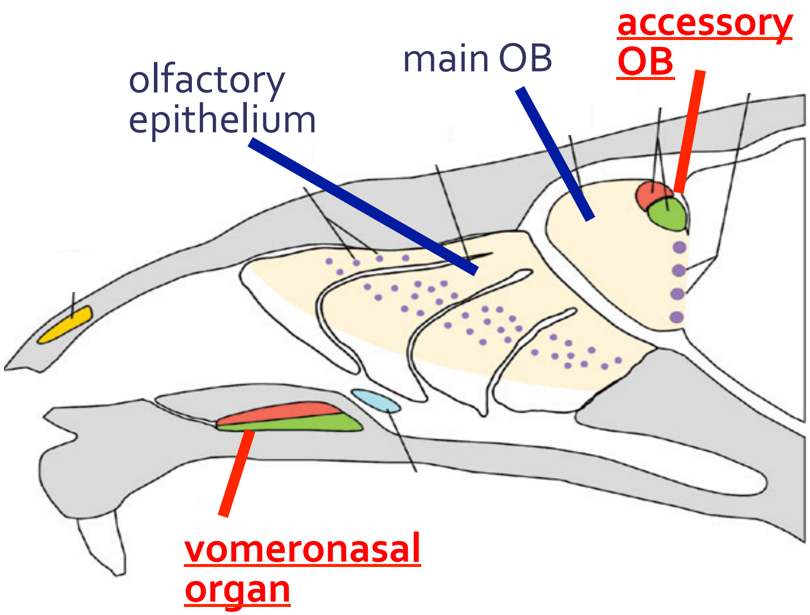
Mating-dependent plasticity in the female accessory olfactory bulb

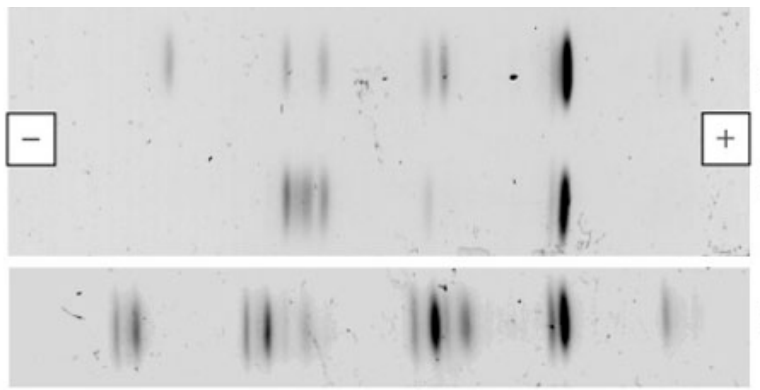
Ian Davison, Dept of Biology, Boston University
KITP Olfaction meeting, July / 2015

The accessory olfactory system



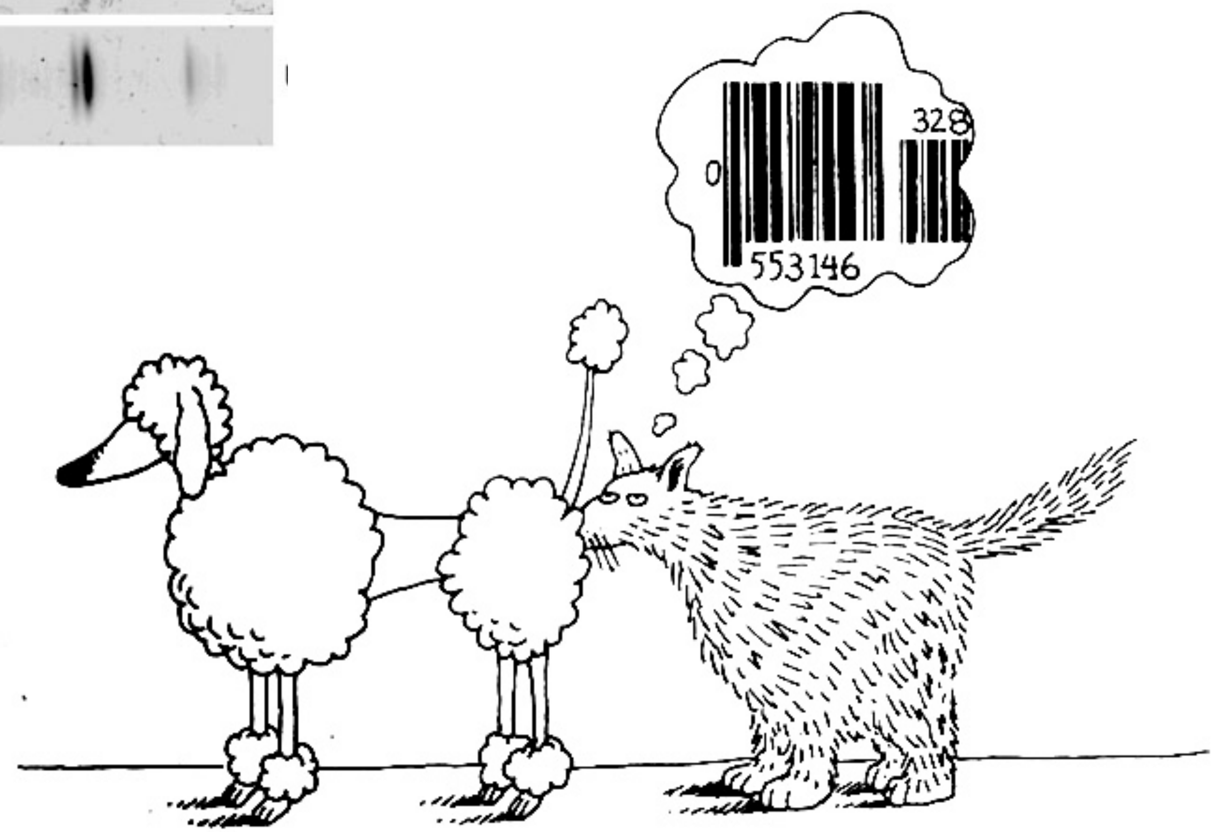
- vomeronasal system: detects primarily non-volatile, high molecular weight chemical cues

The accessory olfactory system



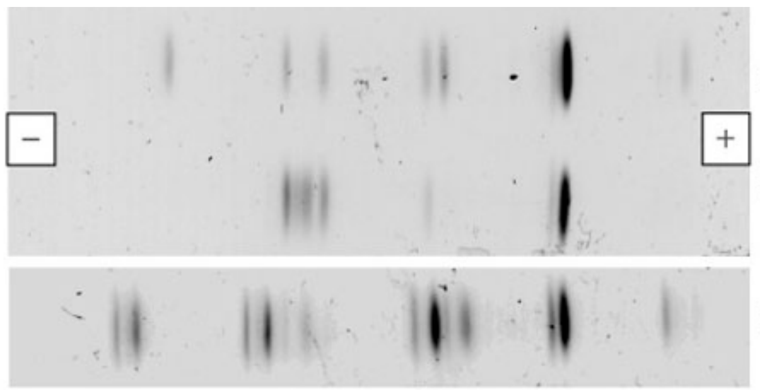
Hurst et al. (2001)

- each individual has a unique set of secreted chemosignals



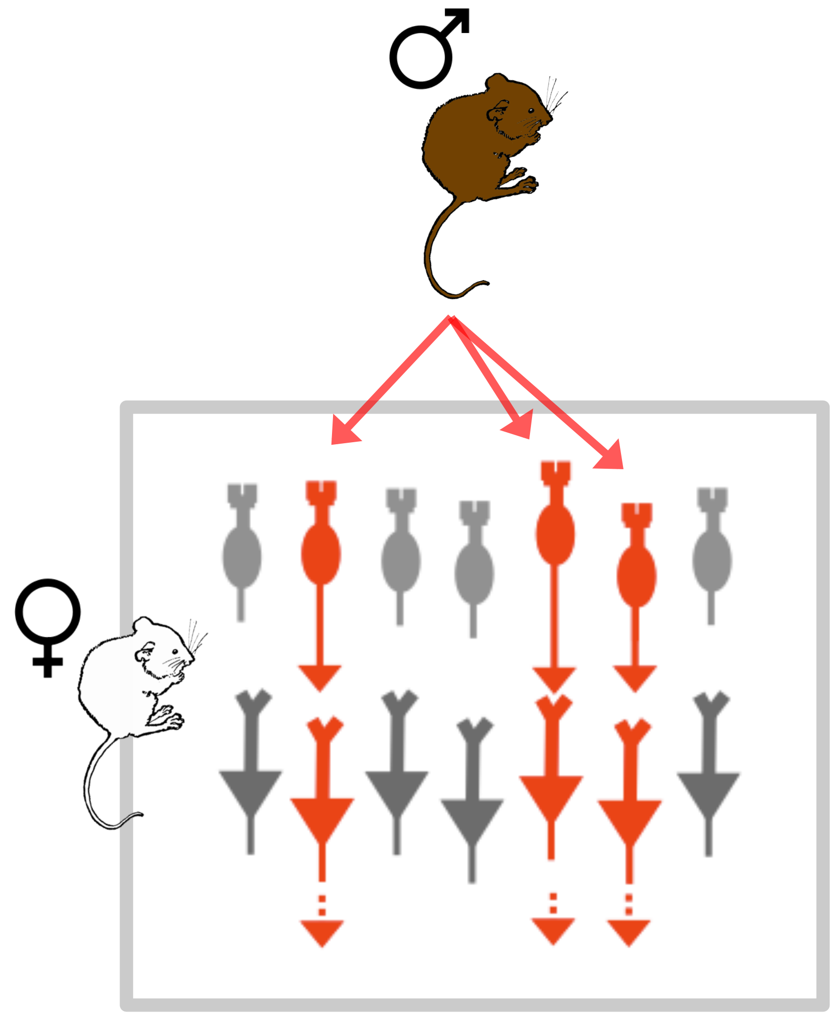
- forms a sensory 'fingerprint' identifying a specific individual

The accessory olfactory system

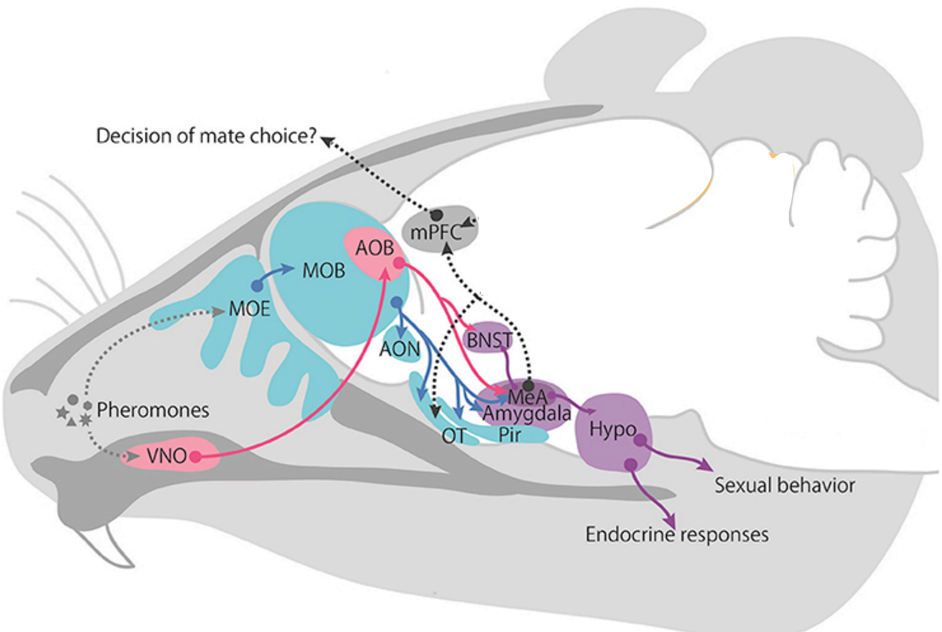


Hurst et al. (2001)

- drives a pattern of neural activity in the AOB unique to that individual.

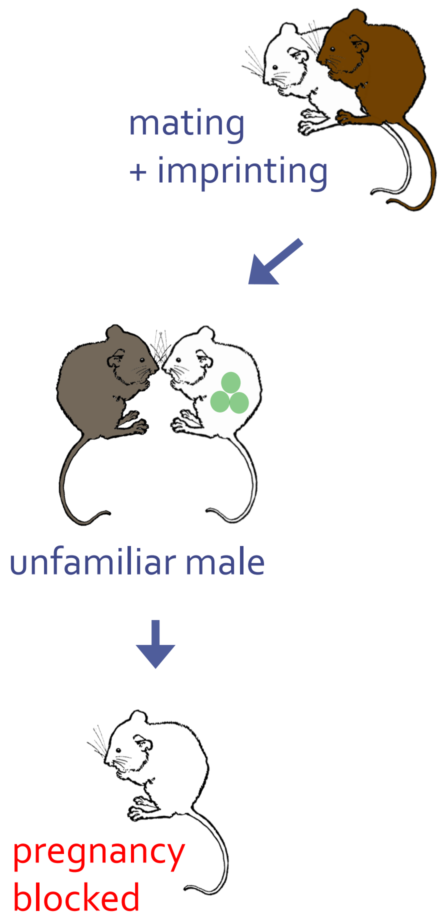


The accessory olfactory system



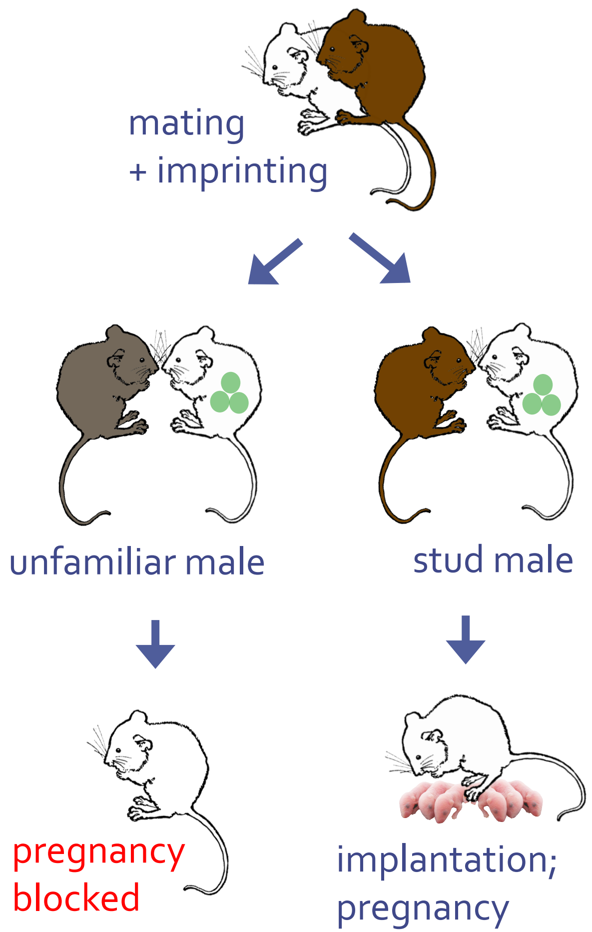
Social behaviors:
reproduction,
parenting,
aggression

Rapid sensory imprinting: the Bruce effect



- the 'Bruce Effect': male-induced pregnancy block in mice

Rapid sensory imprinting: the Bruce effect



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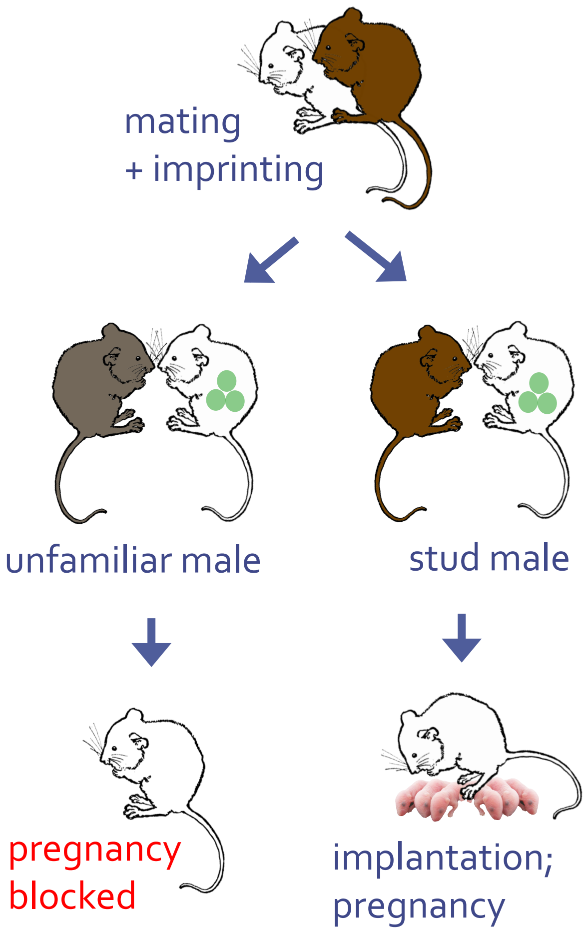
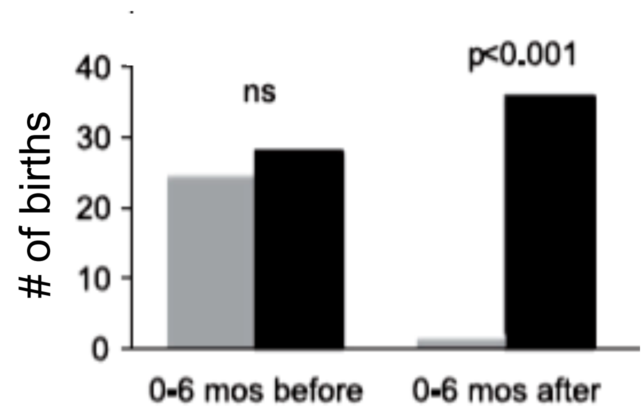
Rapid sensory imprinting: the Bruce effect





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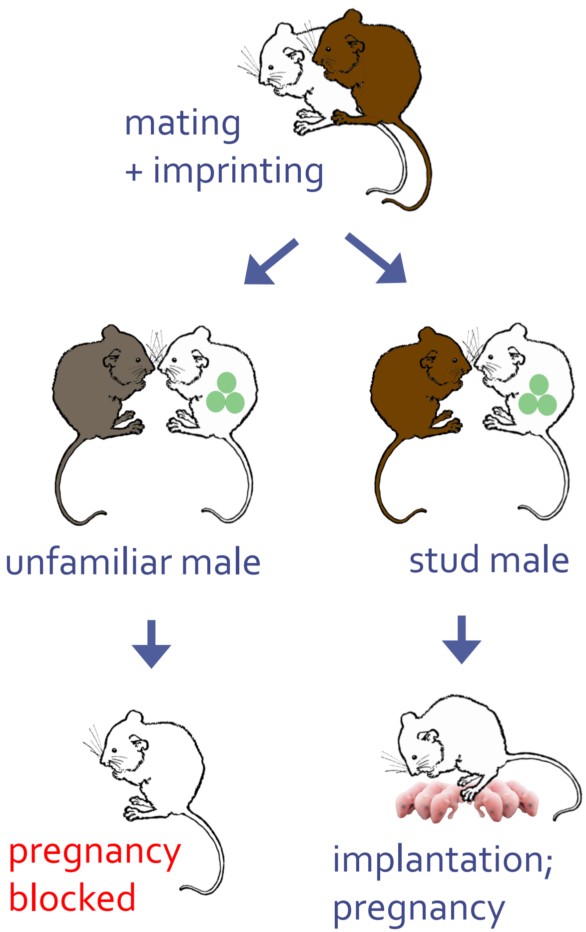
Rapid sensory imprinting: the Bruce effect



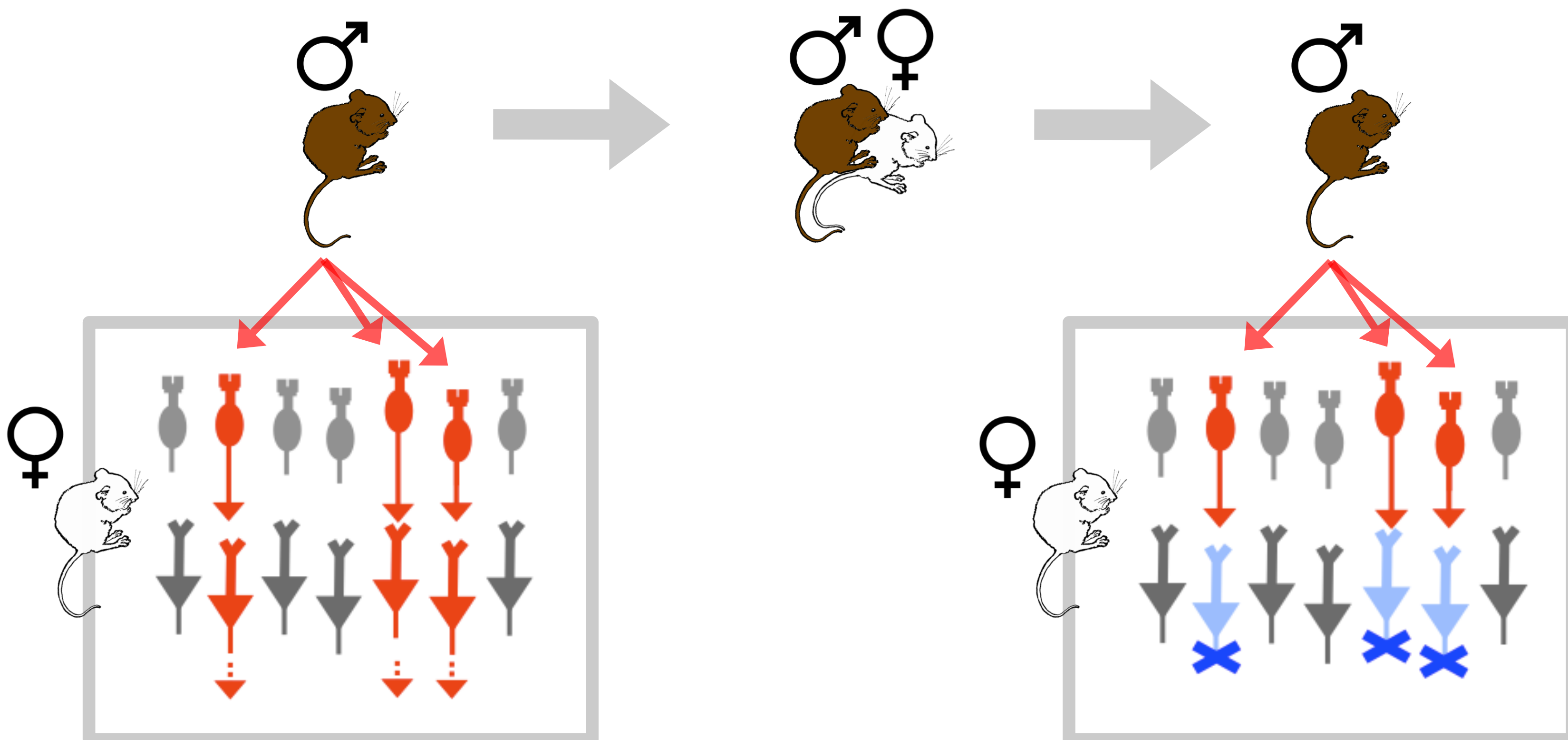
- the 'Bruce Effect': male-induced pregnancy block in mice

Rapid sensory imprinting: the Bruce effect

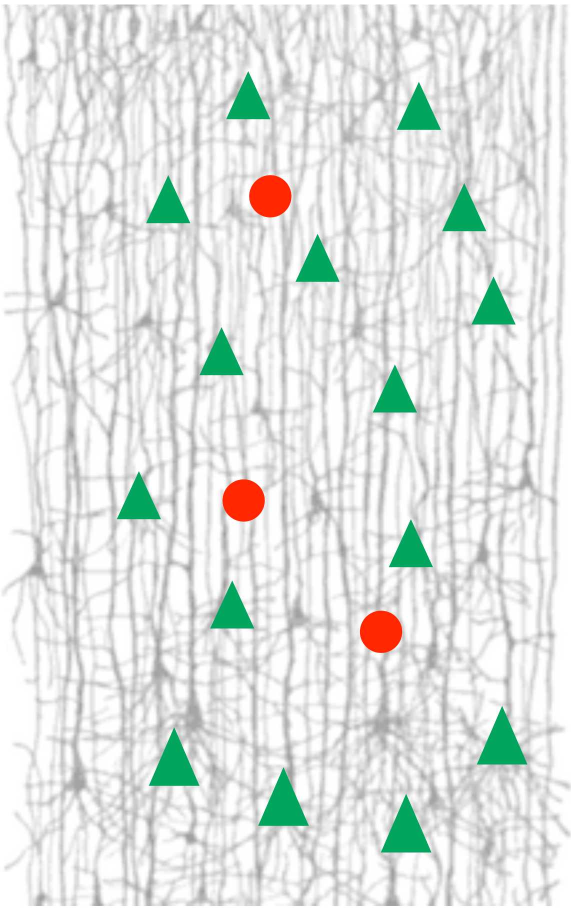
neural activity pattern encoding specific individual (stud)

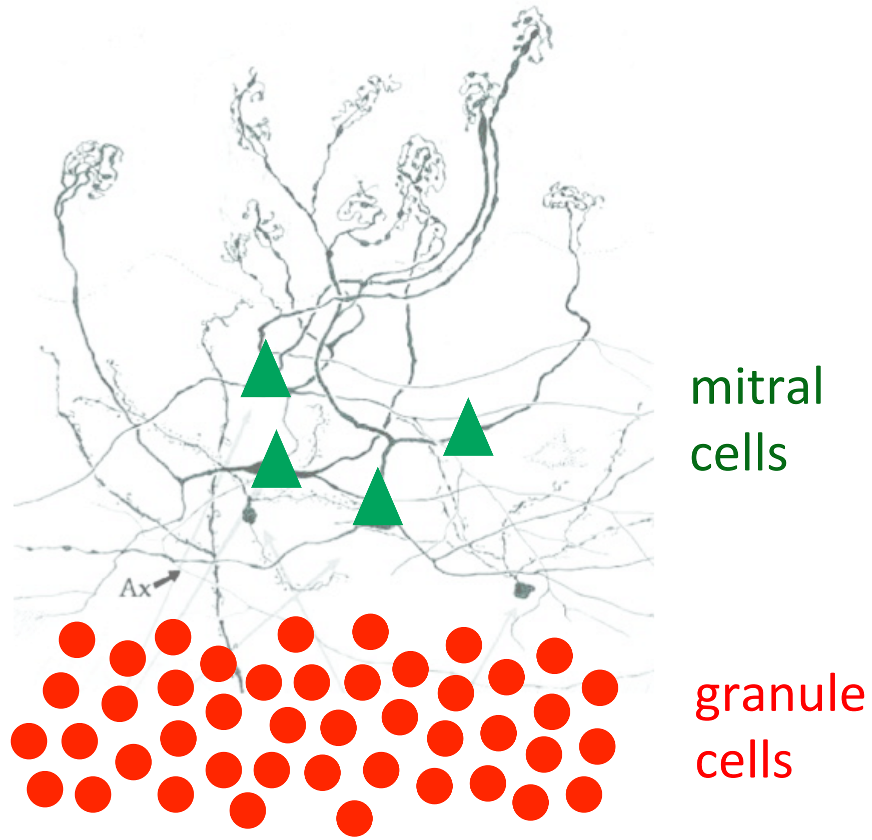
imprinting: mating & sensory exposure

cell-specific suppression of output



Inhibitory circuits in accessory olfactory bulb



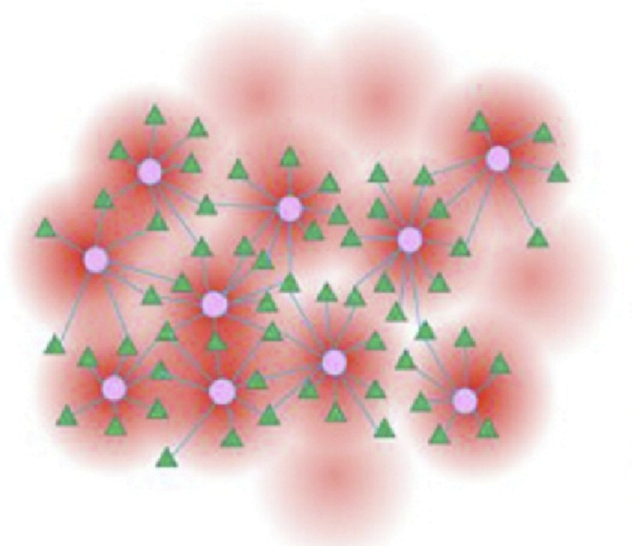


neocortex: ≈ 1:5

olfactory bulb: ≈ 10:1

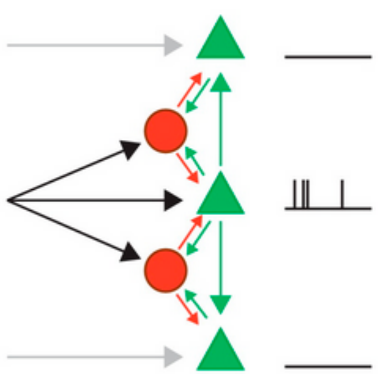
apologies to Mizrahi

Inhibitory circuits in accessory olfactory bulb

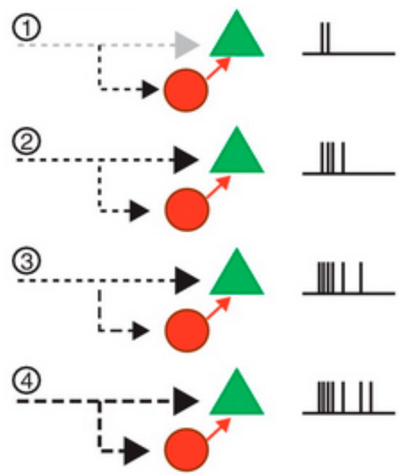


- common inhibitory motifs for shaping neural output:

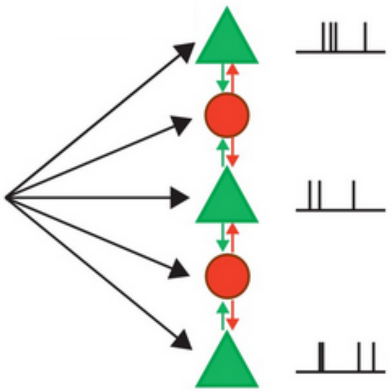
lateral inhibition



normalization

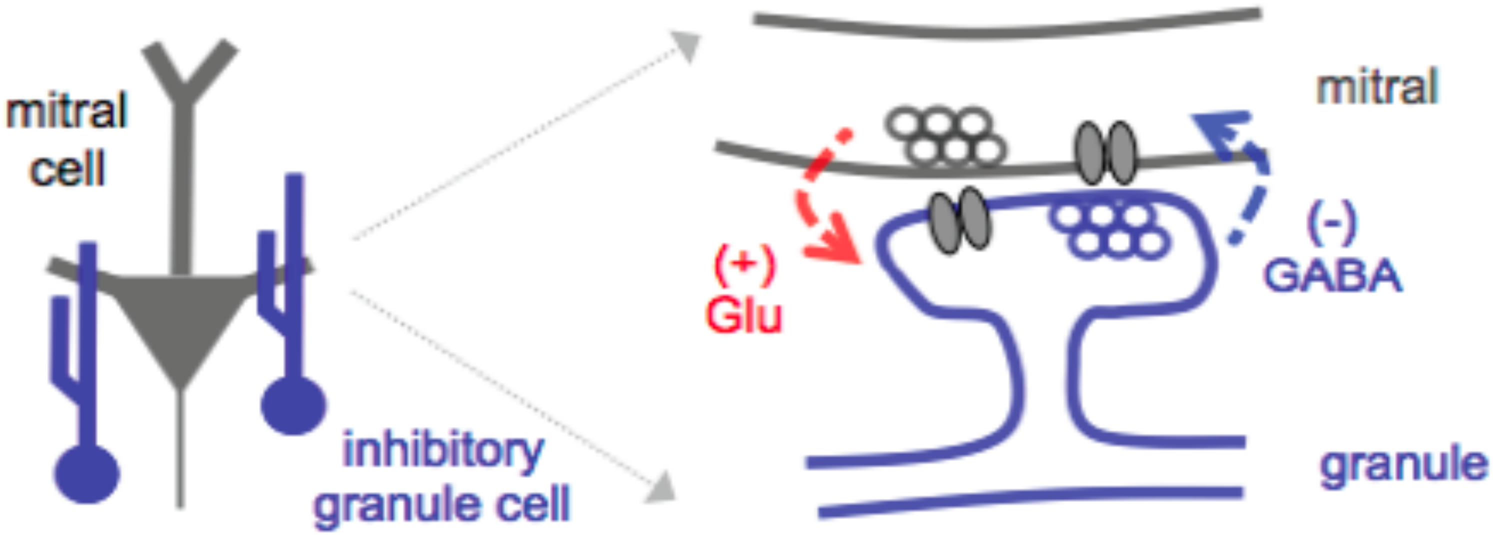


decorrelation



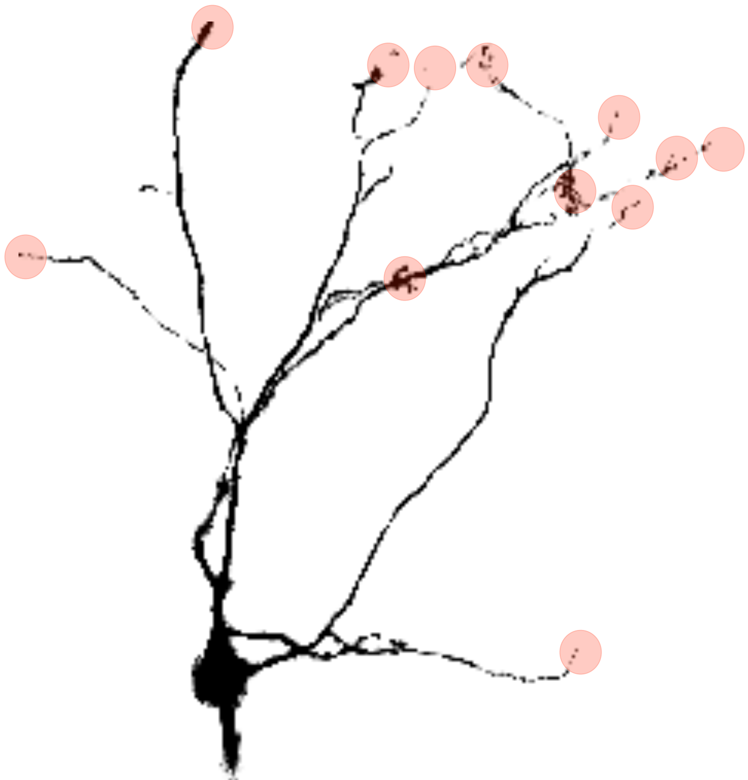
after Yuste

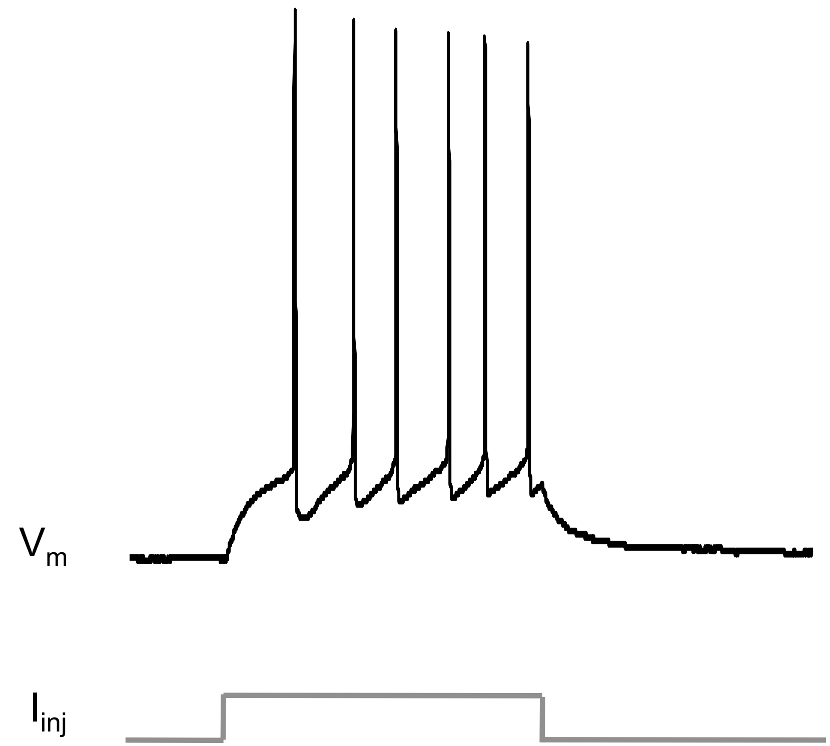
Inhibitory circuits in accessory olfactory bulb



excitatory & inhibitory neurons communicate through specialized, unusual dendritic synapses

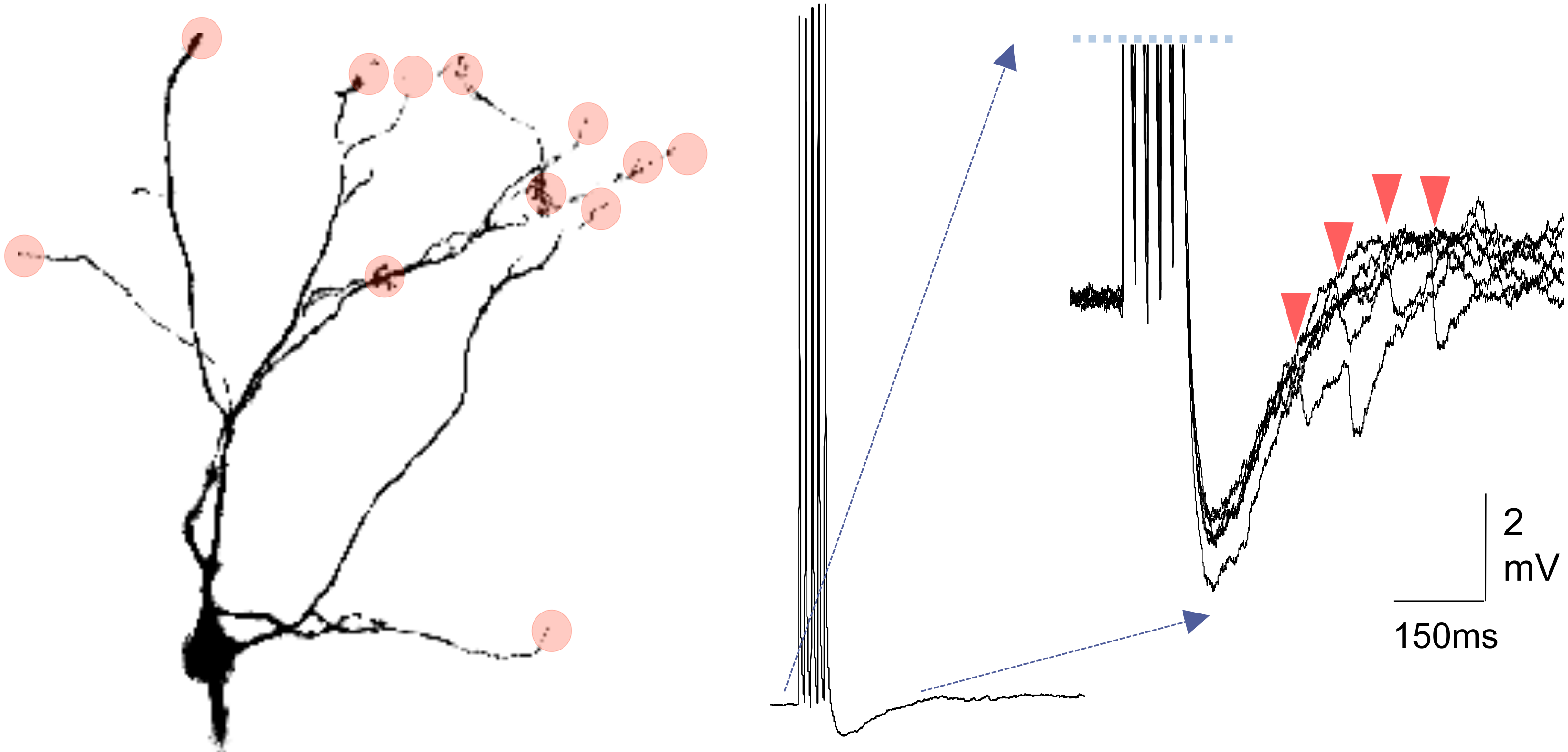
Inhibitory circuits in accessory olfactory bulb





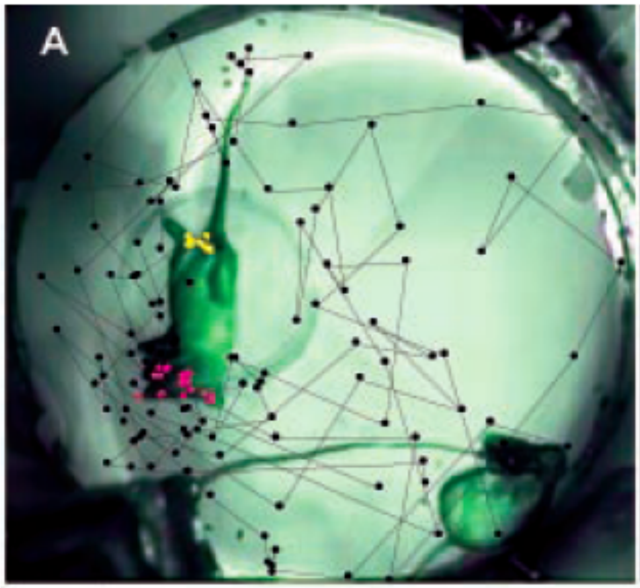
- action potential trains drive modest self-inhibition AOB mitral cells

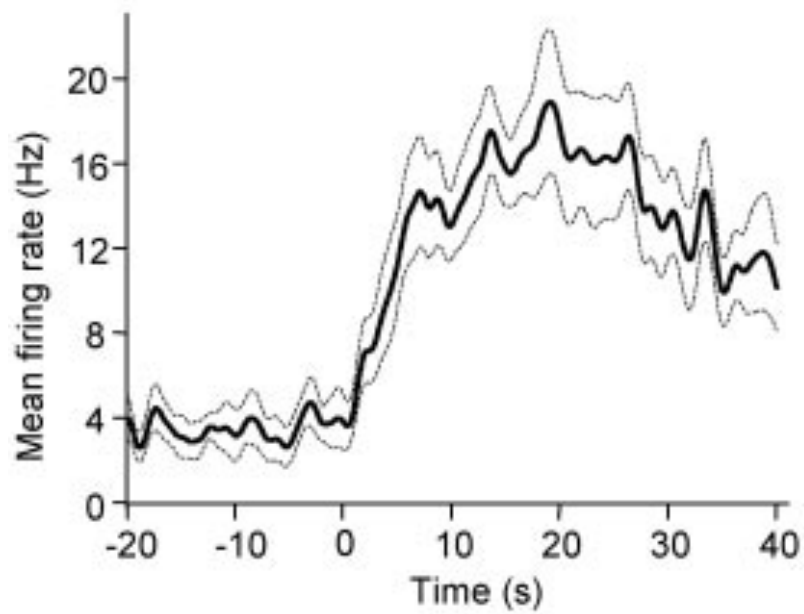
Inhibitory circuits in accessory olfactory bulb



- rapid action potential trains drive only modest self-inhibition in AOB mitral cells

Inhibitory circuits in accessory olfactory bulb

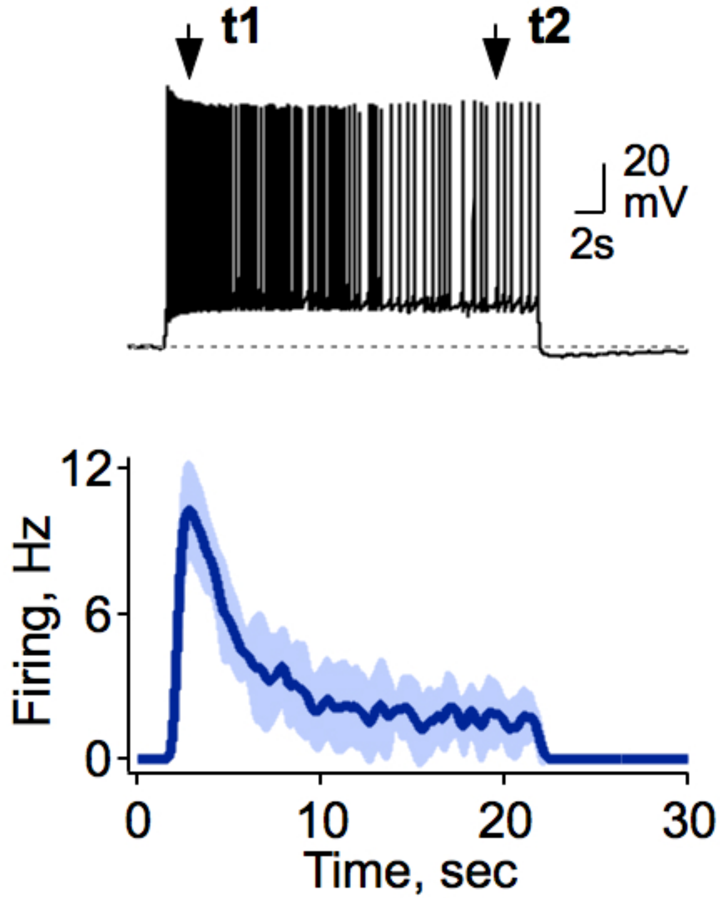




Luo & Katz, 2003

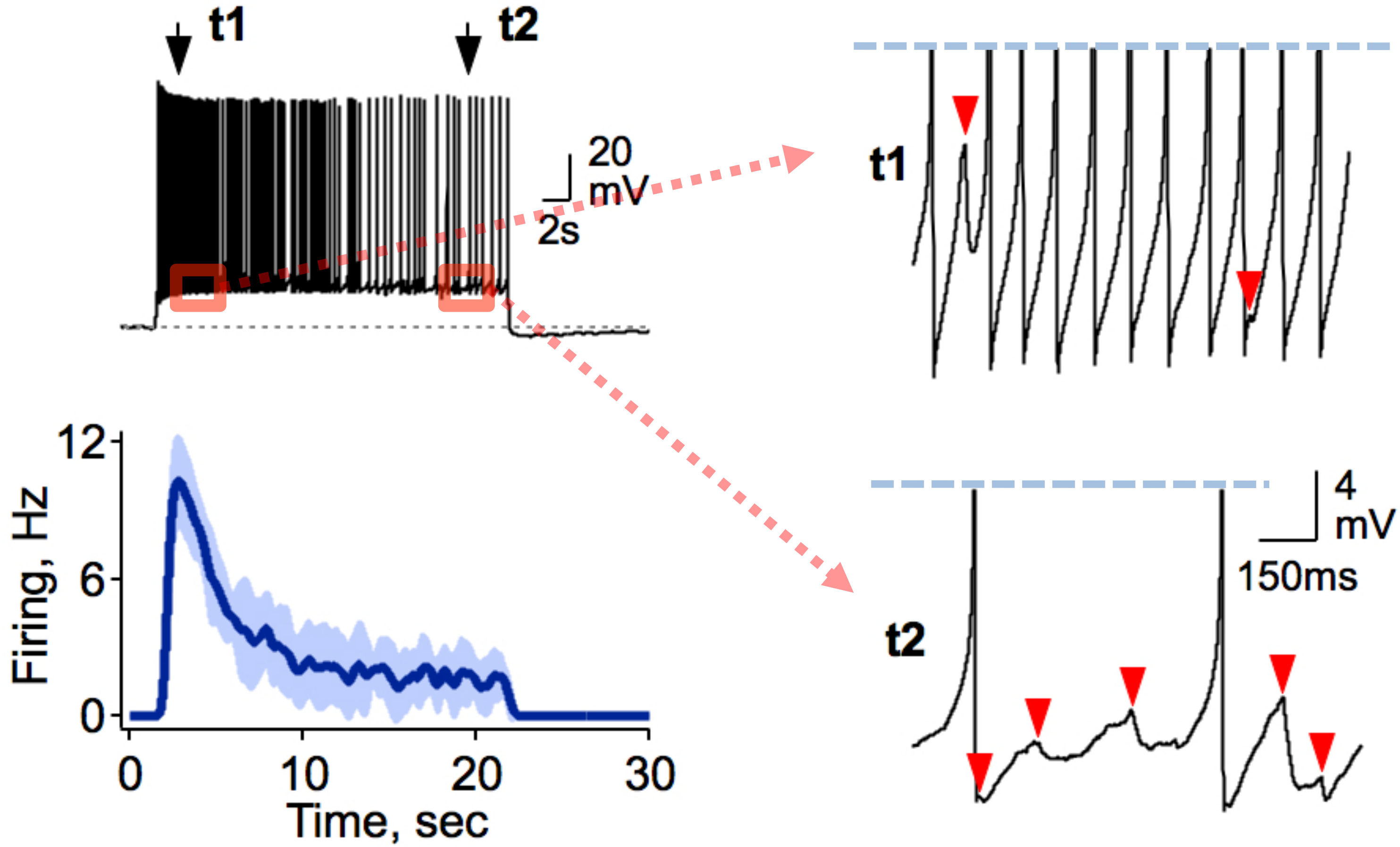
- during natural sensory behaviors, AOB mitral cells are active for long periods – TENS of SECONDS

MC self-inhibition emerges slowly



- long-lasting activity recruits strong self-inhibition in AOB mitral cells

MC self-inhibition emerges slowly



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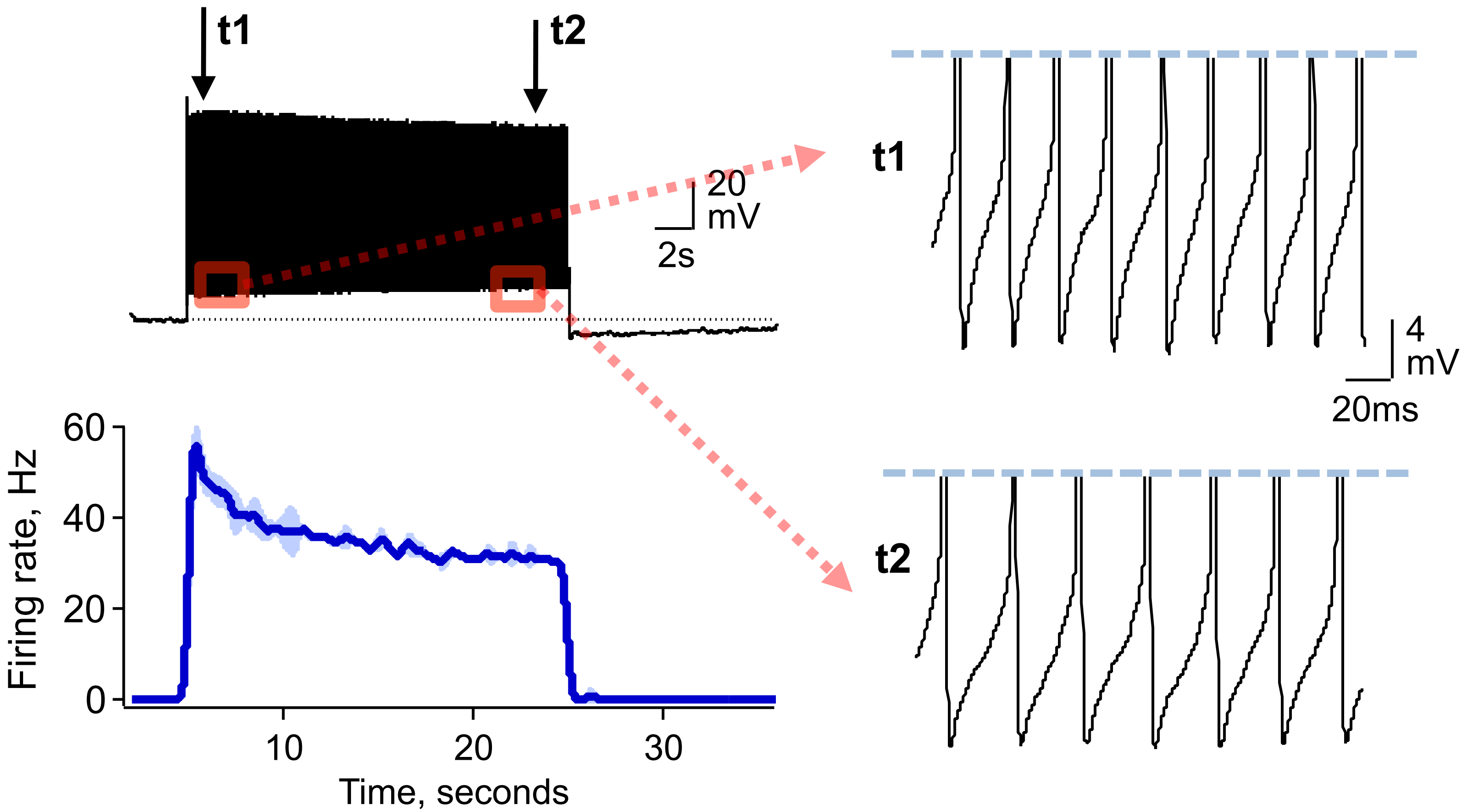
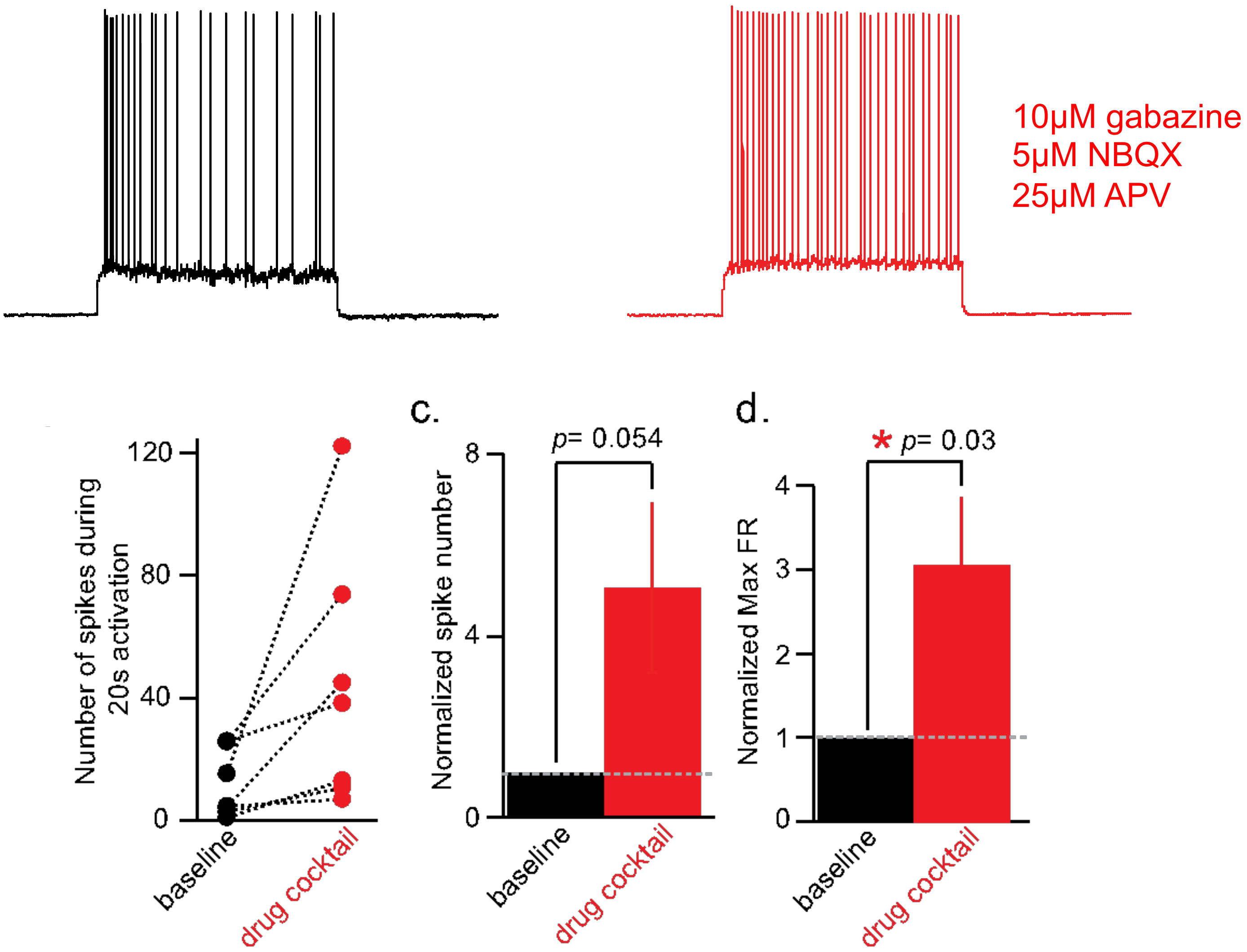


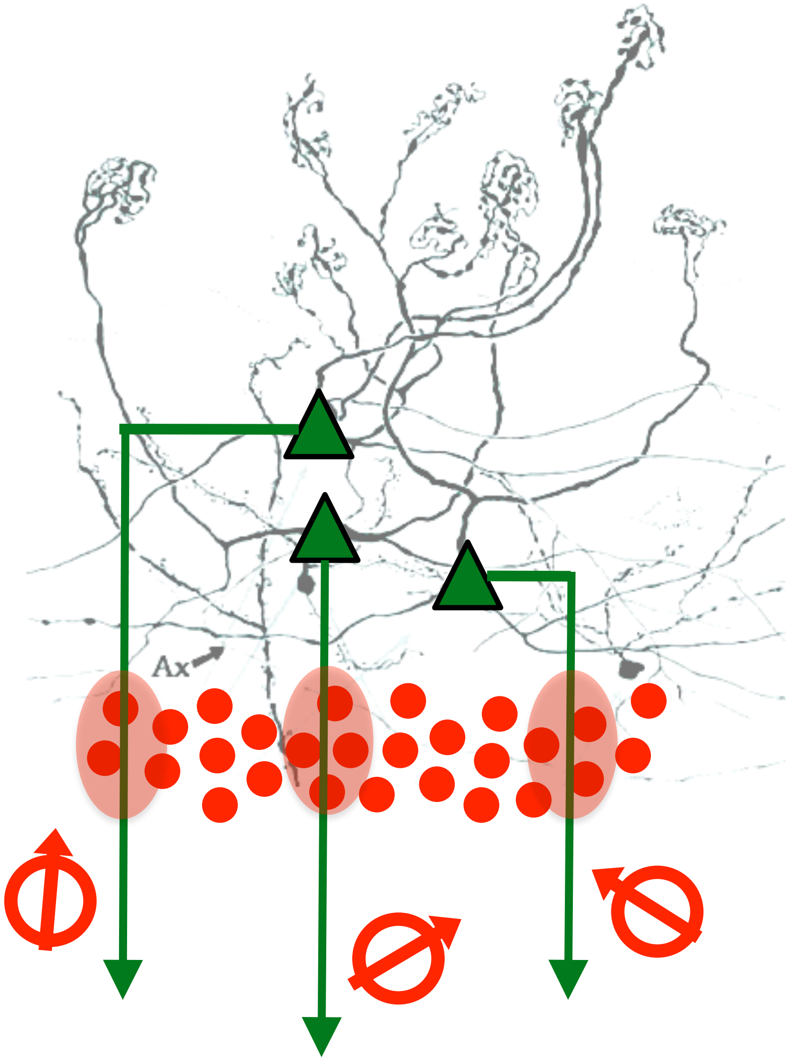
- mitral cells in MAIN olfactory bulb show minimal self-inhibition

MC self-inhibition regulates output



- pharmacology confirms that AOB output is strongly regulated by inhibition

Inhibitory circuits in accessory olfactory bulb

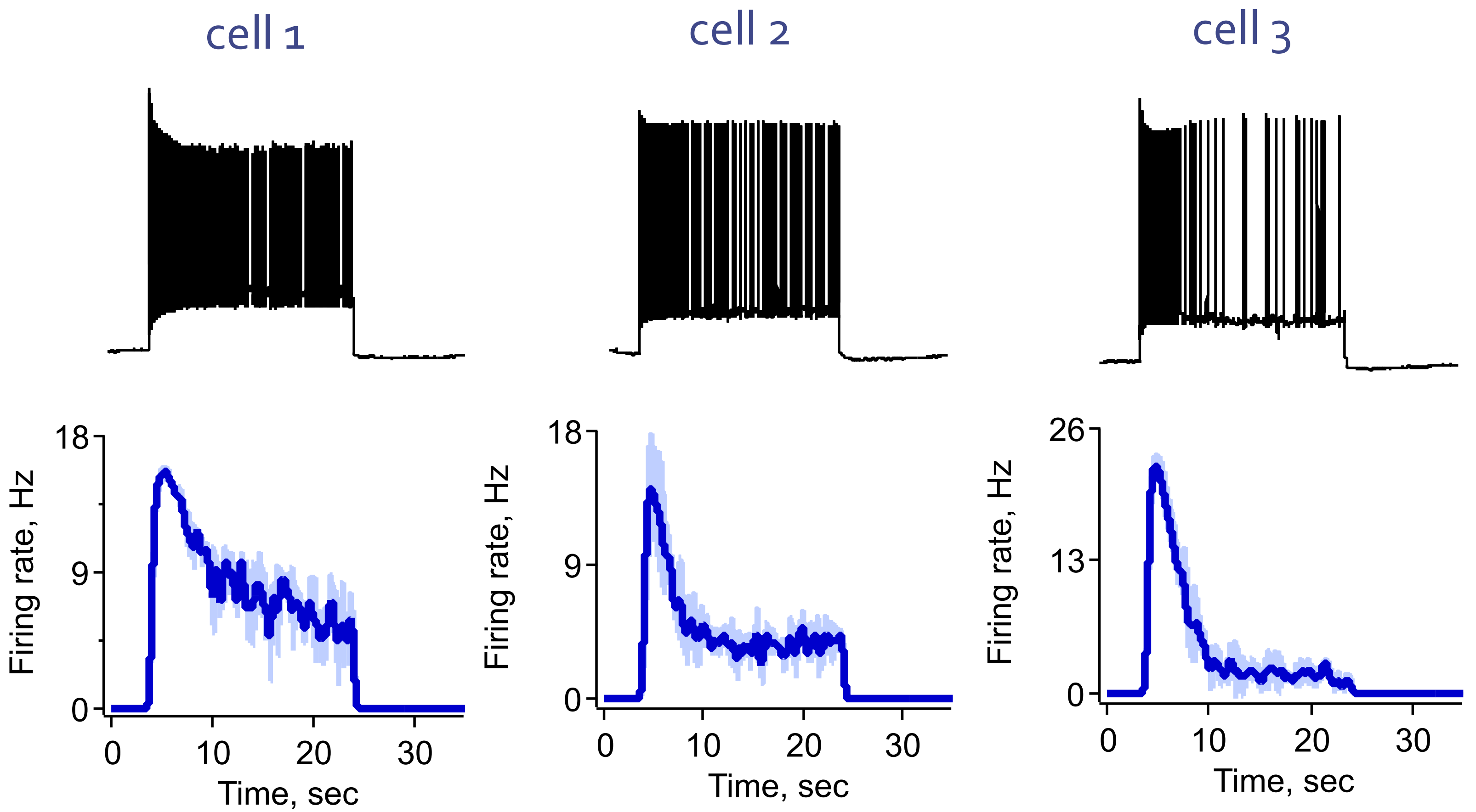


(1) Individual AOB projection neurons can recruit extremely strongly feedback inhibition

(2) Inhibition can strongly regulate AOB output; degree of suppression varies

(3) Inhibition emerges relatively slowly over time

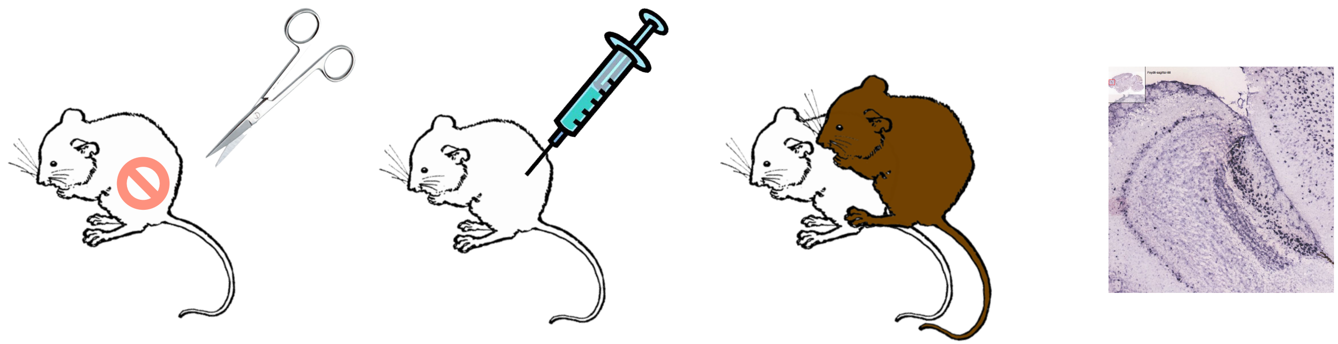
Inhibitory circuits in AOB



- different mitral cells show widely varying levels of inhibitory suppression

Measuring synaptic changes after imprinting

- do mating and sensory exposure drive changes in inhibitory function in the AOB?



8 weeks | ~ 7 days | ~ 4.5 hrs | ~ 4.5 hrs

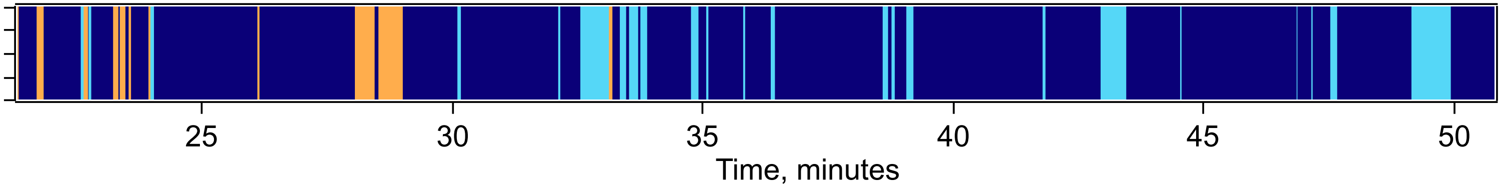
ovarectomy & estrogen implant

induce estrus via progesterone

mating & sensory exposure

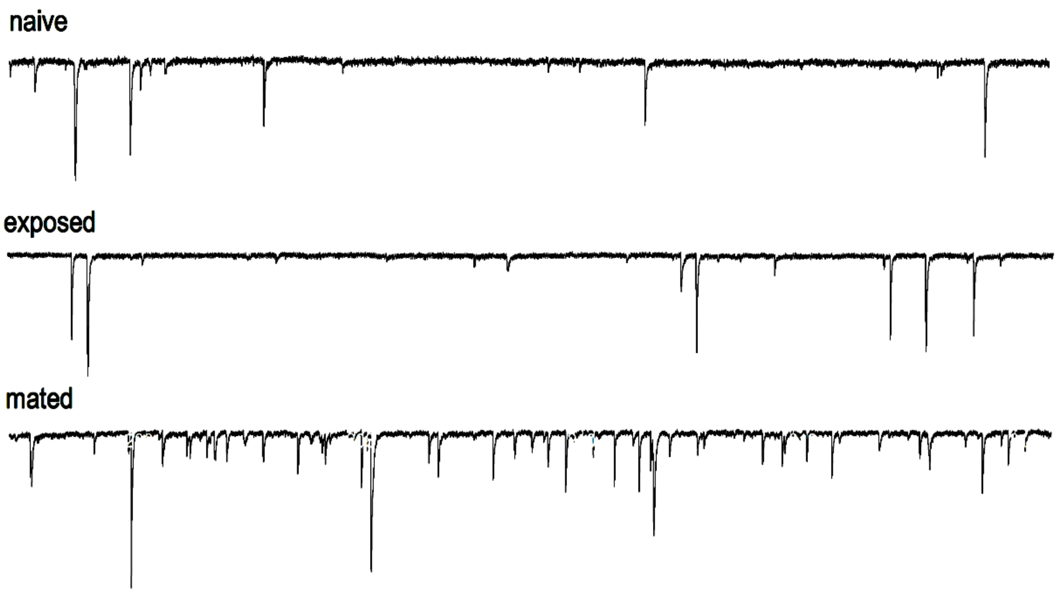
sacrifice, brain slice recording

Behavioral interactions during imprinting

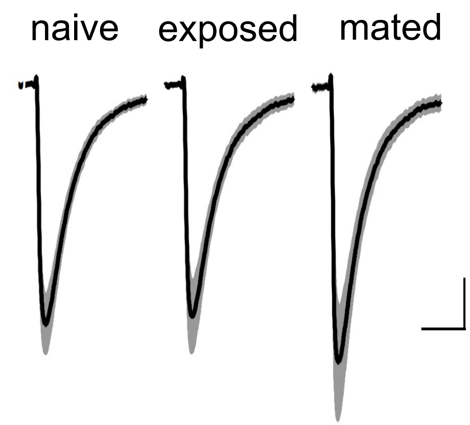


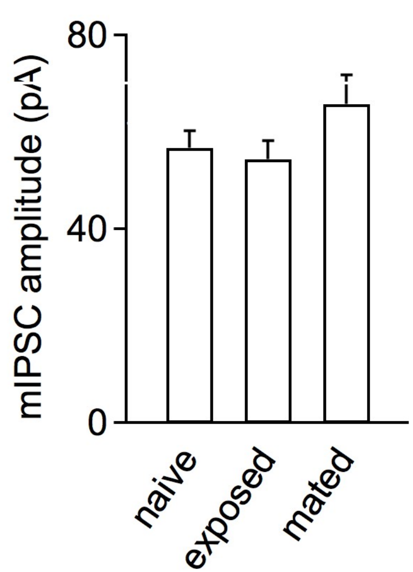
- behavioral interactions are intermittent and repetitive

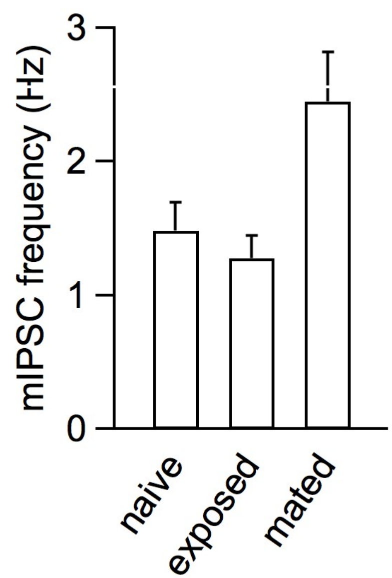
Mating enhances inhibitory input to MCs



average

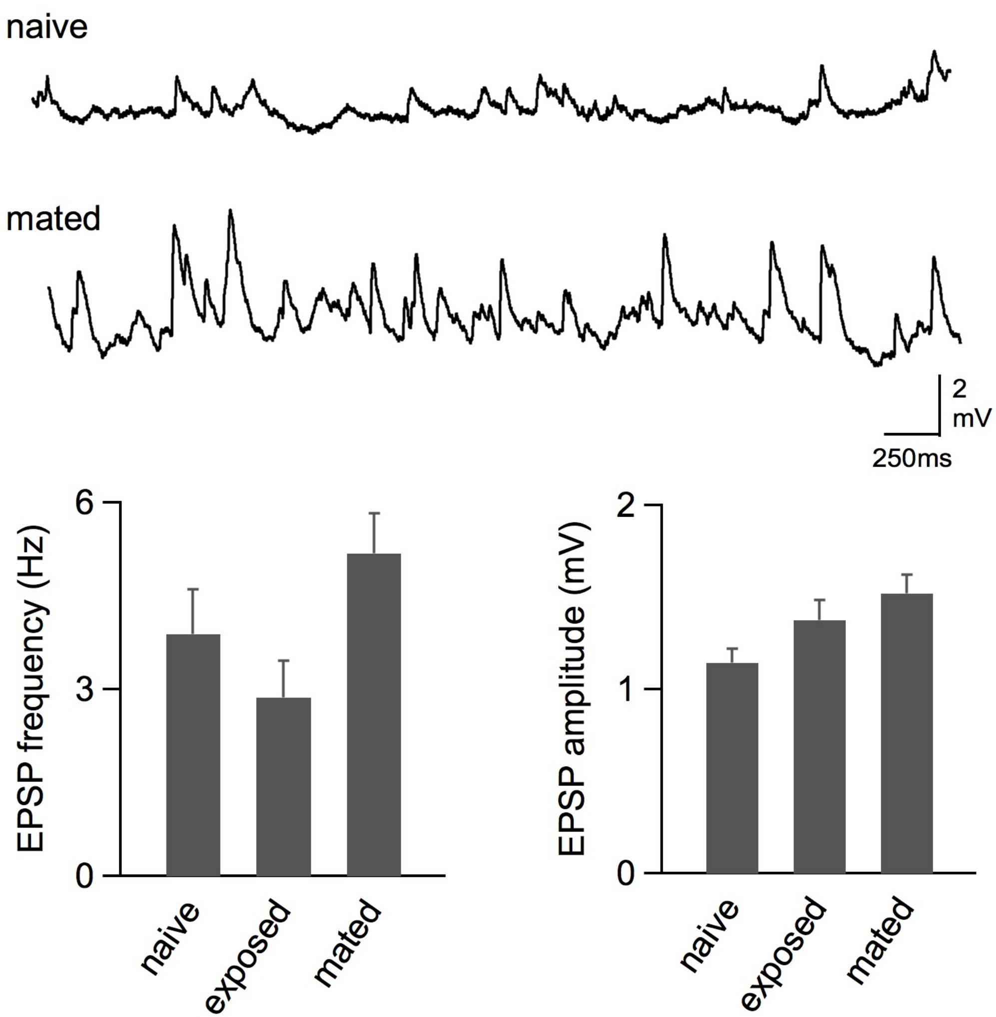






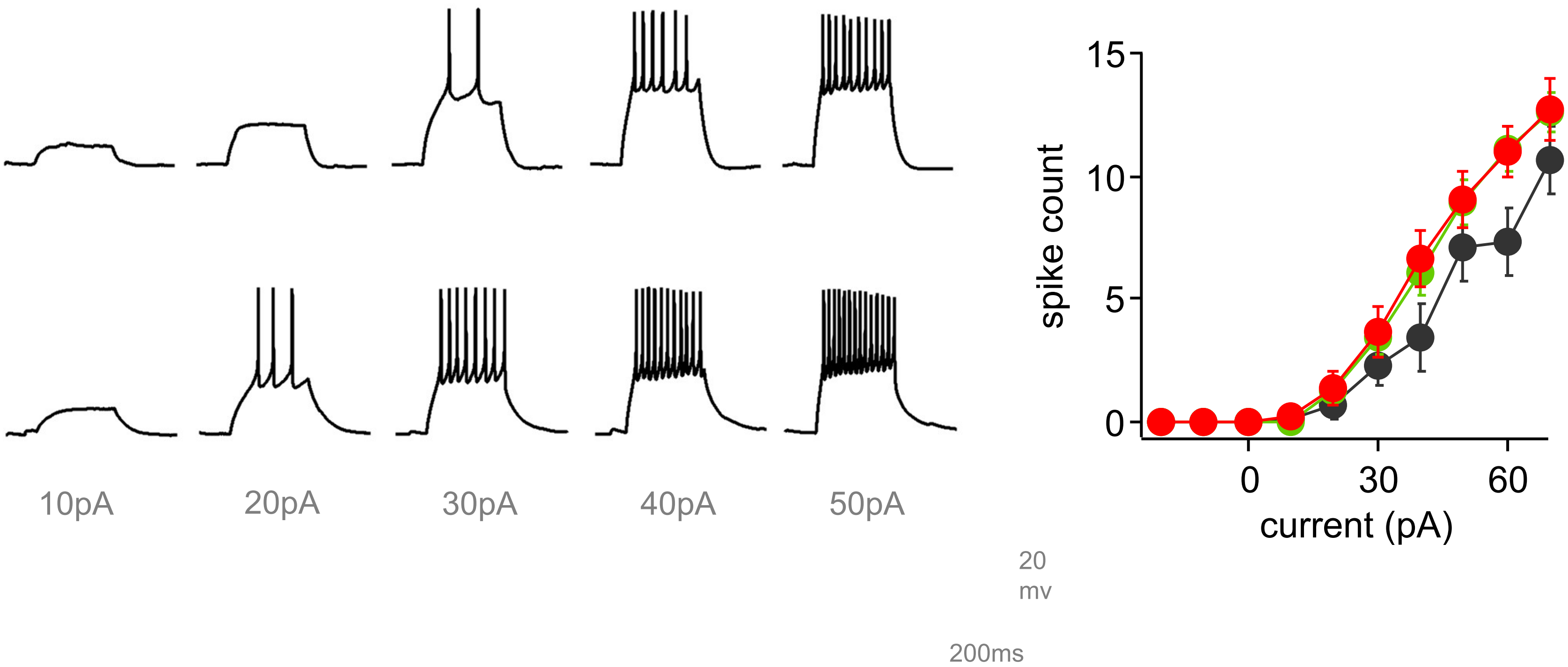
- frequency of miniature inhibitory postsynaptic currents is increased after imprinting

Mating enhances excitatory input to GCs



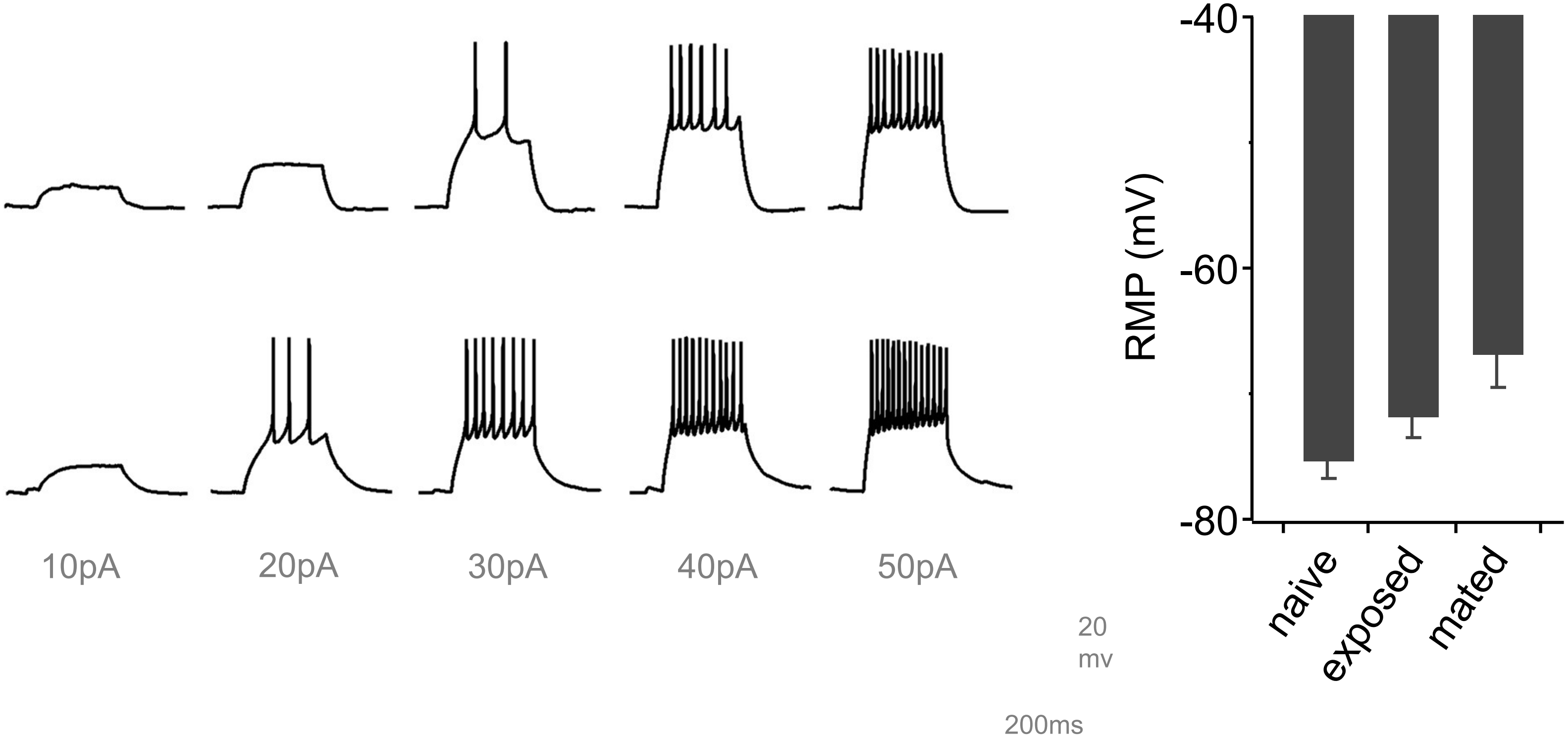
- both amplitude and frequency of spontaneous EPSPs are increased after mating

Mating enhances interneuron excitability



- after mating, granule cells become more excitable
  → show increased firing for the same stimulus

Mating enhances interneuron excitability



- after mating, granule cells become more excitable
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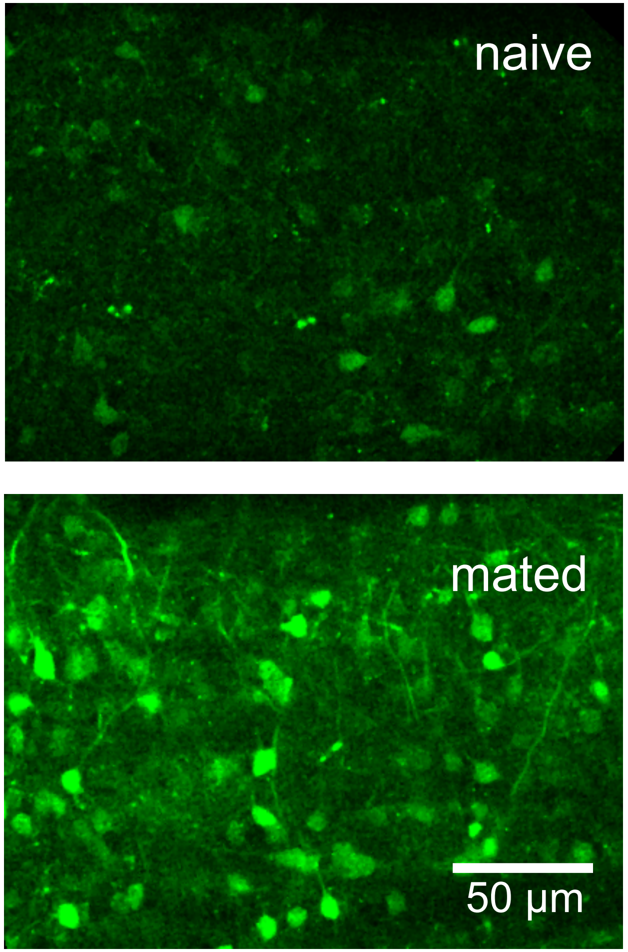
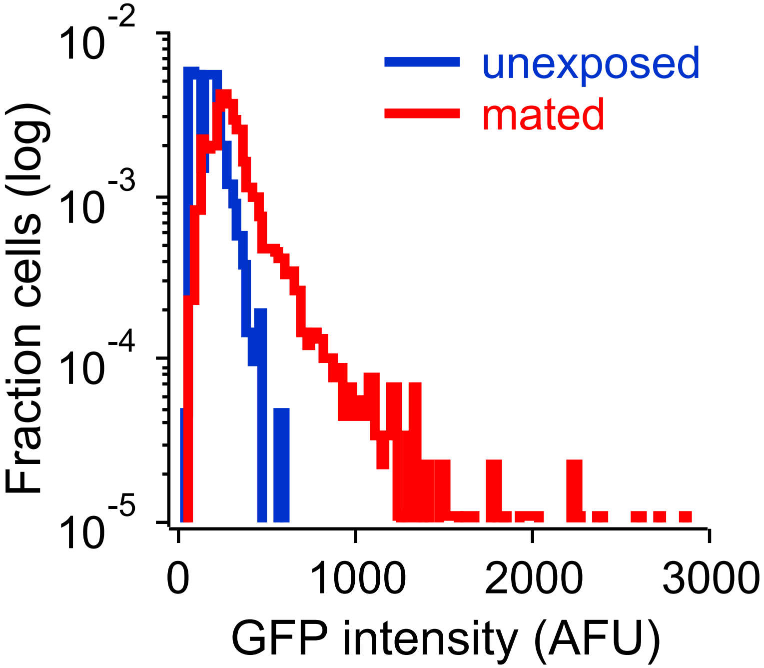
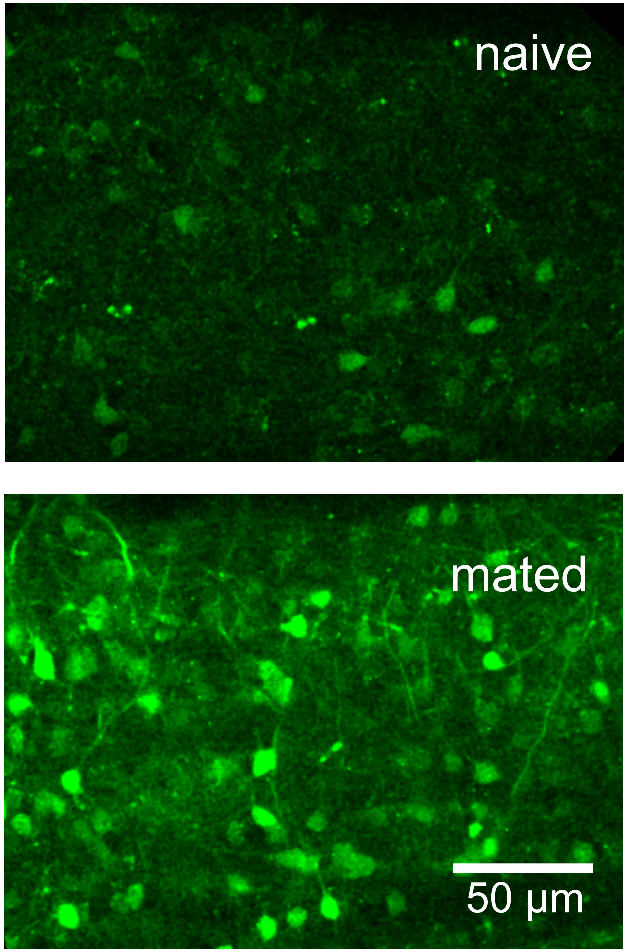
Testing the cellular specificity of plasticity

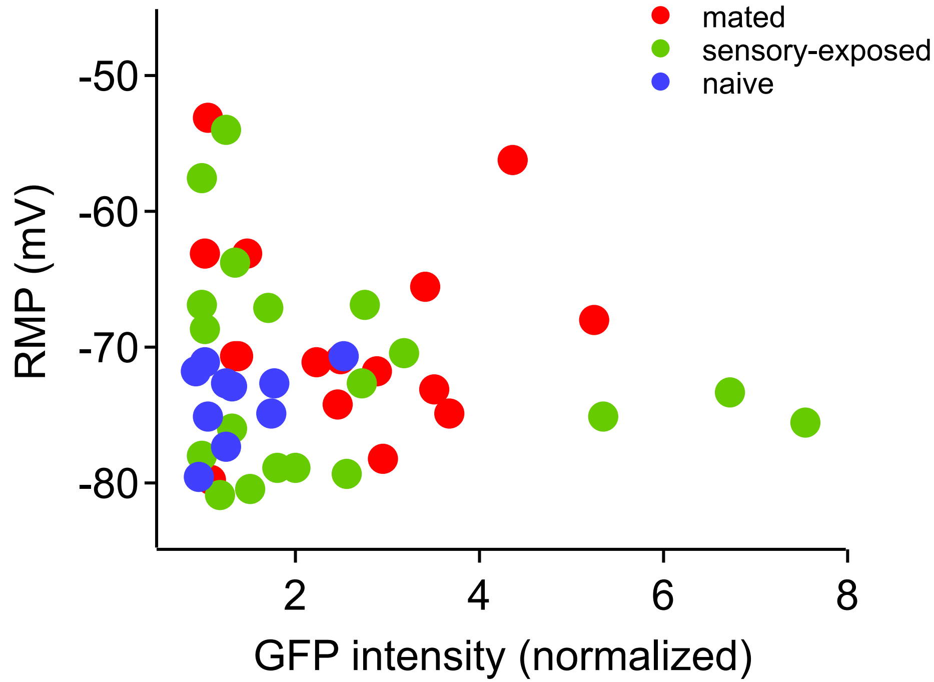




- mating induces robust GFP expression in AOB granule cells

Testing the cellular specificity of plasticity





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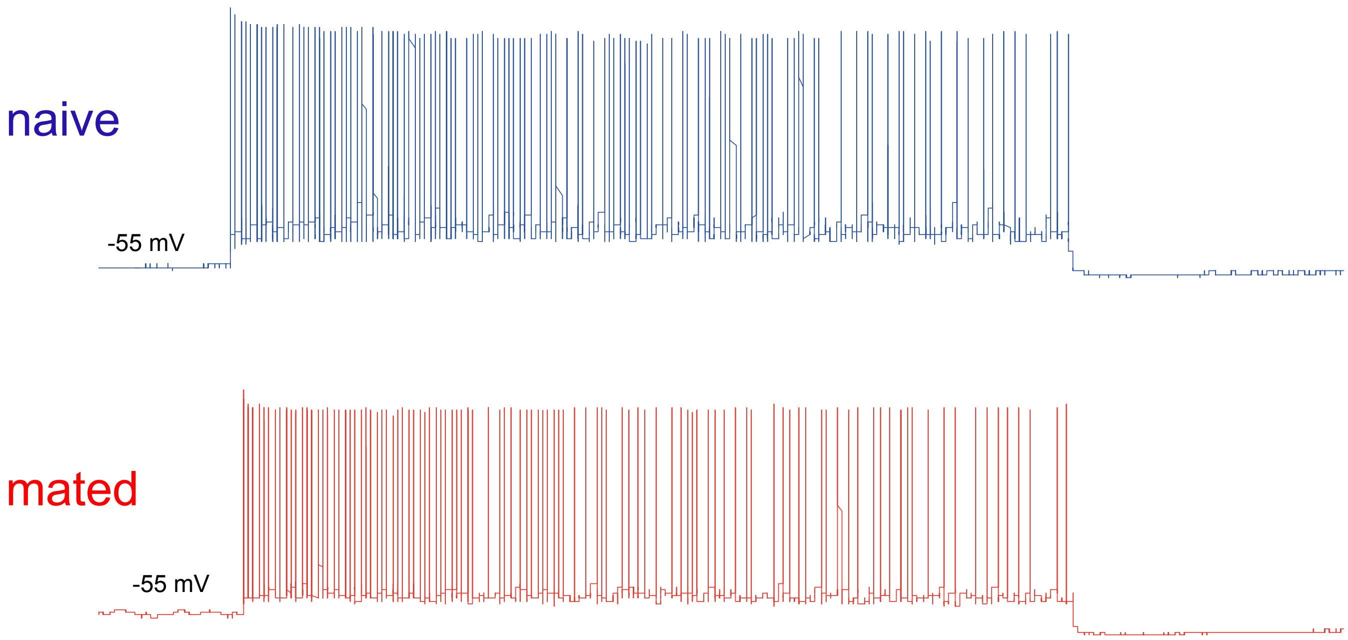
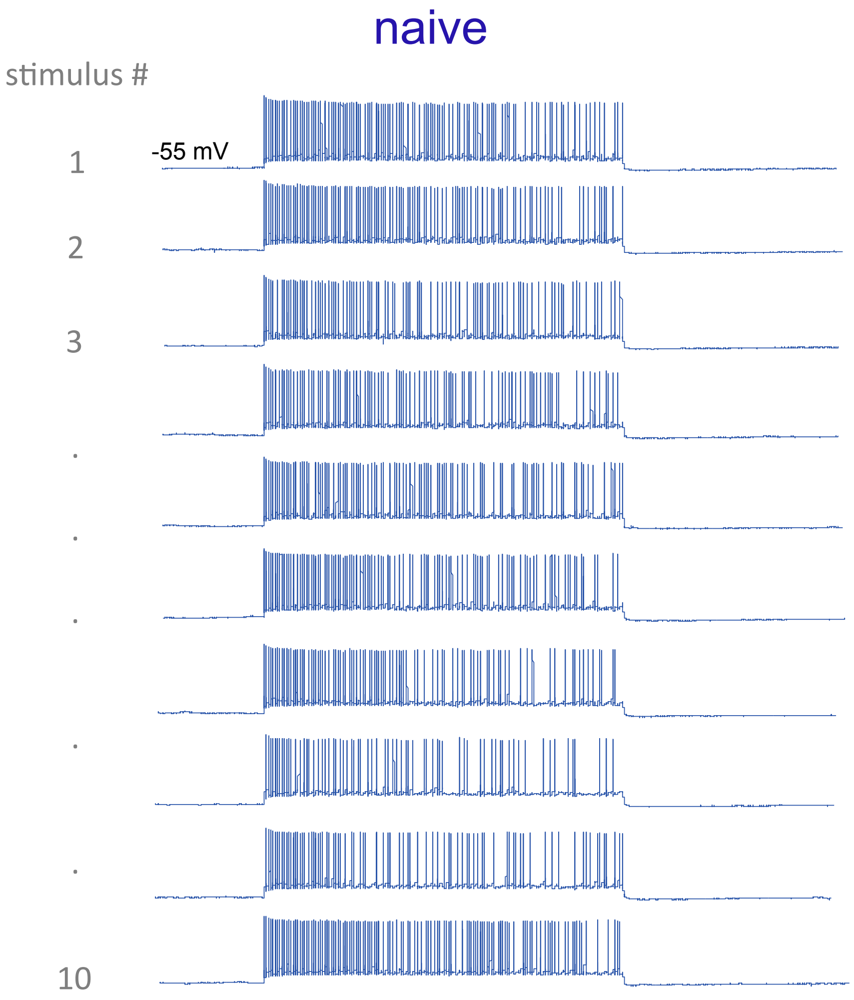
Output of mitral cells after mating



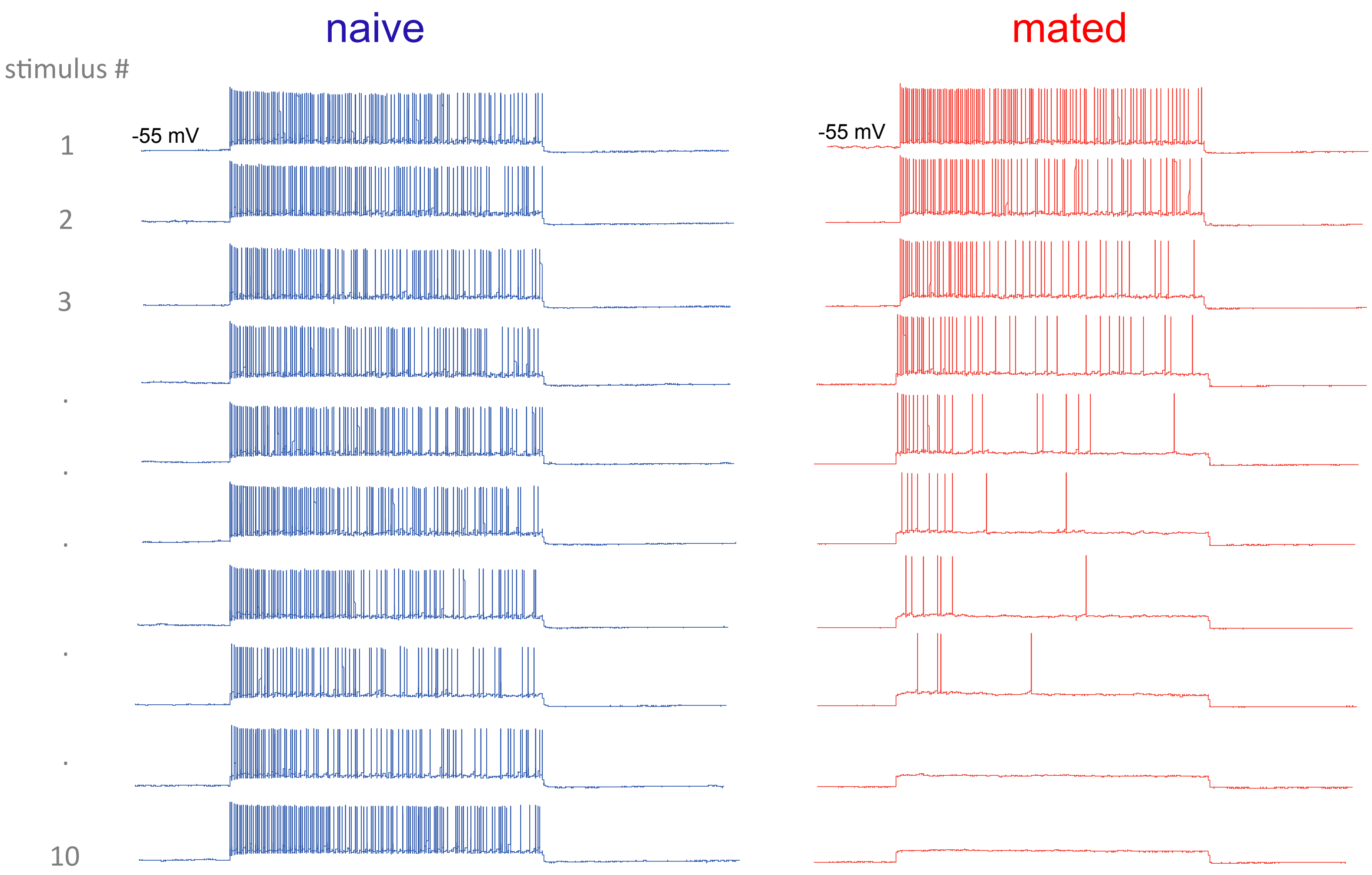
- initial responses to first stimulus are similar for mitral cells naive and mated animals

Output of mitral cells after mating



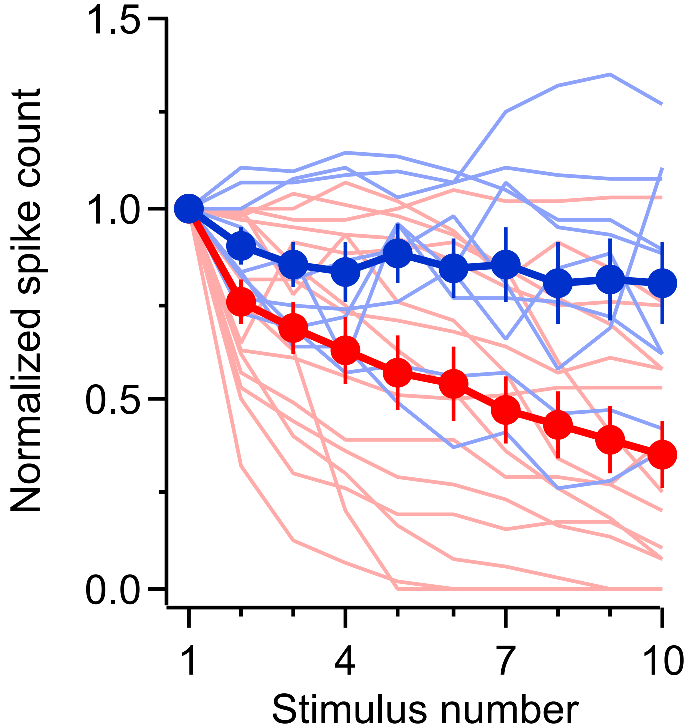
- dynamics of MC output are strongly altered after mating

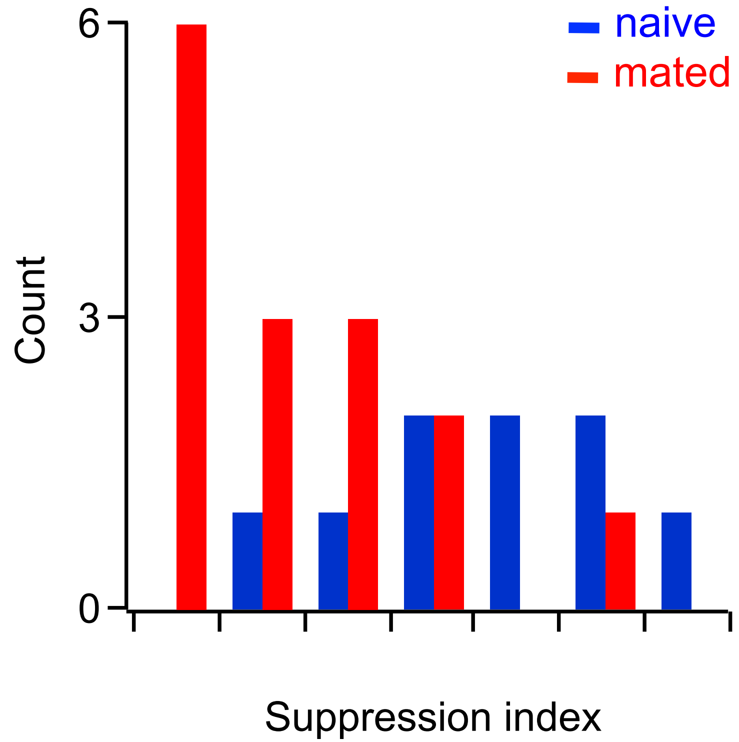
Output of mitral cells after mating



- dynamics of MC output are strongly altered after mating

Mating leads to slowly emerging suppression

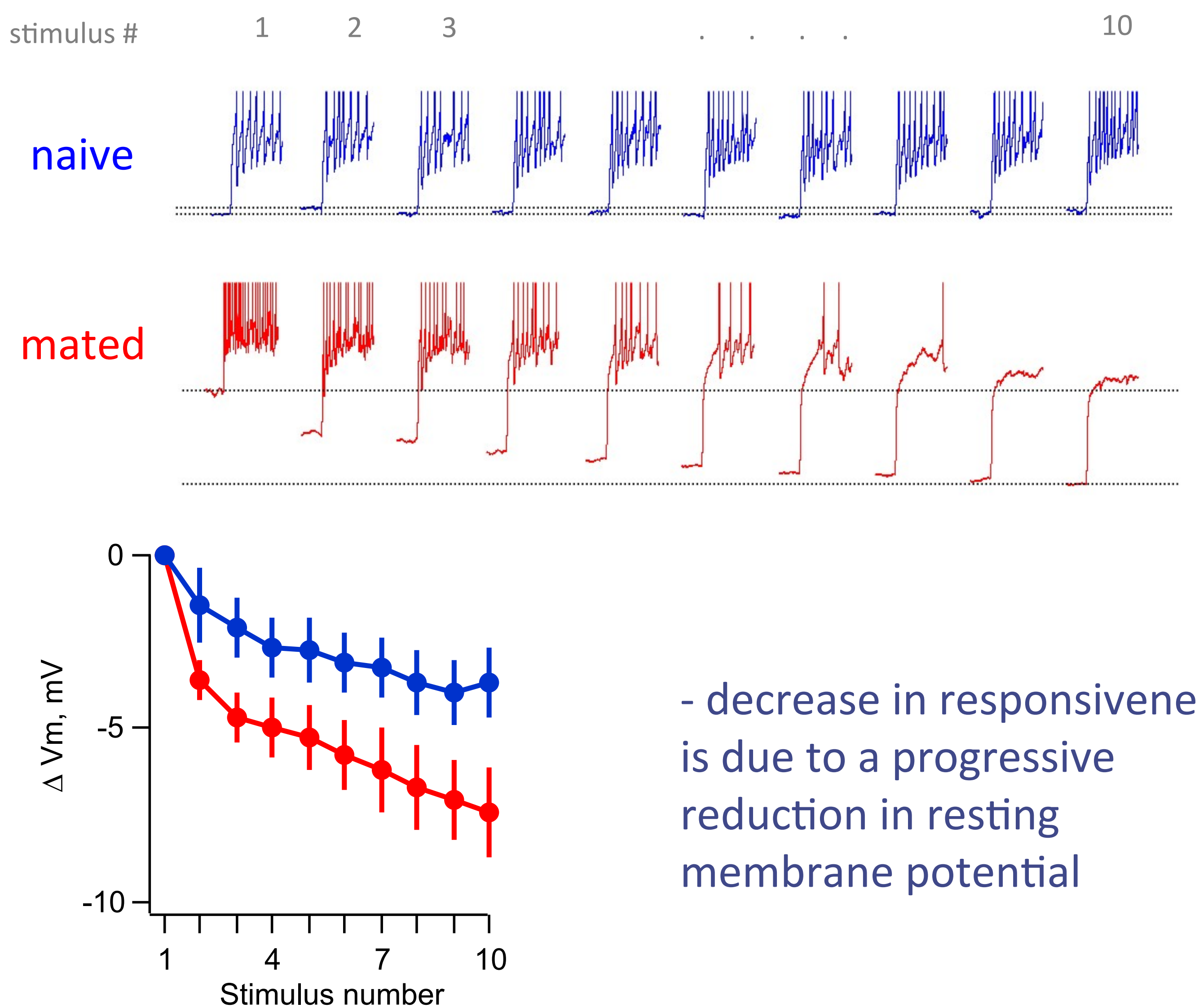




- after imprinting, many MCs show marked drops in firing for repeated stimuli

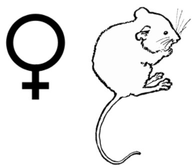
- population distribution for reduced responsiveness

Mating leads to slowly emerging suppression

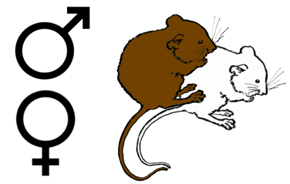


- decrease in responsiveness is due to a progressive reduction in resting membrane potential

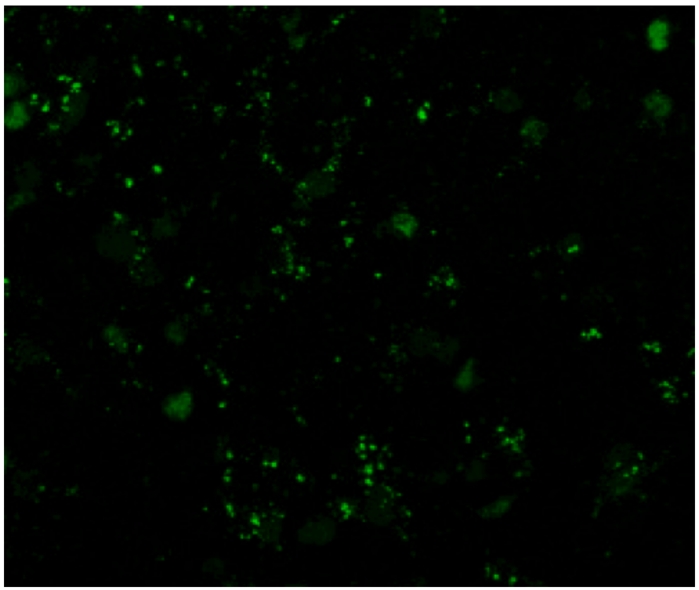
Cellular specificity of learning (ii)

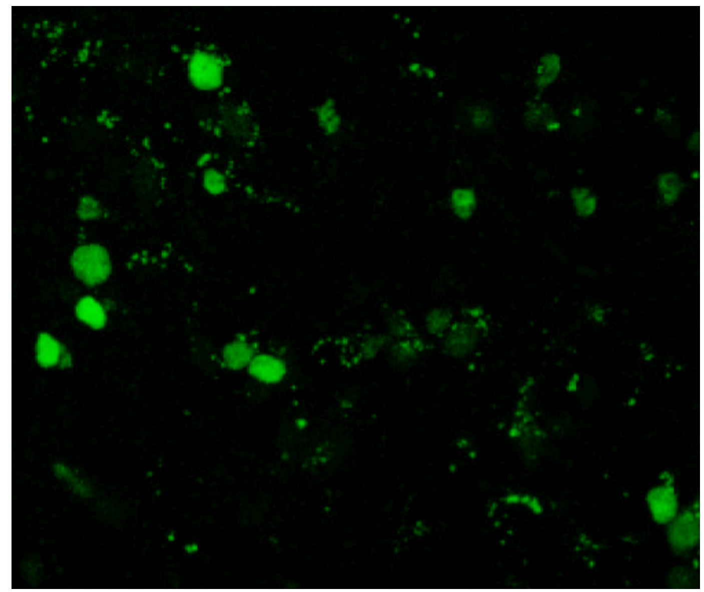


naive
female



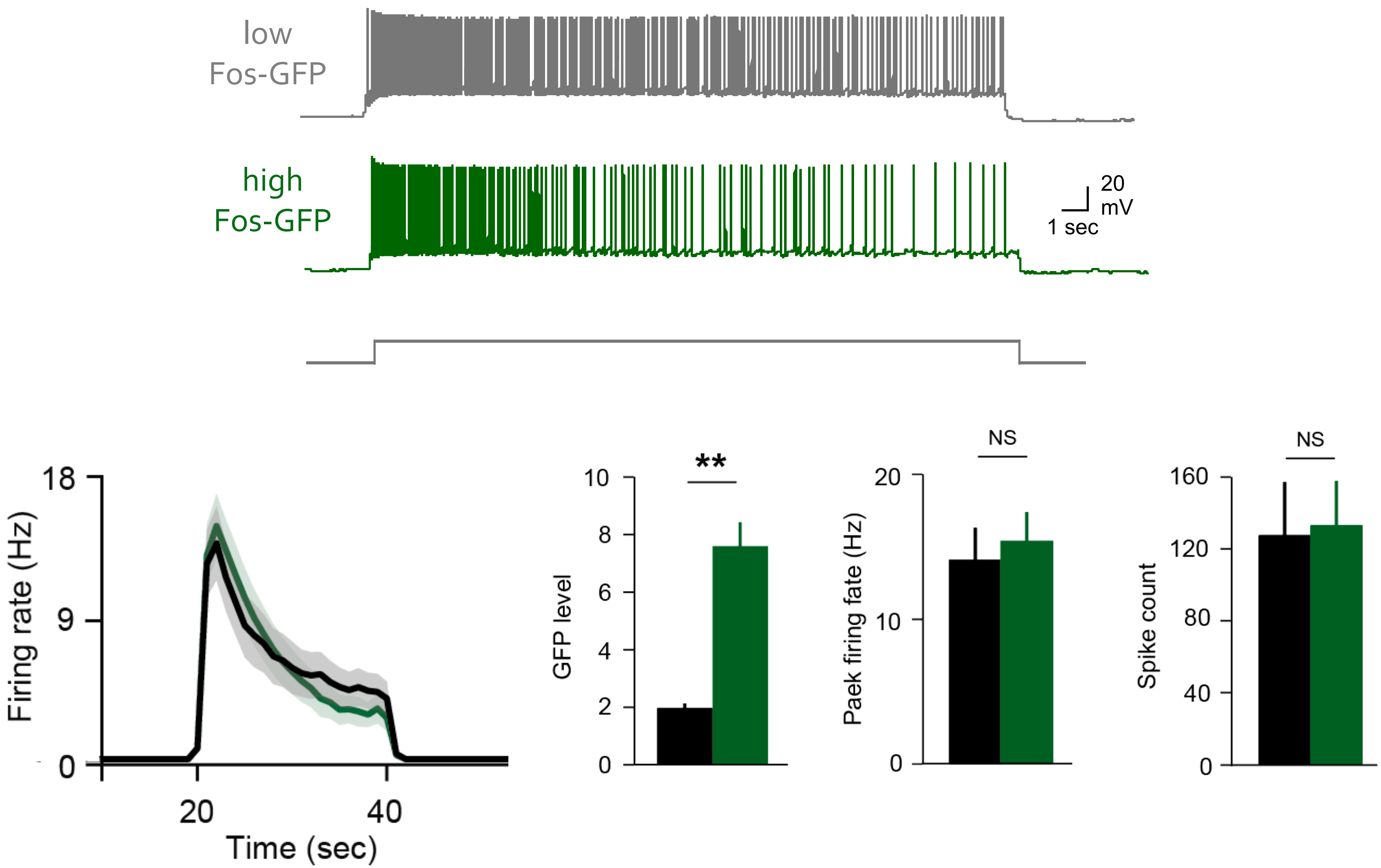
mated
female





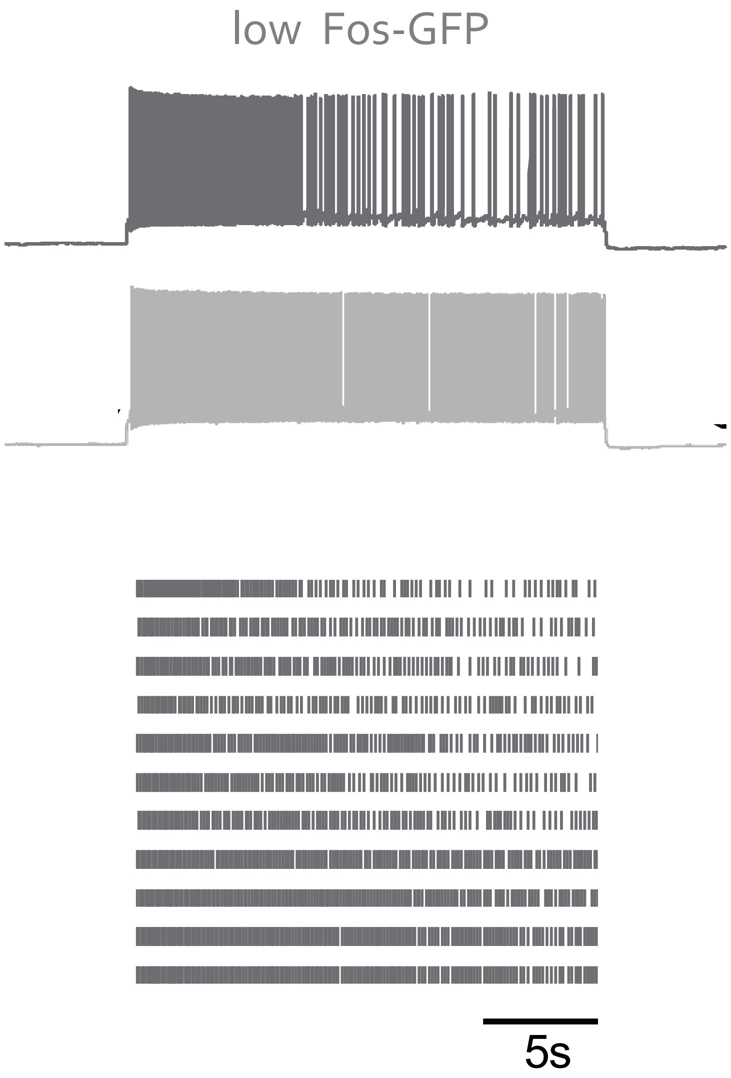
- a subset of stud-activated MCs are labeled with Fos-GFP after mating
- allows targeted recordings of cells encoding the learned cue

Cellular specificity of learning (ii)



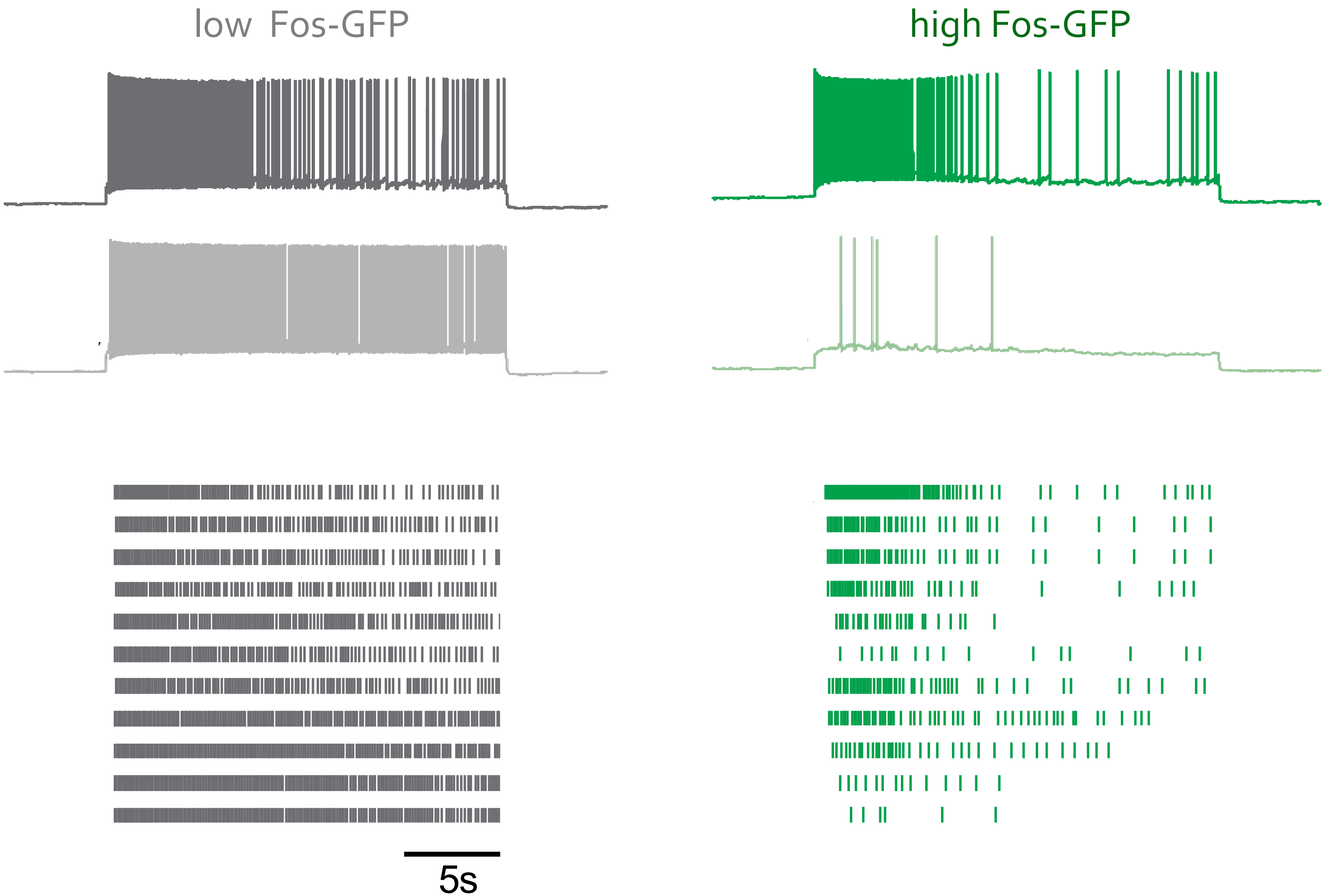
- neurons activated during prior mating experience are more strongly suppressed than cells lacking GFP expression

Cellular specificity of learning (ii)



- stud-activated neurons become unresponsive over time

Cellular specificity of learning (ii)



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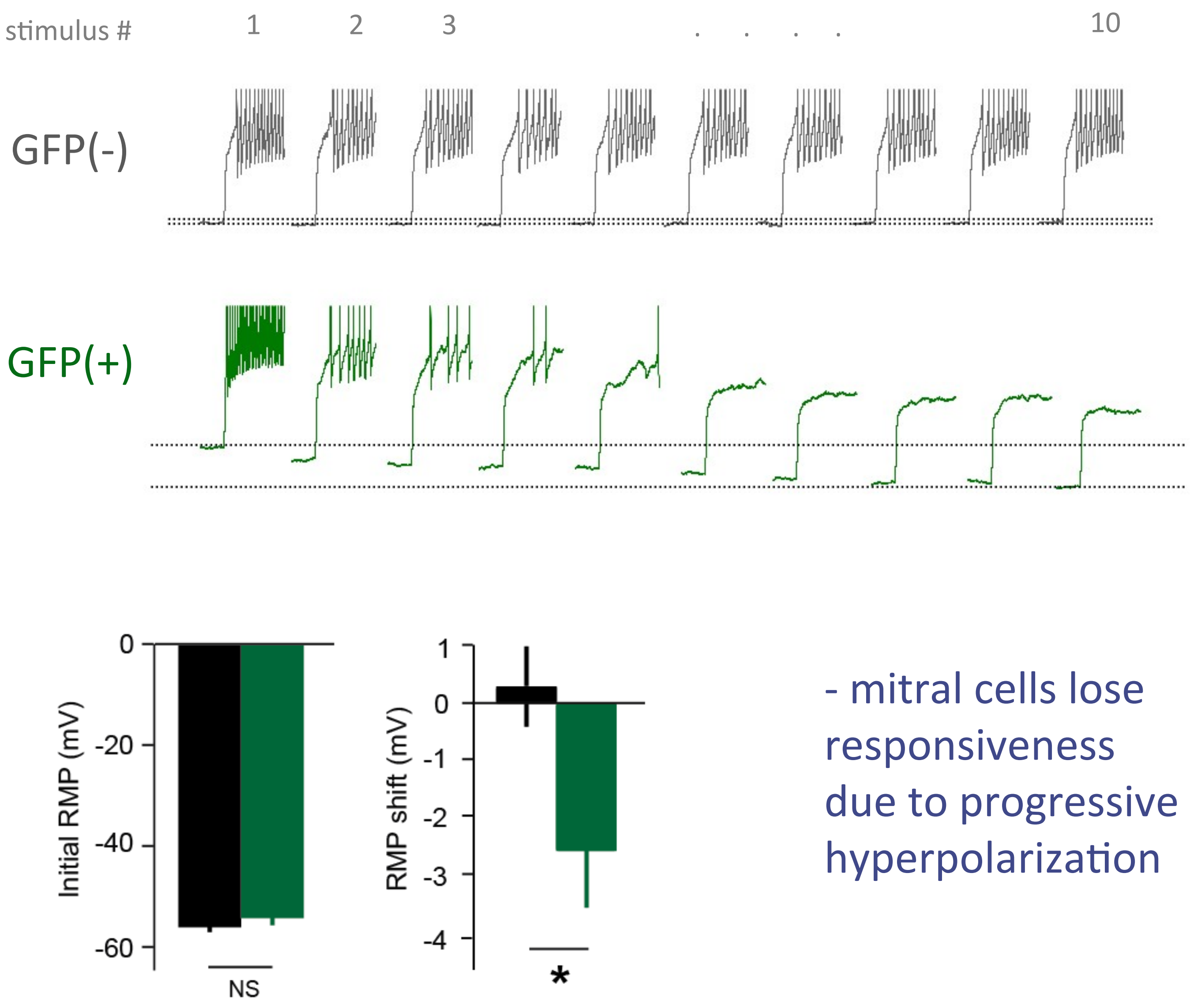
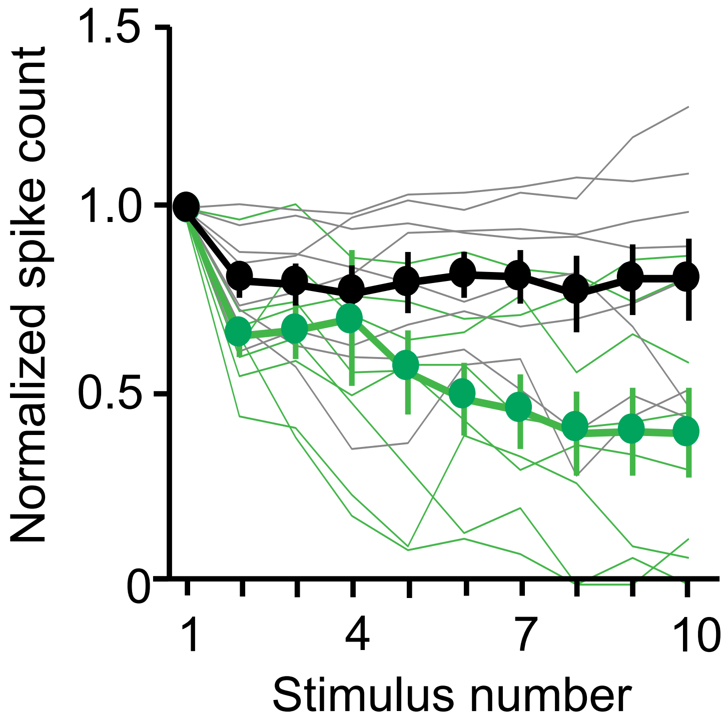
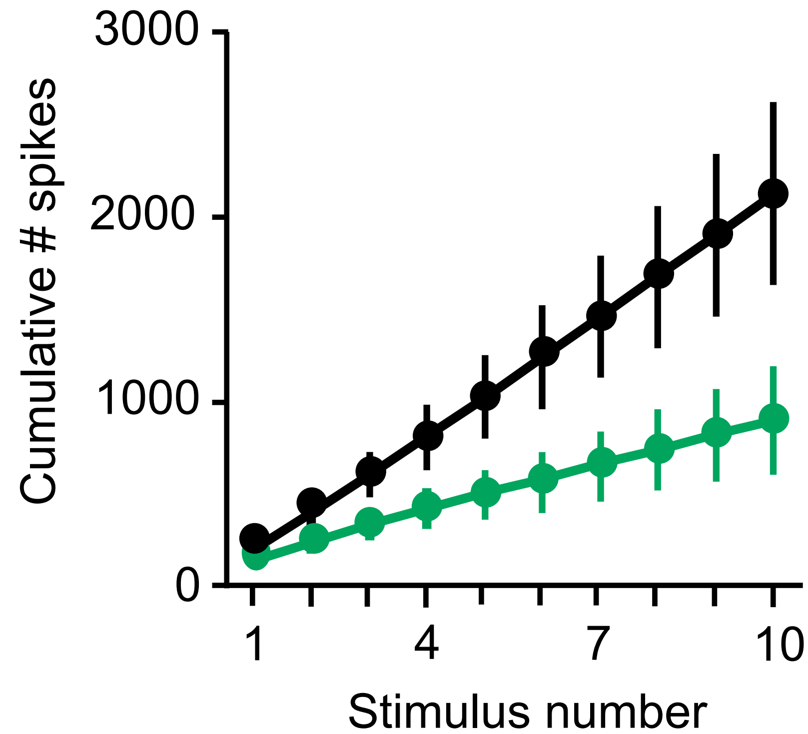
Mating leads to slowly emerging suppression



- mitral cells lose responsiveness due to progressive hyperpolarization

Cellular specificity of learning





- stud-encoding mitral cells show a striking loss of responsiveness

- cumulative output from the AOB is strongly reduced

AOB plasticity after mating – key points

(1) Inhibition is upregulated; changes in multiple points in the inhibitory feedback pathway

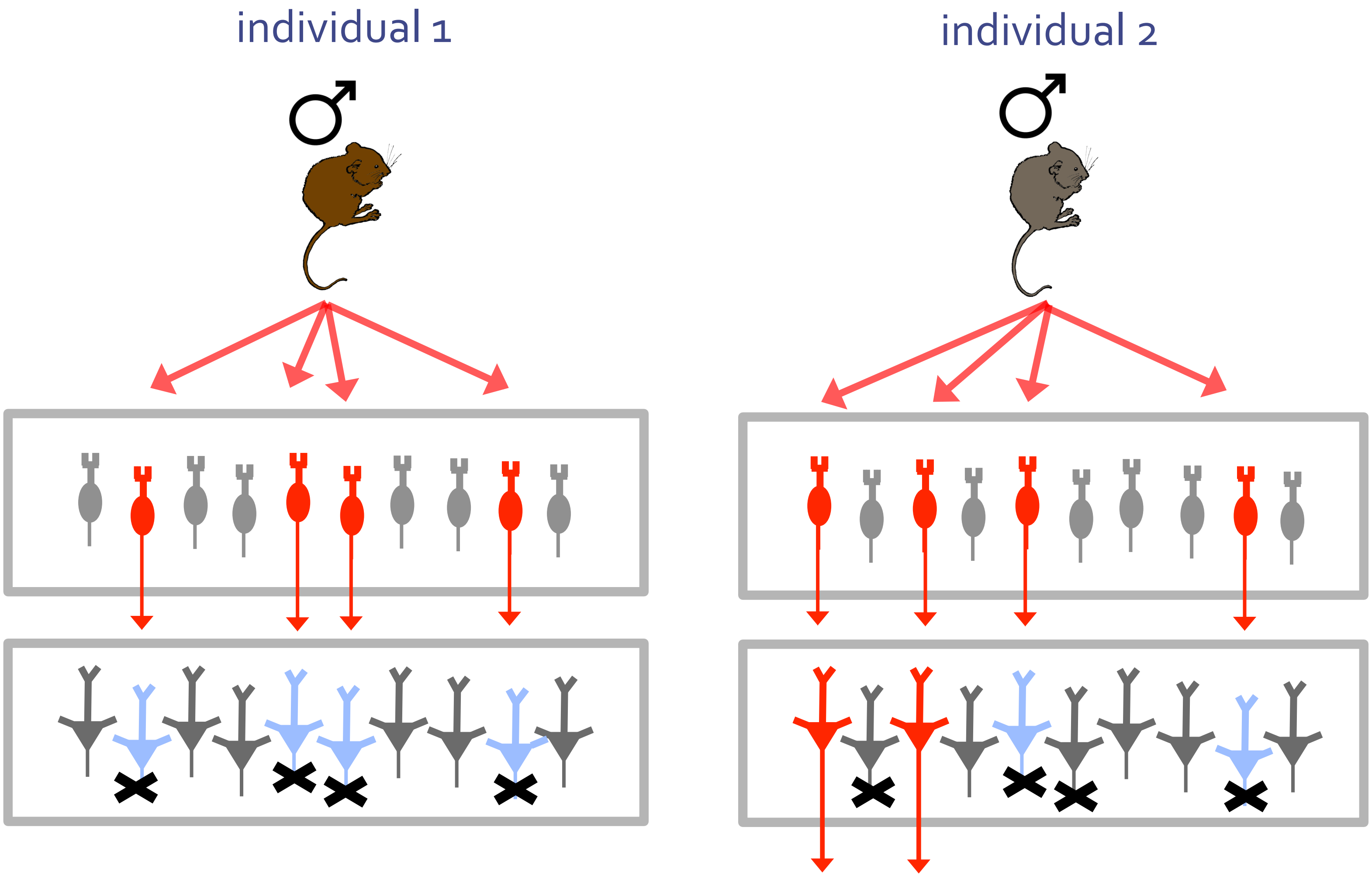
(2) Inhibitory plasticity is broadly distributed, with no obvious cellular specificity

(3) Imprinting also leads to plasticity in intrinsic excitability

(4) Mitral cell activity acquires a strong history-dependence: initial responses are similar, but responses to subsequent stimuli are markedly reduced

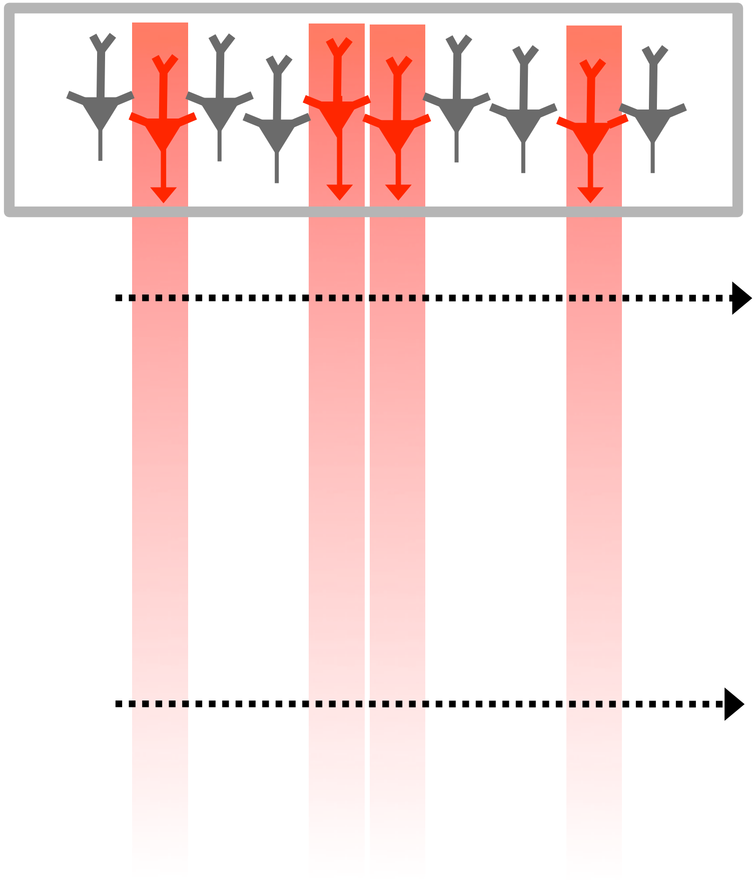
(5) Dynamic regulation of mitral cell responses is specific to the neurons representing the stud male.

Reducing memory interference?



slow temporal filtering may prevent learning from obscuring sensory cues from other individuals

Separate timescales for hormones and behavior?



early: sensory information fully available for detection, discrimination, and rapid behavioral decisions; limits memory interference

late: lowered sensitivity reduces the impact of the imprinted pheromones on neuroendocrine status

slow temporal filtering may allow separation of behavioral and neuroendocrine effects

THANKS

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