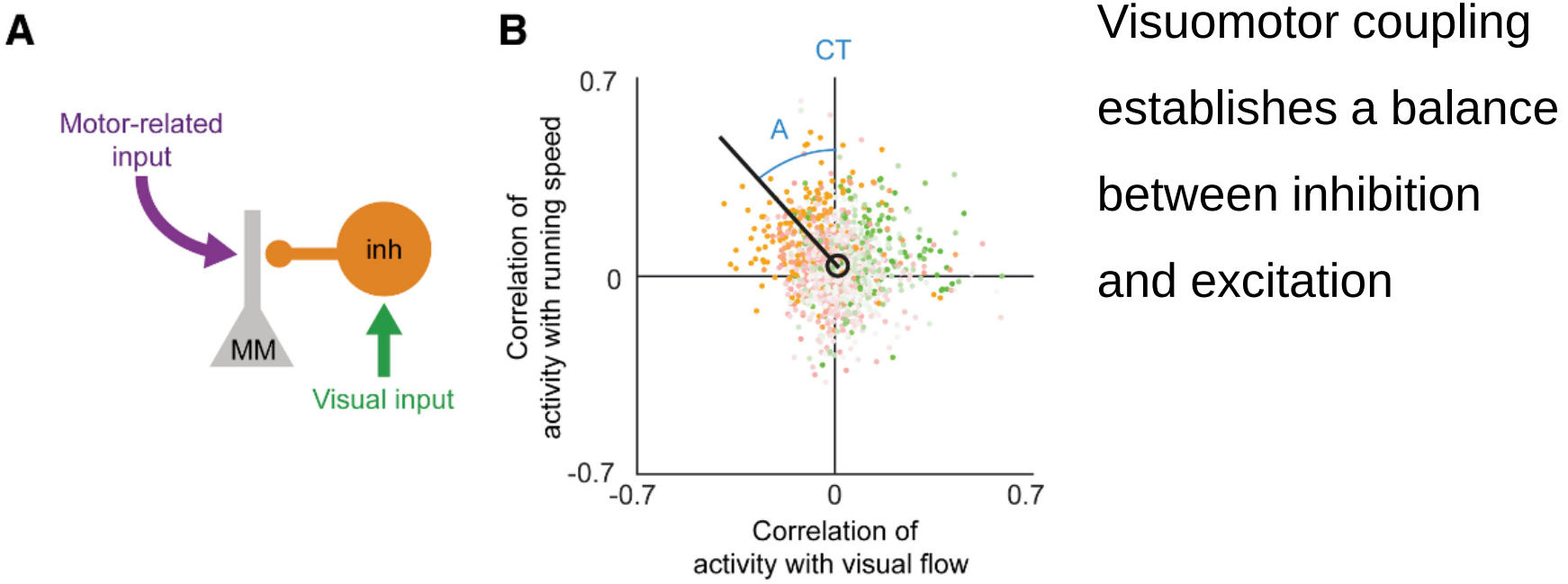
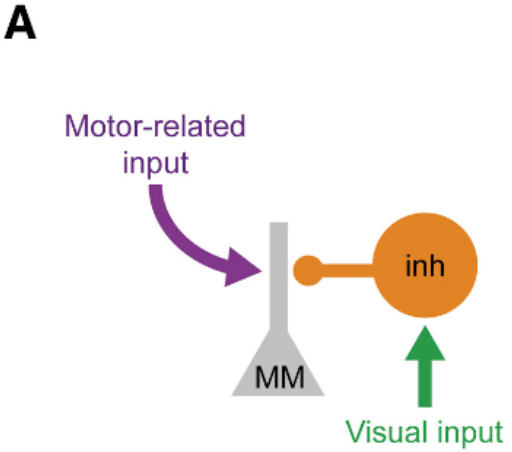


Visuomotor coupling establishes a balance between inhibition and excitation

Mismatch response

- Which inhibitory neurons?
  - Cre-driver lines for selective expression of GCaMP6f in
    - SST
    - VIP
    - PV



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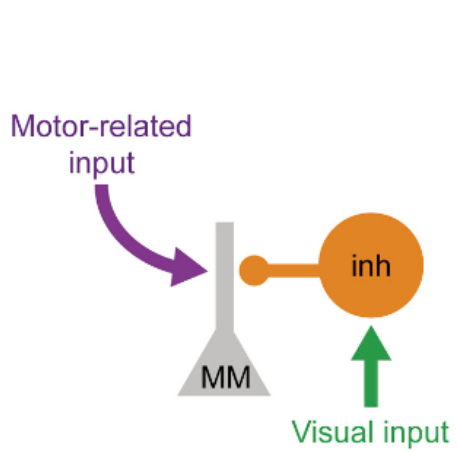

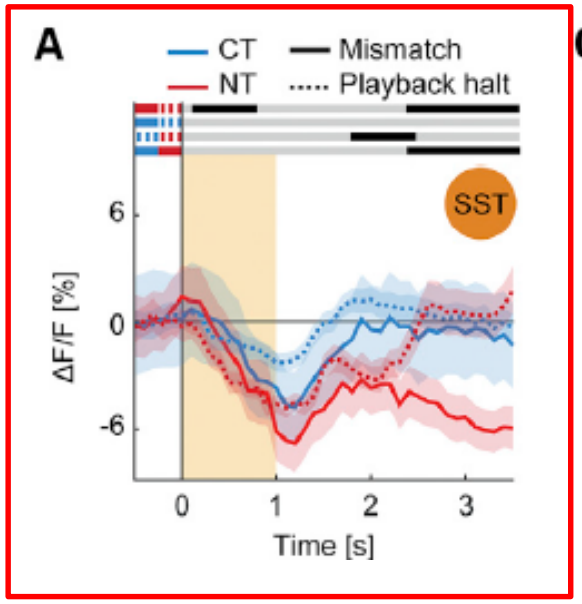

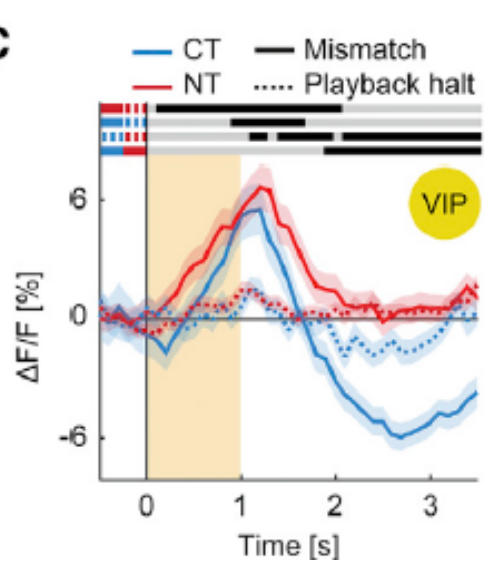

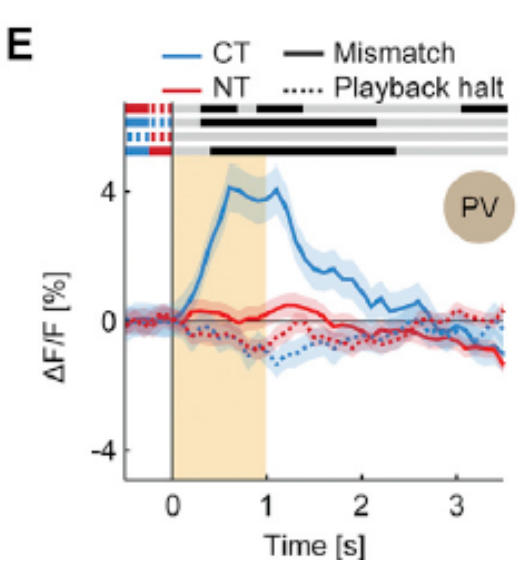

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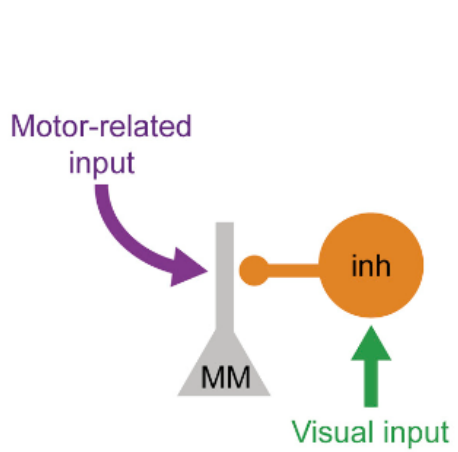

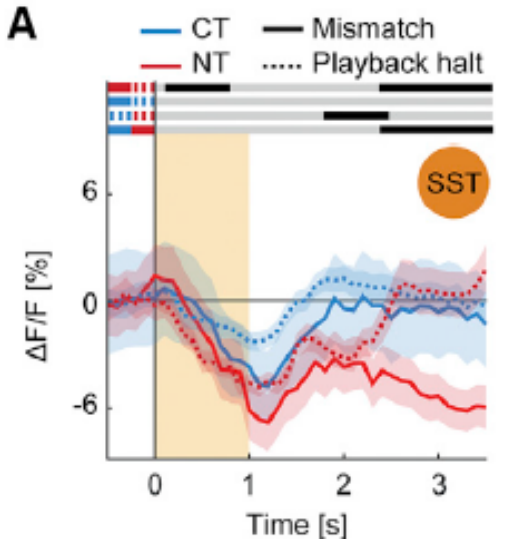

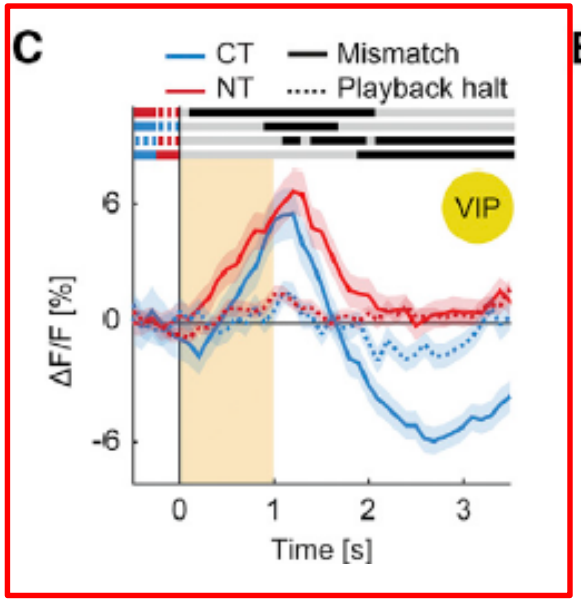

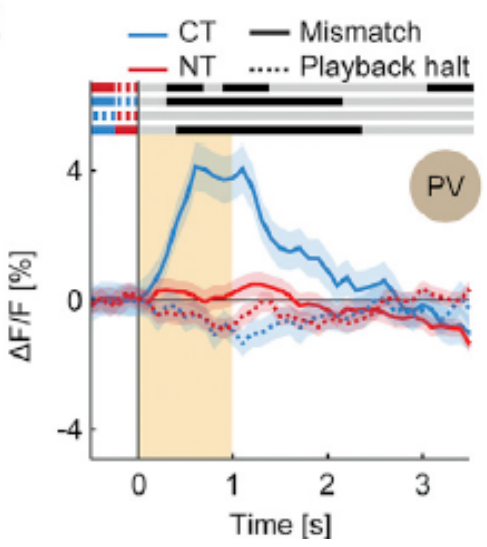

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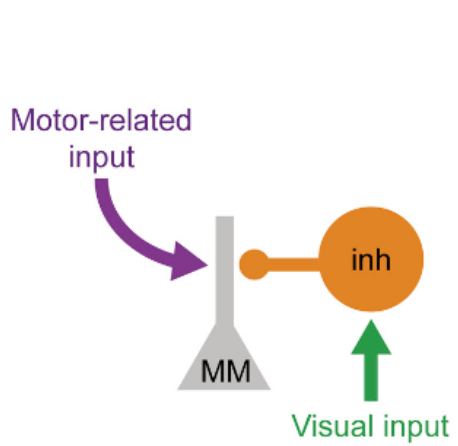

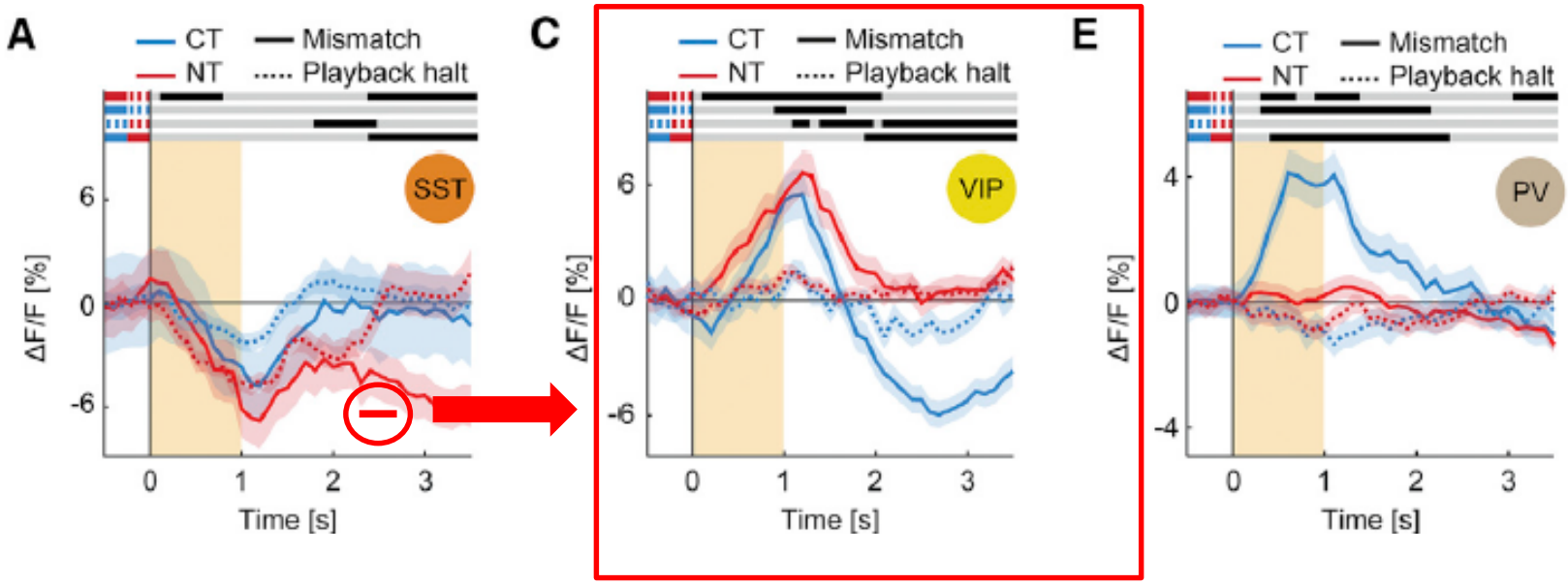

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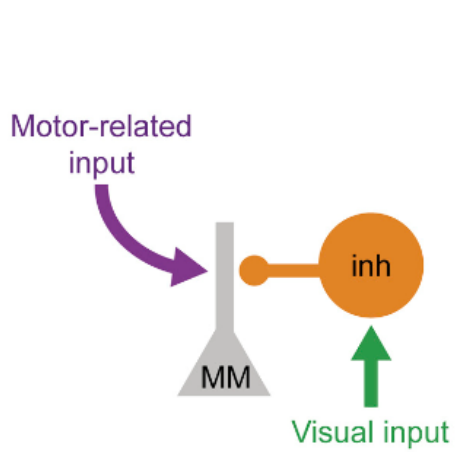
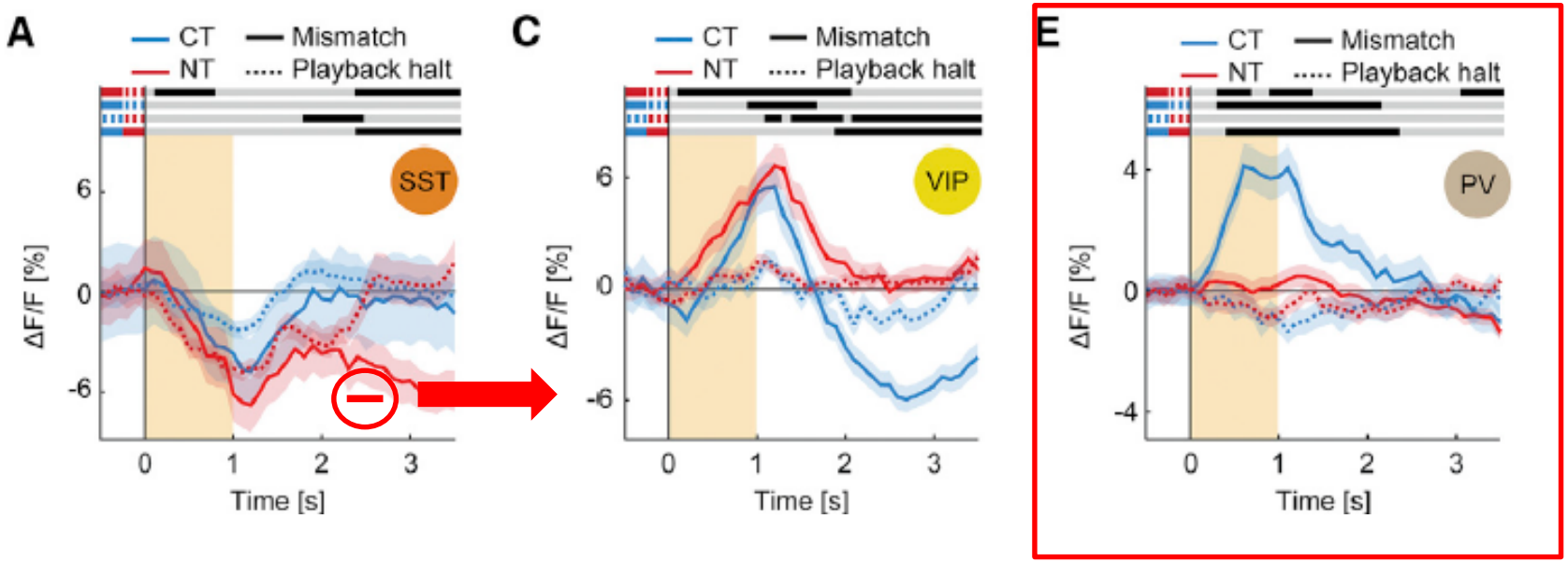
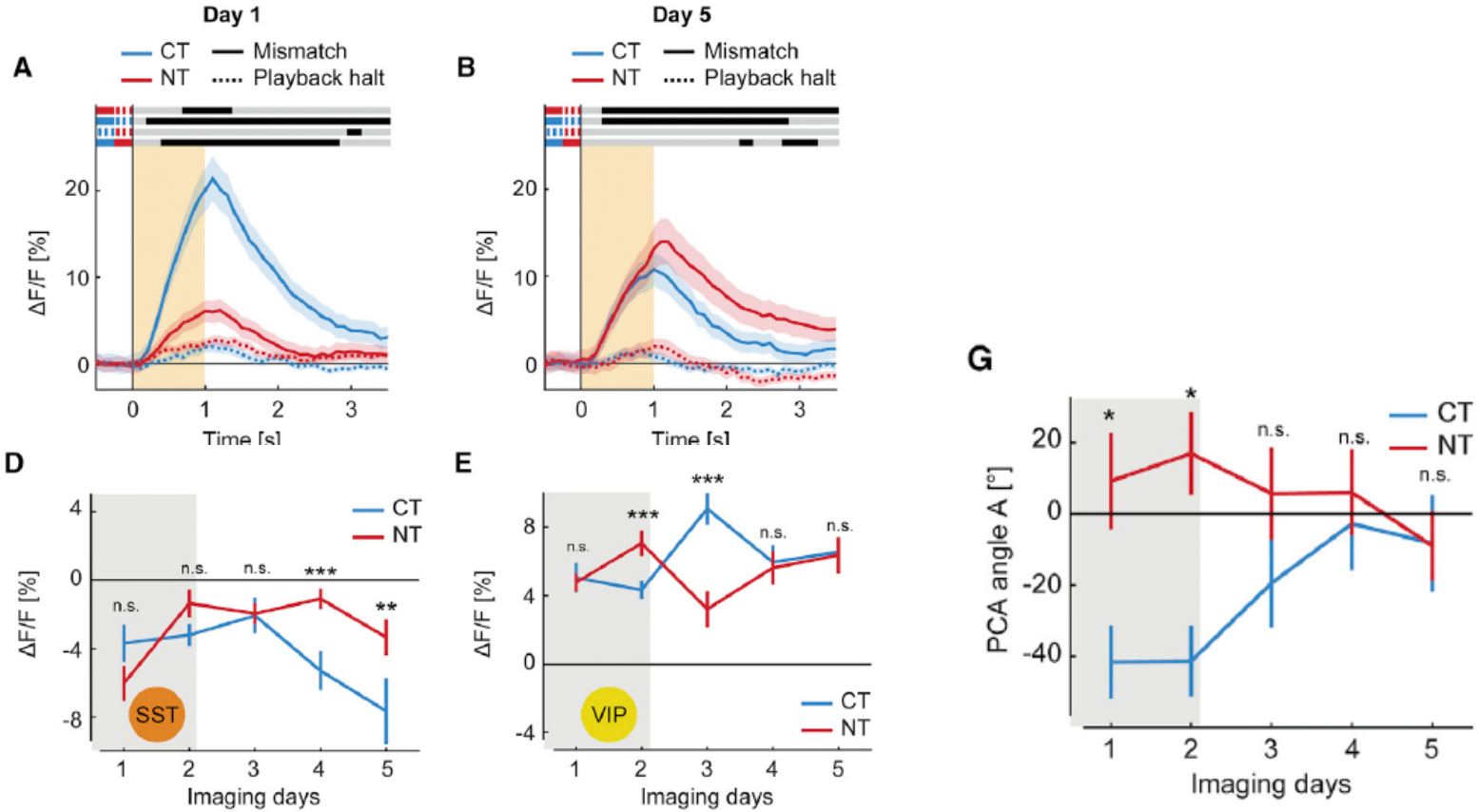


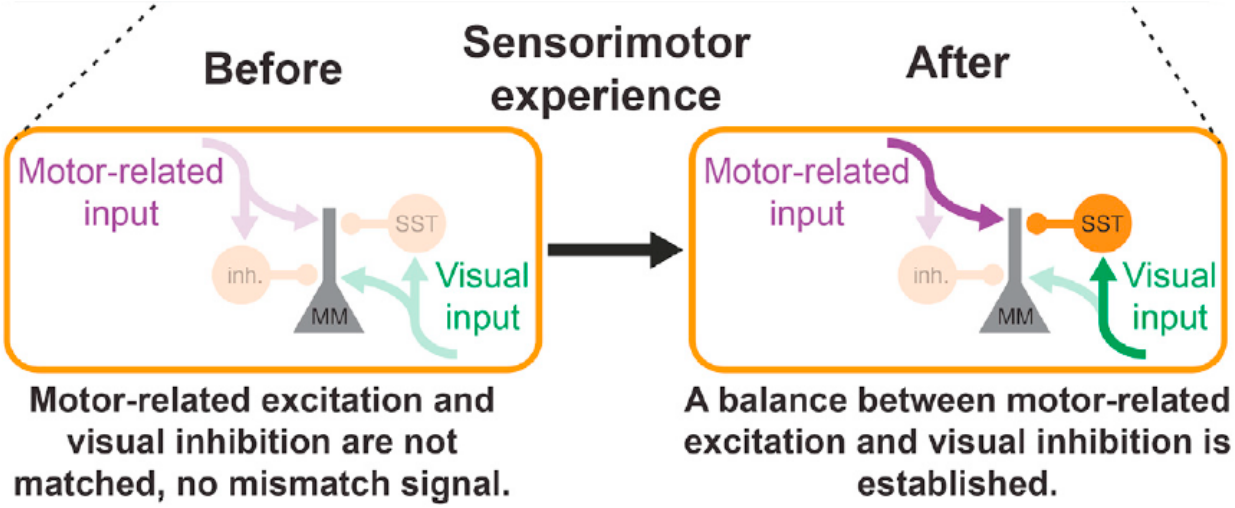


Restoration of normal visuomotor integration

- Exposure to normal light/dark cycle, and open- and closed-loop conditions



Conclusions



Mismatch response = consequence of predictive coding strategy

- V1 layer 2/3 excitatory mismatch and a subset of VIP interneurons receive excitatory, motor-related input
- SST neurons more strongly driven by visual input

- ➢ Artificial restriction of visuomotor coupling to only a subset of movements leads to an overrepresentation of the visuomotor processing of these movements.
- ➢ Needs to be unlearned for normal visuomotor behavior

Virtual reality for freely moving animals

Nature, 2017

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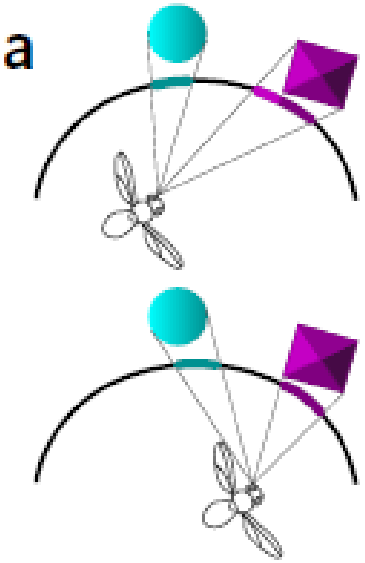
- VR systems require movement restrictions

- FreemoVR = VR system for freely moving animals
  - Instant, disruption-free environmental reconfigurations and interactions between real organisms and computer-controlled agents
  - Animal tracking + precise spatial calibration of computer displays + computer game technology > draw realistic and perspective-correct images from animals perspective



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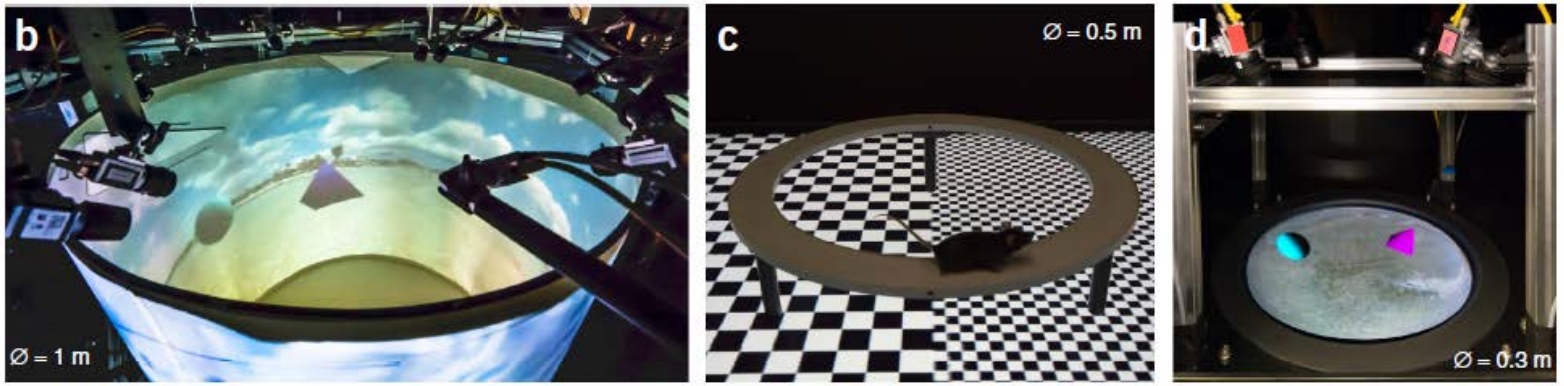
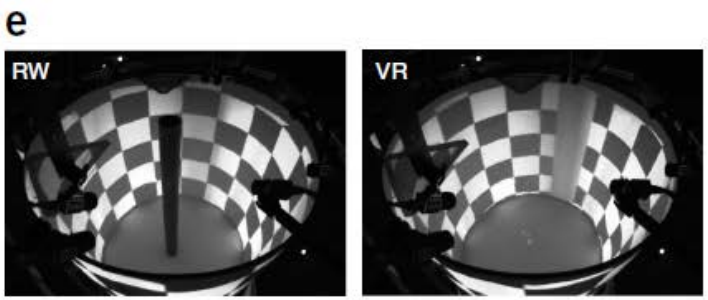
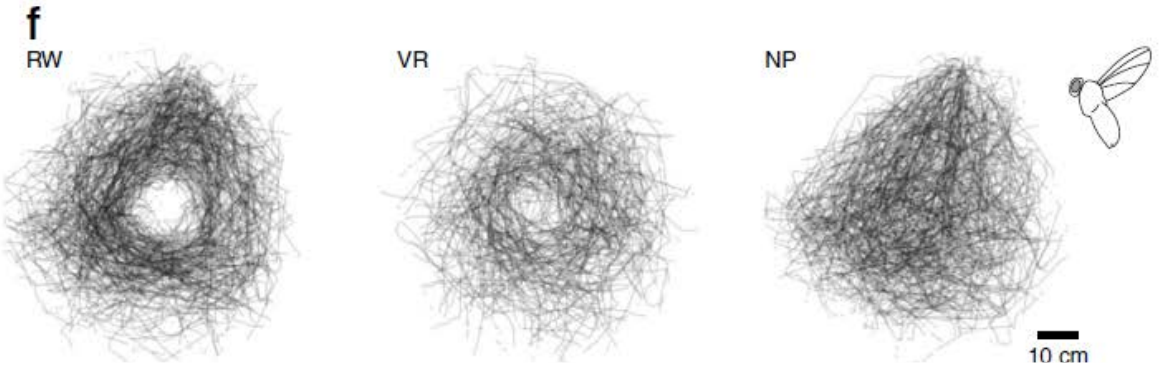


  - Validated for fly, mouse and fish

Validation

- Behavioral response to virtual objects





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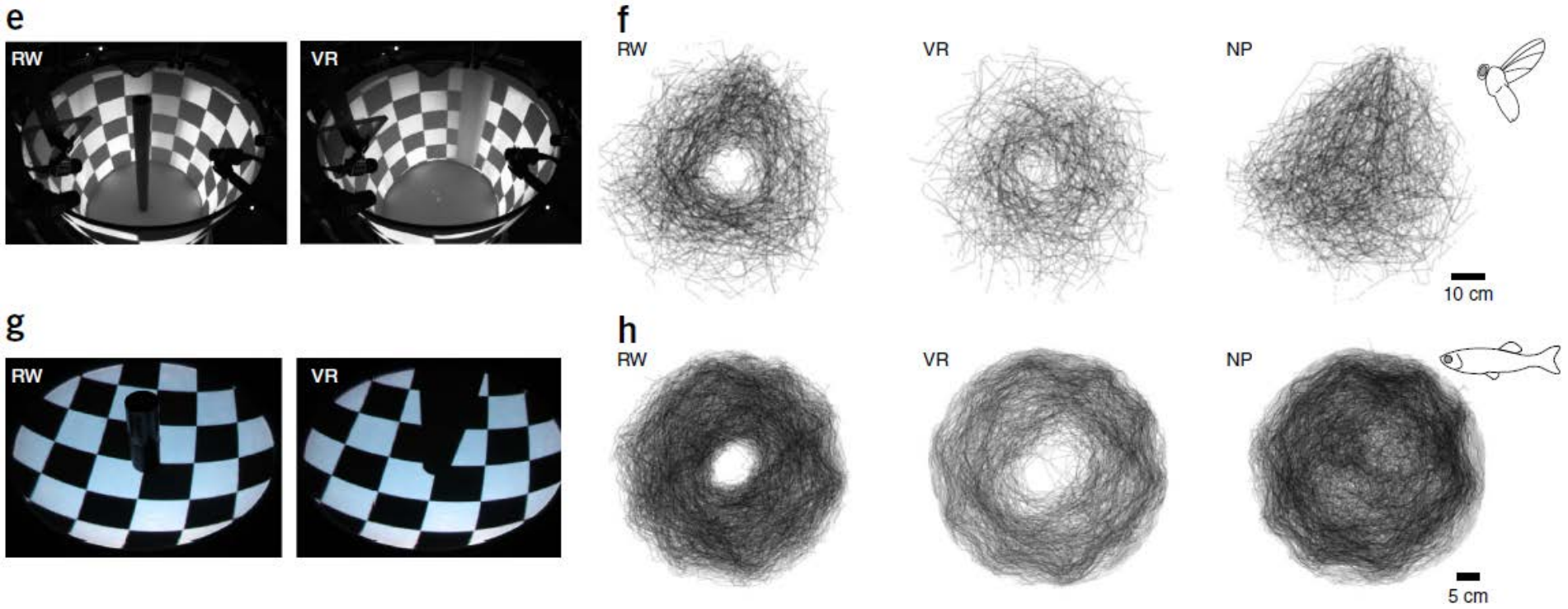
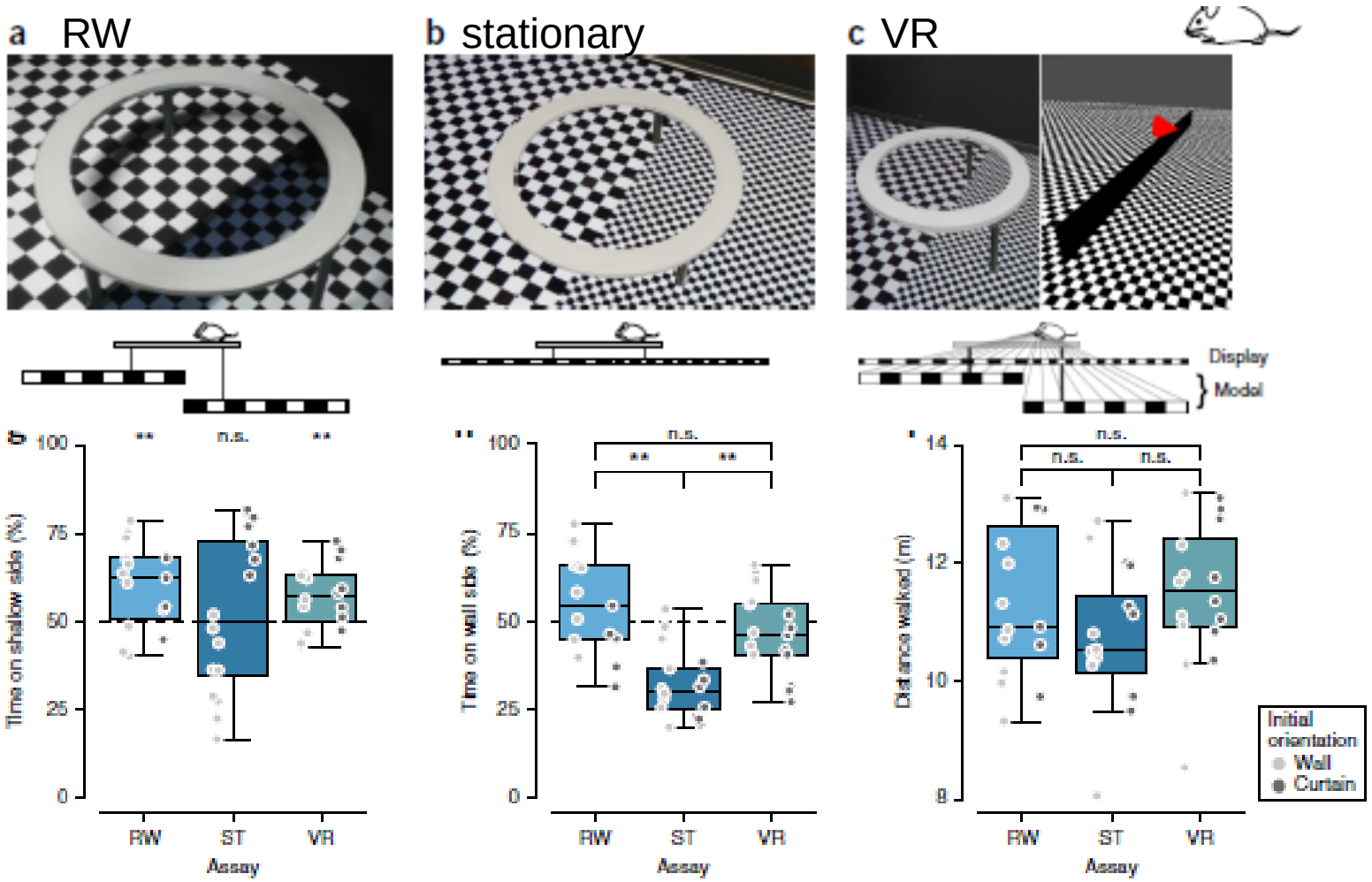
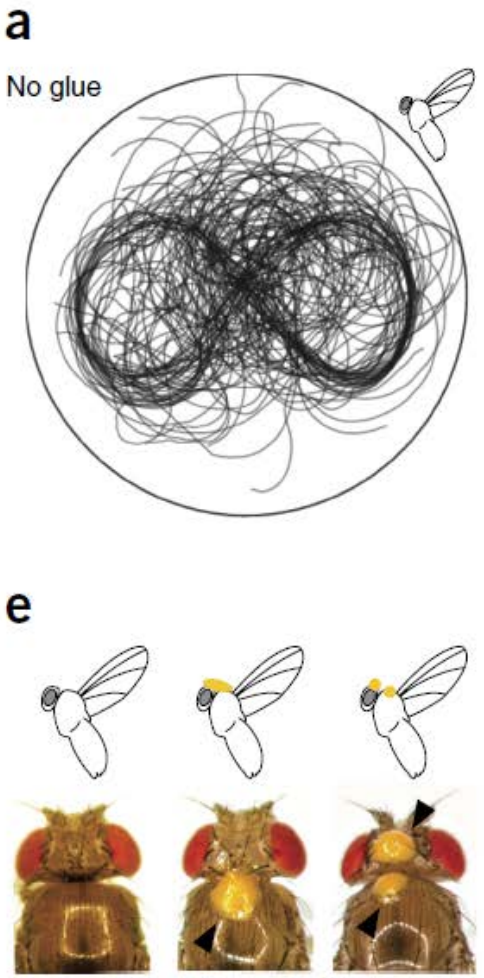


Validation

- Height aversion (mice)



Head immobilization



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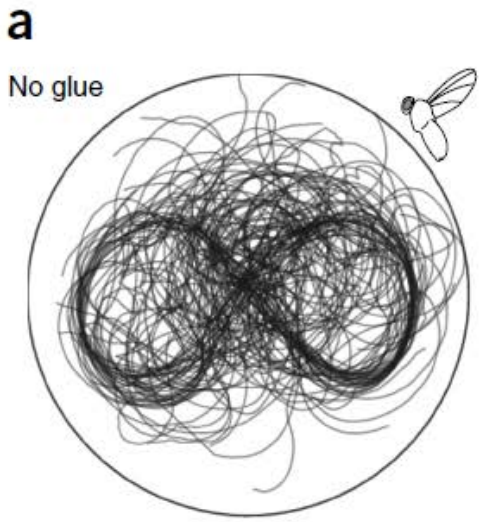

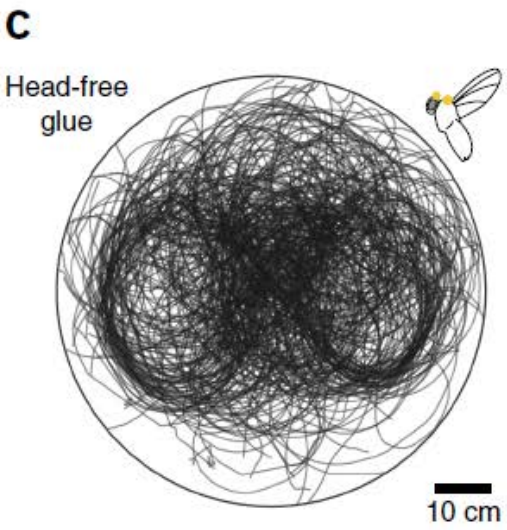

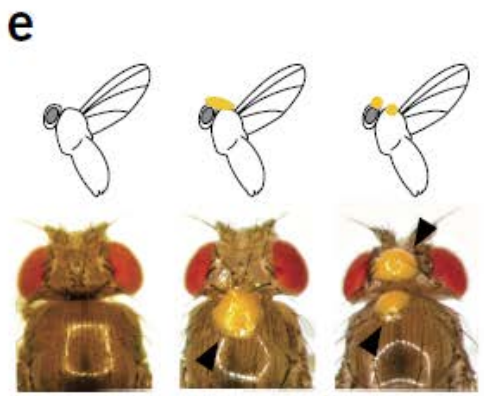

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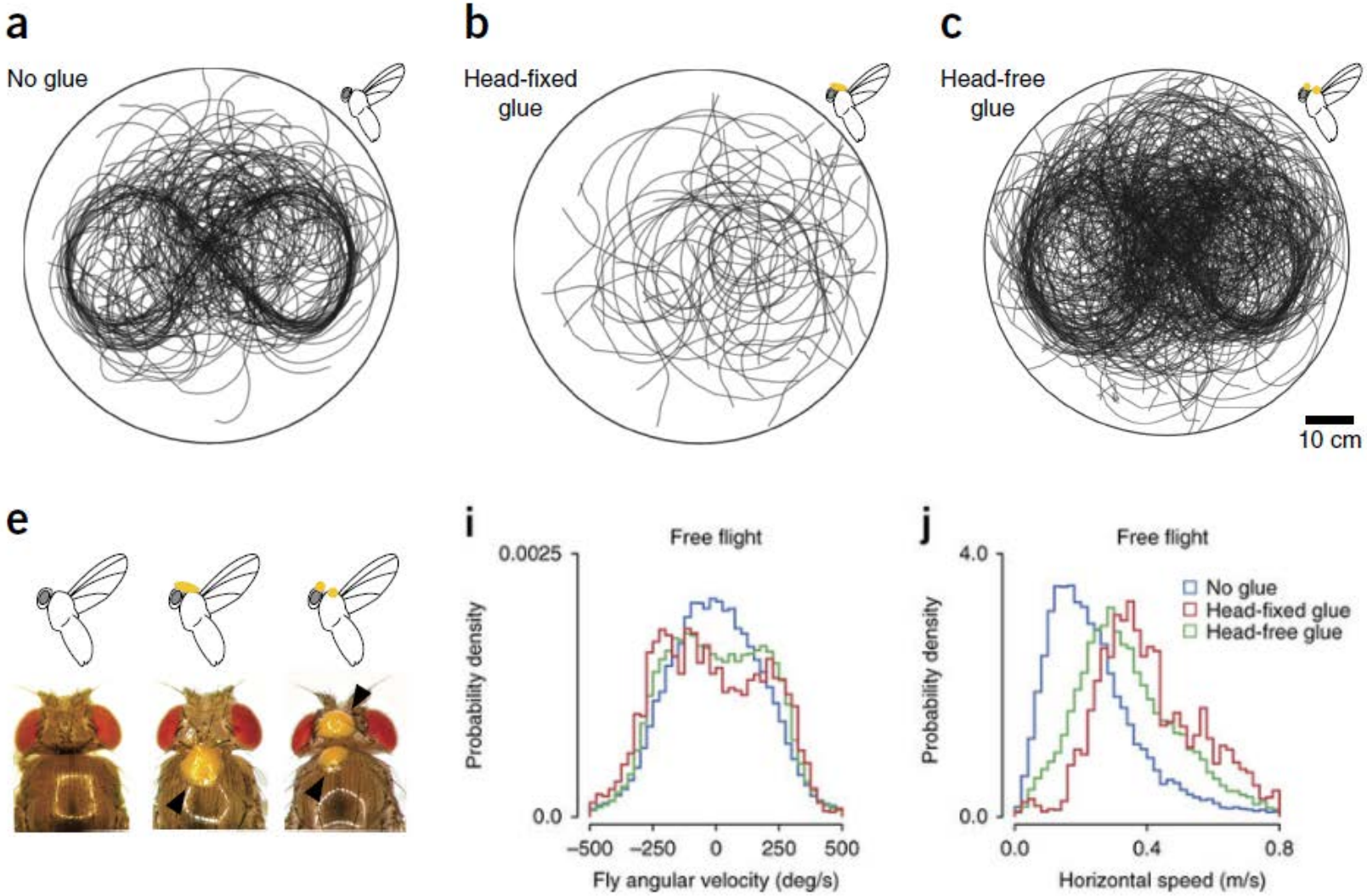
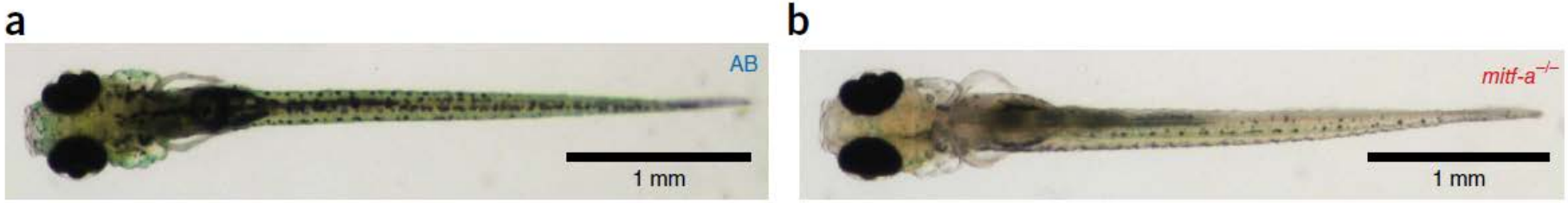


FreemoVR enables novel experimental designs…

- Subtle visuomotor deficit in *mitf-a* mutant zebrafish



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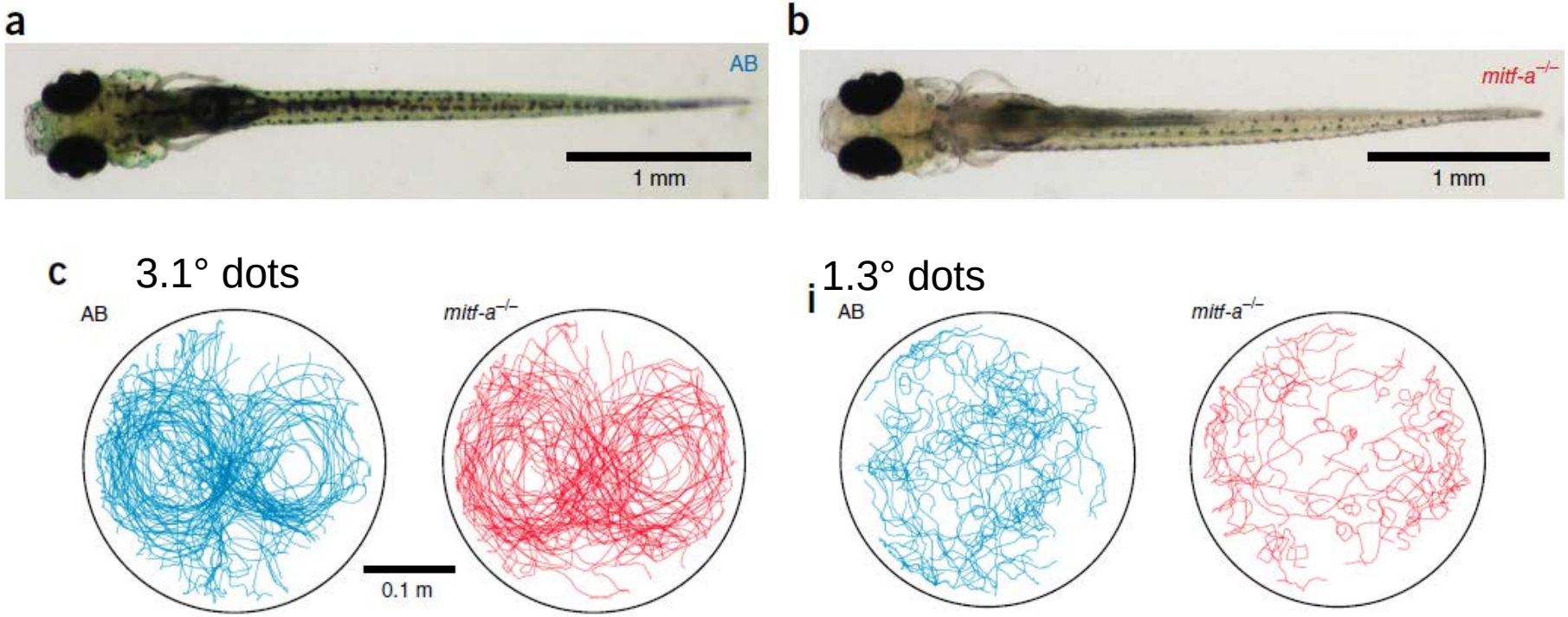

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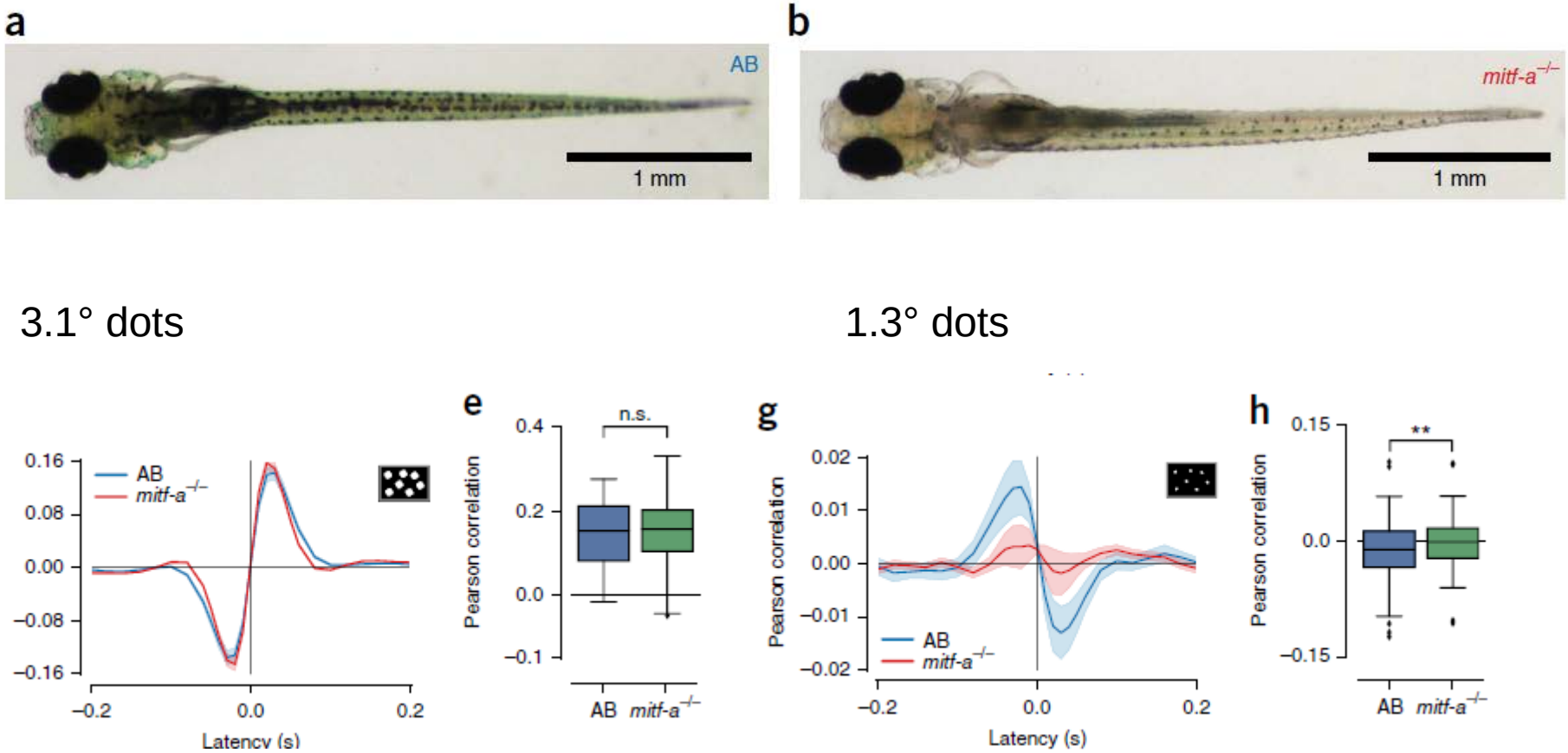
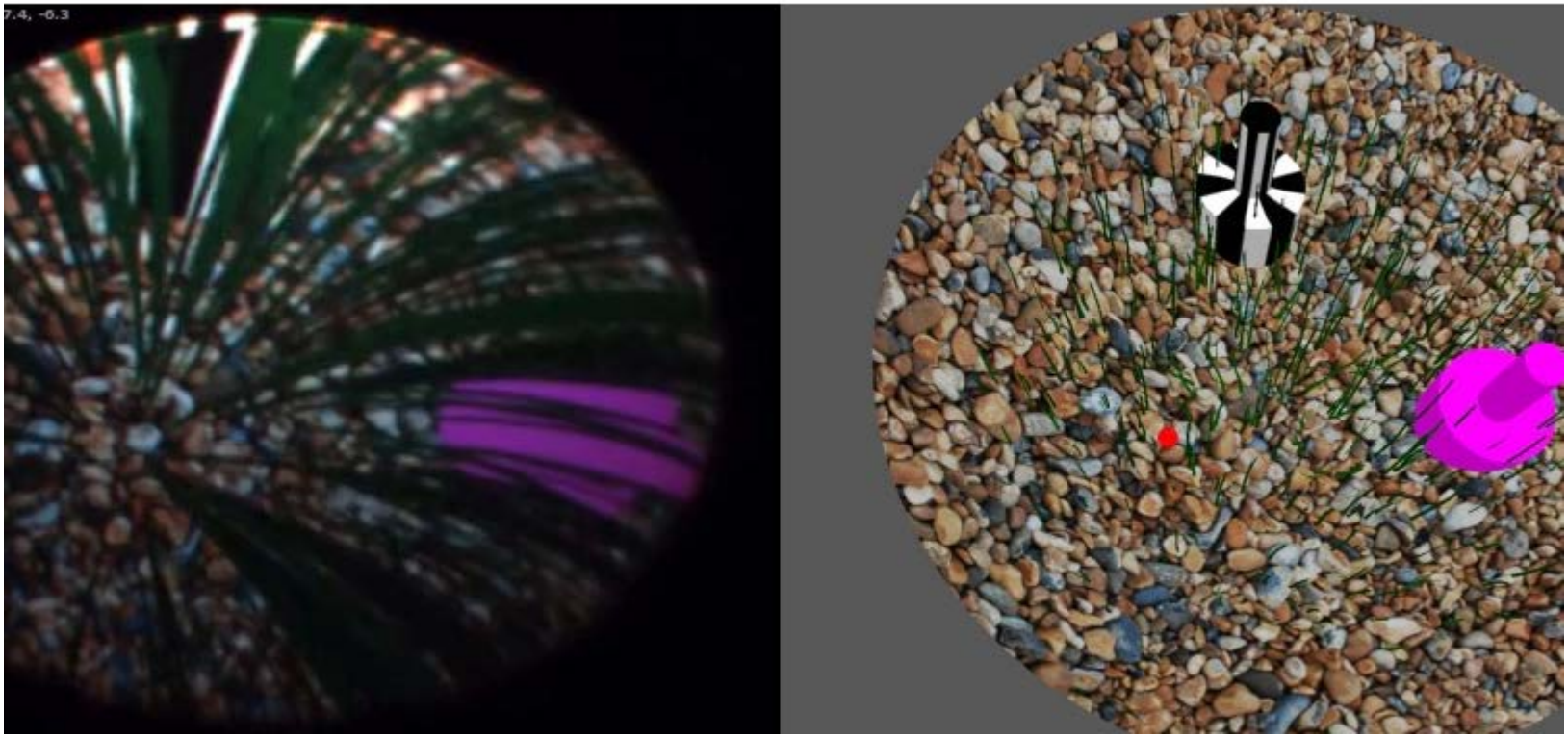


- VR system can discover even small deviations from WT behavior in freely moving animals

- Virtual teleportation: decision-making assay for fish
  - Checkerboard or plant world?



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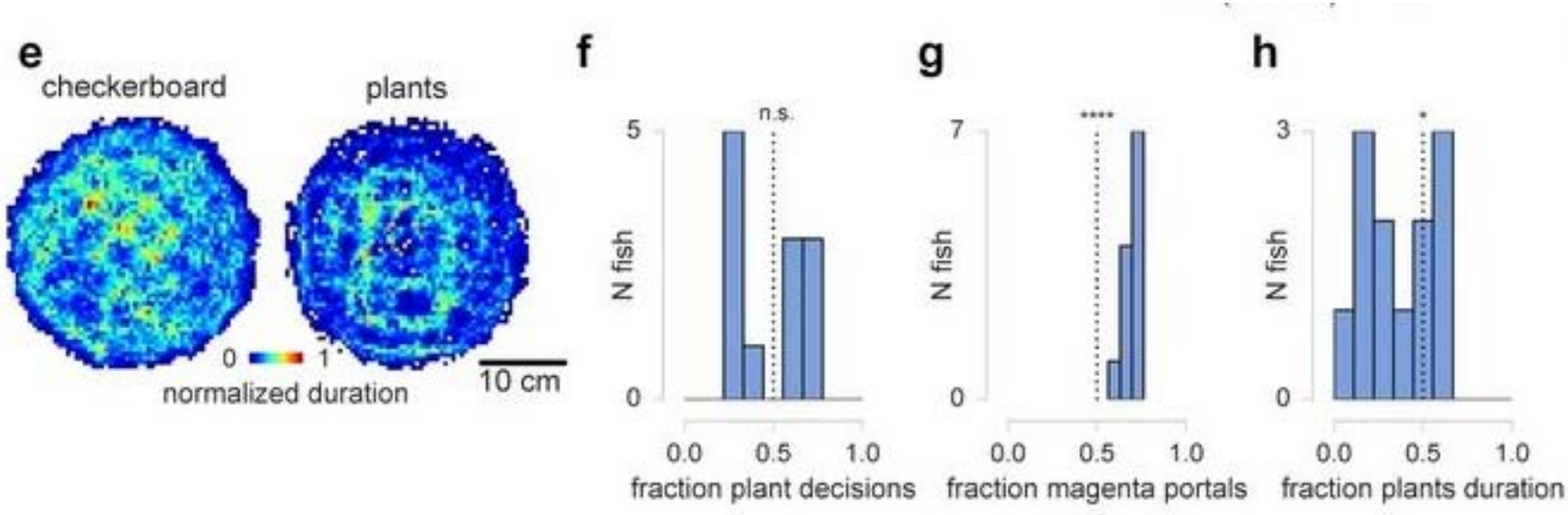

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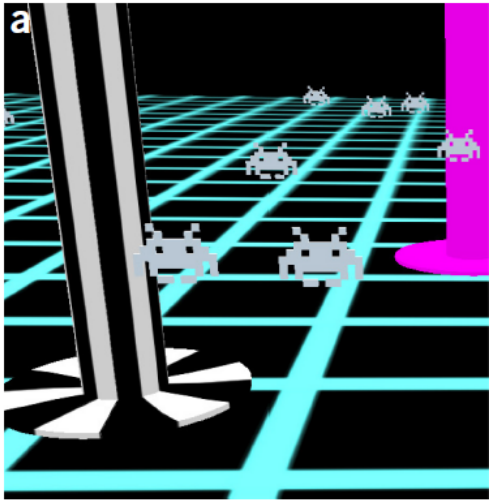
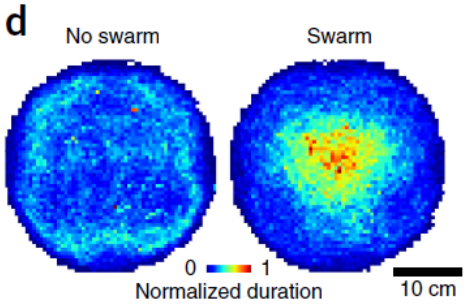
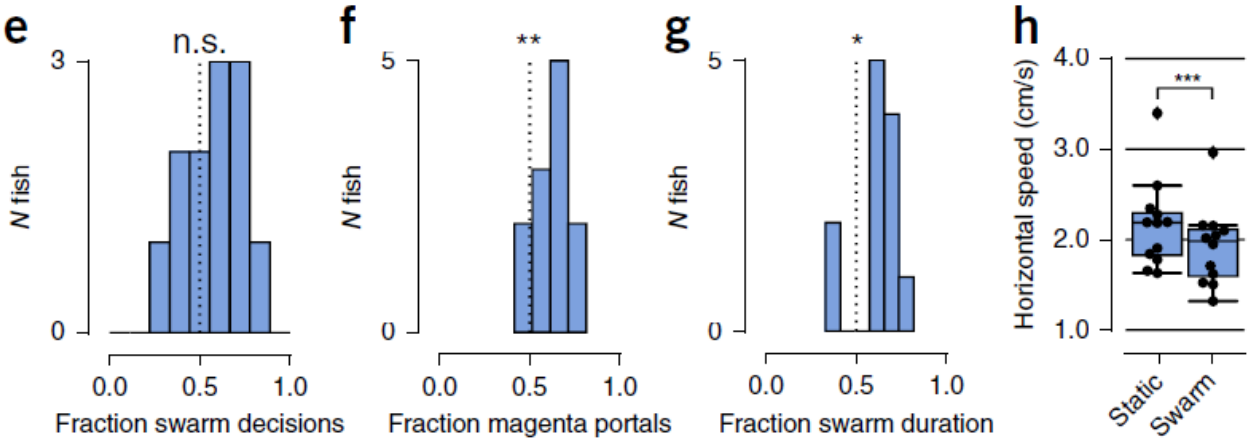
  - Virtual swarm (space invadors)







- Virtual teleportation: decision-making assay for fish
  - Checkerboard or plant world?
  - Virtual swarm (space invadors)

  - Scene specific swimming speeds
  - Preference for portal appearance
  - Occupancy differences
  - No learning

- Social responsiveness
  - Virtual swarm: personal vs. social information in movement decisions

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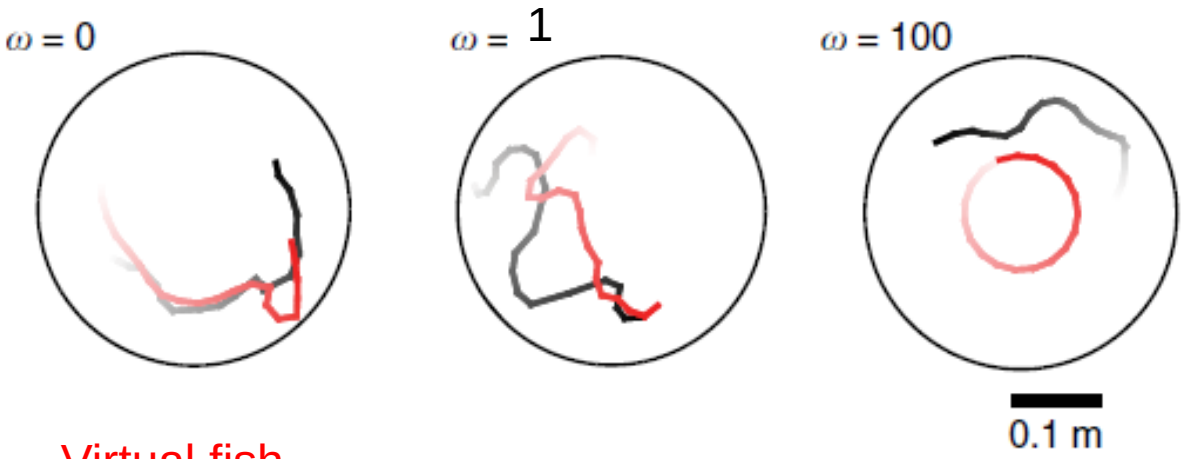

Virtual fish

Real fish

Advantages and limitations

- Setting to allow naturalistic behaviors
- Closed-loop
- Study of
  - Visual processing
  - Spatial navigation + cognition (i.e. Acharya 2016, Chen 2013)
  - Spatial learning and memory (water maze)
  - (multimodal) sensory integration
  - (Social) interactions, collective behaviour

- Restraint

- Stimulus repertoire limited
- No stereovision
- Only single animals
- no eye position tracking or angular orientation
- Animals with certain visual requirements
- Time lag – what is realistic for animals?
- Limit the movement of the animal in VR

Current Zoology, Thurley, 2016

Thank you!