The Contribution of Adult-Born Interneurons to Olfactory Bulb Circuit Functions

Laboratory for Perception and Memory
— Pasteur Institute & CNRS —
Paris - France

Main Objectives

1) Adult-born neurons boost learning and memory

2) Unique features of new neuron synaptic output

3) Top-down control of adult-born neuron activity

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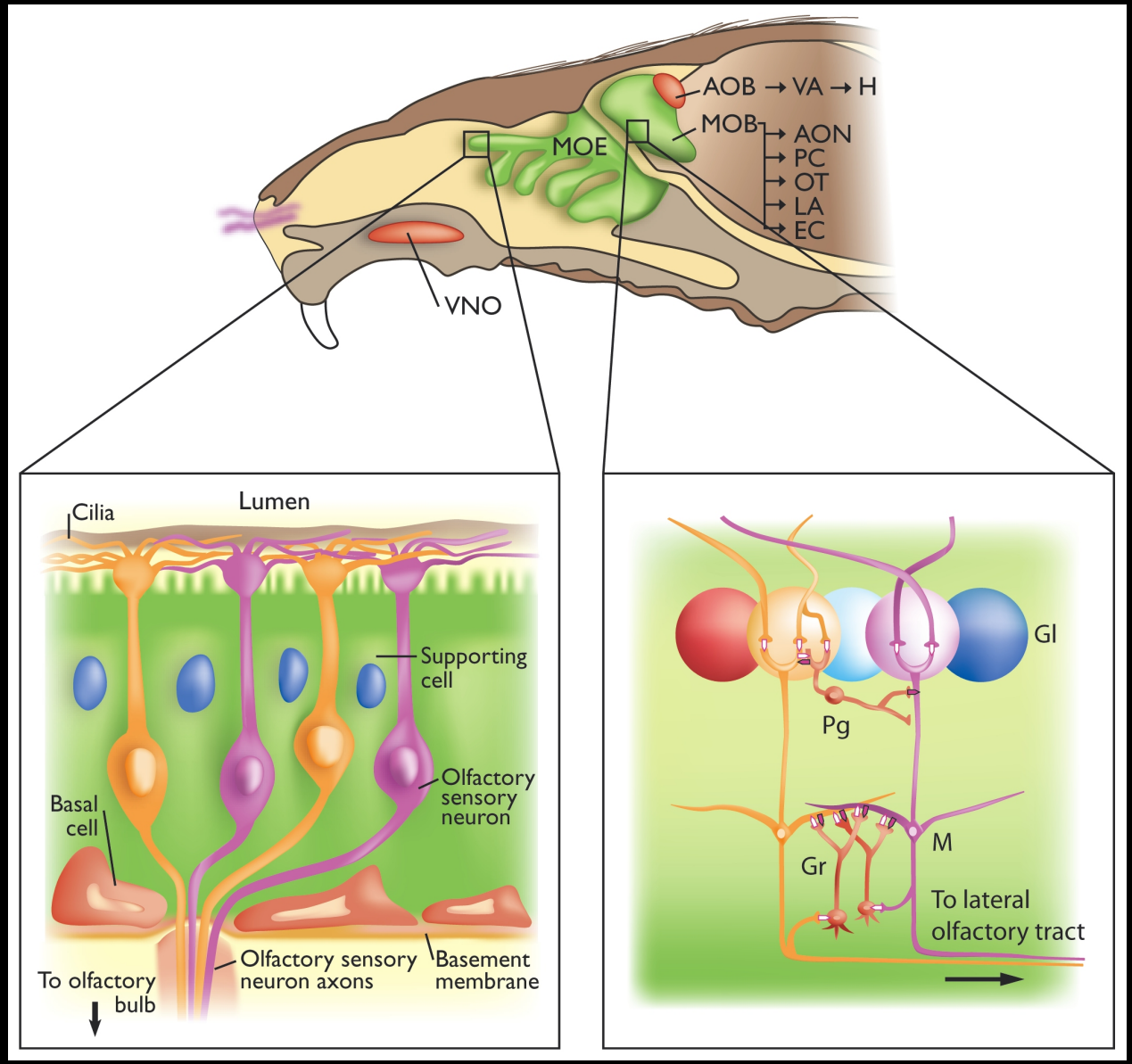
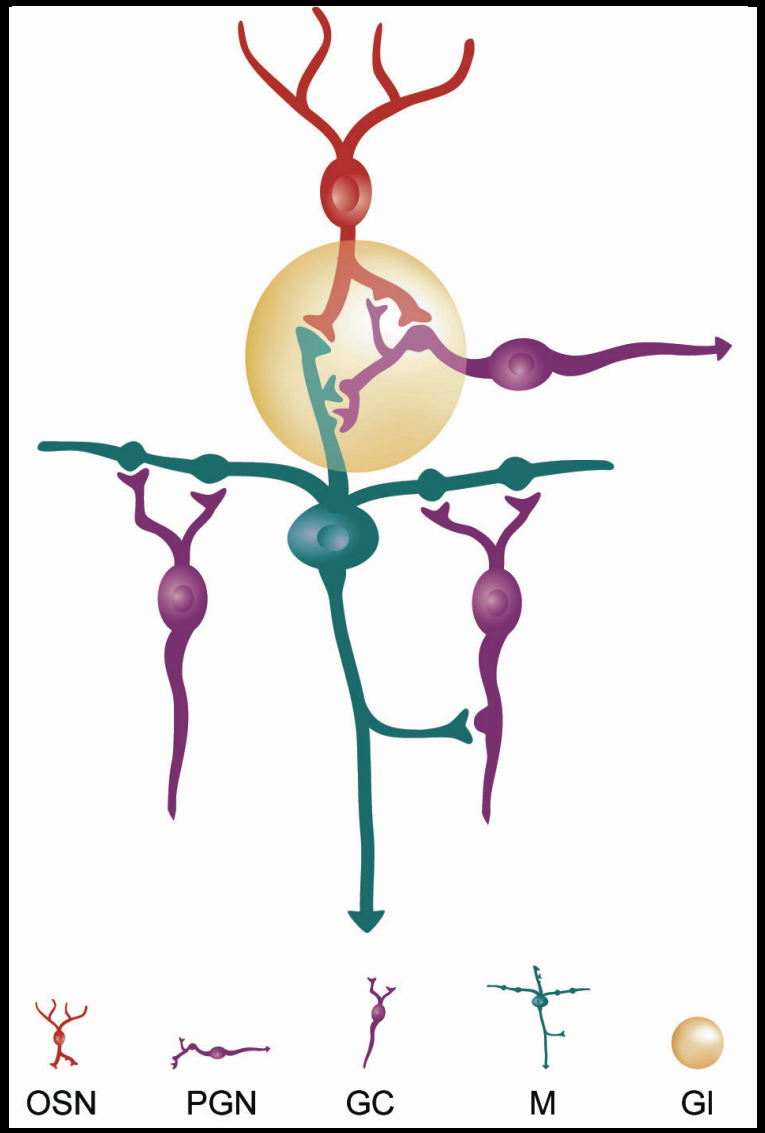
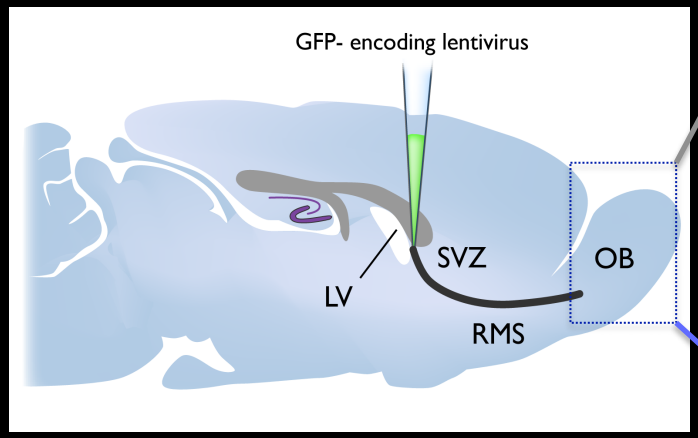
The Rejuvenating Olfactory System

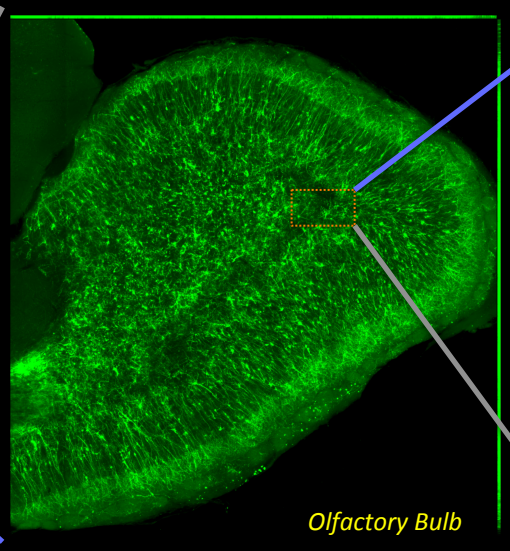


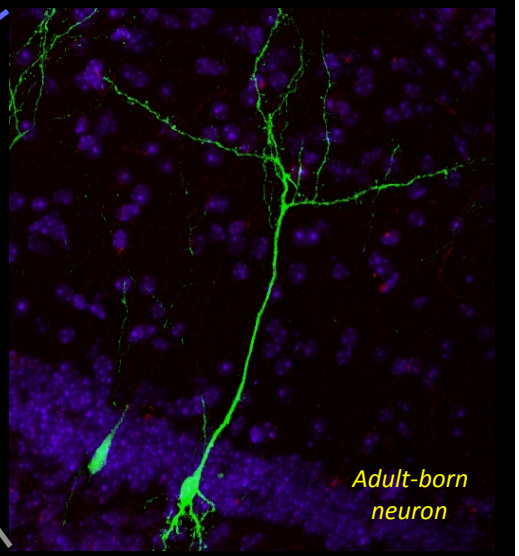
The Canonical Microcircuit

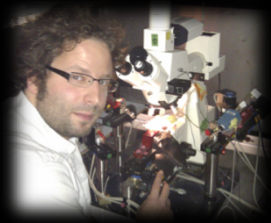


Identifying newborn neurons in adult brain circuits









Antoine Nissant
Resarch assistant / CNRS

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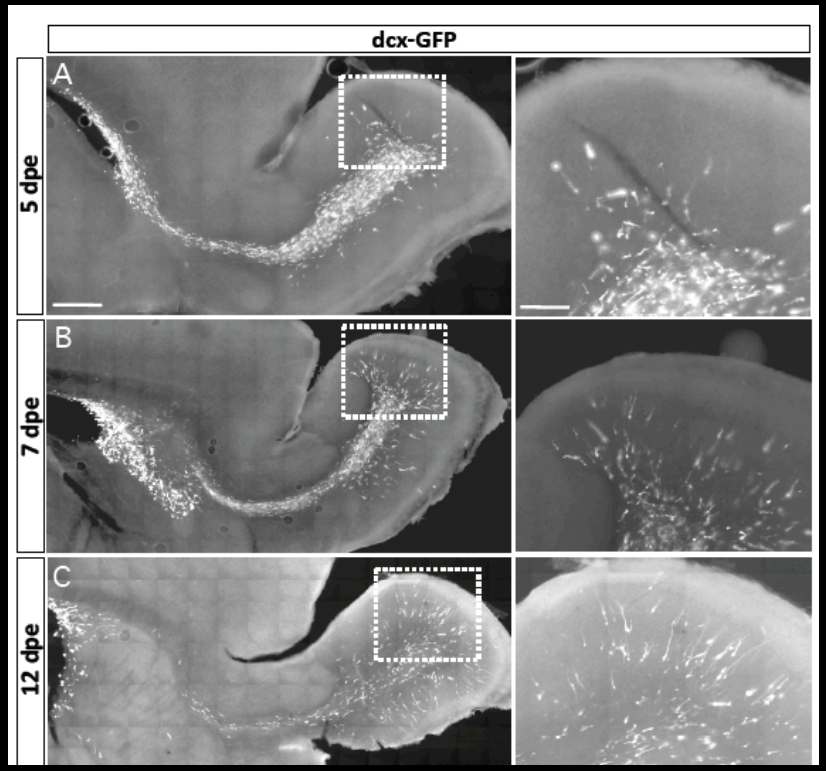
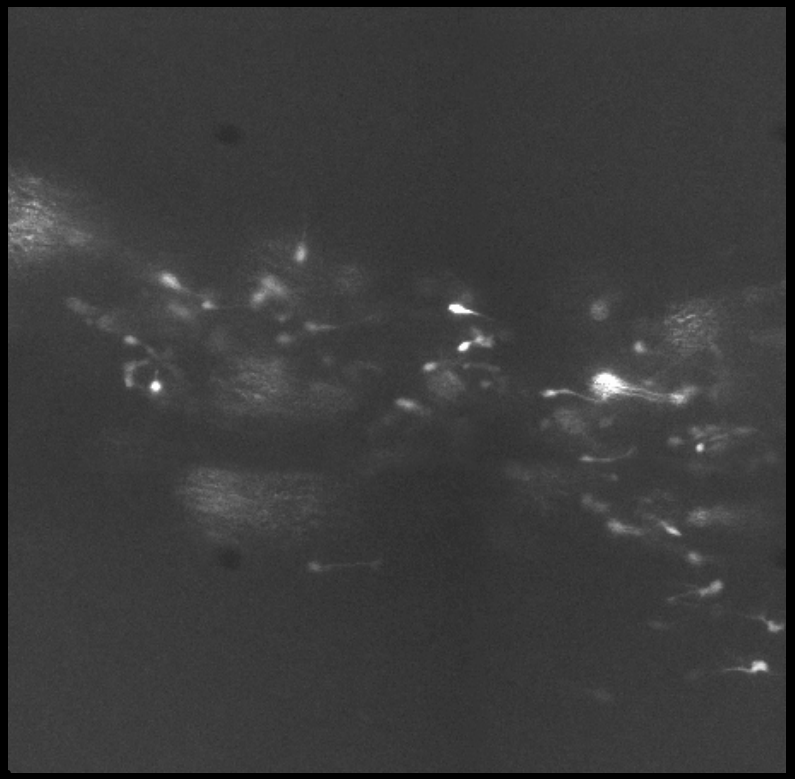
A journey in the forebrain

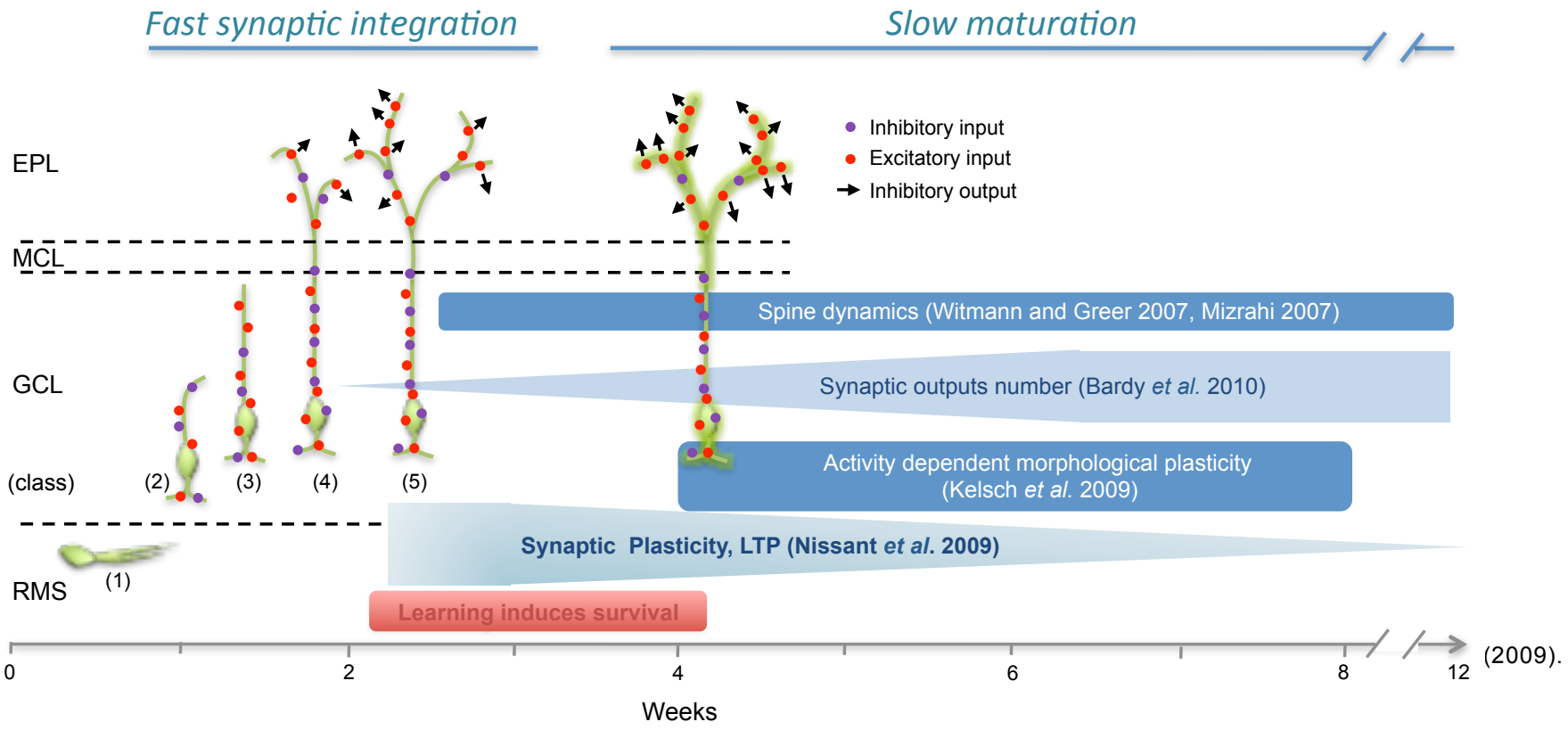




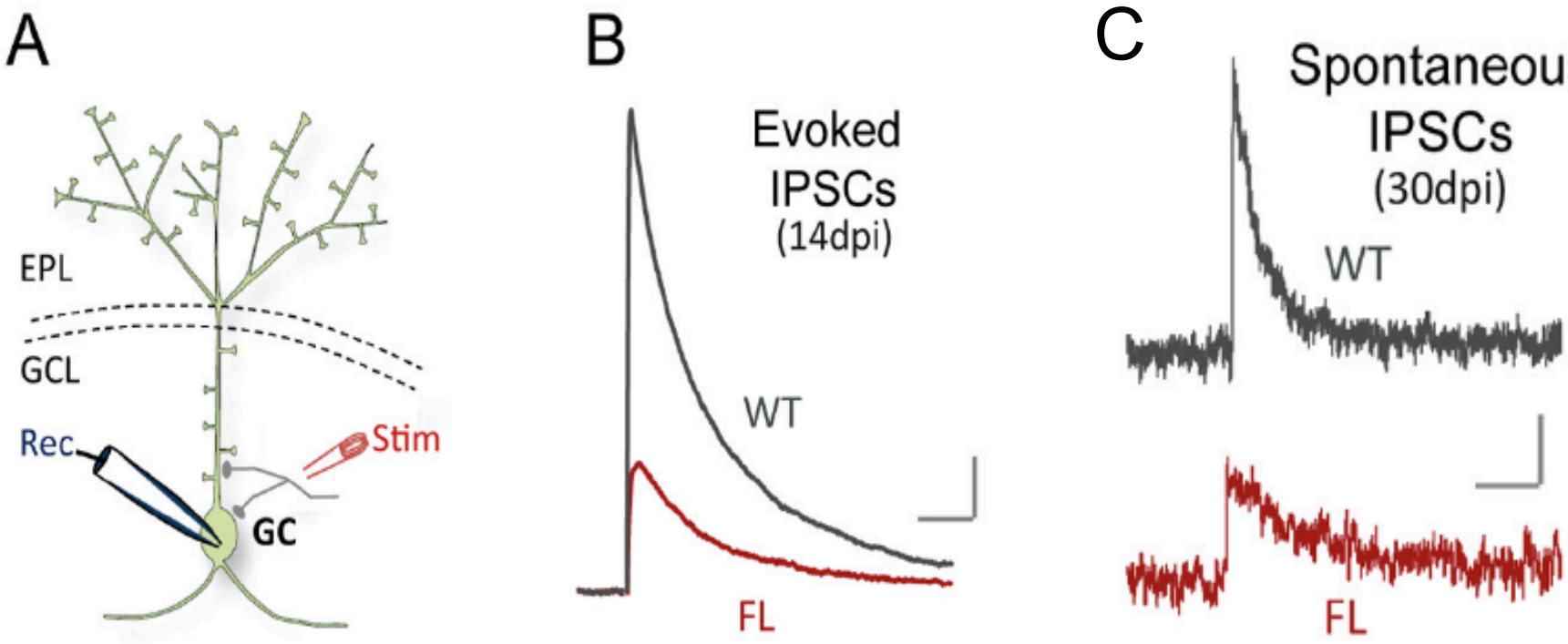
J. Neurosci. 31: 7551-62 (2012).

Maturation of newborn neurons plasticity

A

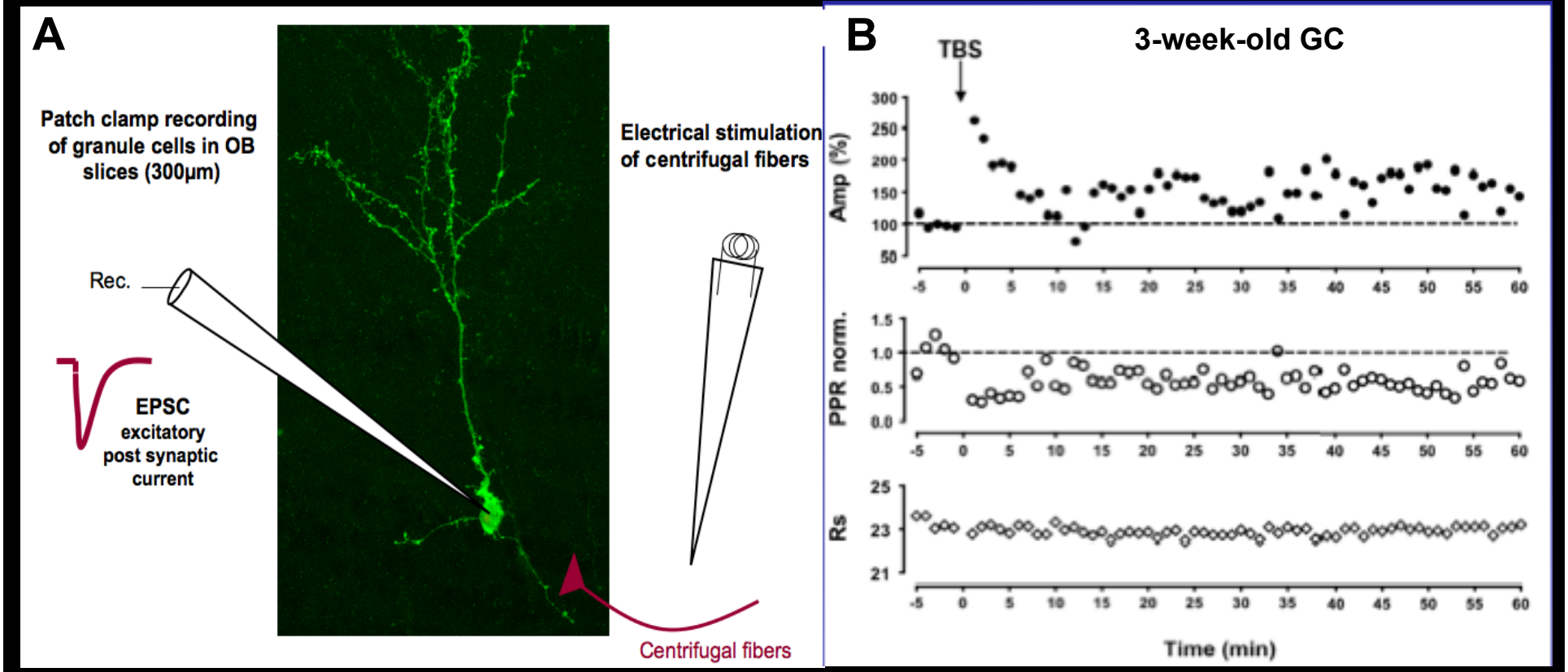


Maturation of newborn neurons plasticity



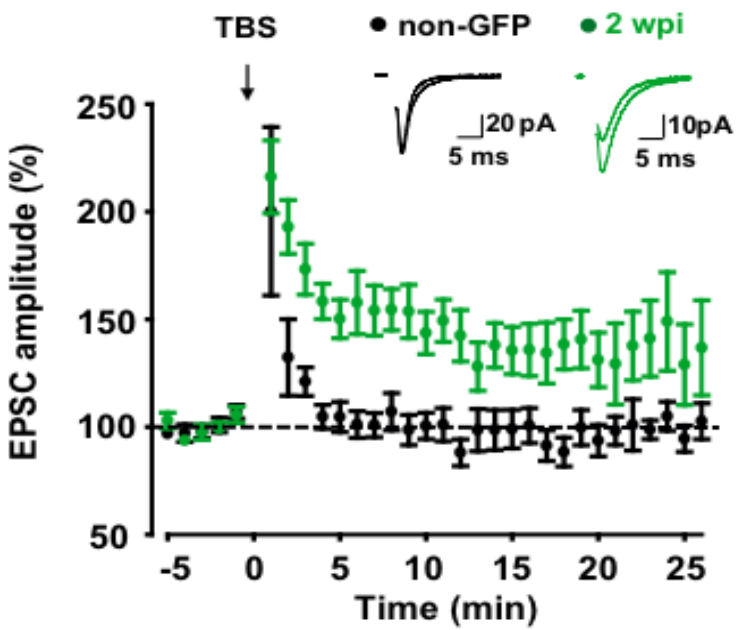
Pallotto et al., J Neurosci 2012

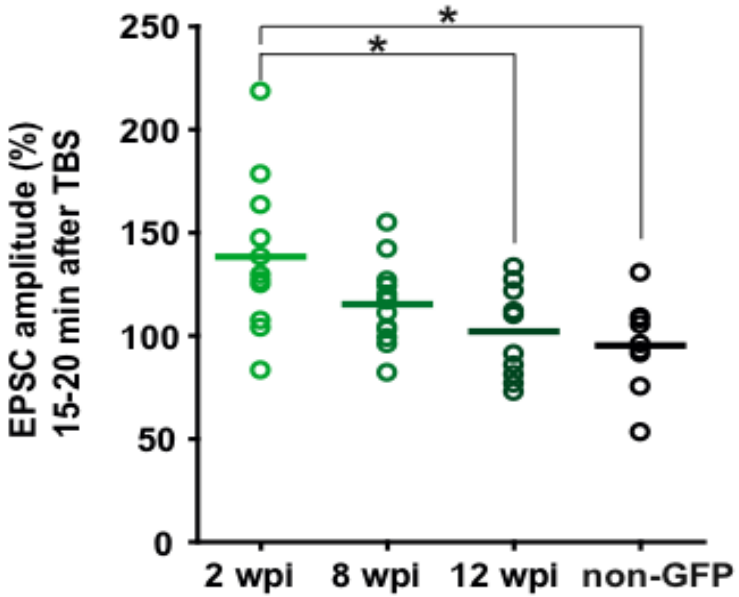
Newborn neurons display plasticity



Nissant *et al.*, Nature Neurosci. (2009)

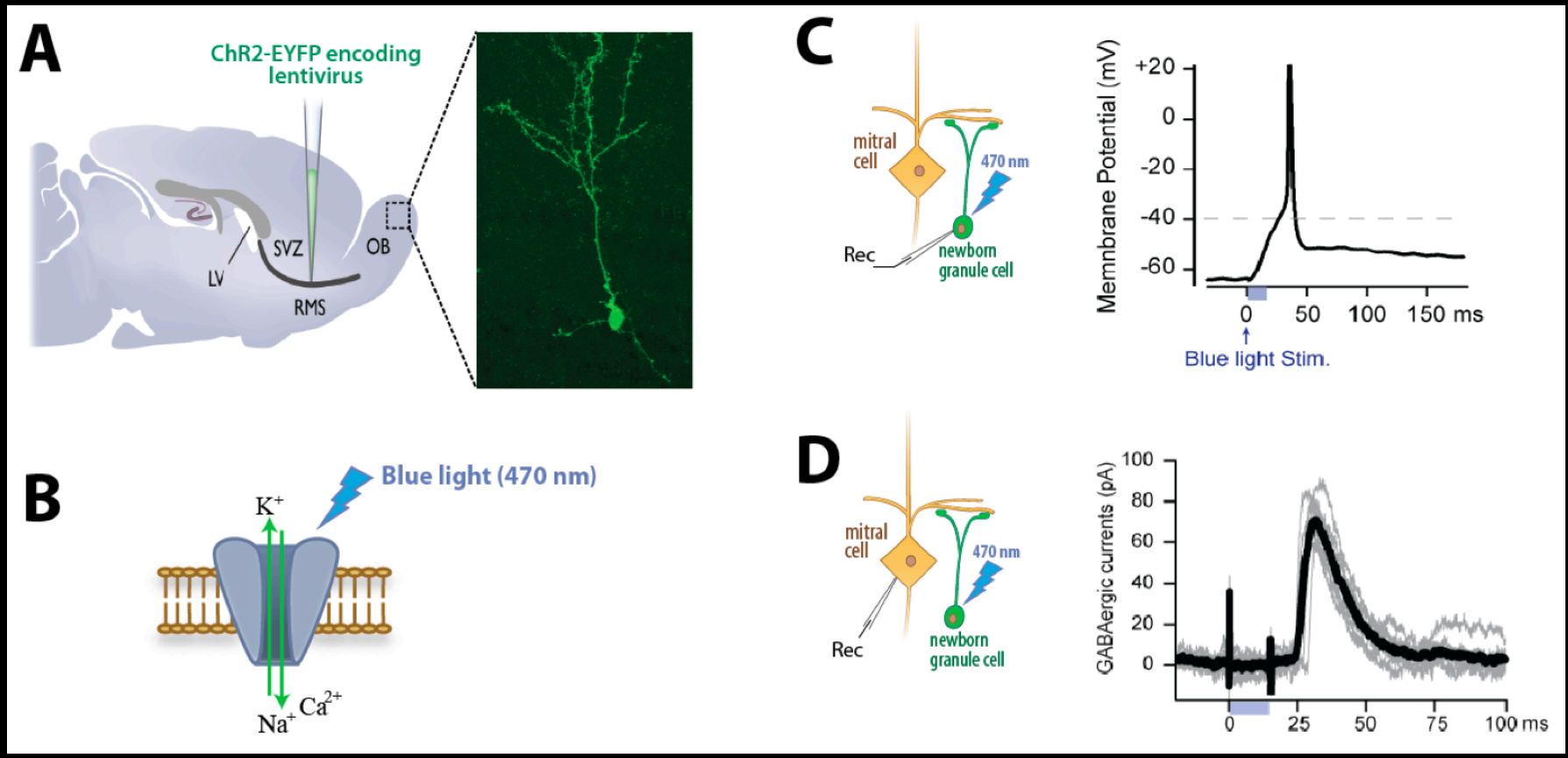
Newborn neurons are transiently amenable





Nat. Neurosci. 12, 728-730 (2009).

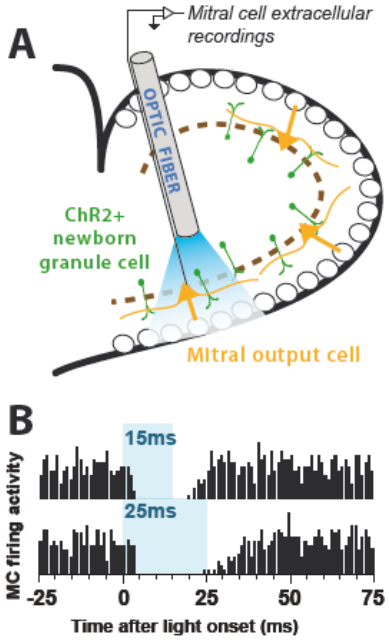
Nature of the output signal?



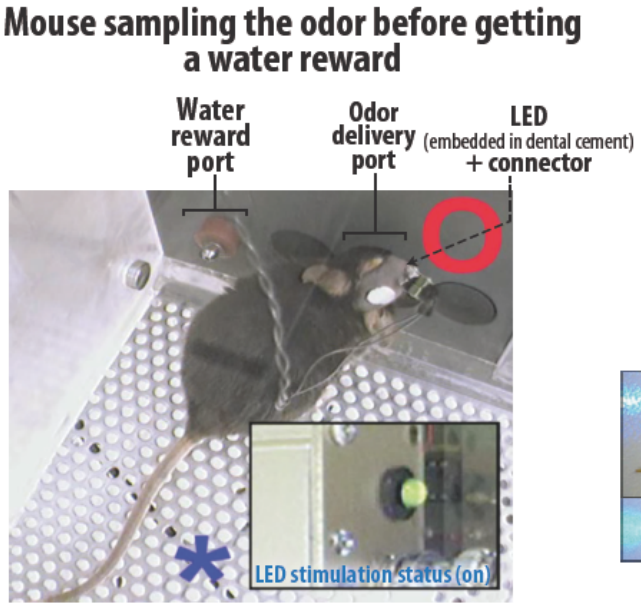
Bardy *et al.*, J. Neurosci. (2010)

Remote control of adult-born neurons firing by light

In vivo recordings in the awake head-fixed mouse

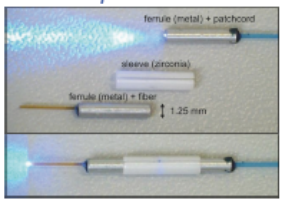


Optogenetic control during operant conditioning



Headfixed LED

Optic fibers



Custom-built olfactometer designed for optogenetics available at www.olfacto-meter.com

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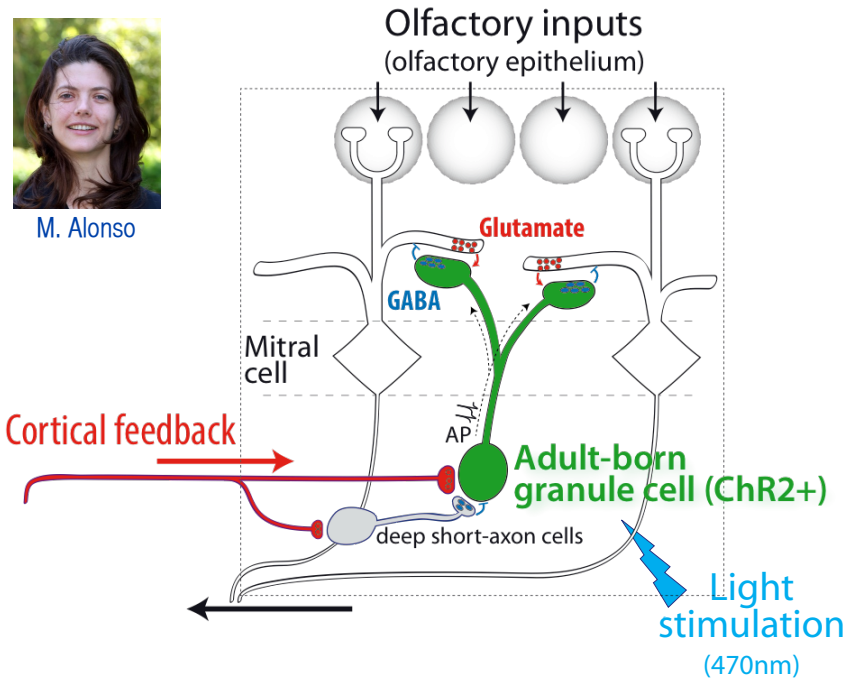
Gilles Gheusi
Assistant prof. (Univ. Paris 13)

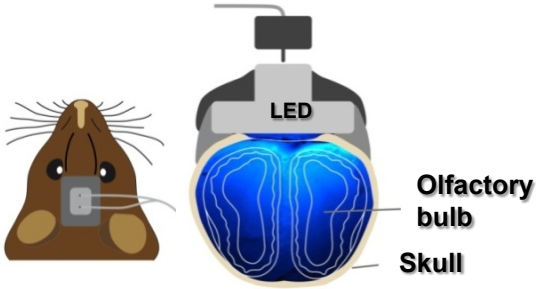
Mariana Alonso
Research associate (Inst. Pasteur)

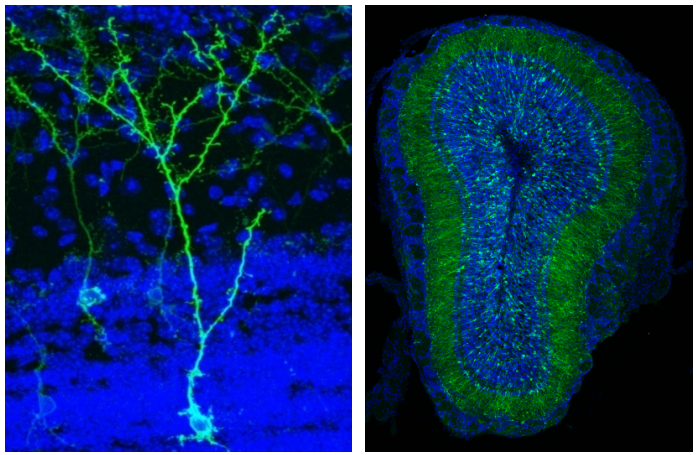
Sebastien Wagner
Engineer (Letten Foundation)

Effect of adult-born neurons activation on olfactory learning

M. Alonso

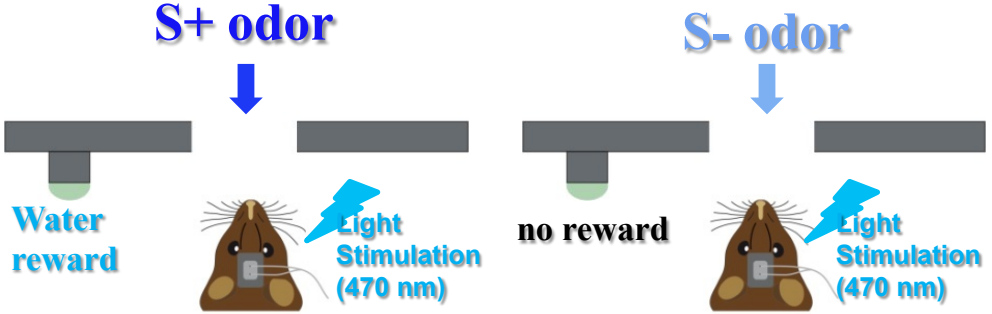






ChR2+ adult-born granule cell

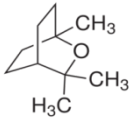
Olfactory discrimination learning



Alonso et al. Nat Neurosci 2012

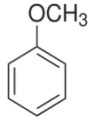
Easy and difficult learning tasks

Easy task



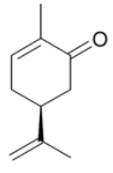
Cineole

vs



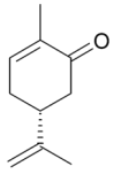
Anisole

Difficult task



Carvone+

vs



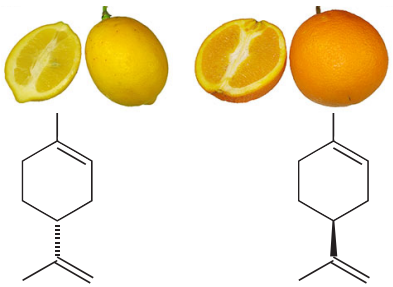
Carvone-

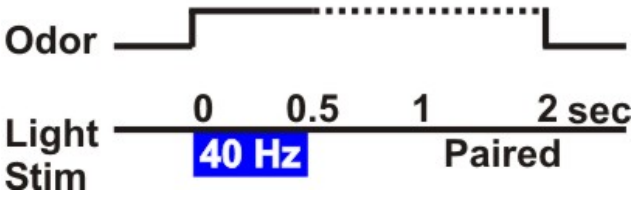
Only activation during S+ presentation accelerates difficult learning

"difficult"
odor discrimination
learning

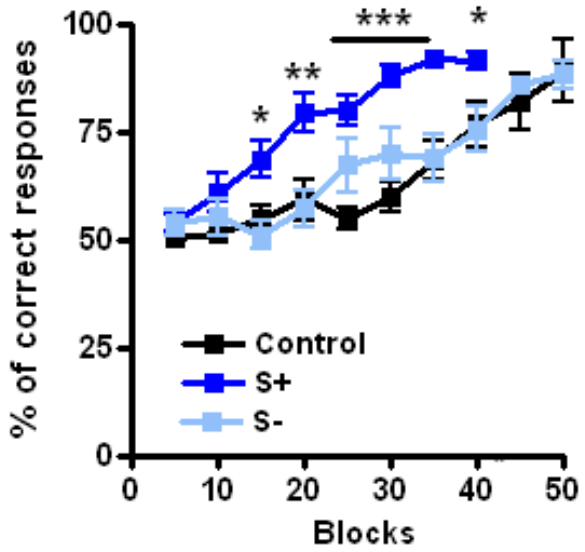
(R)-Limonene *vs* (S)-Limonene

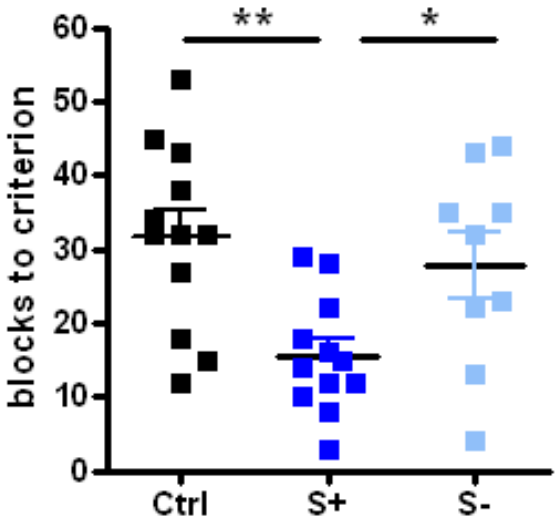
(lemon) (tangerine)





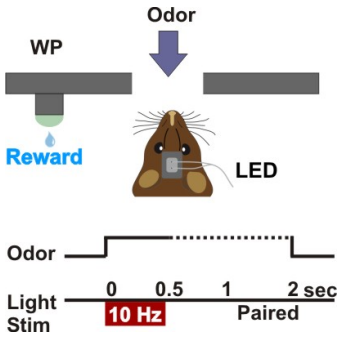
Light stimulation on
S+ odor OR S- odor

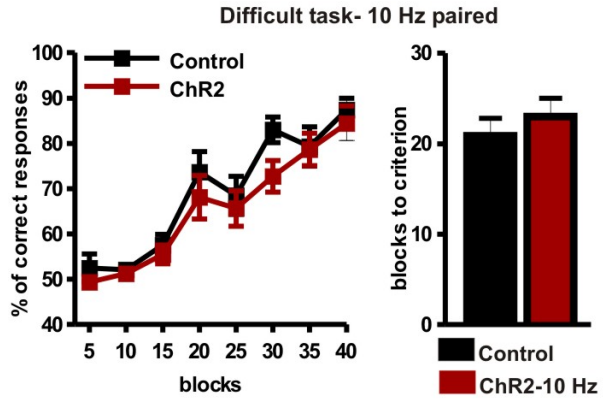


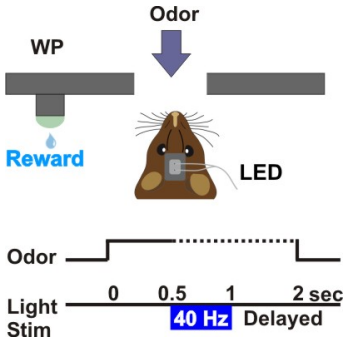


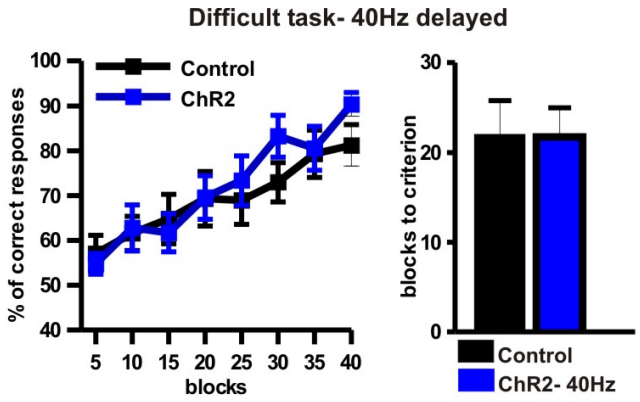
Question for the future: Top-down activation of GC during learning encodes odor reward value?

Learning facilitation depends on light frequency

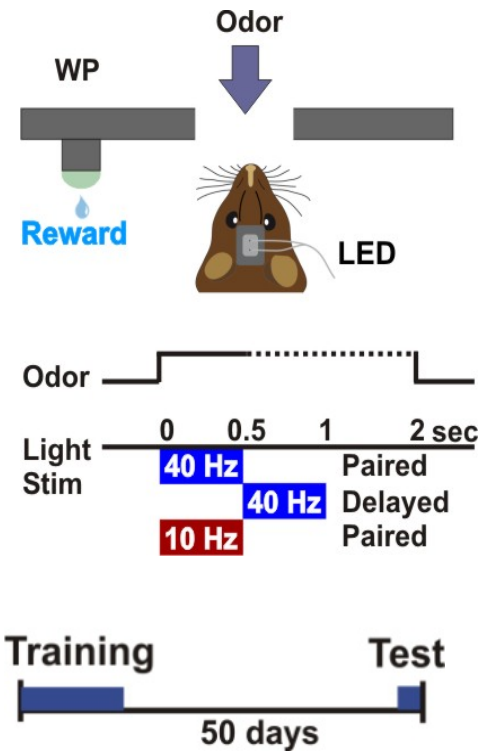


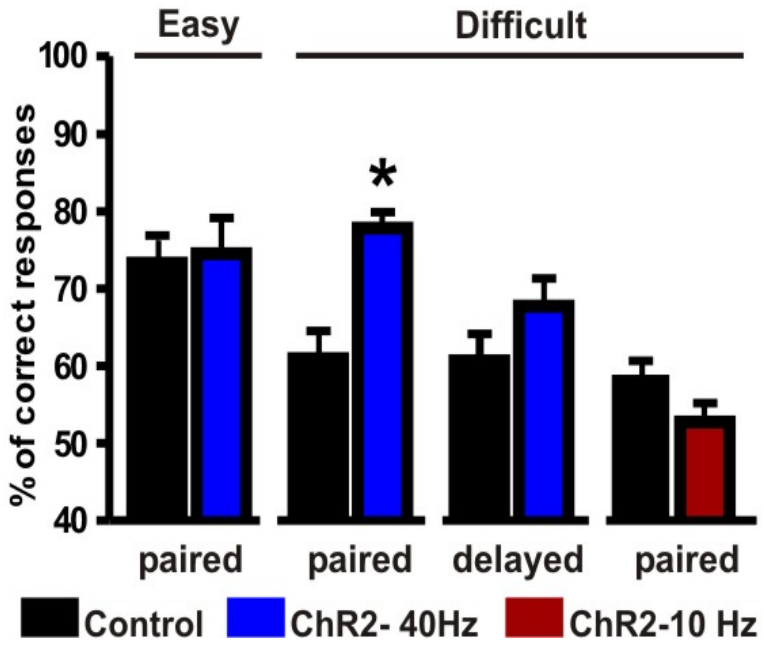




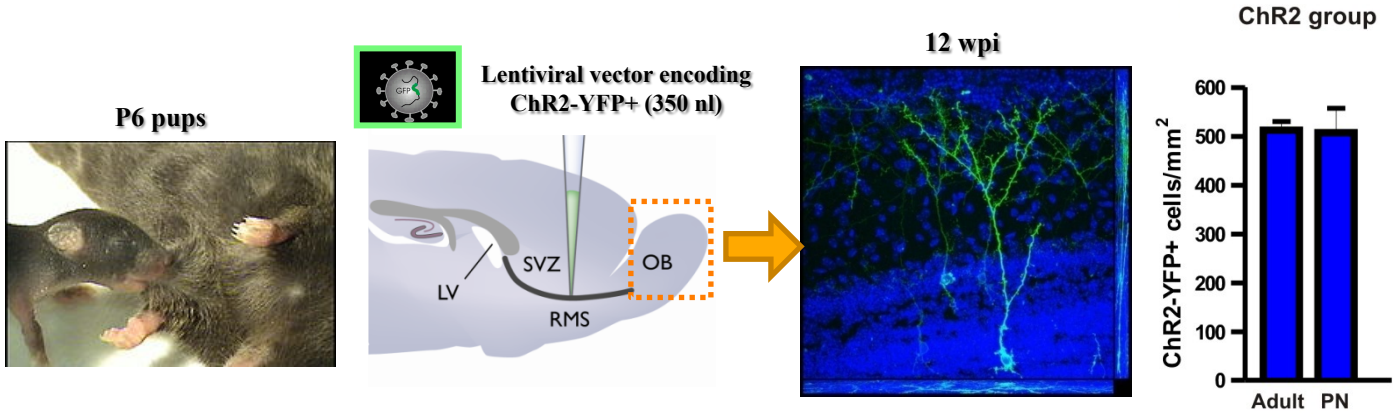


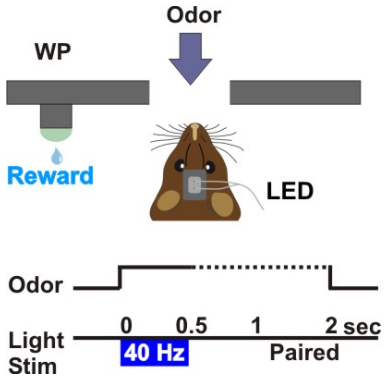
Long-term memory is improved by new neurons activation

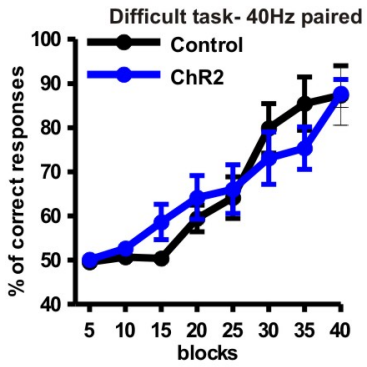


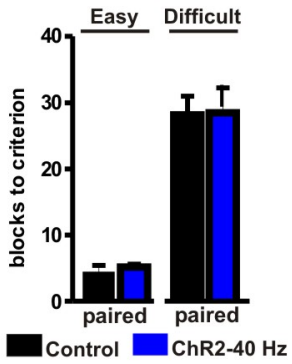


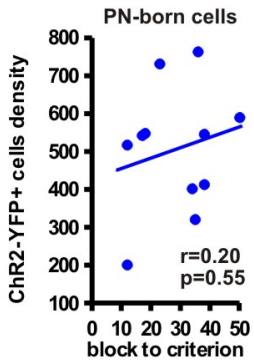
Stimulation of early-born neurons does not improve learning



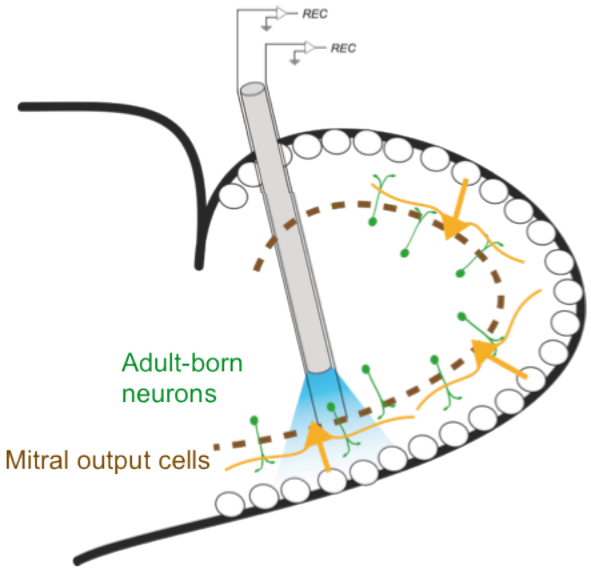




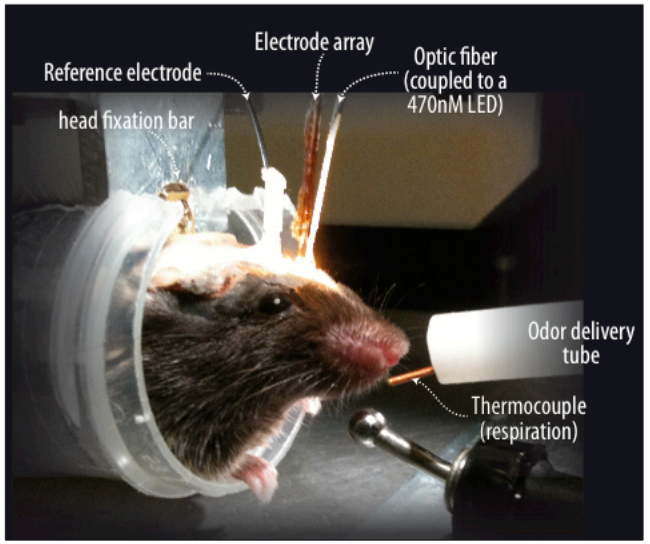




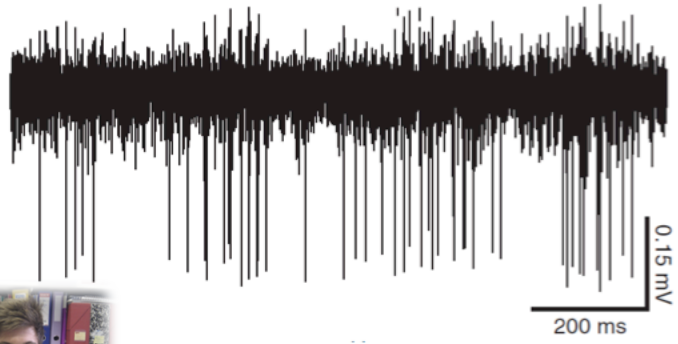
In vivo recording in awake mice

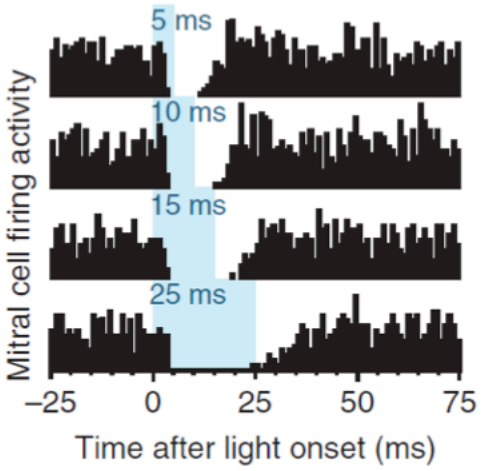


Awake head-fixed mitral output cell recordings



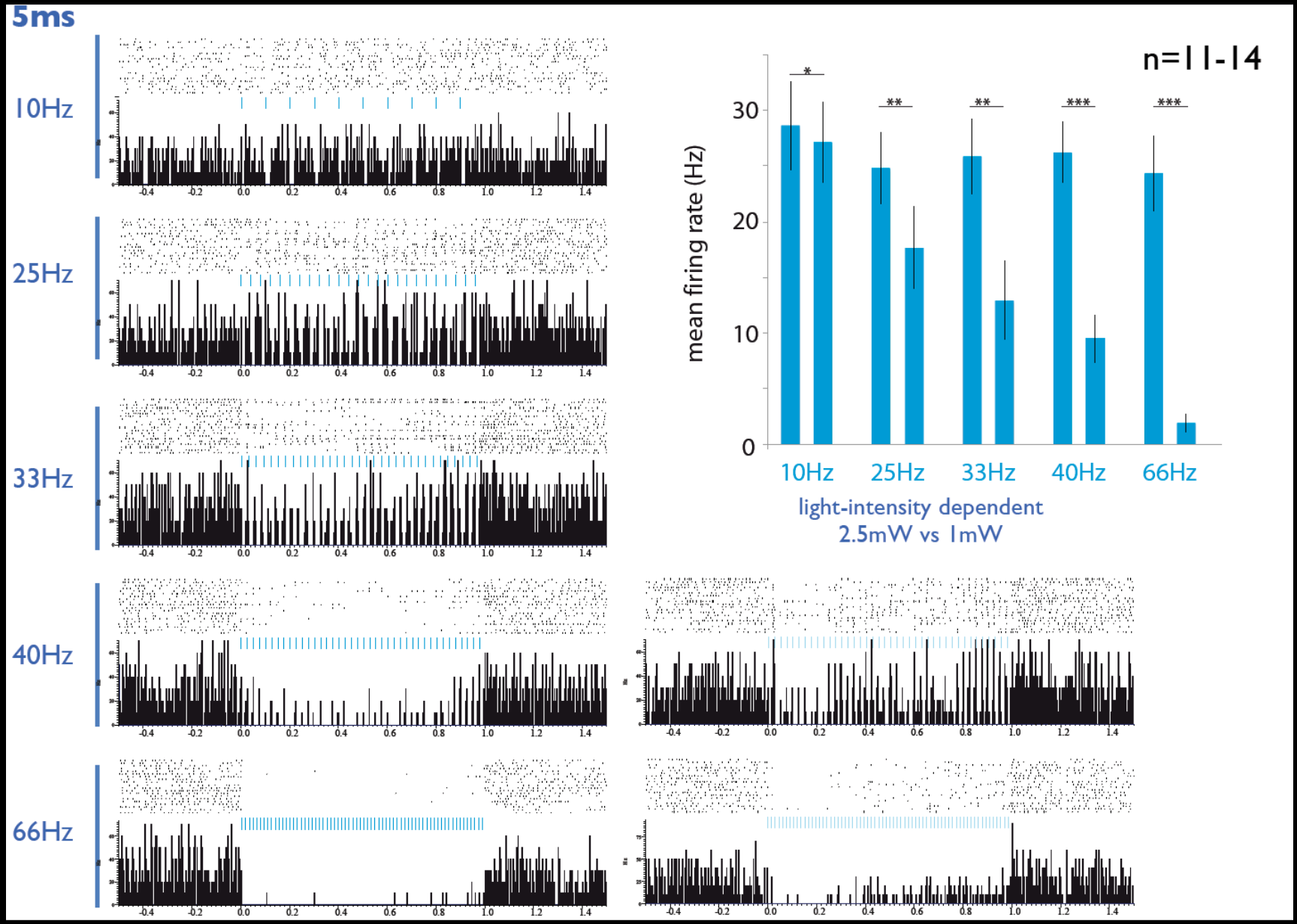
Firing activity of a mitral output cell



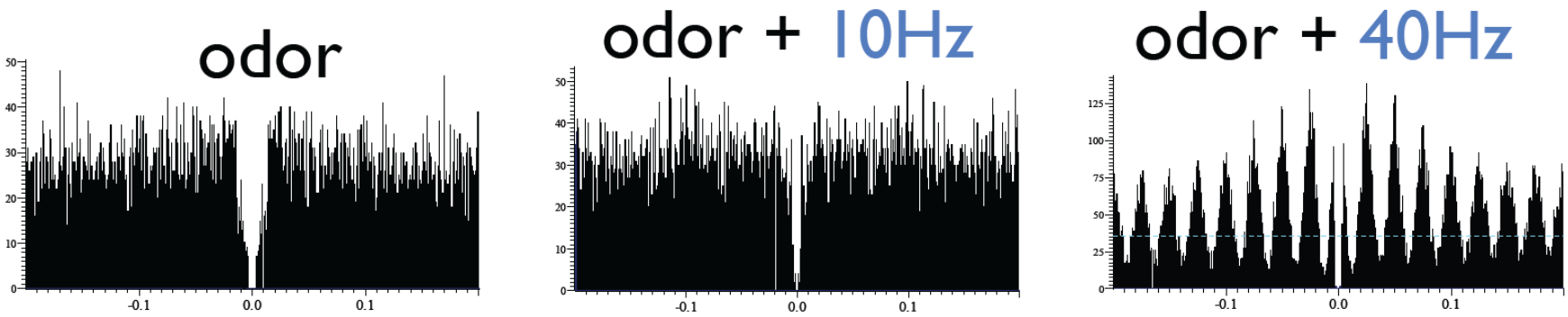


Gabriel Lepousez

Firing pattern of output neurons



40Hz stimulation increases the regularity of odor evoked spiking



Summary - Part 1

Smell (Cluny Museum, Paris)

- *Activation of new interneurons facilitates discrimination learning.*
- *New neurons improve difficult but not easy tasks.*
- *Synchronization of output neurons improves learning*

Are adult-generated neurons unique in any way compared to developmentally born neurons?

- Unique intrinsic properties?

- Unique connectivity?

- Unique synaptic transmission?

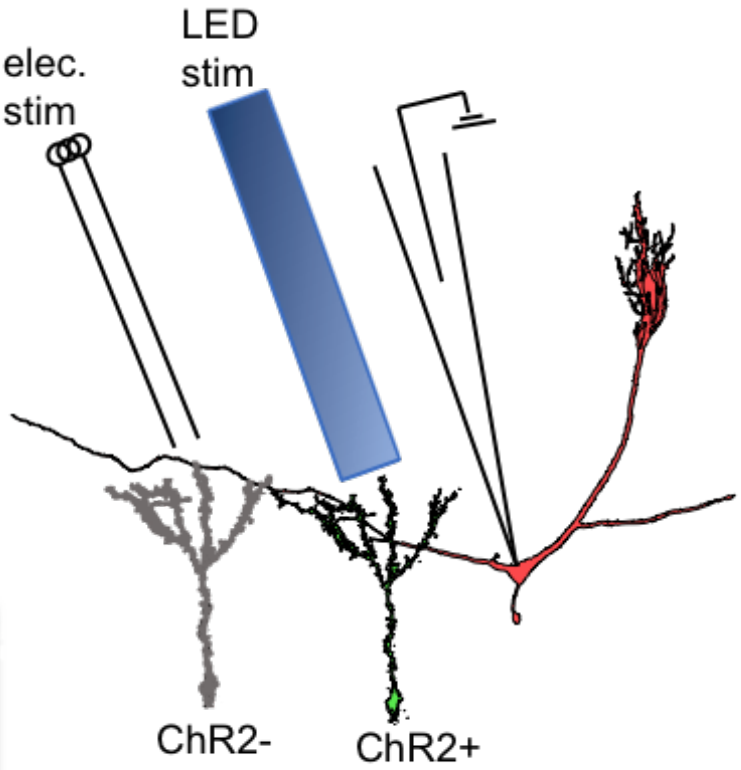
Main Objectives

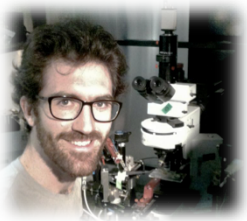
1) Adult-born neurons boost learning and memory

2) Unique features of new neuron synaptic output

3) Top-down control of adult-born neuron activity

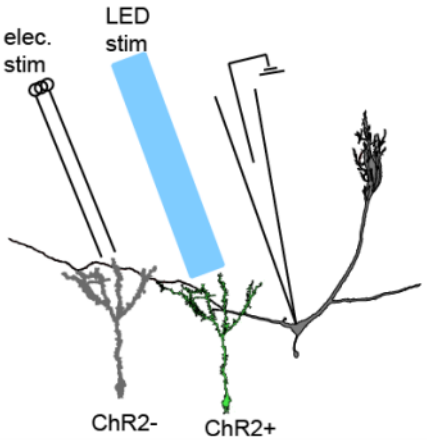
A comparative screen for finding differences in synaptic physiology between GCs of different ages

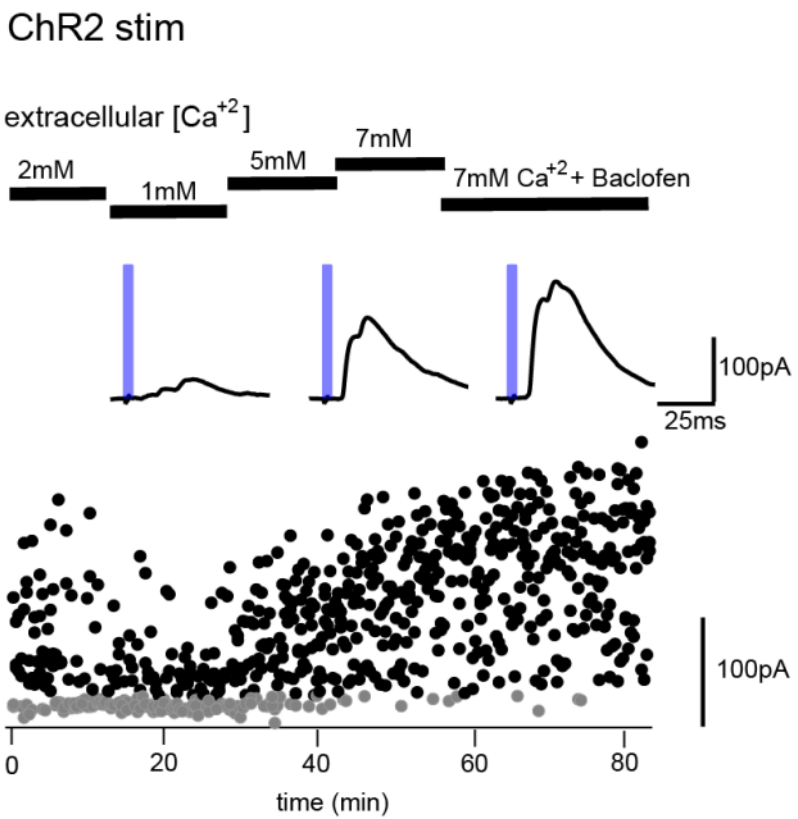


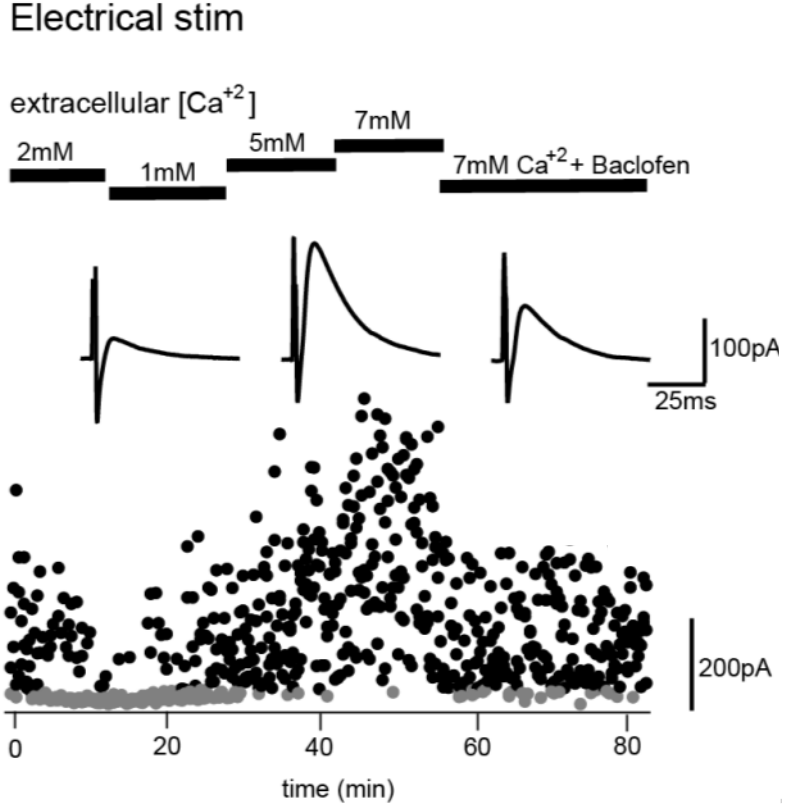


Matt Valley
Post-doc / ANR

Differential effect of baclofen (GABA-B agonist) on adult-born GCs

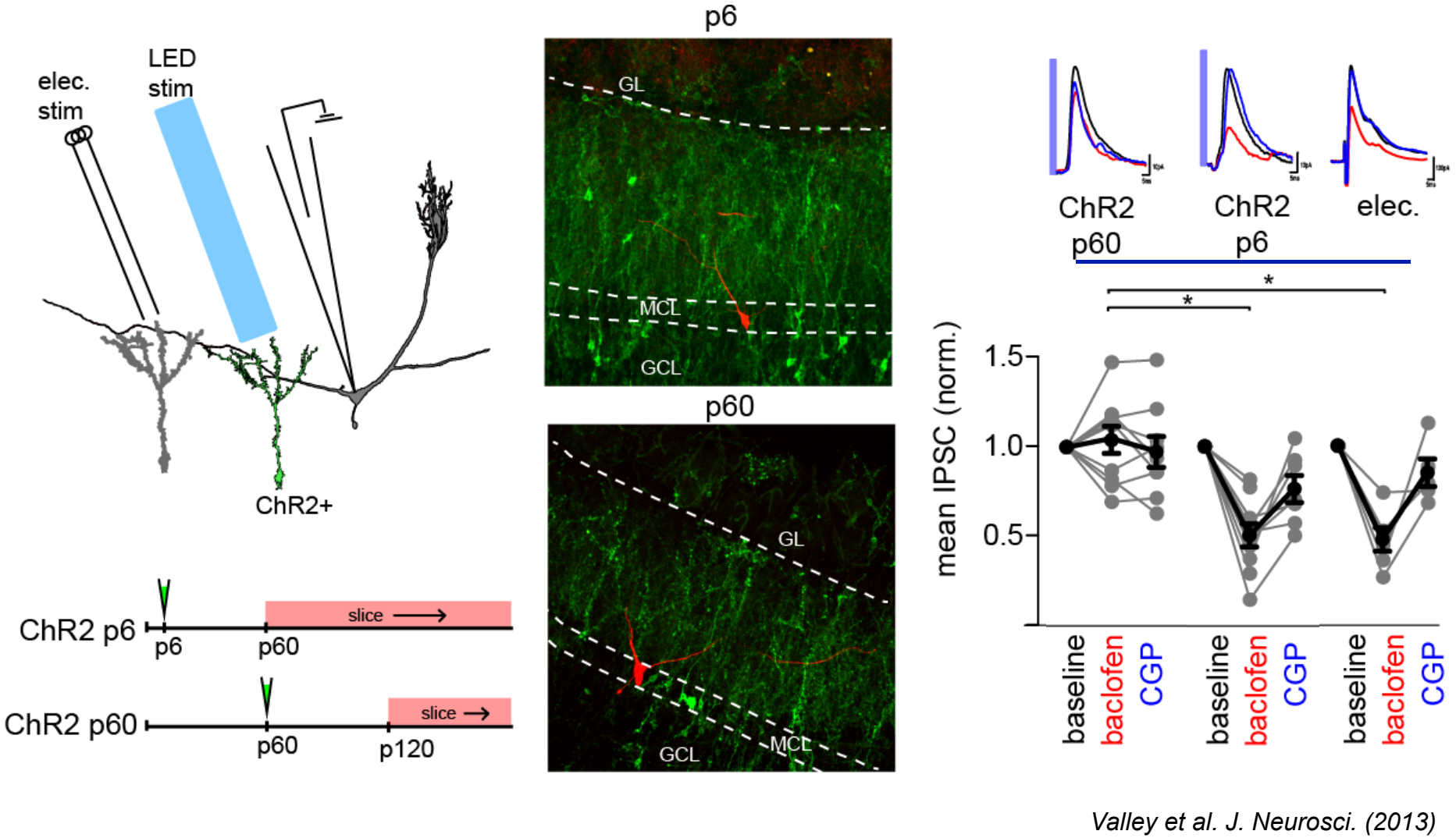






Valley et al. J. Neurosci. (2013)

Comparison of GABA-B function in GCs born at p6 and p60



Valley et al. J. Neurosci. (2013)

Summary - Part 2

Smell (Cluny Museum, Paris)

Adult-born GCs may influence olfactory behavior by showing:

- Long-term potentiation of glutamatergic inputs
- Stronger inhibition in the circuit resulting from non-functional GABA-B signalling
- New patterns of associative connectivity

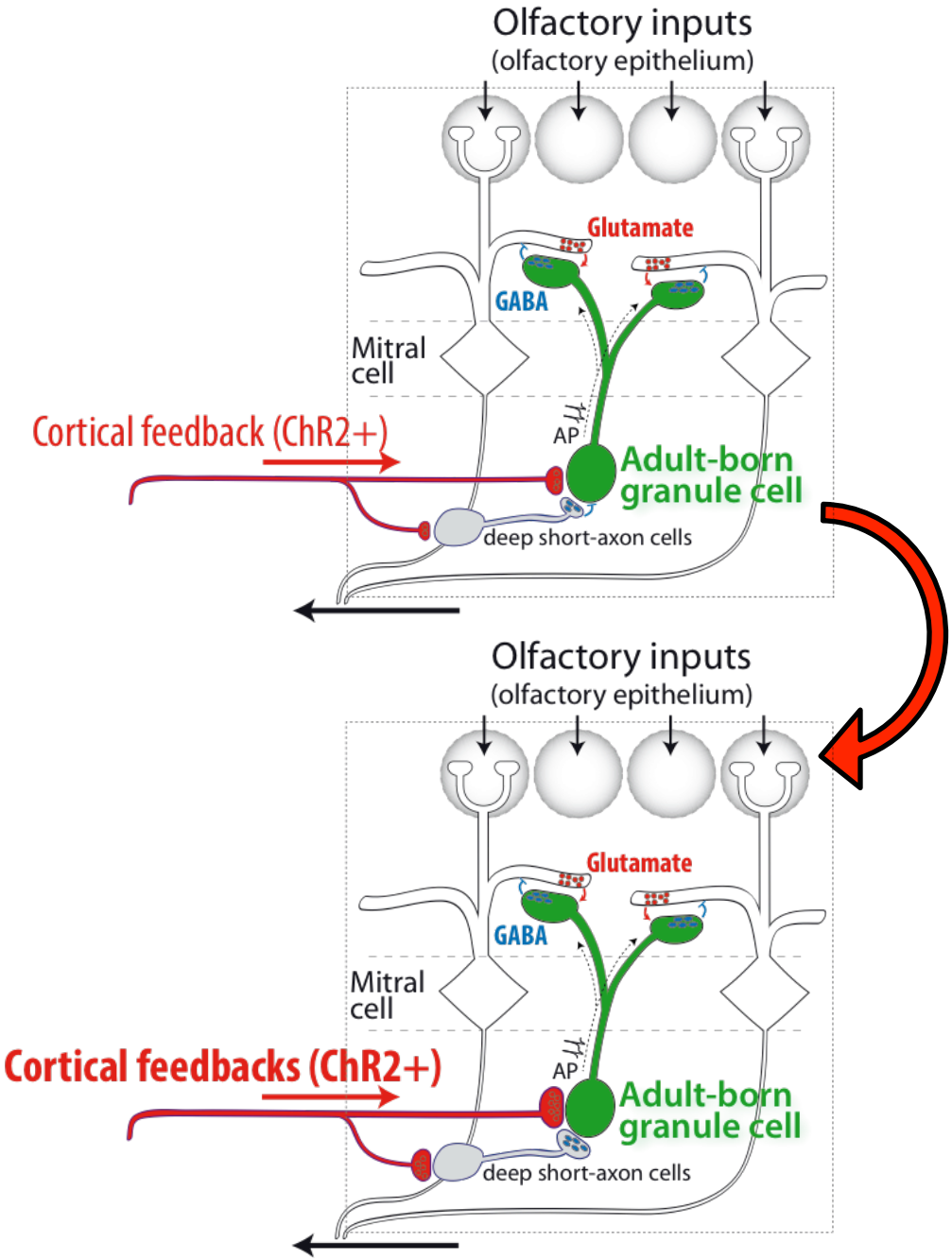
Main Objectives

1) Adult-born neurons boost learning and memory

2) Unique features of new neuron synaptic output

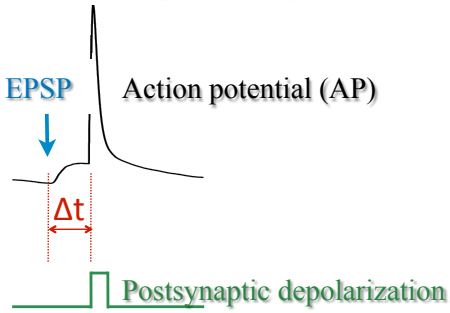
3) Top-down control of adult-born neuron activity

Does learning promote changes in synaptic strength?

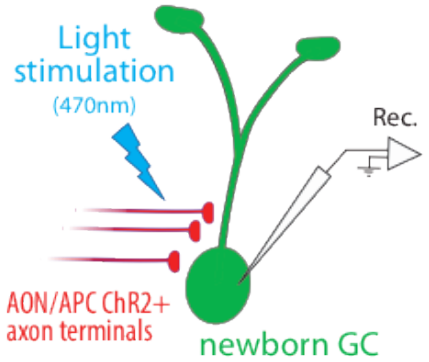


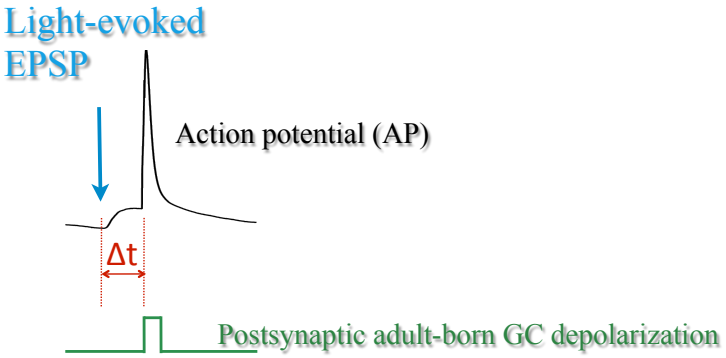
Olfactory learning

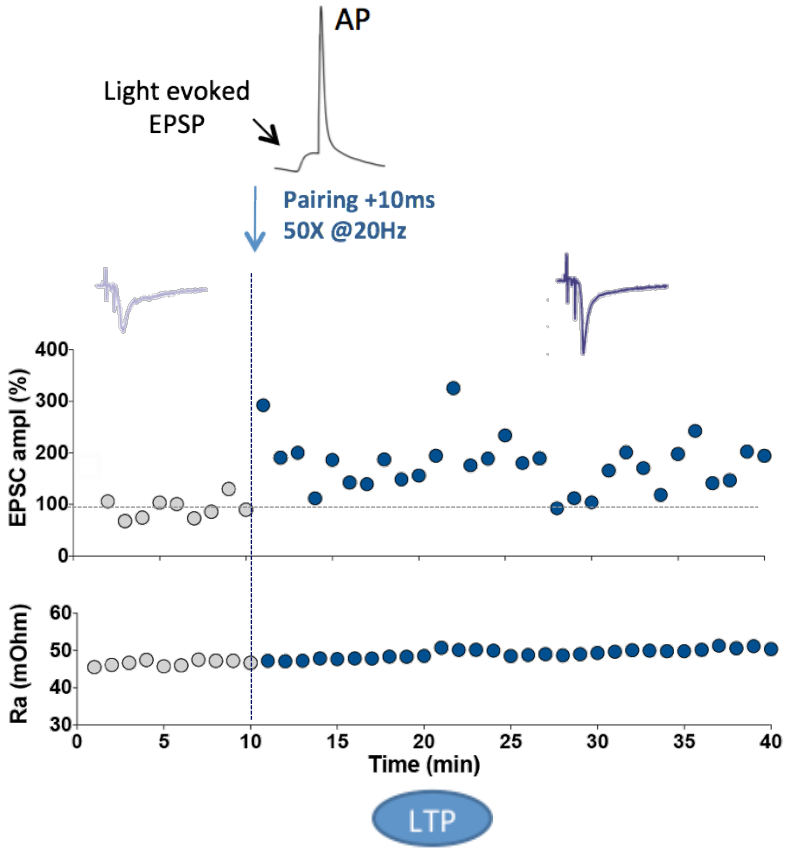
Spike-timing dependent plasticity (STDP) ?

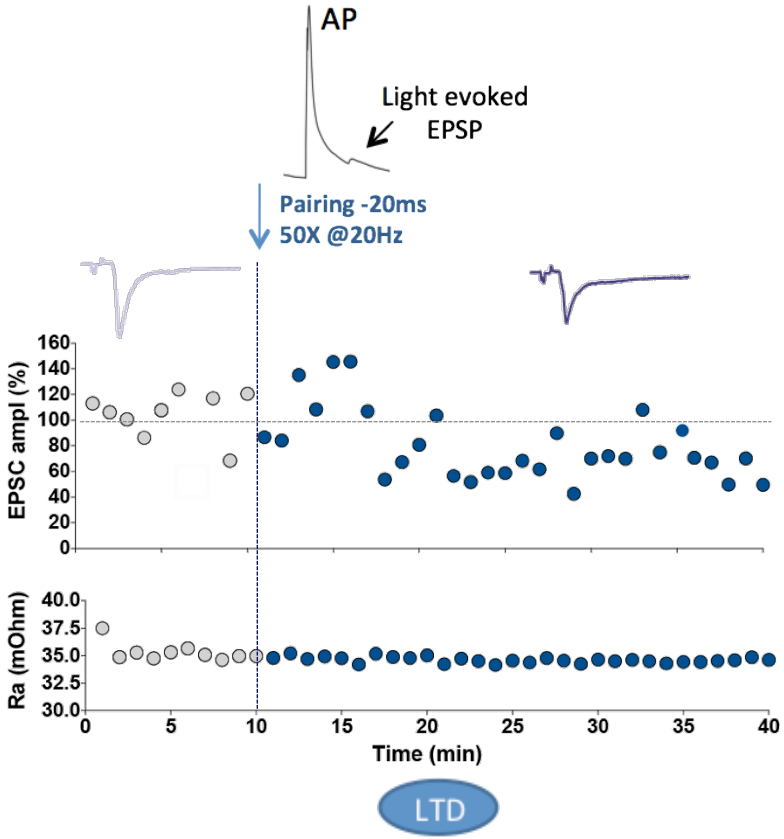


Spike-timing dependent plasticity rules in the cortical feedback loop

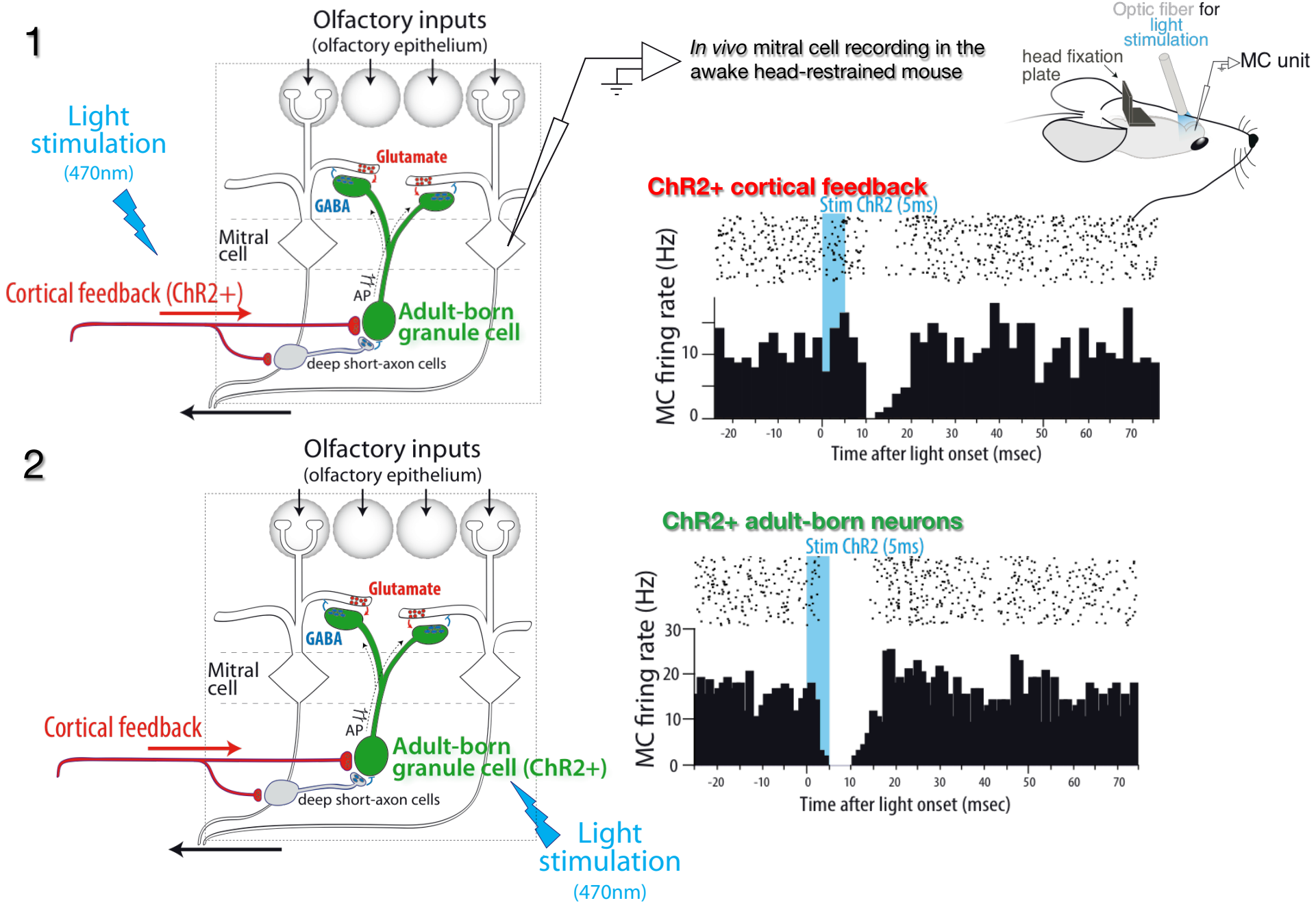






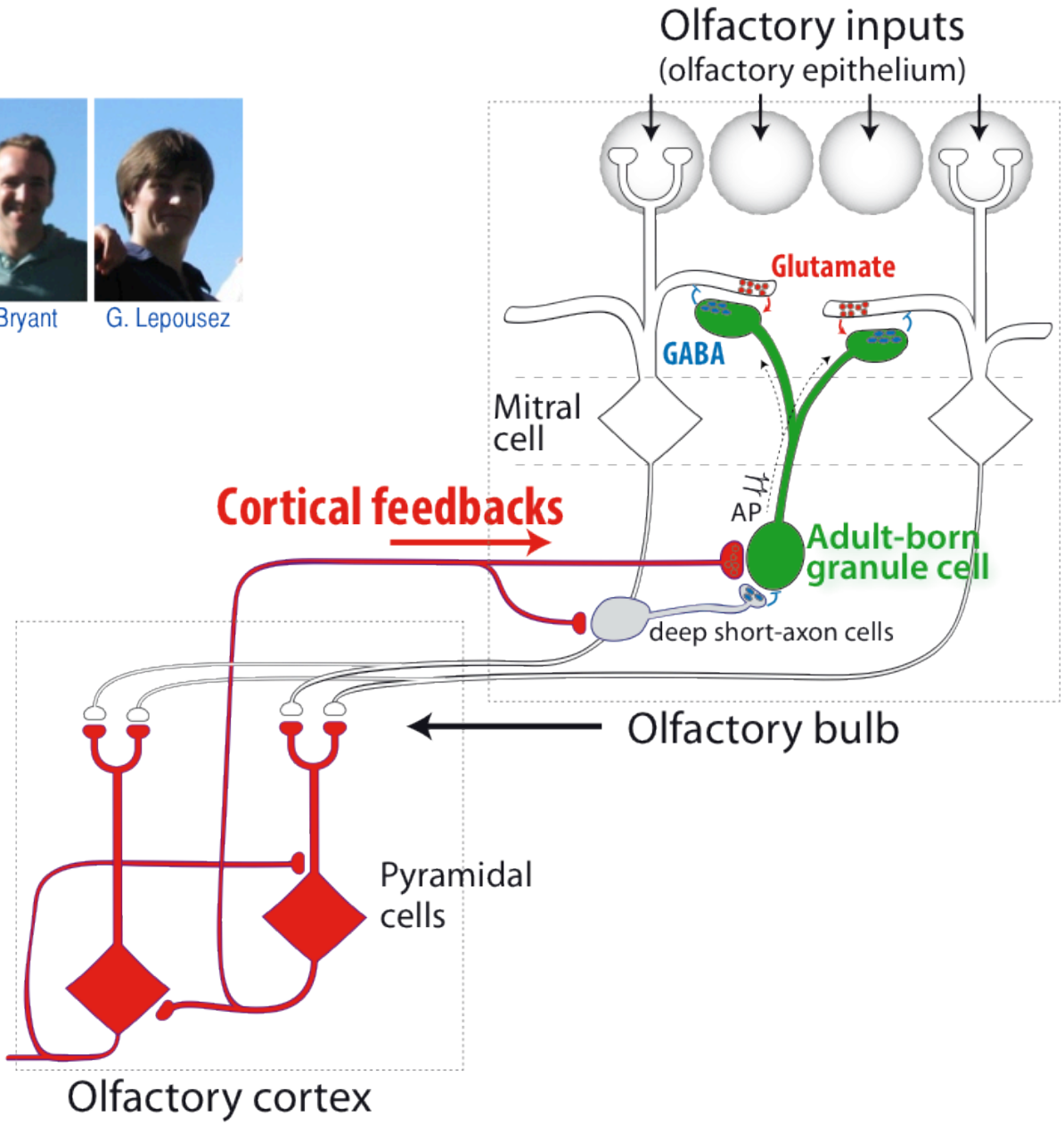


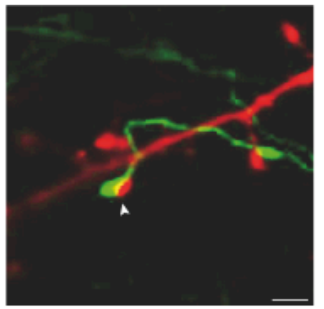
Feed-forward inhibitory circuits sculpt mitral cell firing activity



Olfactory cortical feedback in the olfactory bulb

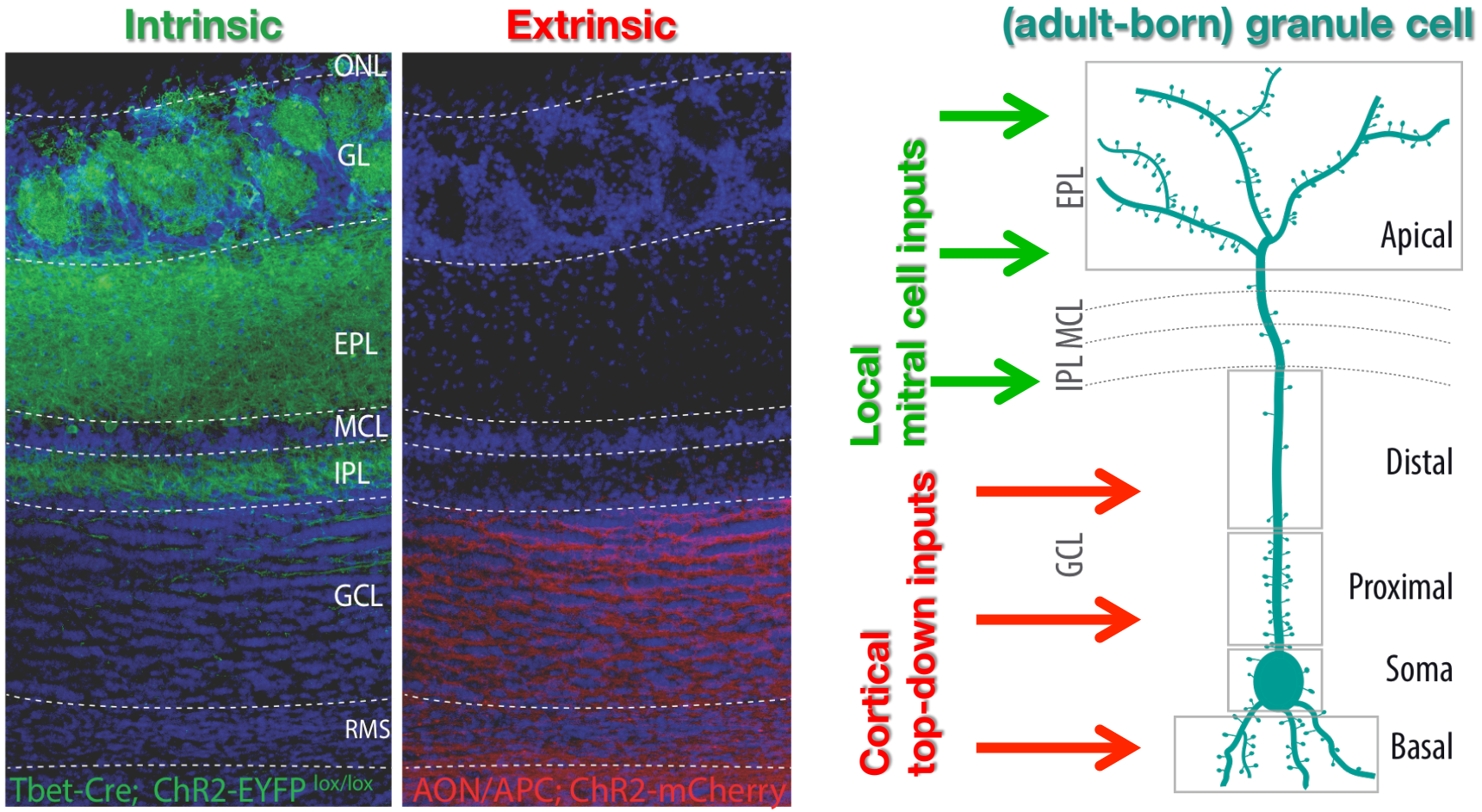

A. Bryant G. Lepousez




synapse/circuit

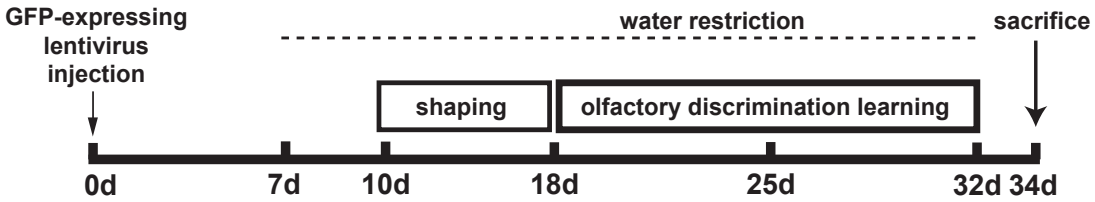
behavior

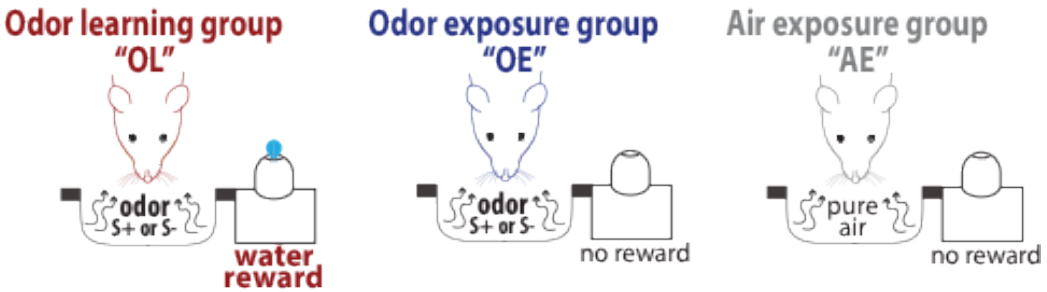
Intrinsic *versus* extrinsic olfactory bulb networks

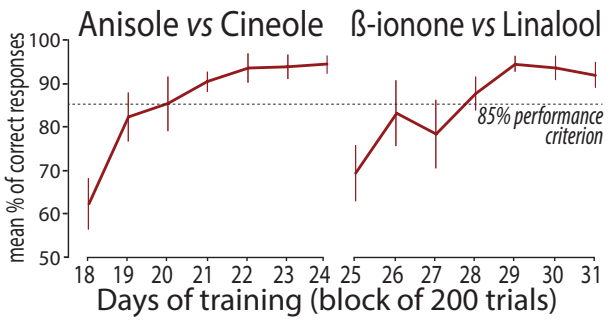


Lepousez et al. PNAS (2014).

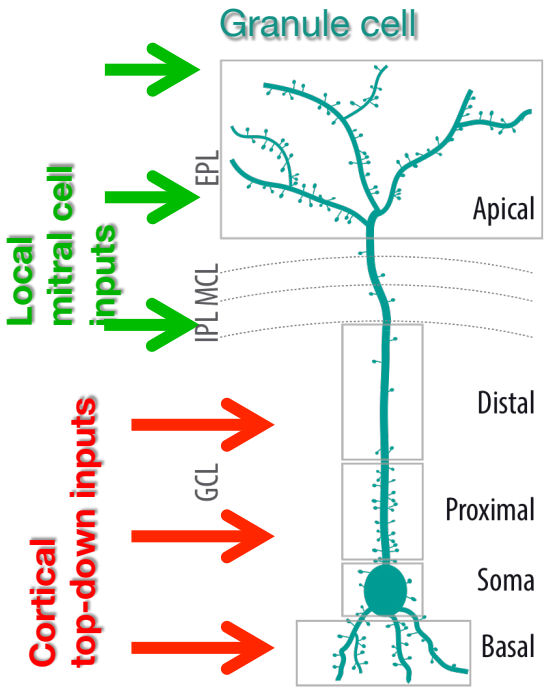
Olfactory discrimination learning

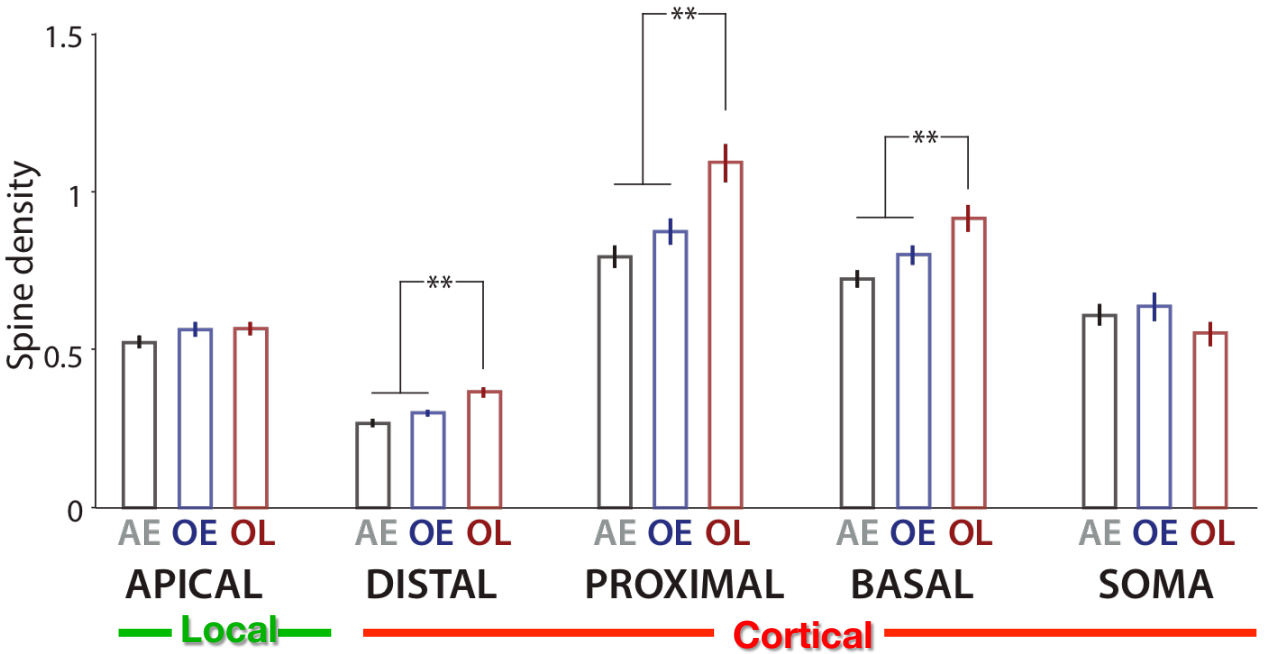


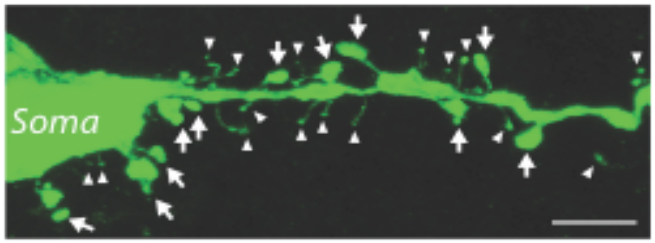




Learning promotes input-specific structural plasticity



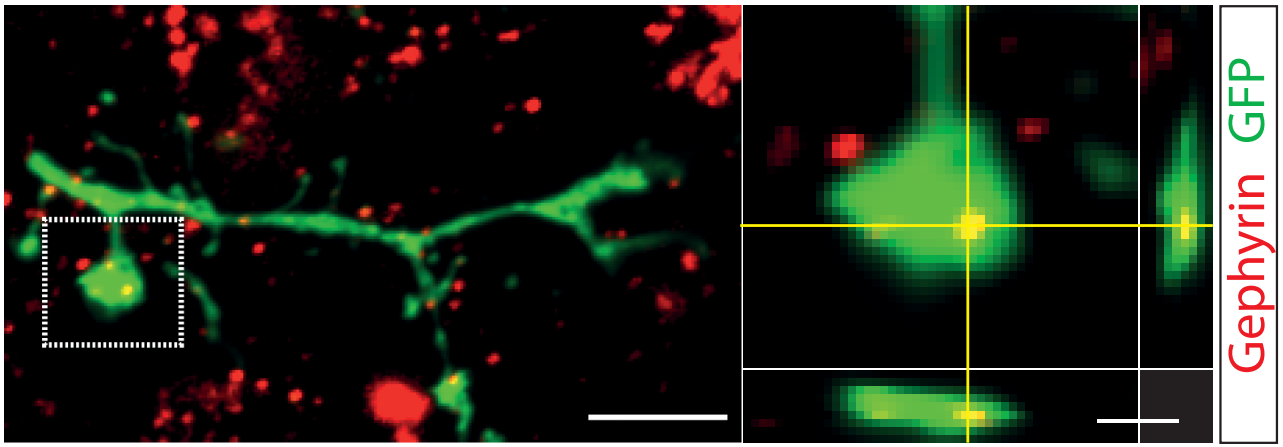


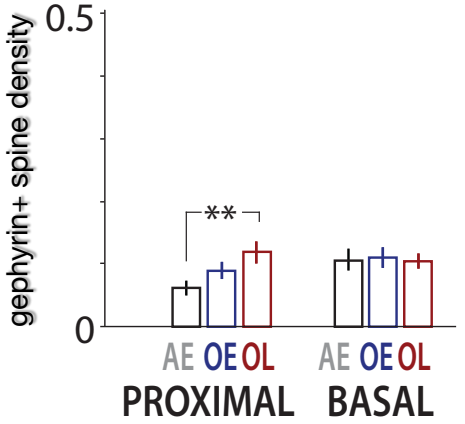


Lepousez et al. PNAS (2014).

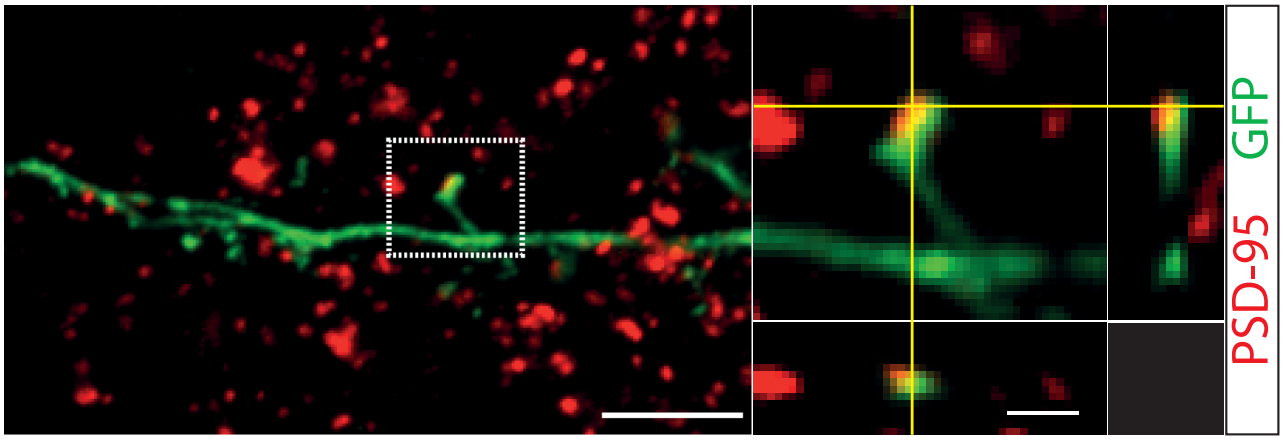
Number of excitatory and inhibitory synapses increase after learning

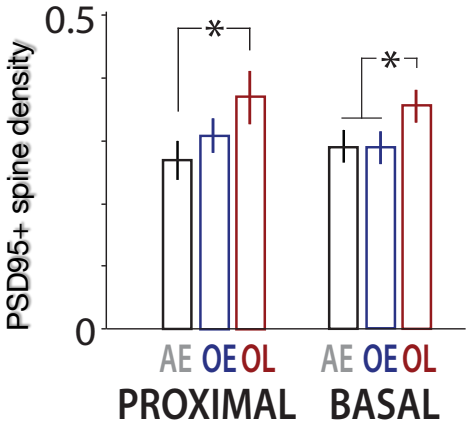
GABAergic inputs





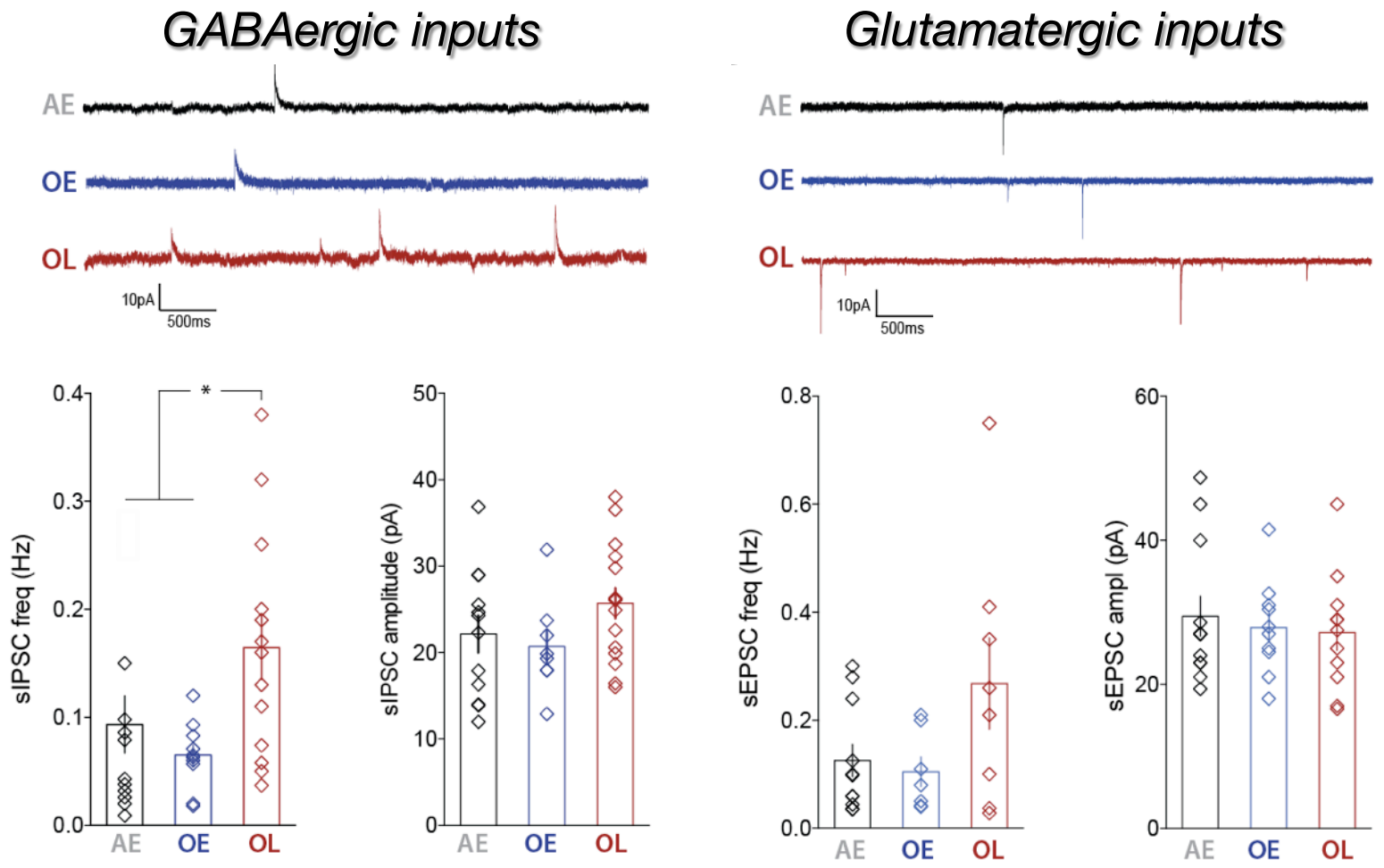
Glutamatergic inputs



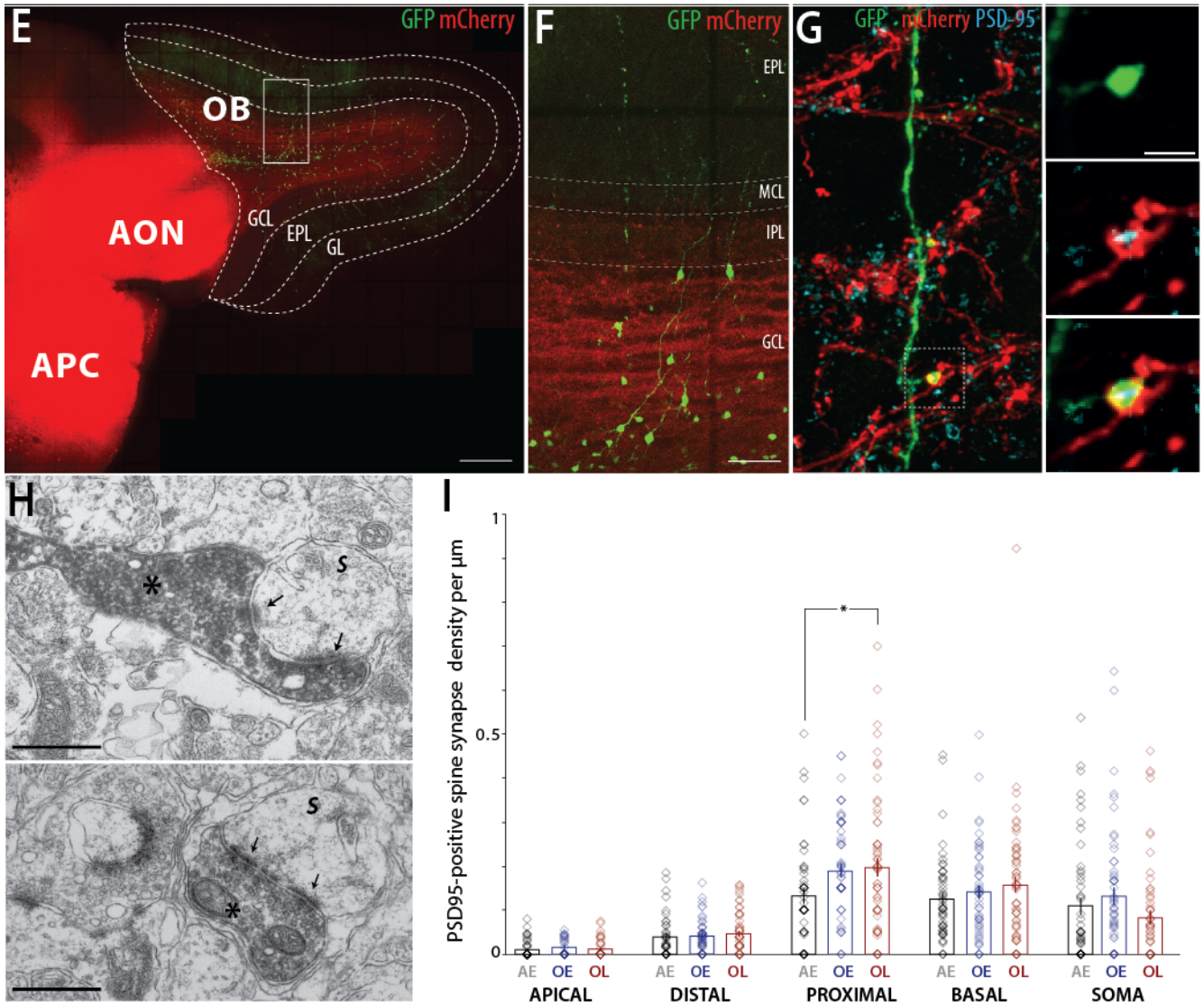


Lepousez et al. PNAS (2014).

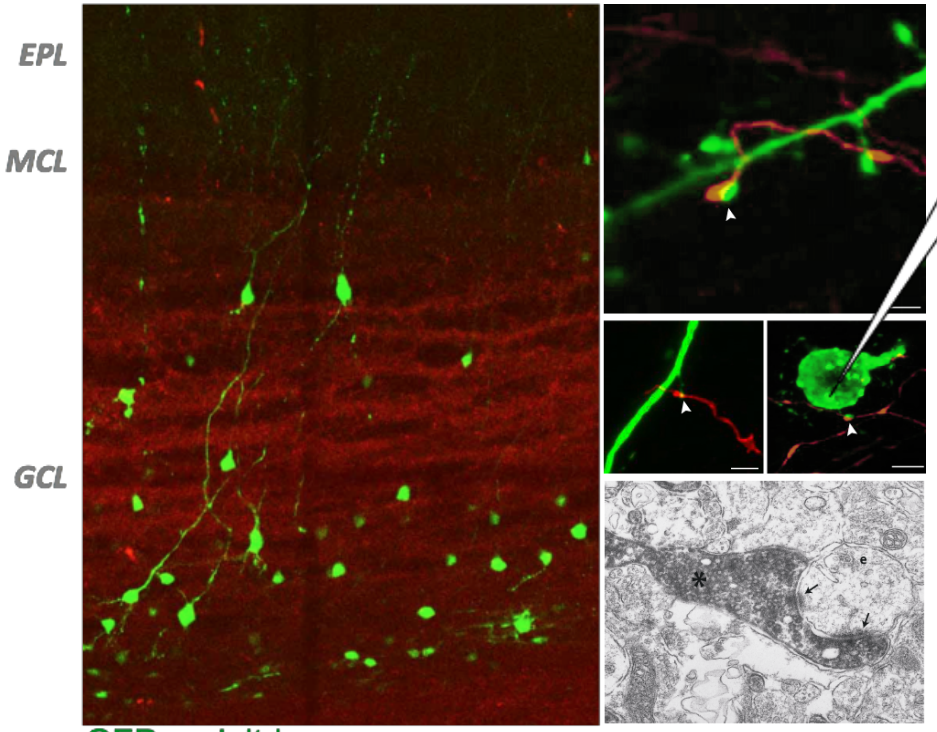
More frequent synaptic events after olfactory learning



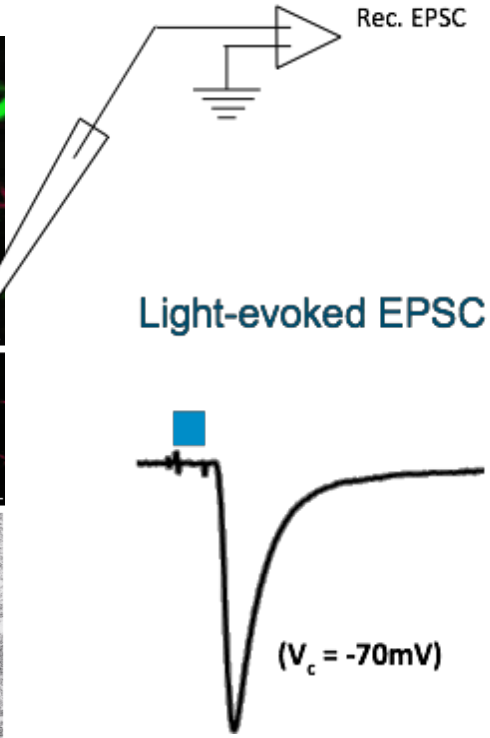
Top-down control of adult-born neuron activity



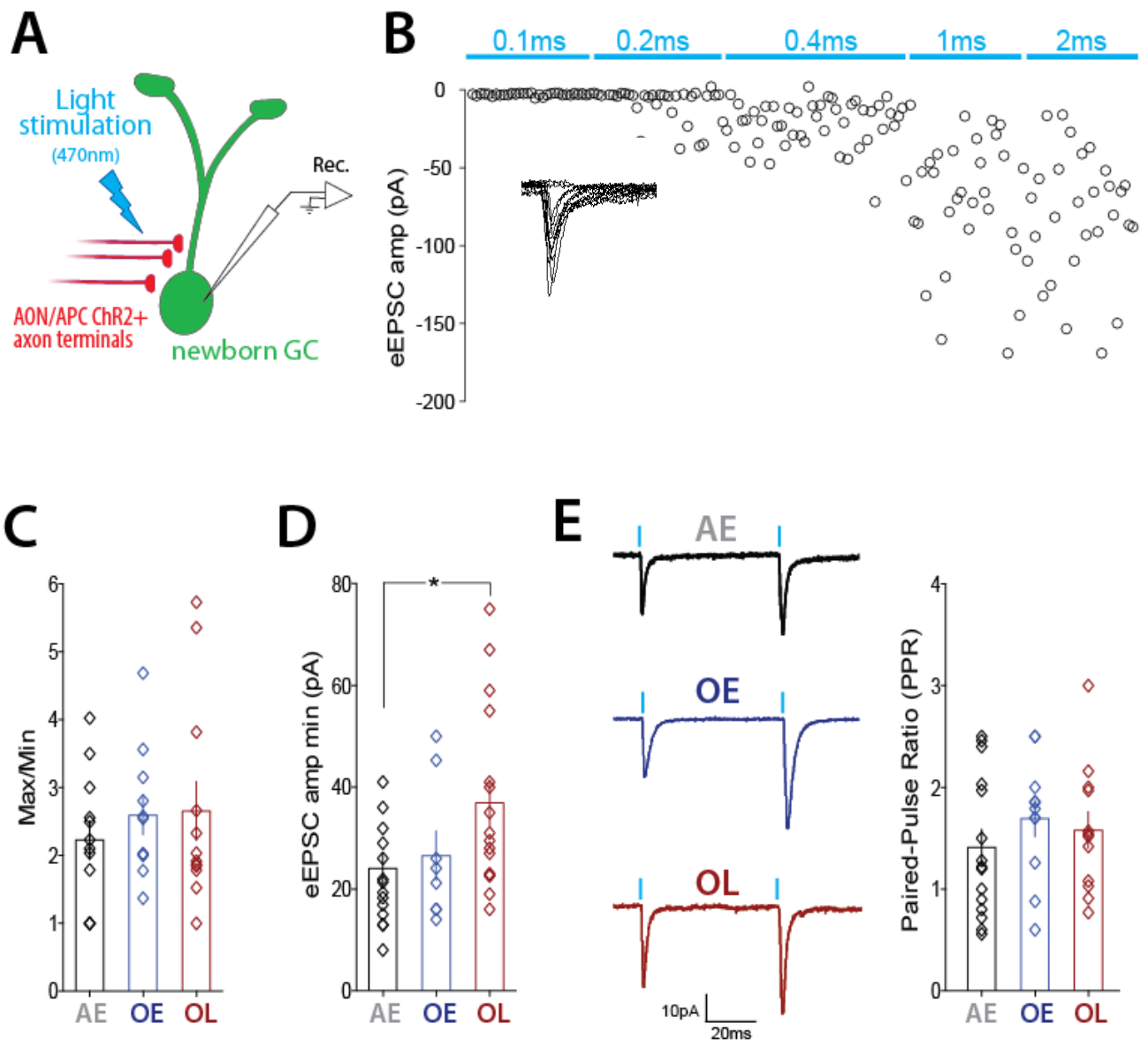
Top-down control of adult-born neuron activity



GFP+ adult-born neurons
ChR2+ cortical axon terminals



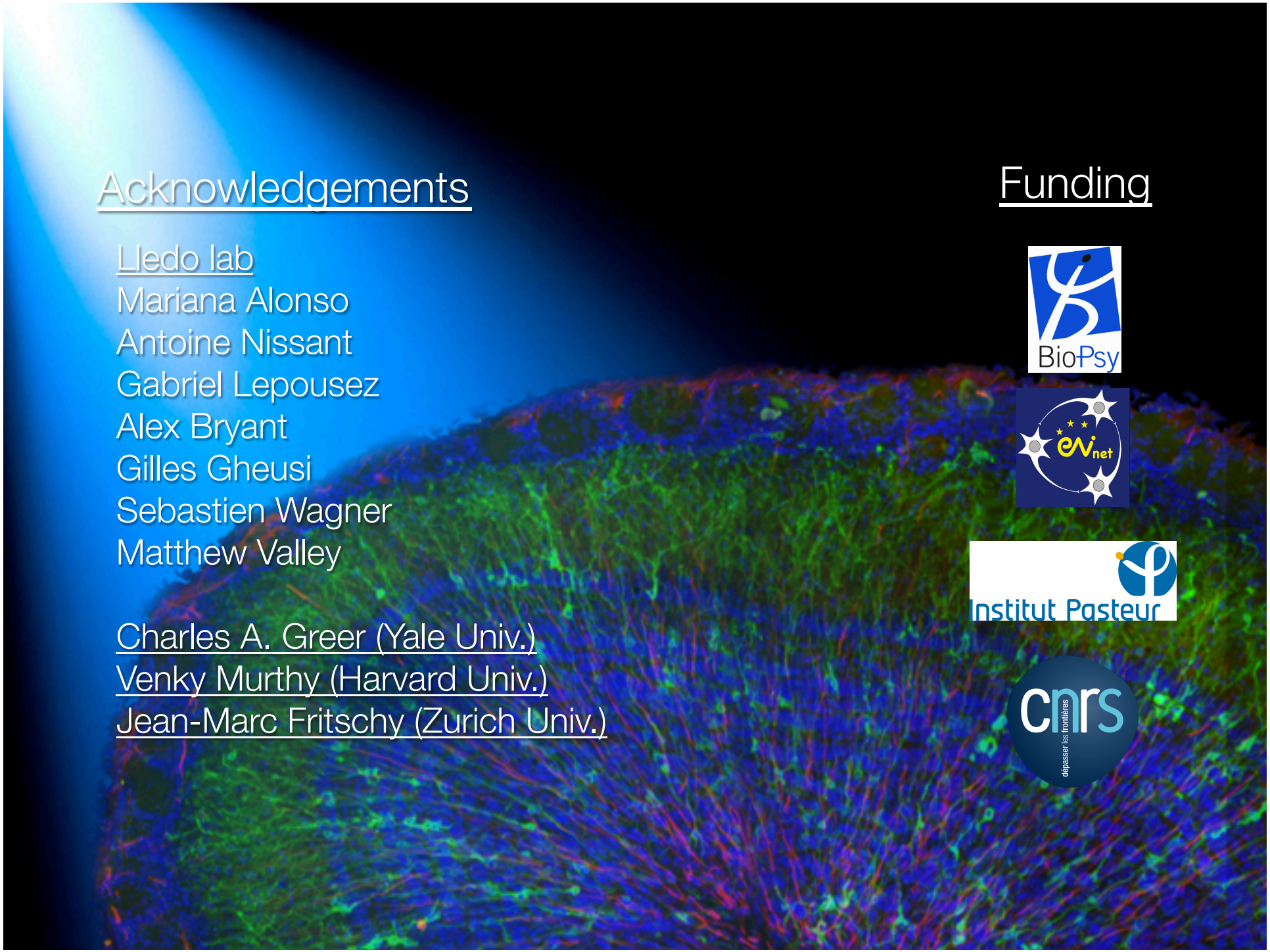
Top-down control of adult-born neuron activity



Summary – Part 3

Smell (Cluny Museum, Paris)

- Learning enhances spines density in a restricted domain of new neurons
- The most plastic dendritic domain is the one that connects the cortical inputs
- This reinforces the top-down influence on early stages of information processing



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