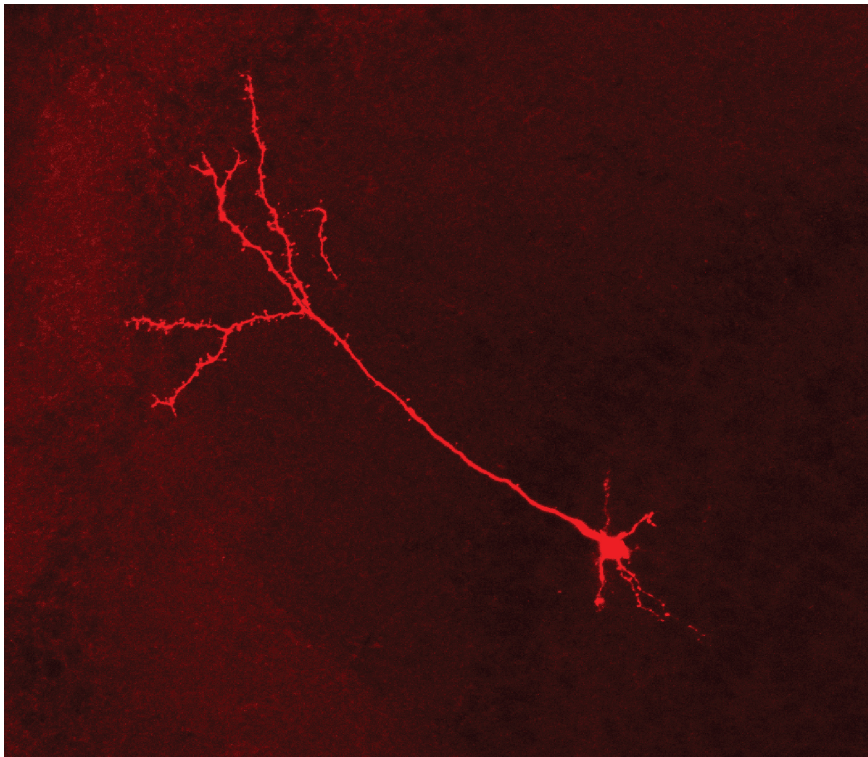


# 'Top-down'- and neuromodulatory influences on granule cell activity



Stephen Shea, PhD  
Cold Spring Harbor Laboratory

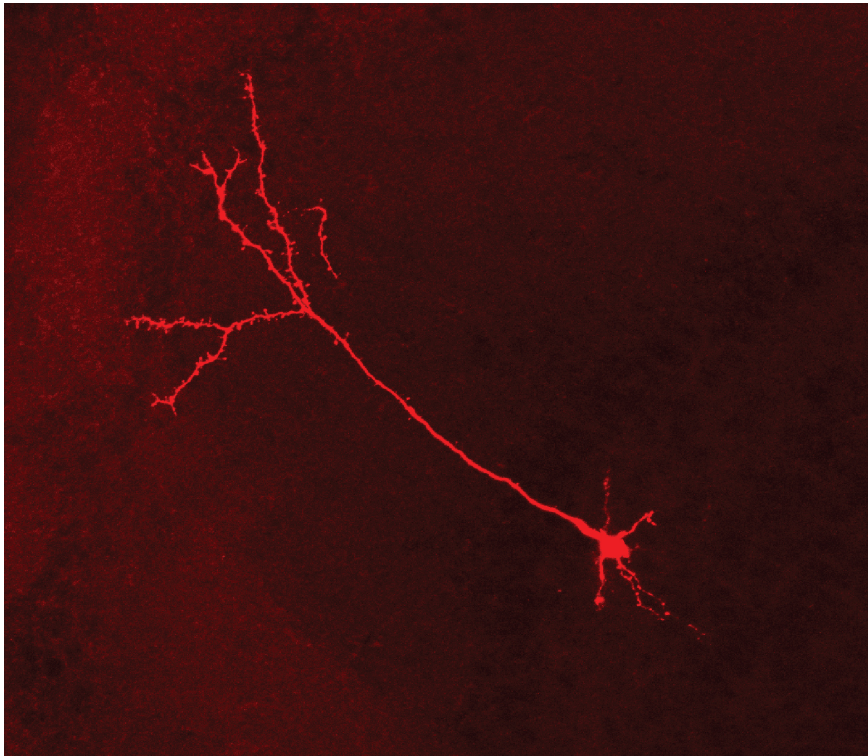


KITP Smell Meeting  
July 6<sup>th</sup> - 10<sup>th</sup> 2015

# 'Top-down'- and neuromodulatory influences on granule cell activity (cf. Schaefer, 2 h ago)



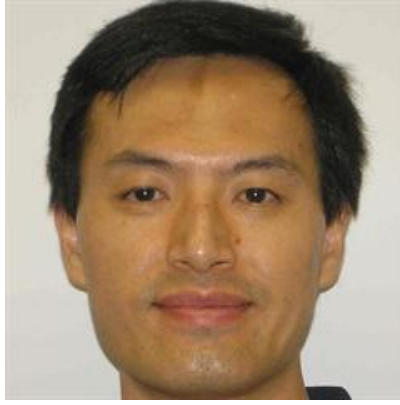
Stephen Shea, PhD  
Cold Spring Harbor Laboratory



KITP Smell Meeting  
July 6<sup>th</sup> - 10<sup>th</sup> 2015



Kerensa Crump  
undergraduate



Billy Lau  
postdoc



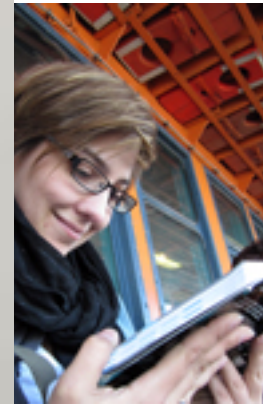
Brittany Cazakoff  
grad student



Heike Demmer  
postdoc



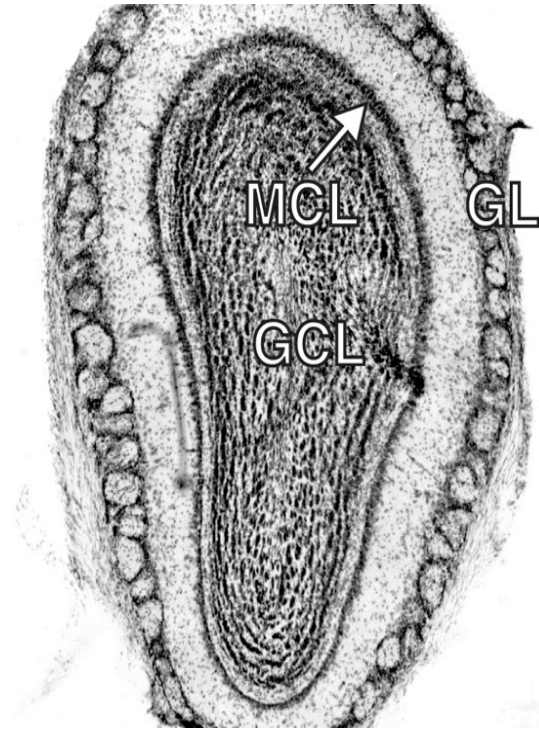
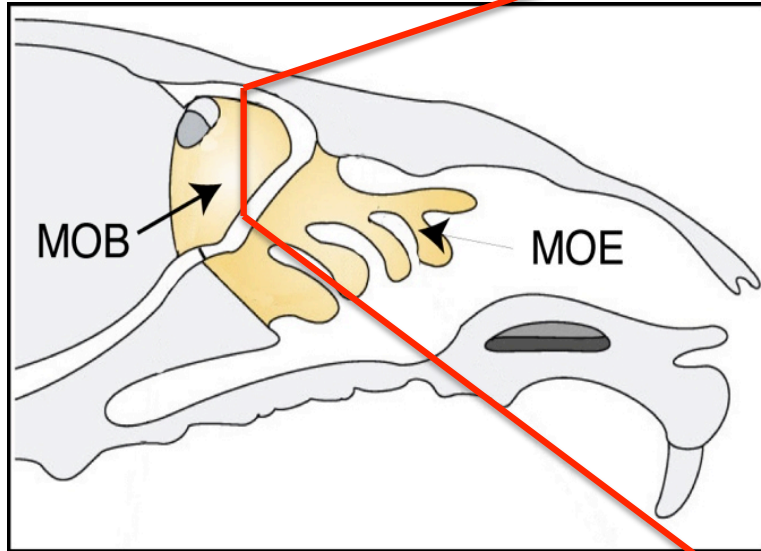
Kerensa Cruikshank  
undergraduate



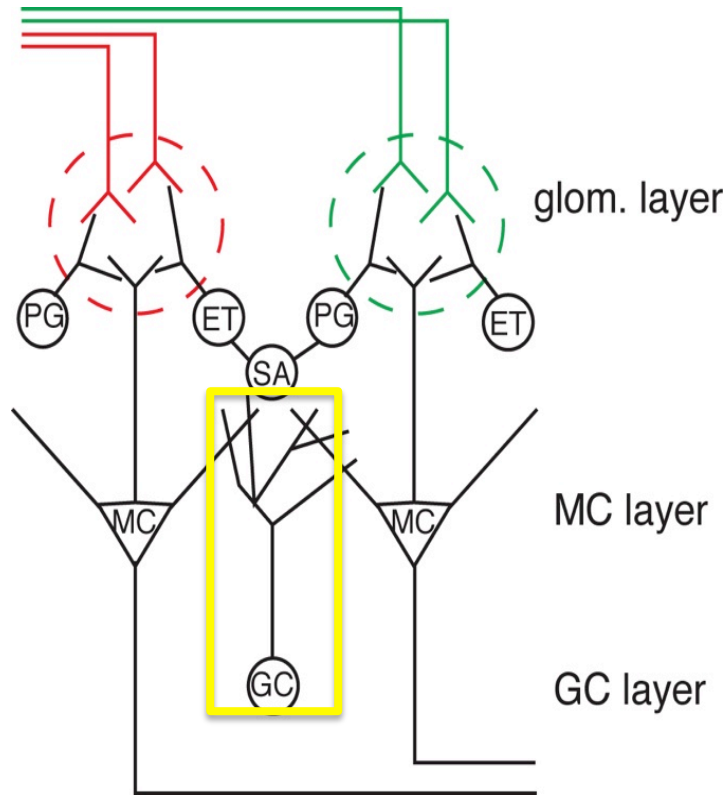
Mike Demmer  
postdoc



# Circuitry of the main olfactory bulb



# Circuitry of the main olfactory bulb



## Granule cells:

Major target of central feedback

Neurogenesis and learning

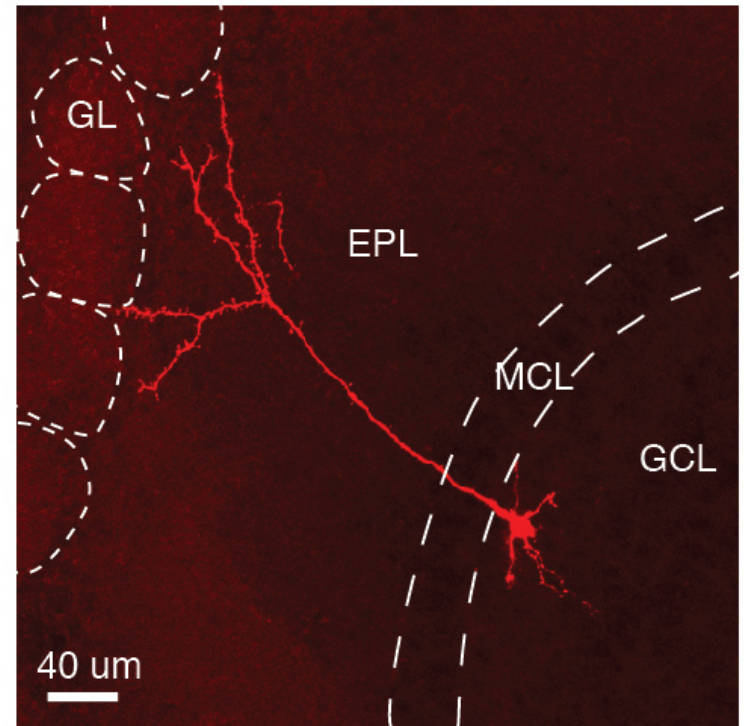
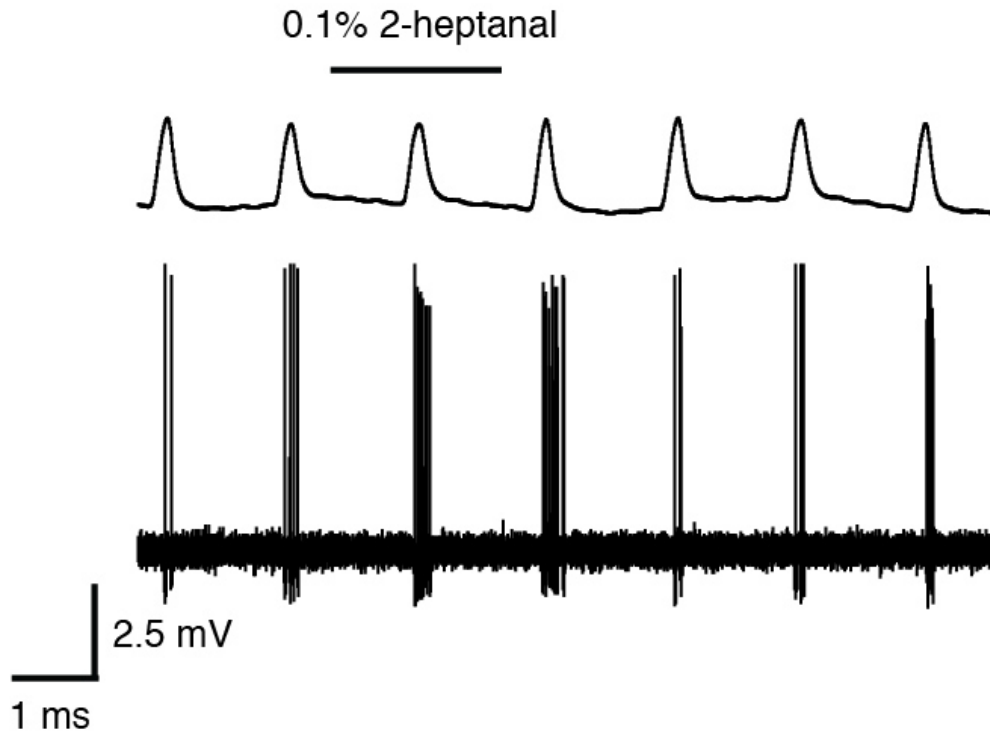
Gain of function leads to enhanced discrimination

Spatial control vs temporal control

State and odor meaning

Yet, no direct observation of their spiking activity during wakefulness or learning

# Recording and labeling granule cells



# Talk Outline

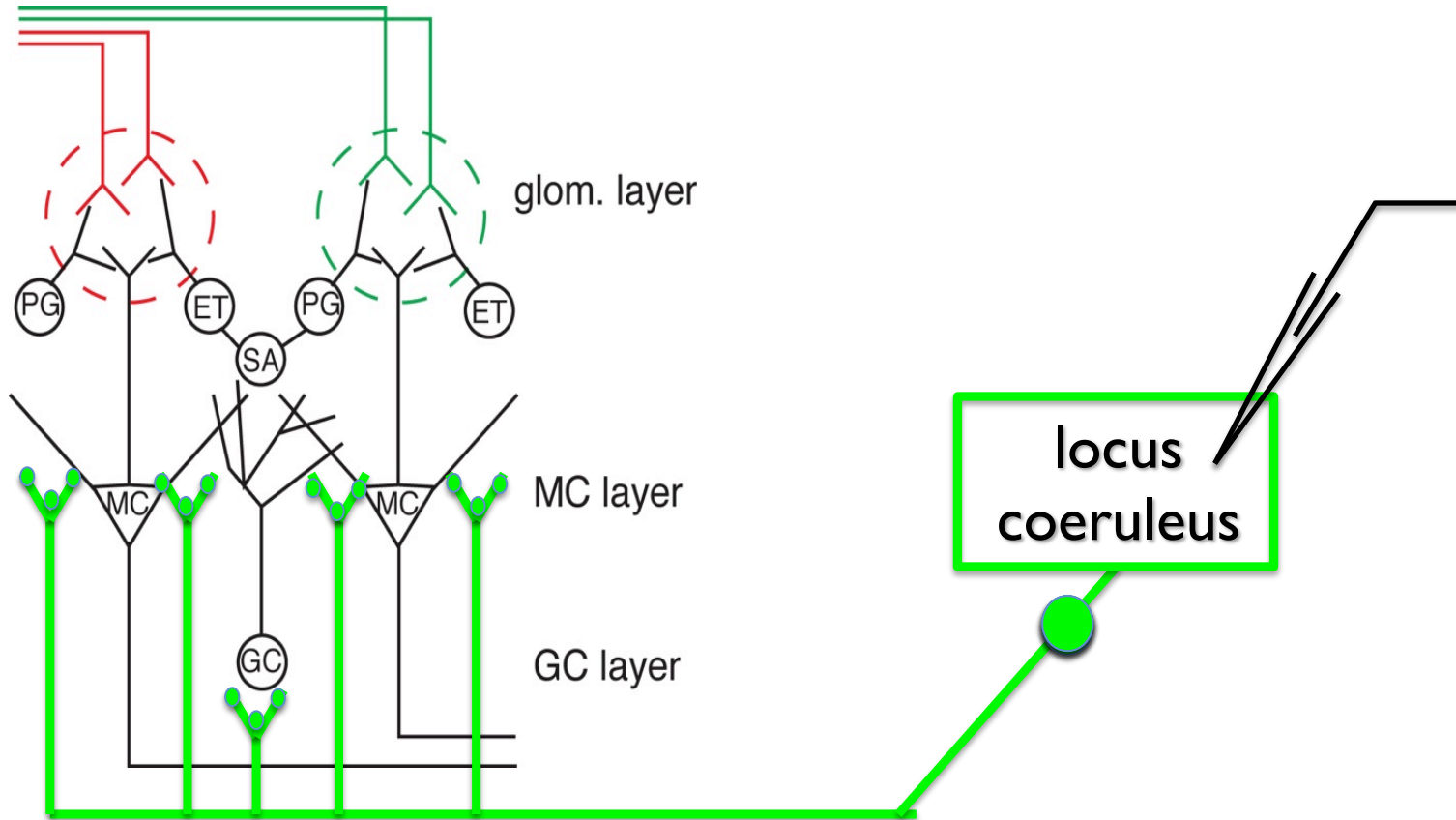
Part 1: Short-term and long-term noradrenergic control of GC activity

Part 2: State-dependent GC activity in awake head-fixed mice

Part 3: Monitoring GC activity during rapid associative odor learning

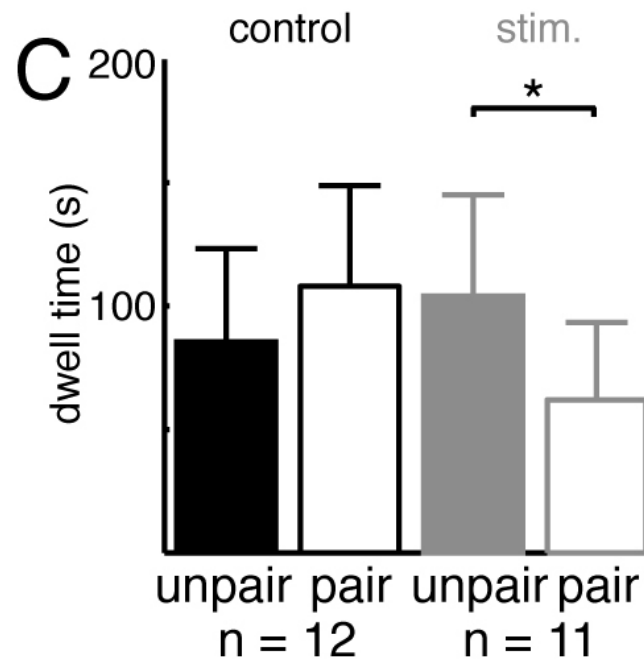
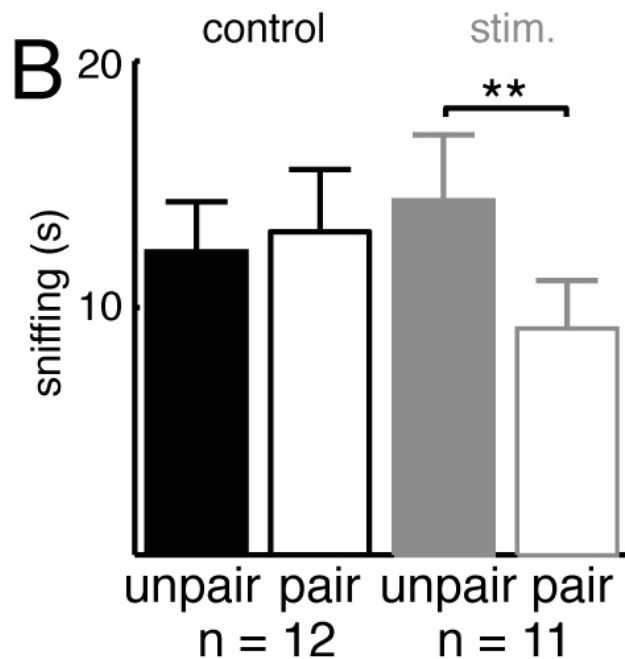
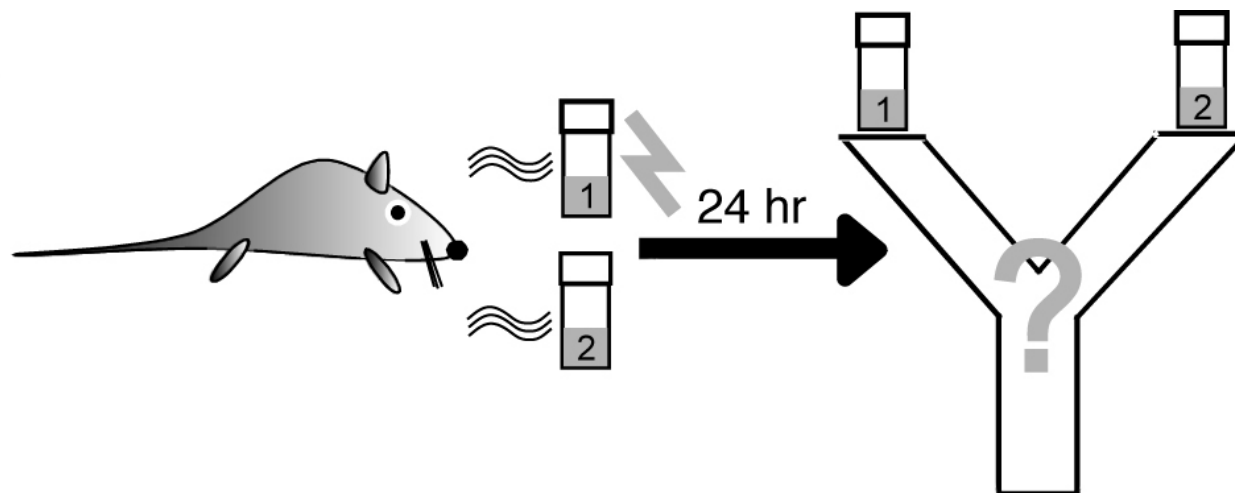


# Circuitry of the main olfactory bulb

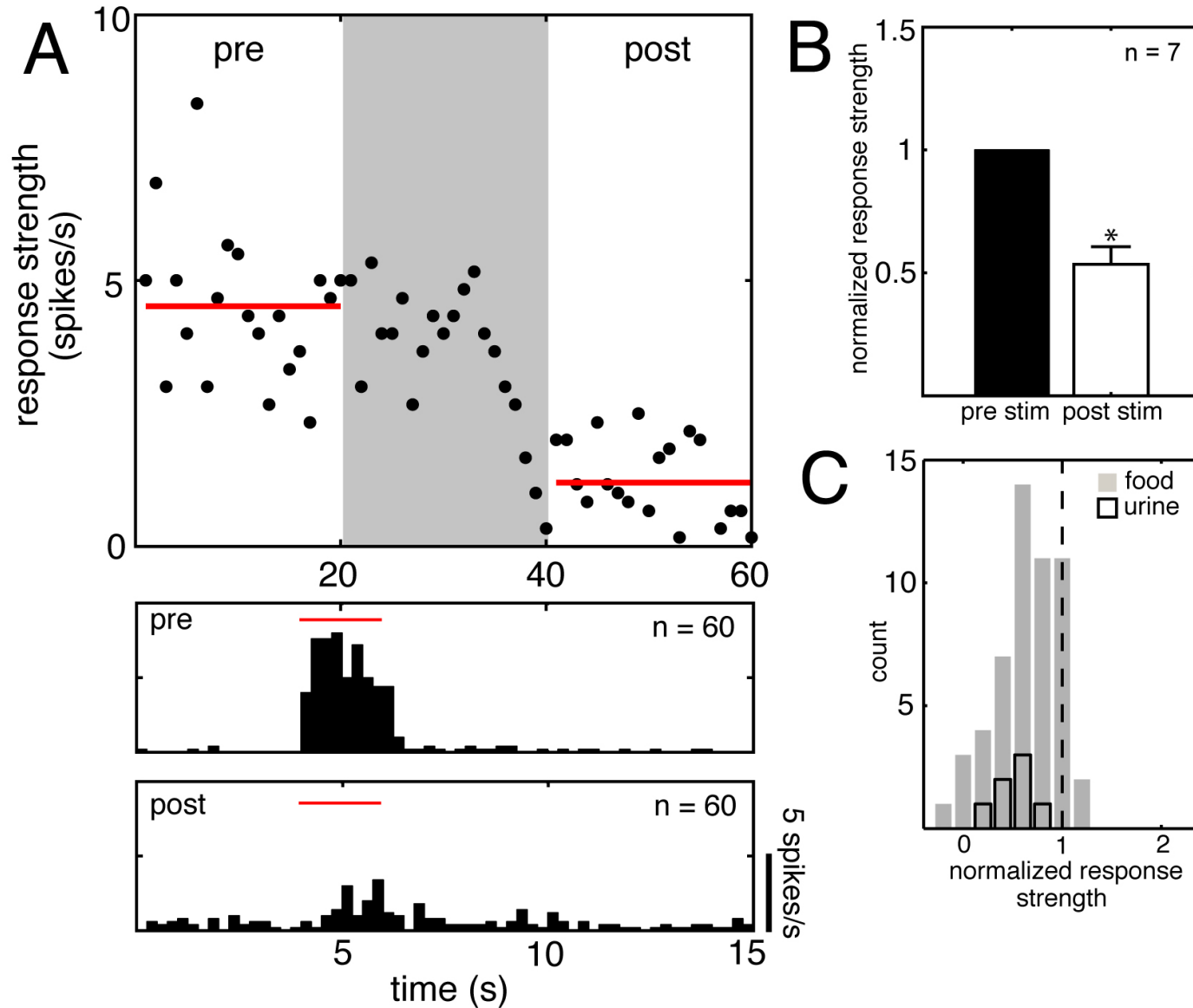


# Odors associated with LC stim are “remembered”

A



# LC stim suppresses odor responses to urine

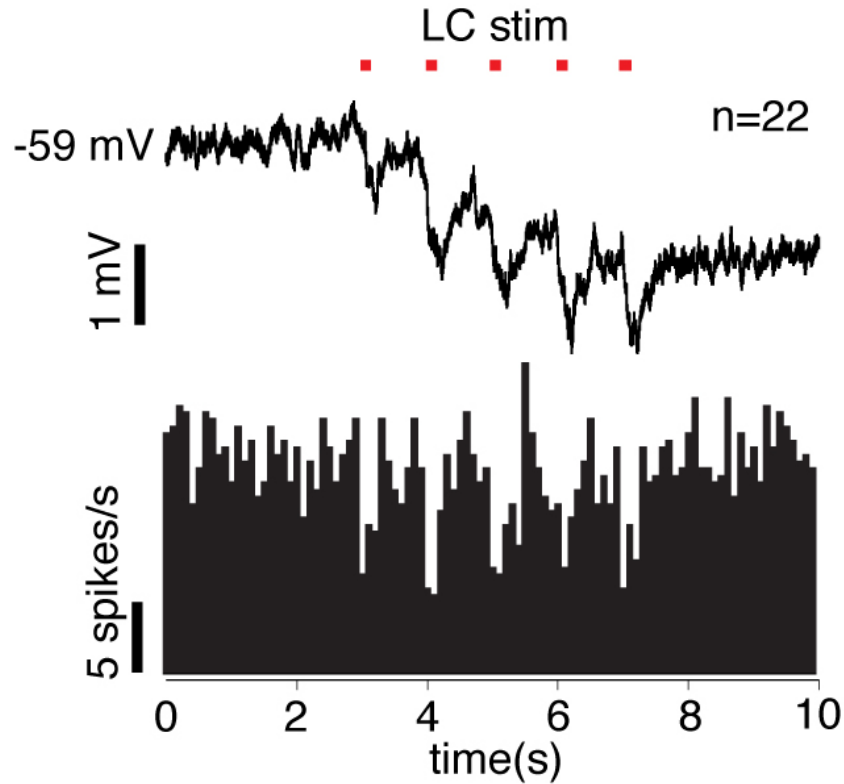


**Noradrenergic modulation:**

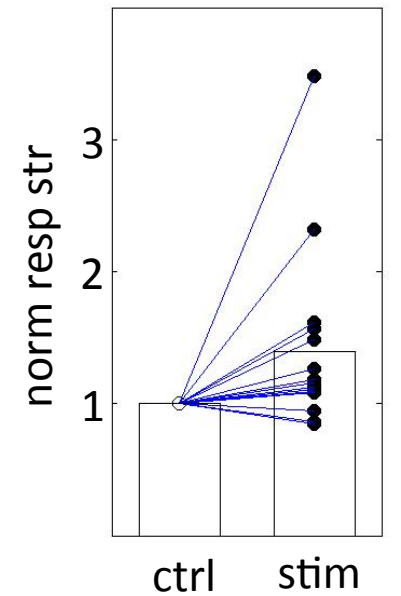
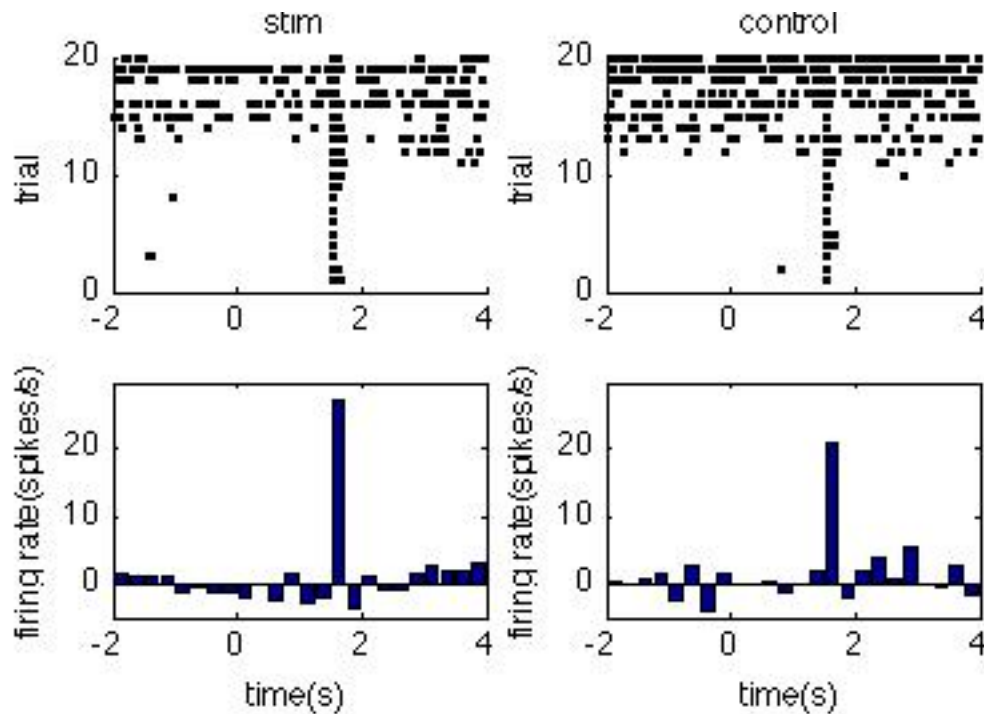
**Short-term vs long-term effects**



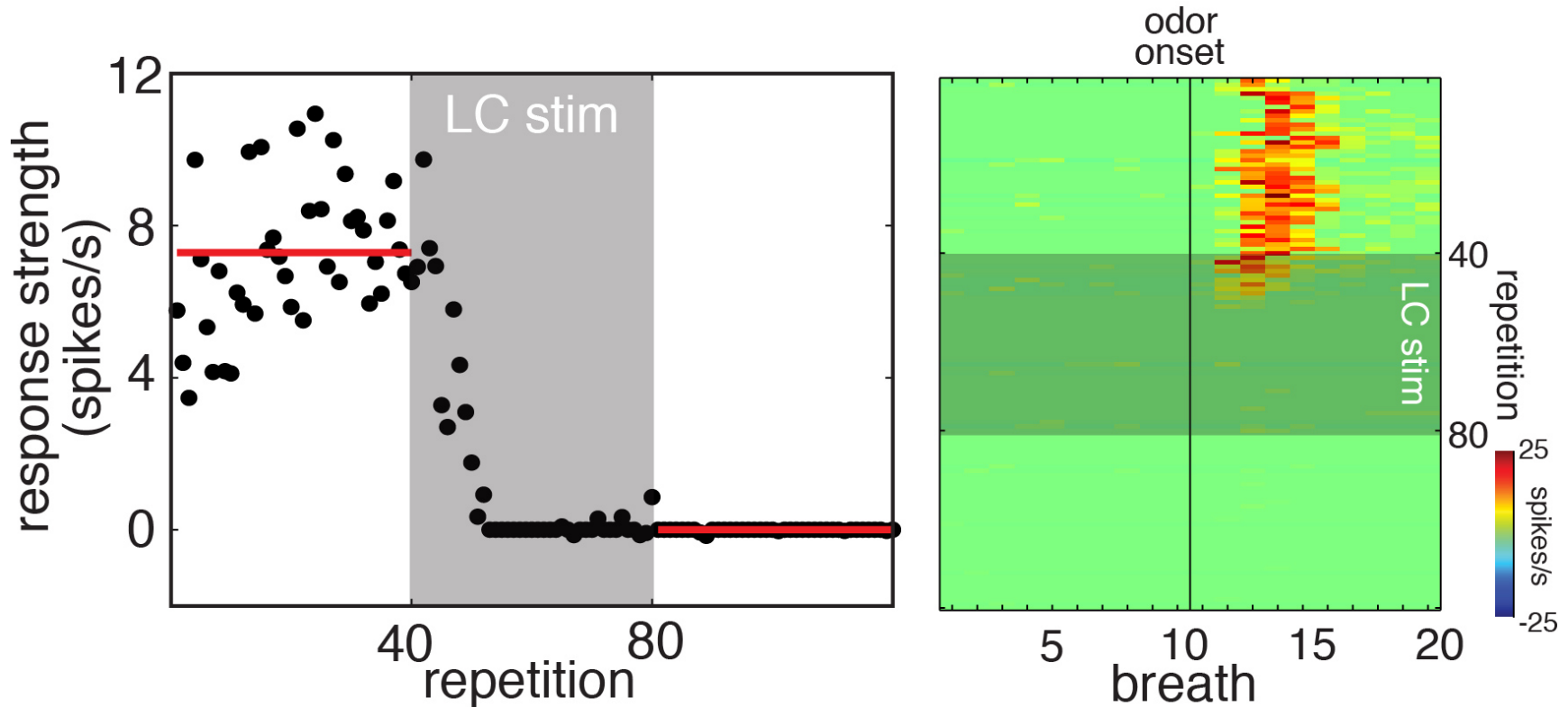
# LC stimulation acutely suppresses GC activity



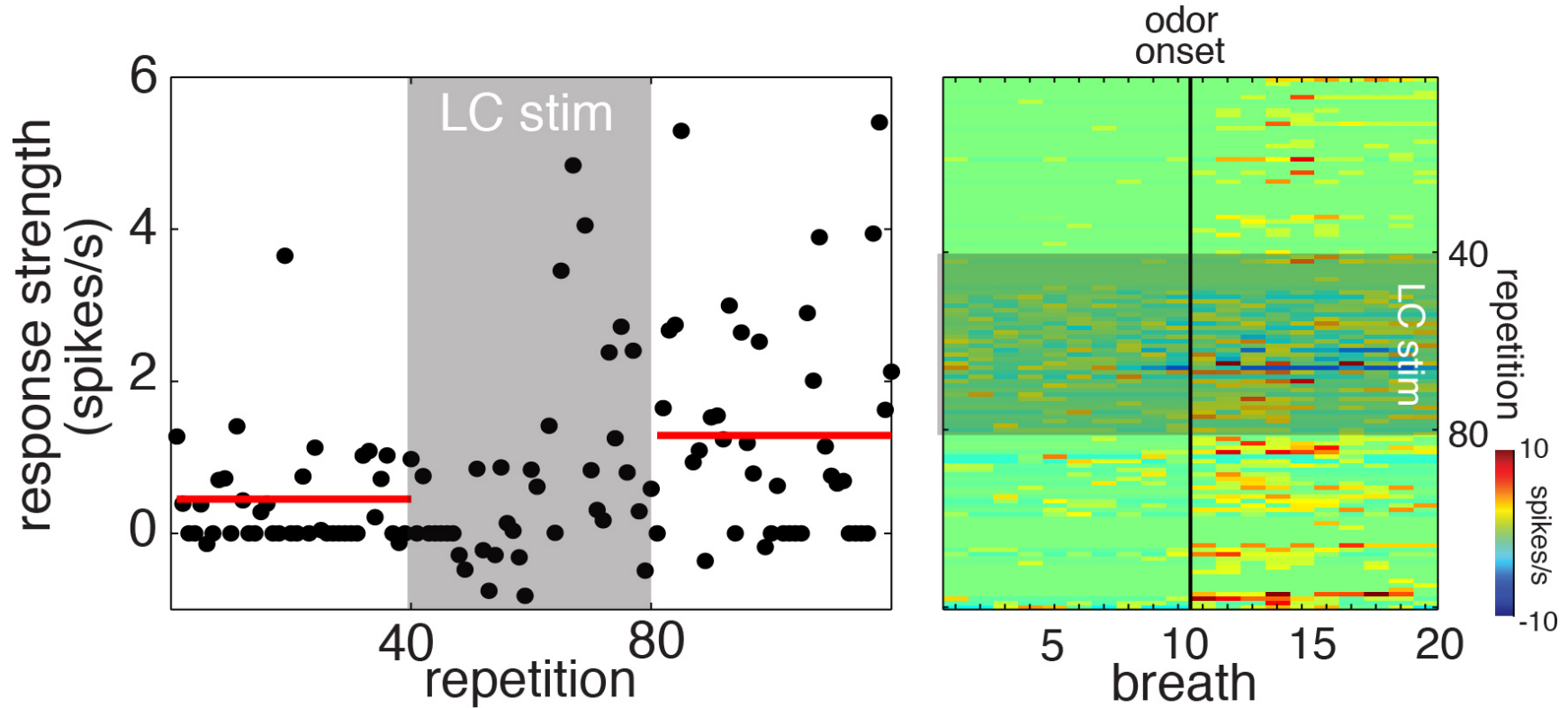
# LC stimulation disinhibits MC responses to sensory input



# LC stimulation modulates the response of granule cells to odors

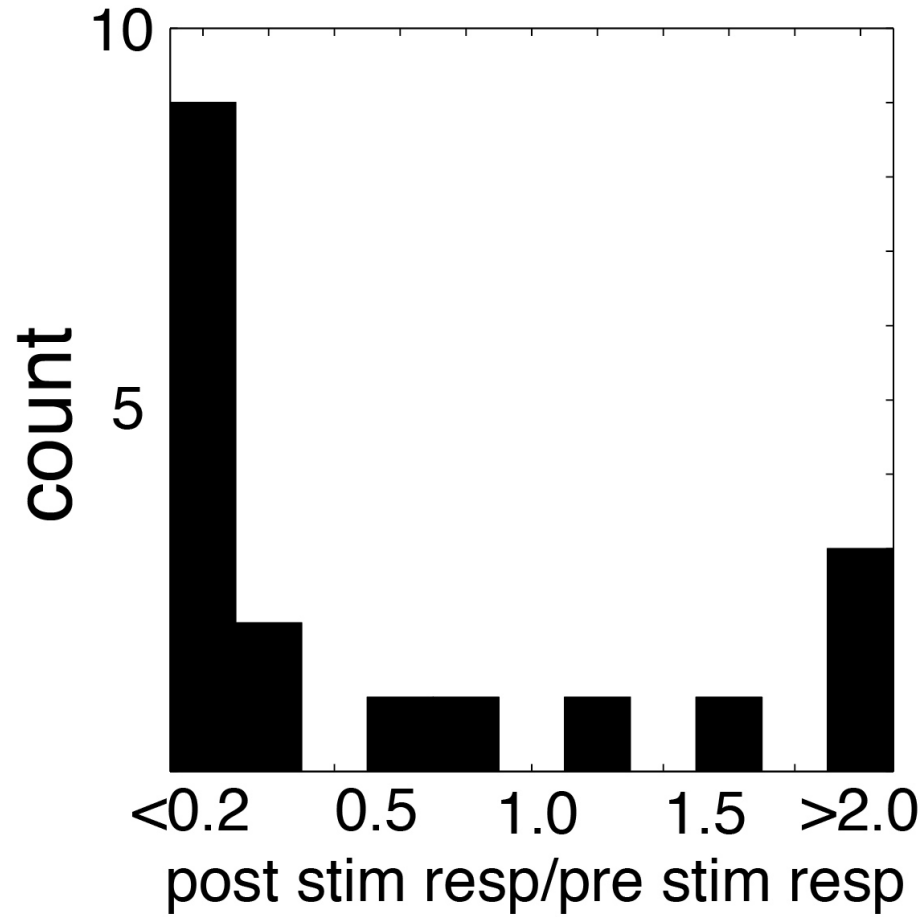


# LC stimulation modulates the response of granule cells to odors

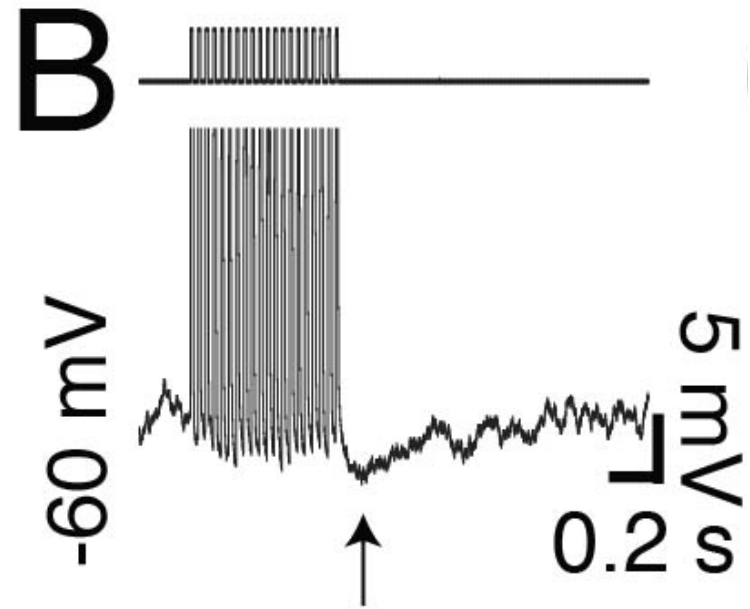
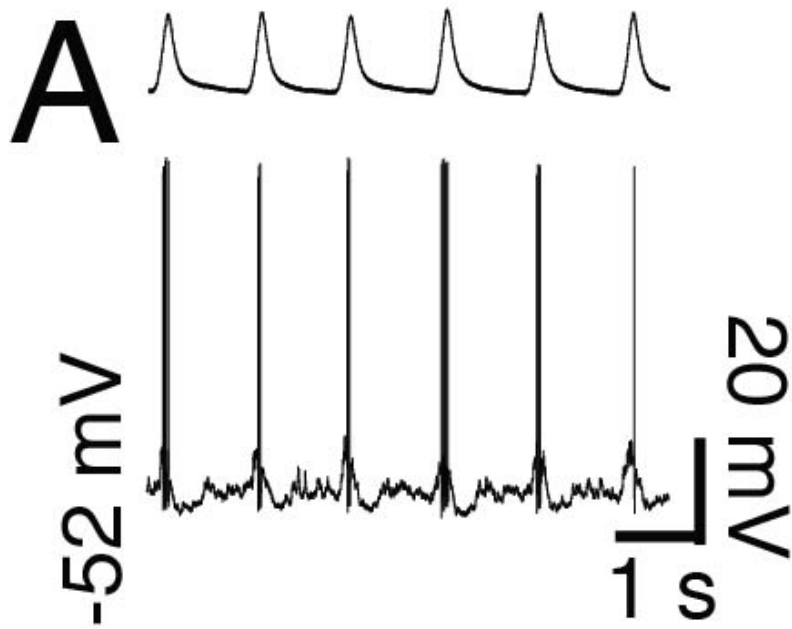




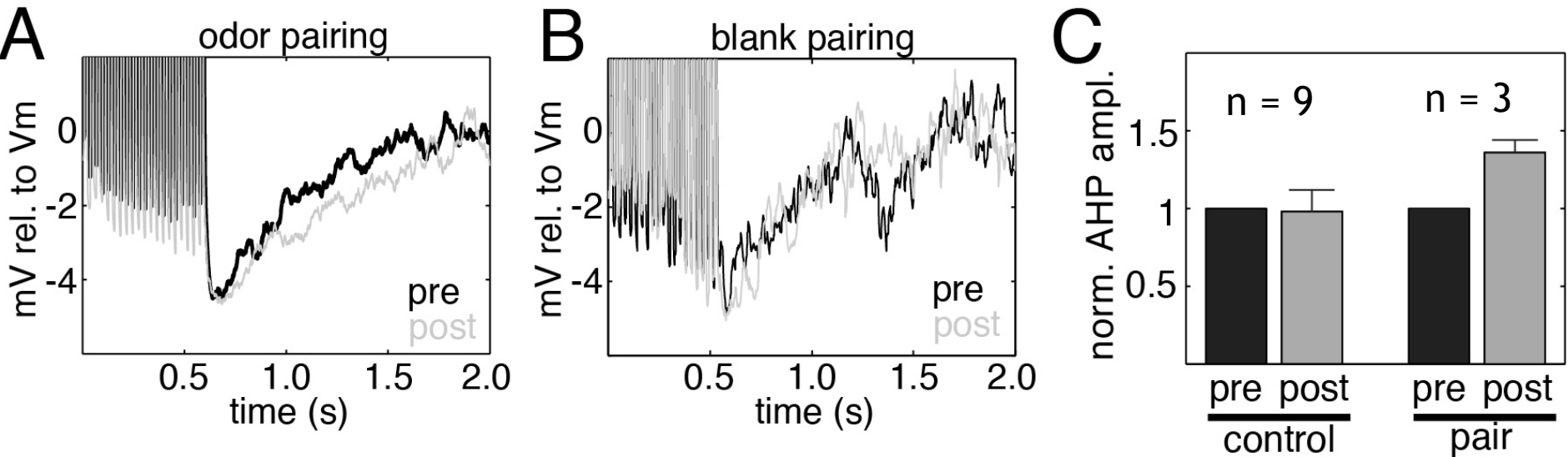
# LC stimulation sparsens GC representations



# Probing granule cell inhibition with *in vivo* whole cell recording



# Granule cell inhibition is specifically enhanced on MCs that are driven by an odor

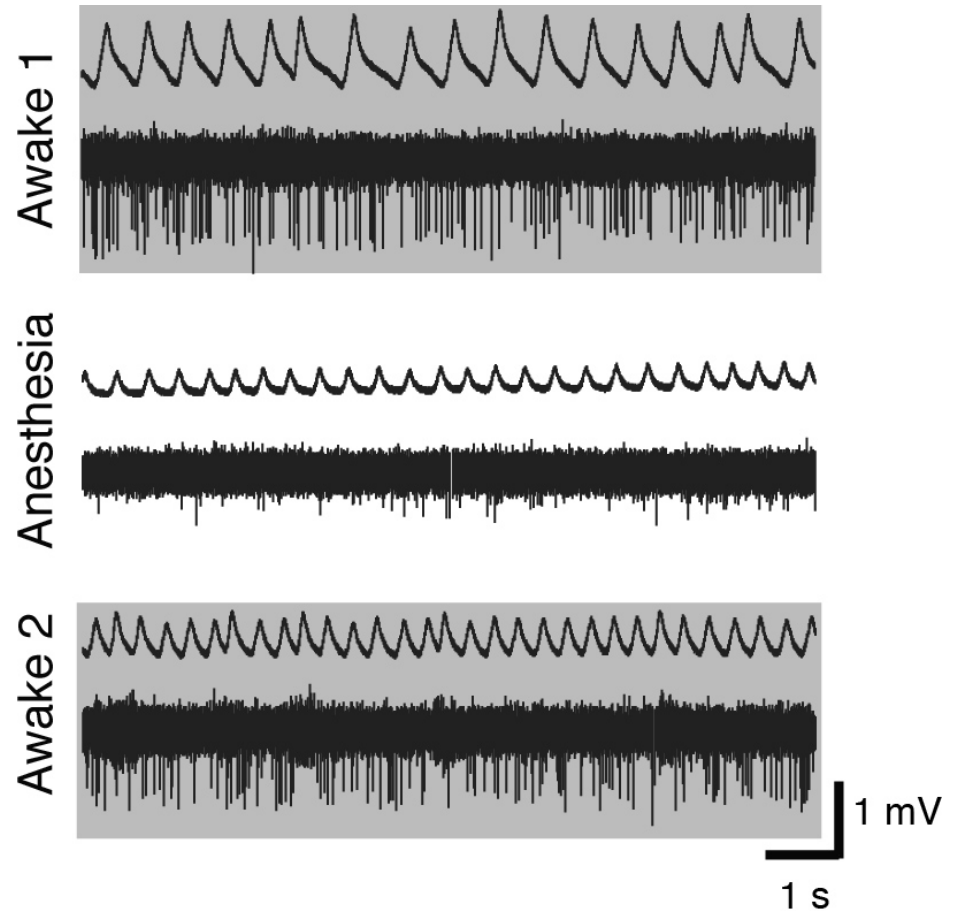
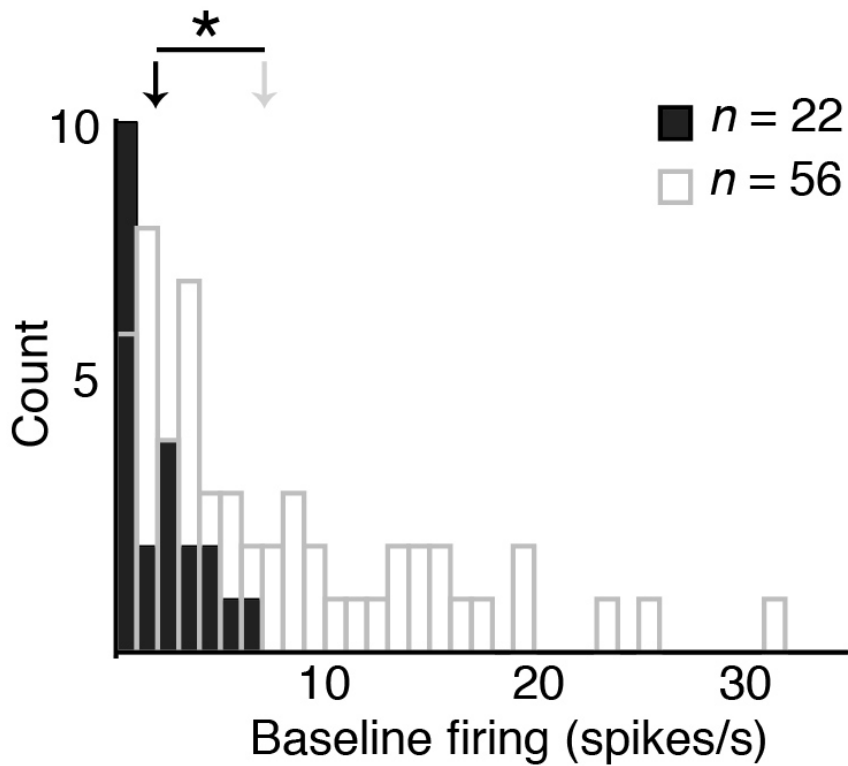


# Part I Conclusions

- Noradrenergic input from LC imprints memories through stimulus-specific habituation in the OB
- LC stimulation activates plasticity as early as the first synapse in the MOB
- A sparse population of GCs becomes activated to suppress specific MCs with amplified feedback inhibition



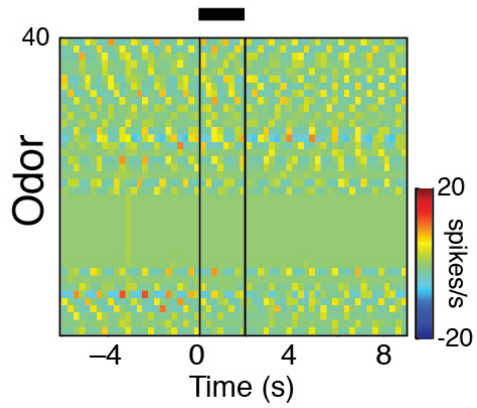
# Granule cell activity is state-dependent



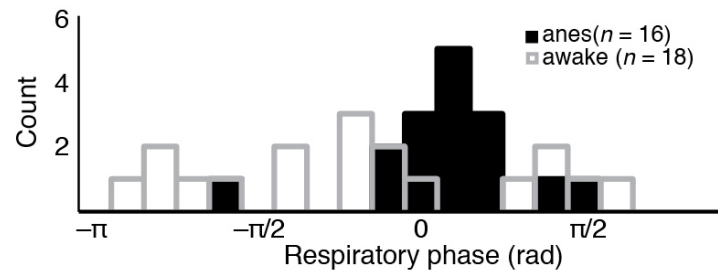
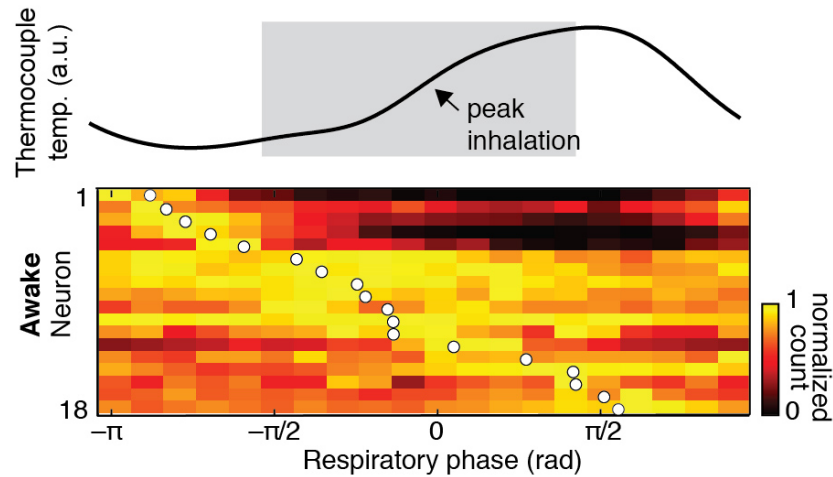
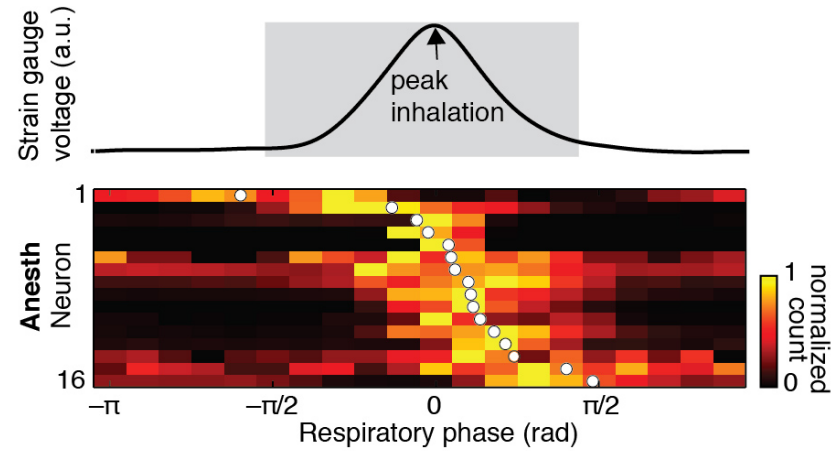
# GC responses are much stronger in awake mice

anesthetized

awake

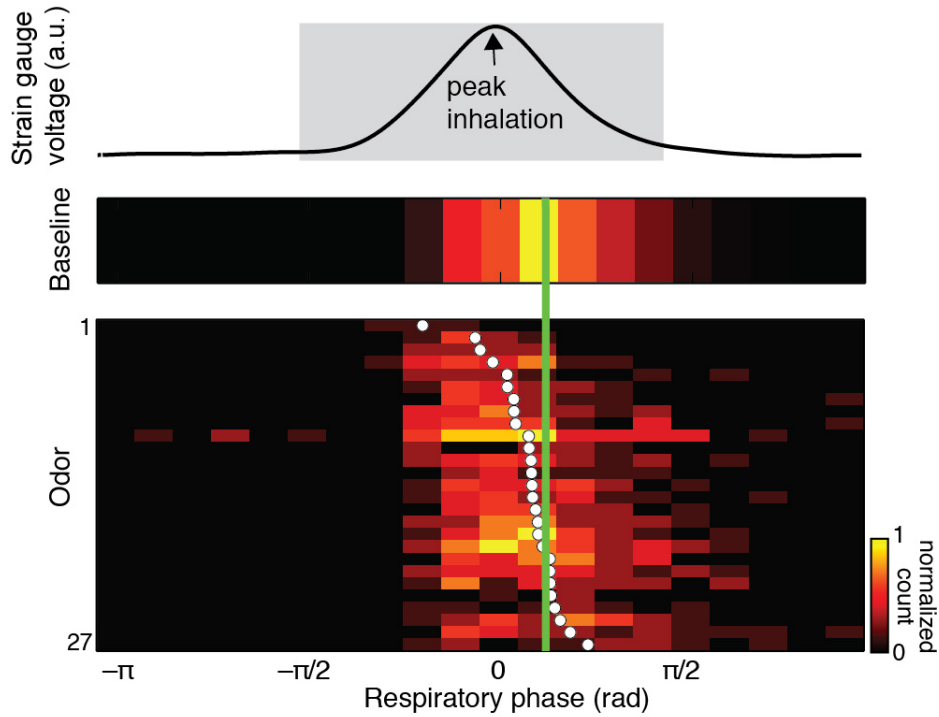


# GC activity uncouples from breathing in awake mice

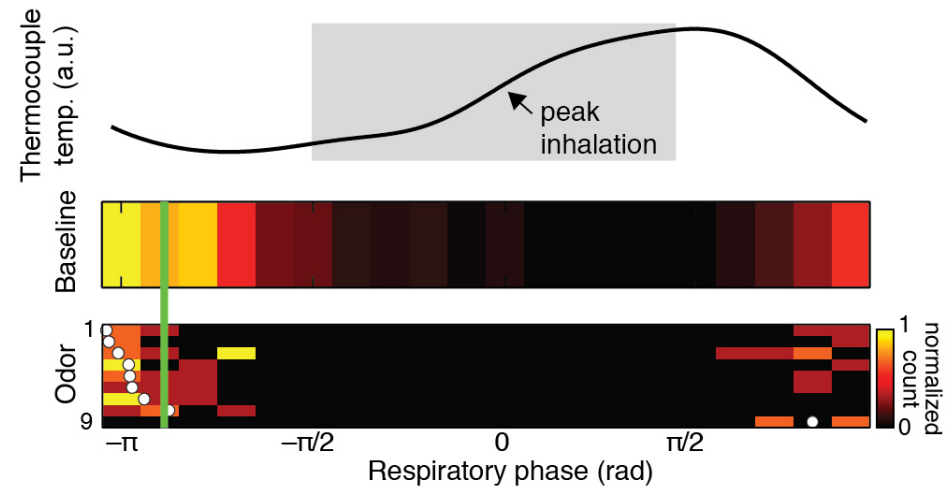


# Breath-coupled GC activity is unchanged by odors

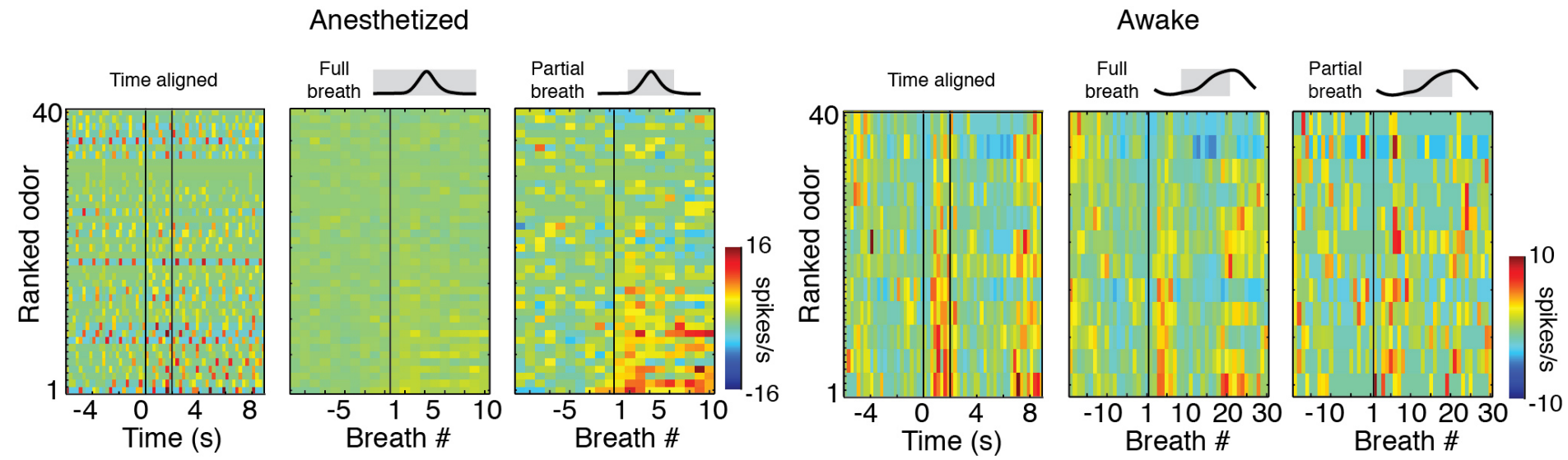
Anesthetized



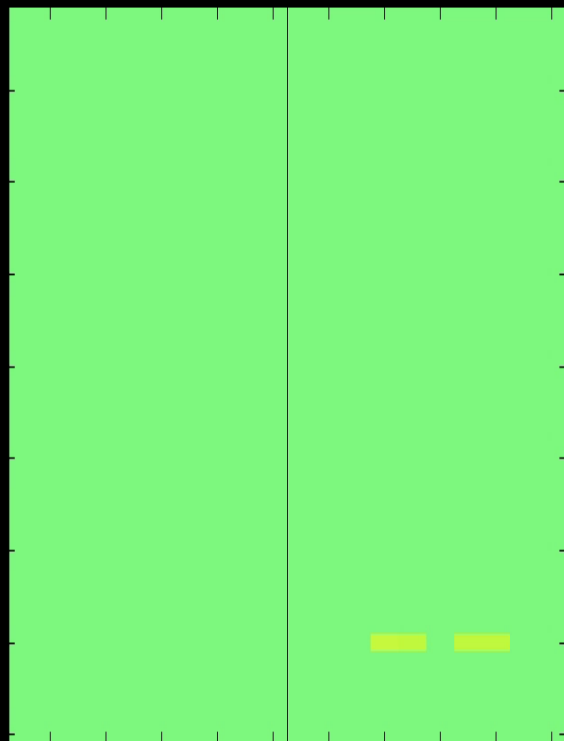
Awake



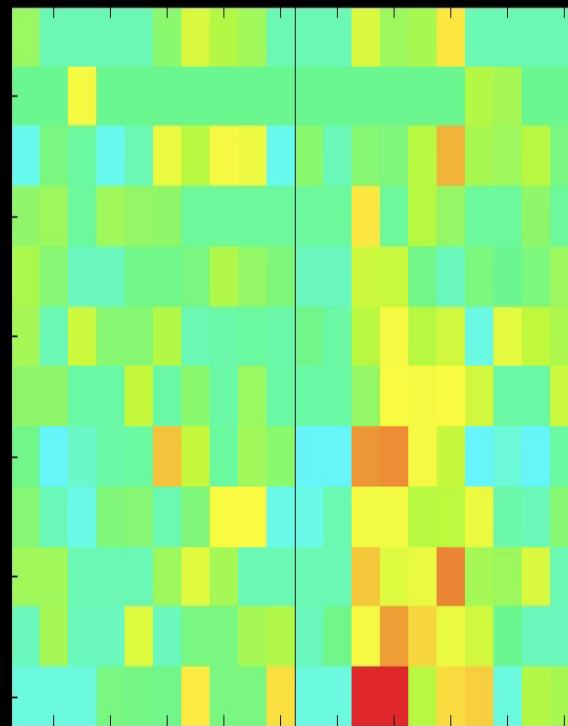
# Distribution of odor information over the breath cycle is state-dependent



anesthetized



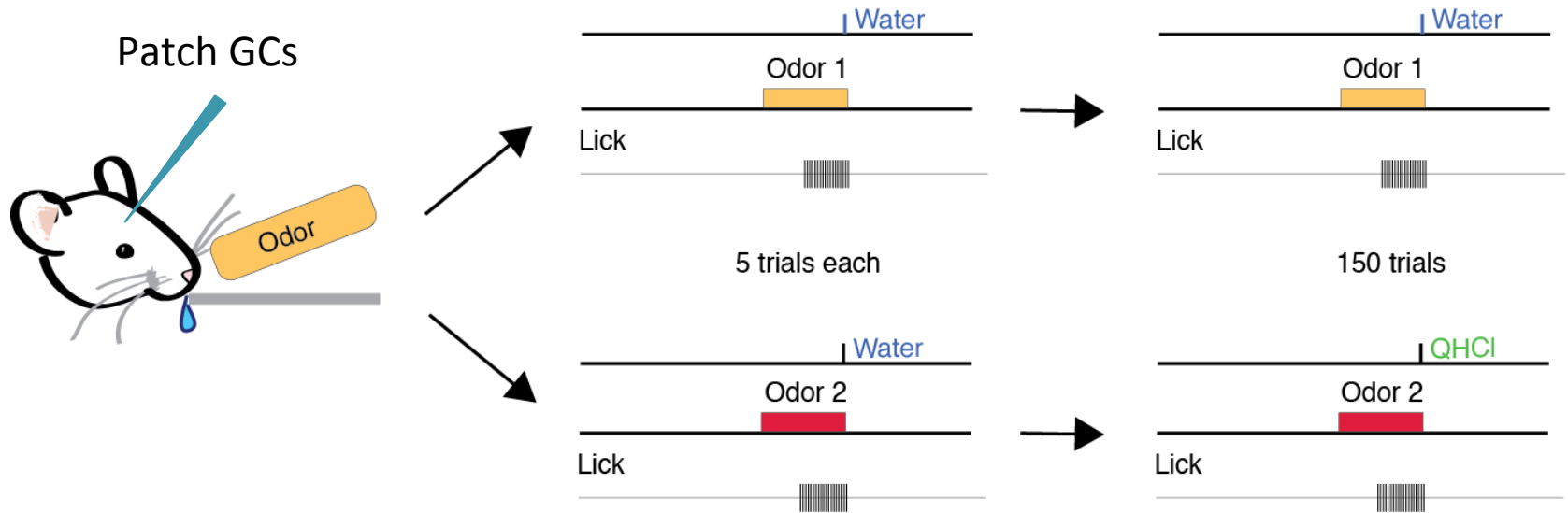
awake



## Part II Conclusions

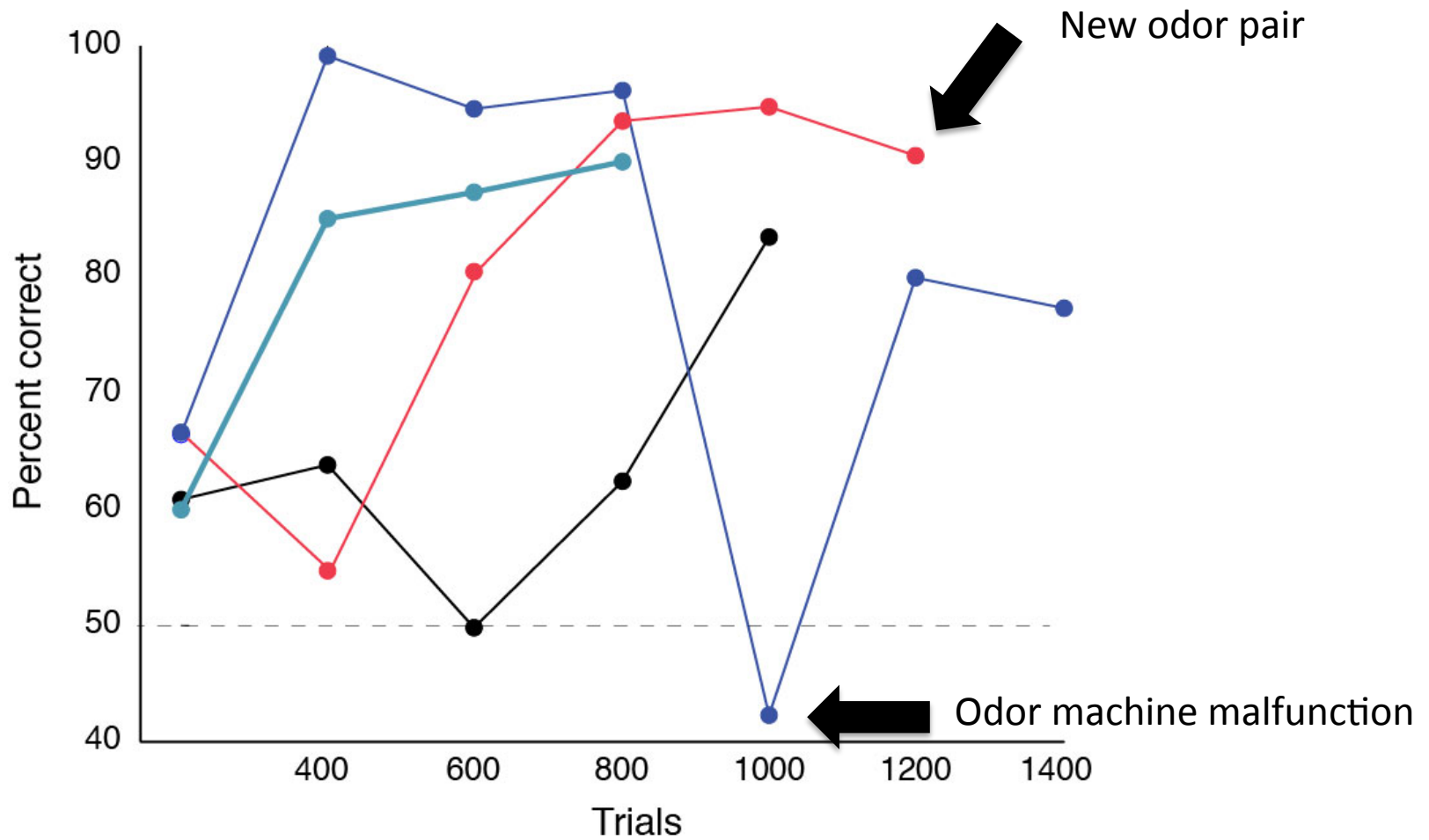
- Granule cells appear to more heavily modulate MOB output in awake mice
- Granule cells are likely to affect which mitral cells are active to an odor, but not likely to affect when with respect to breathing
- Granule cell-mediated population inhibition is organized into synchronous pulses under anesthesia and is organized into rippling waves during wakefulness

# GC physiology during an odor learning task

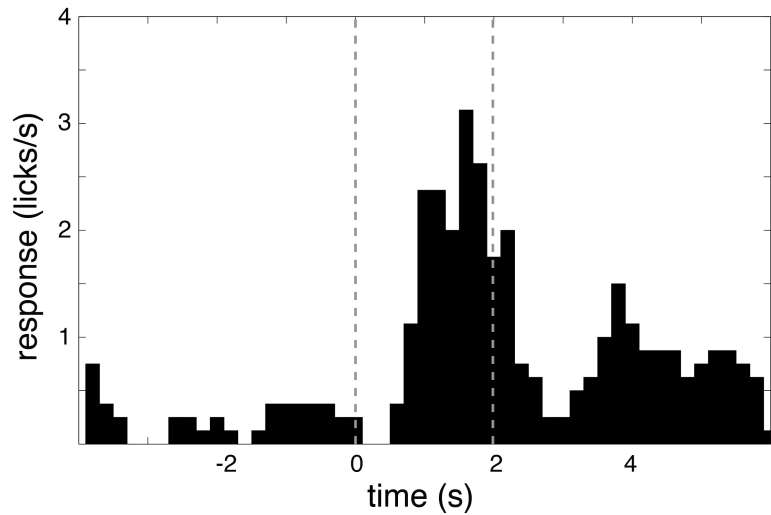




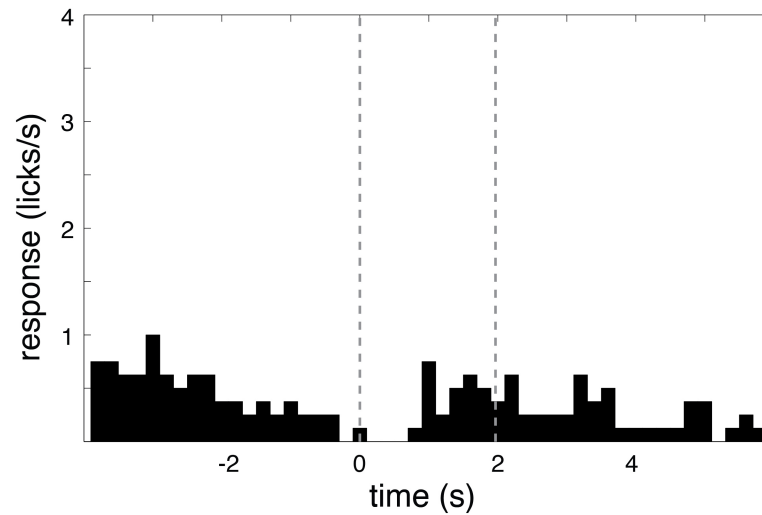
# Mice rapidly learn a Go-NoGo task



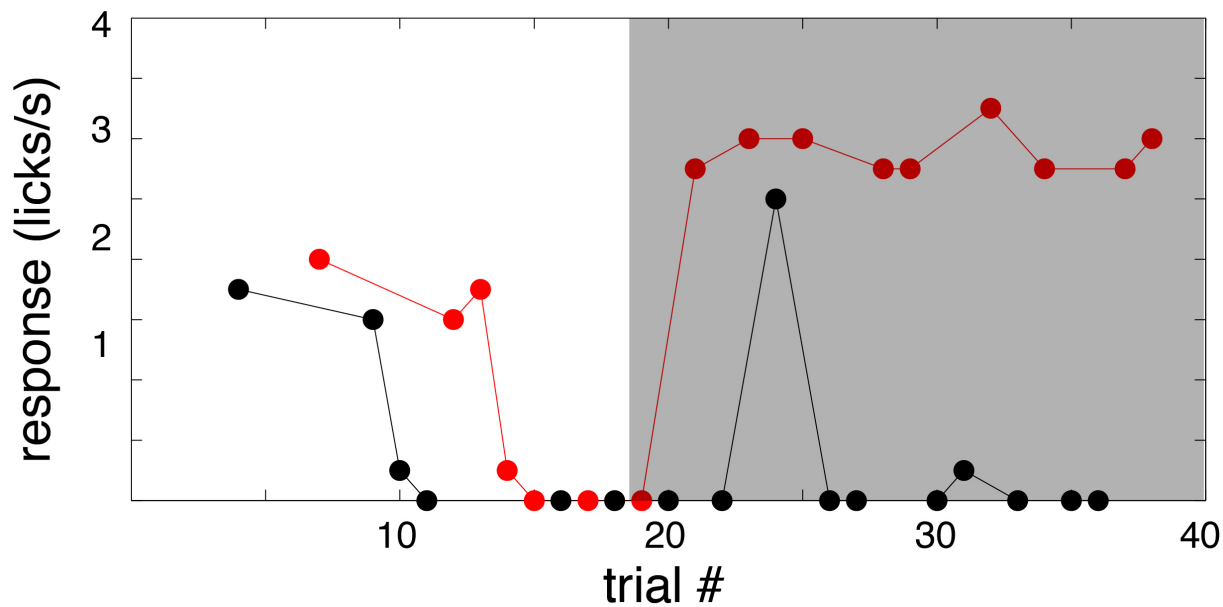
Licking to rewarded odor



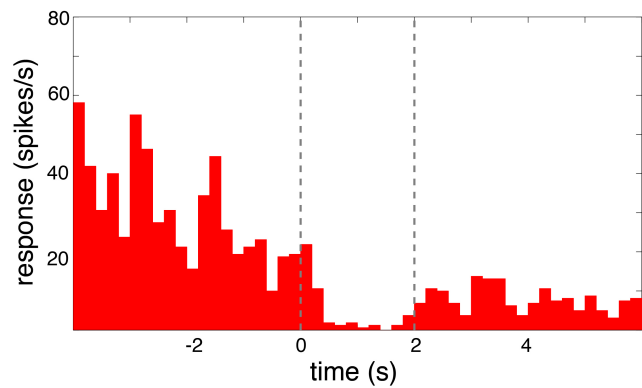
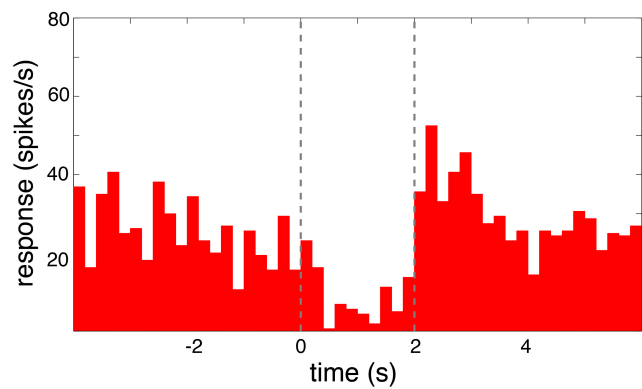
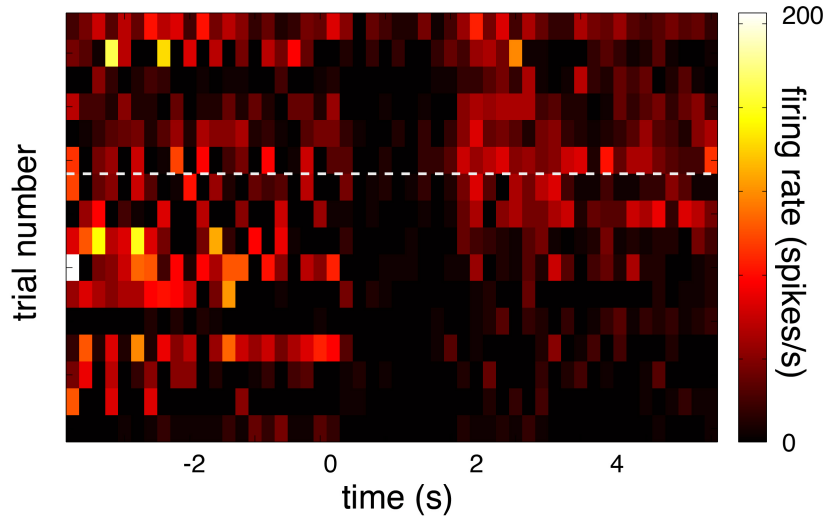
Licking to QHCl odor



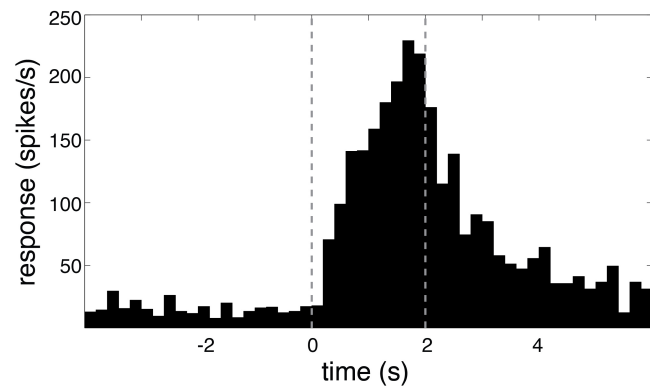
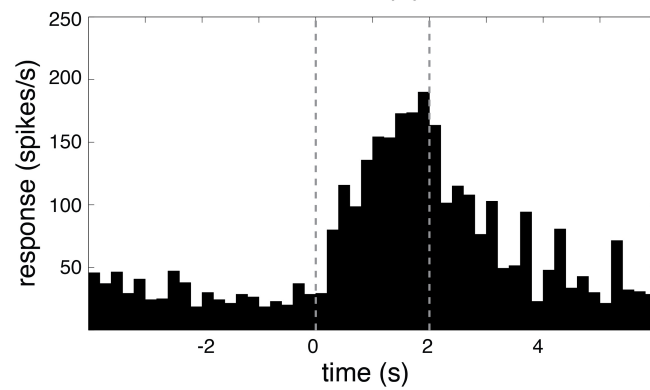
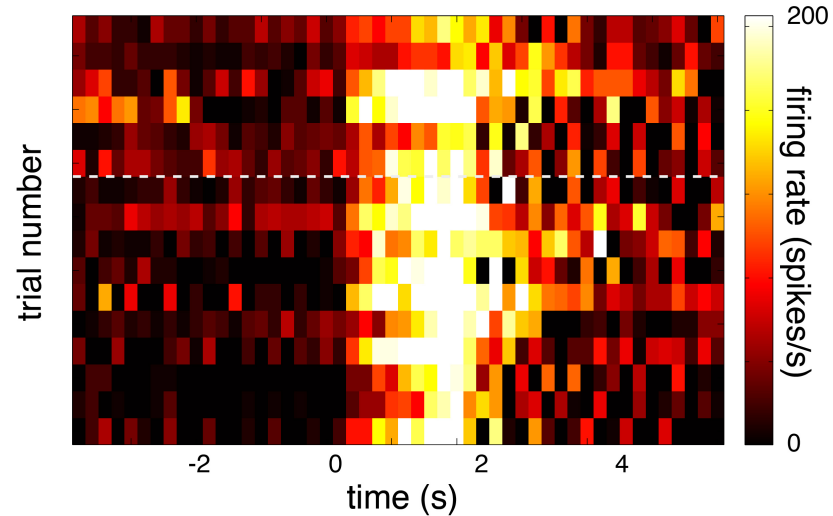
licks to reward odor  
licks to QHCl odor

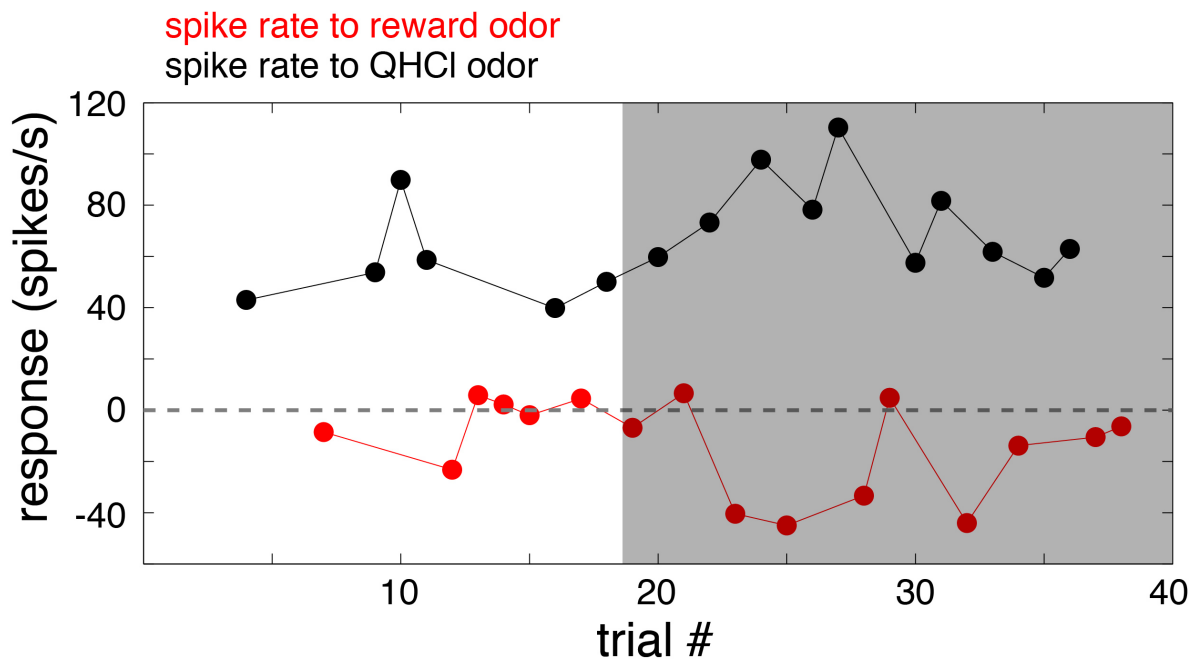
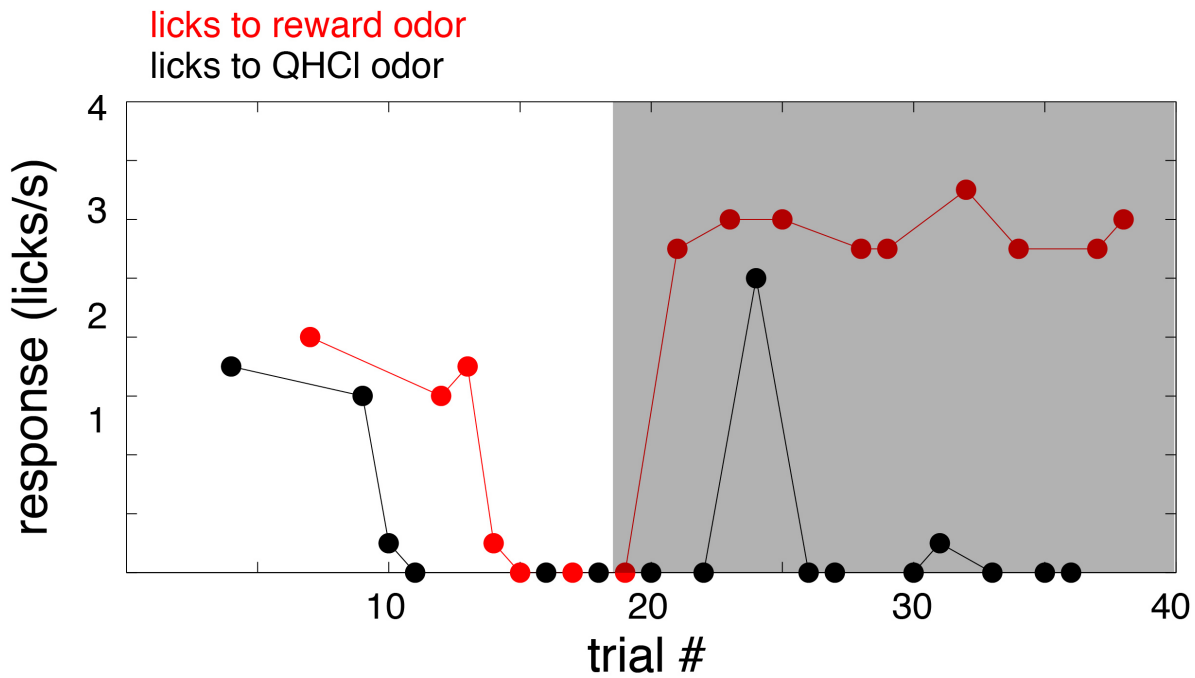


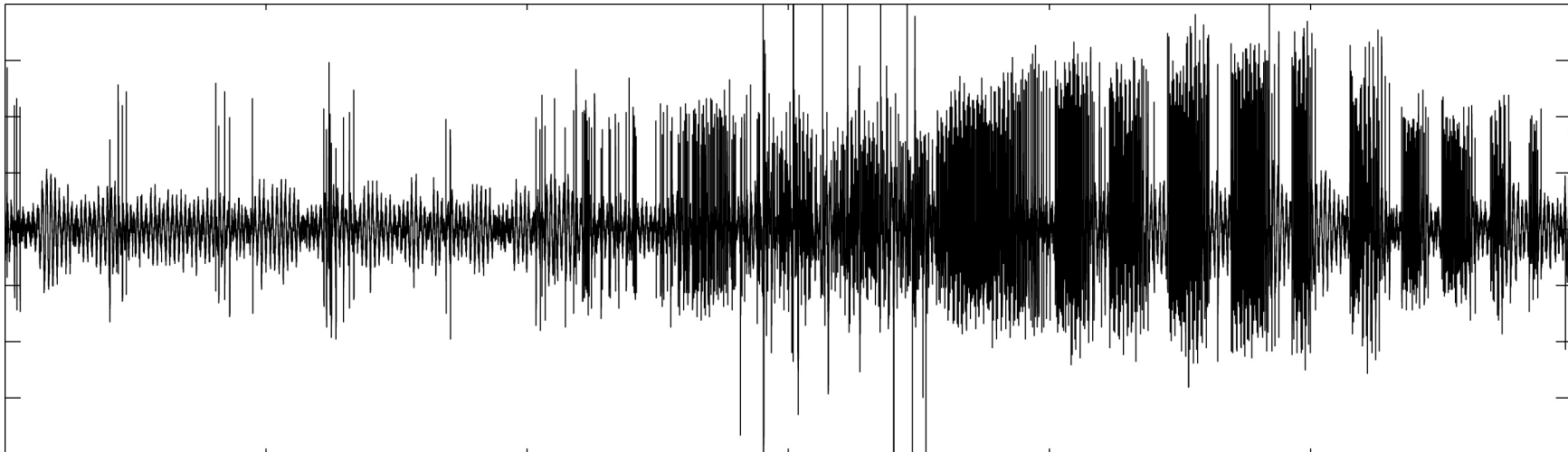
reward odor



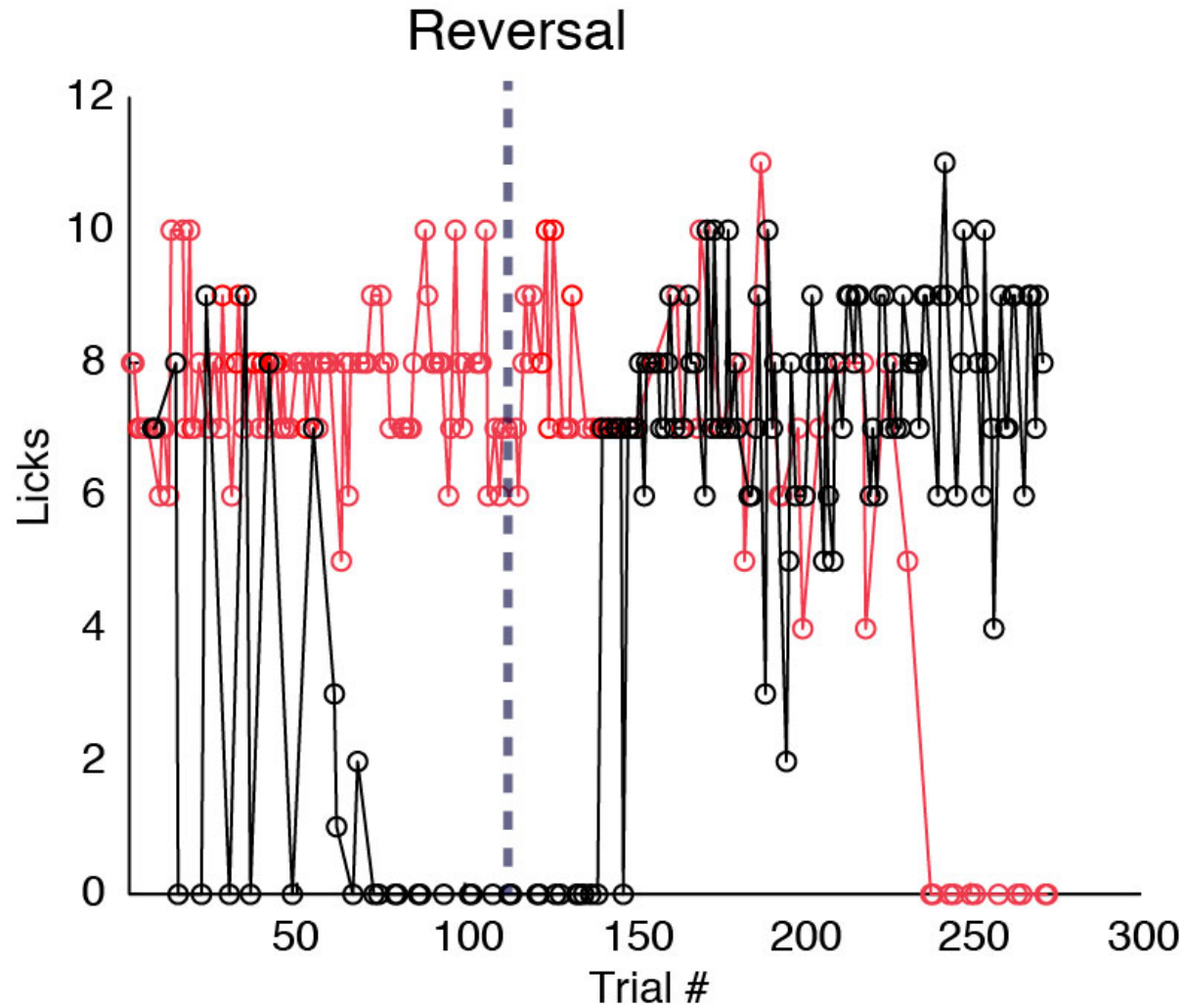
QHCl odor







# New learning occurs in a recordable time frame



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James Newman

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Benjamin Schuman

### HS student

Gabrielle Ewall

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AUTISM RESEARCH INITIATIVE

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