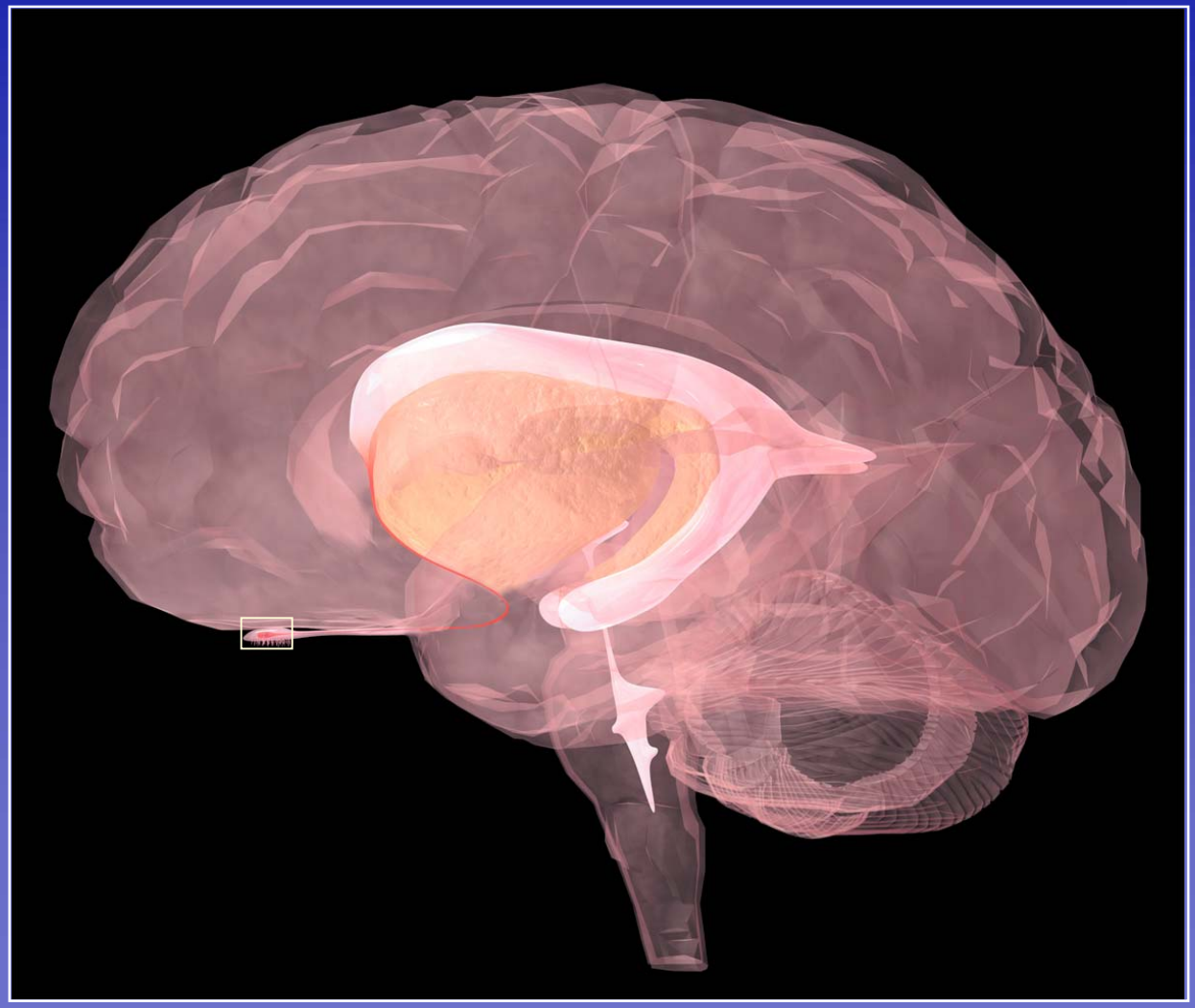
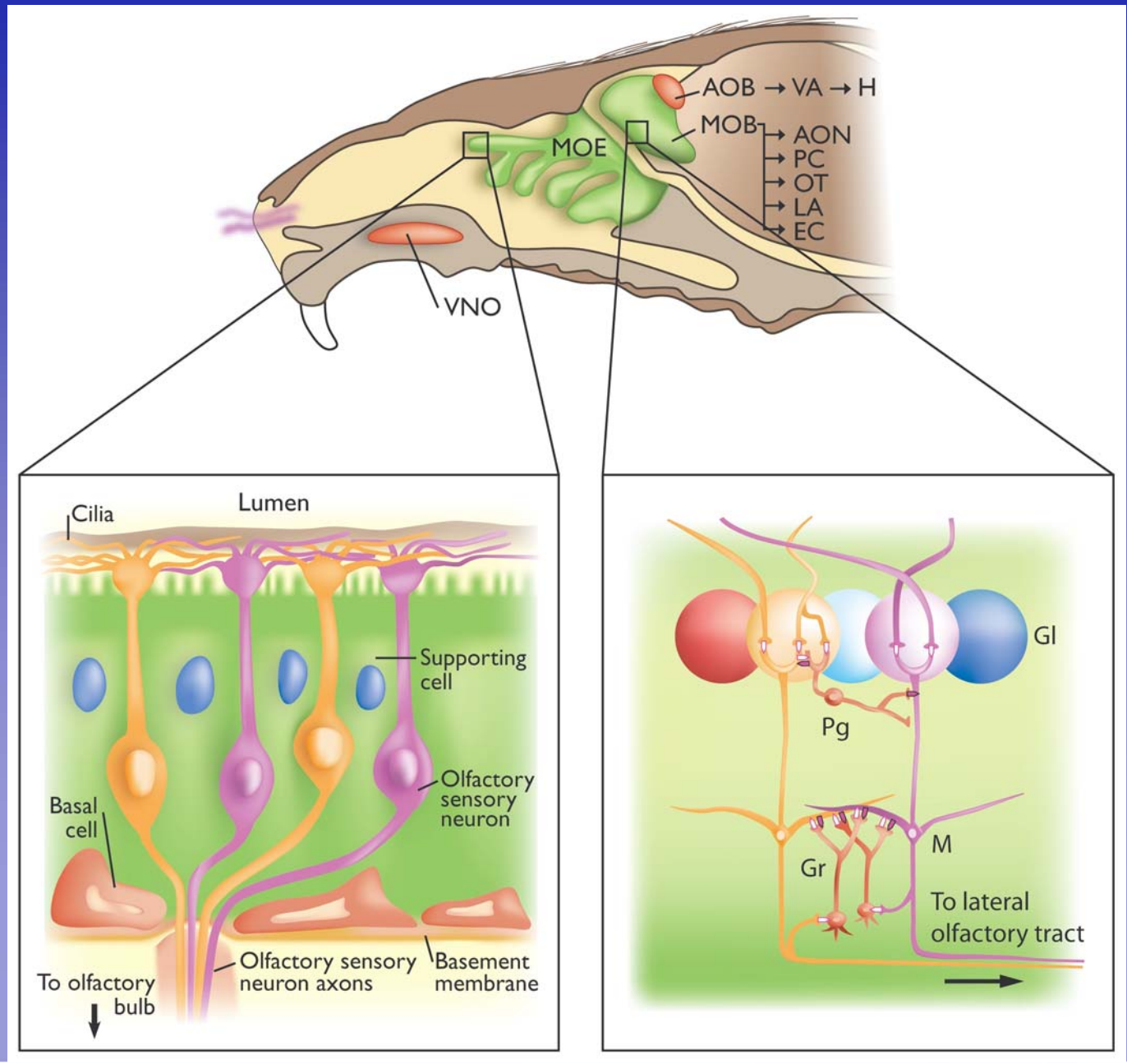
Olfactory Circuits: From Development to Function



Laboratory for Perception and Memory
Institut Pasteur & CNRS

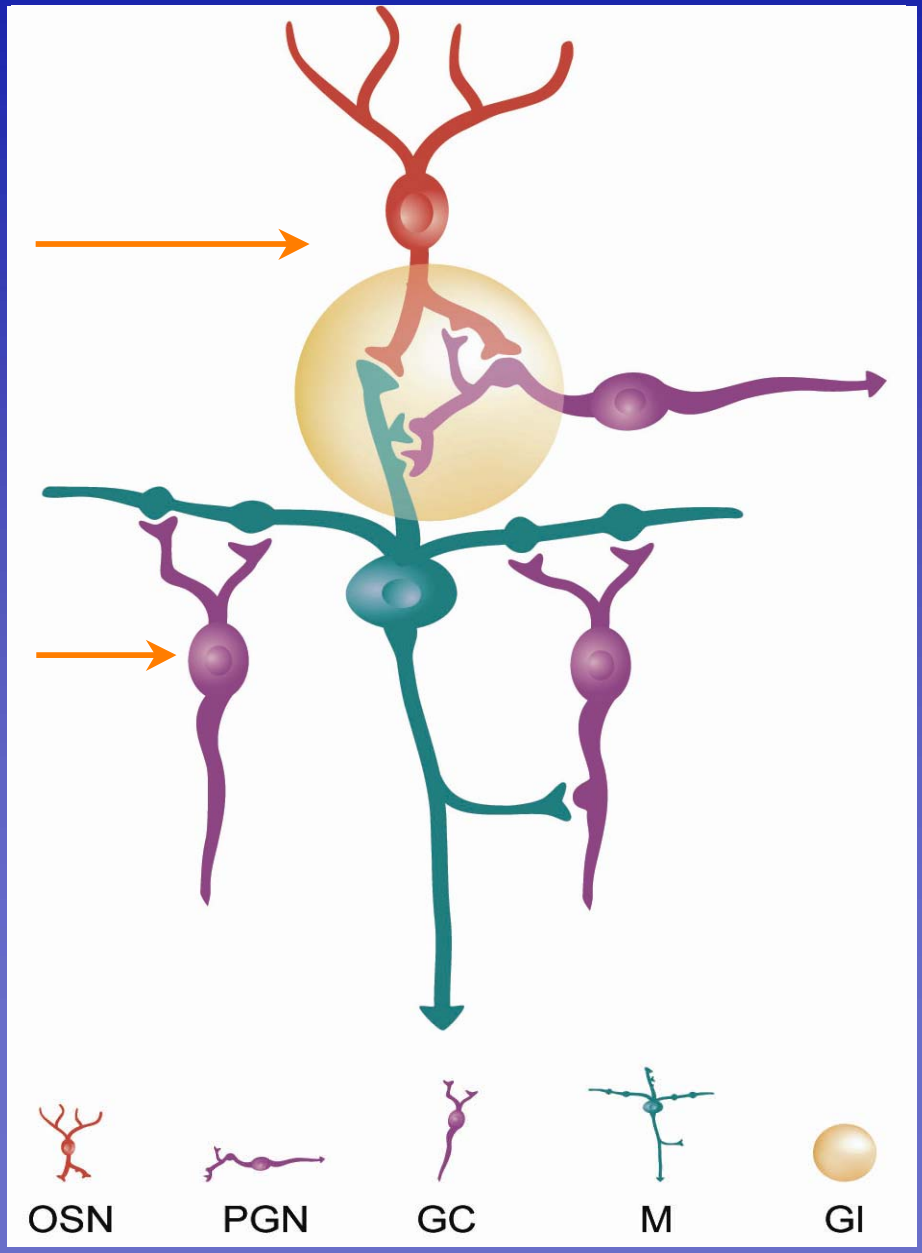
L’autopoïèse du système olfactif



The Canonical Microcircuit

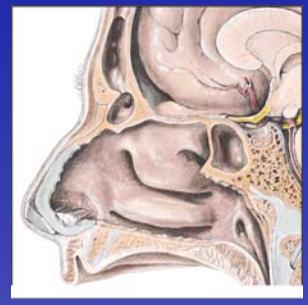
1) Sensory Neurons

2) OB Interneurons

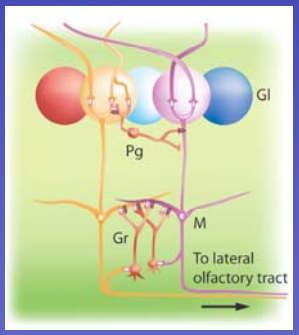


Three Main Parts

1) Neurogenesis of sensory neurons



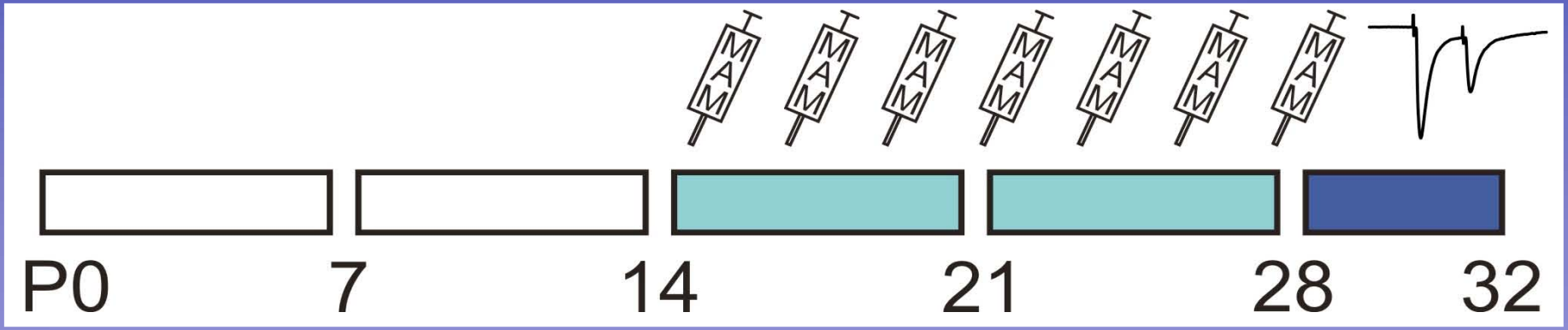
2) Neurogenesis in the central relay



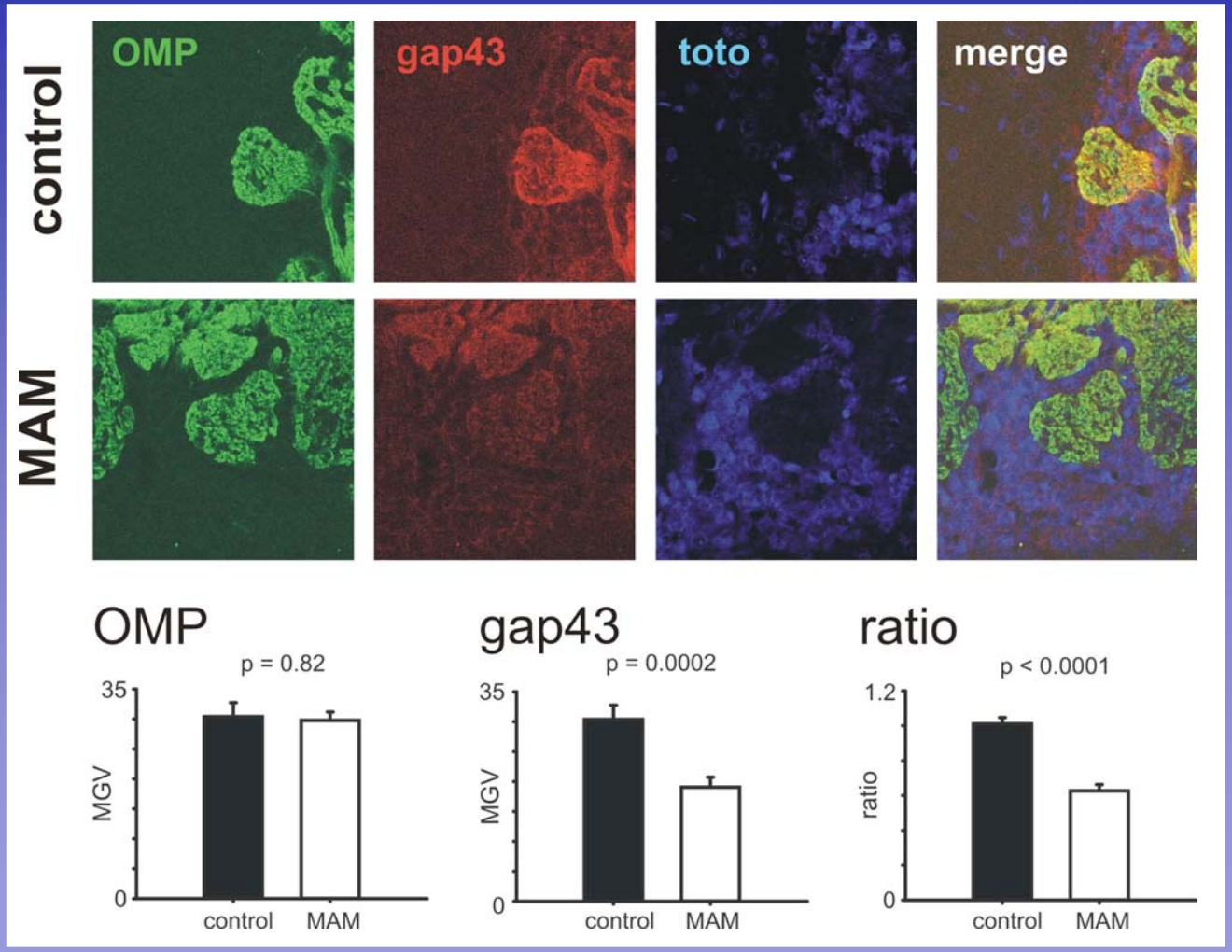
3) Functional significances

Part I. Neurogenesis of Sensory Neurons

- We used methylazoxymethanol acetate (MAM) to kill dividing cells in the OE. Intranasal injections were performed every 48h over a 2-week period.



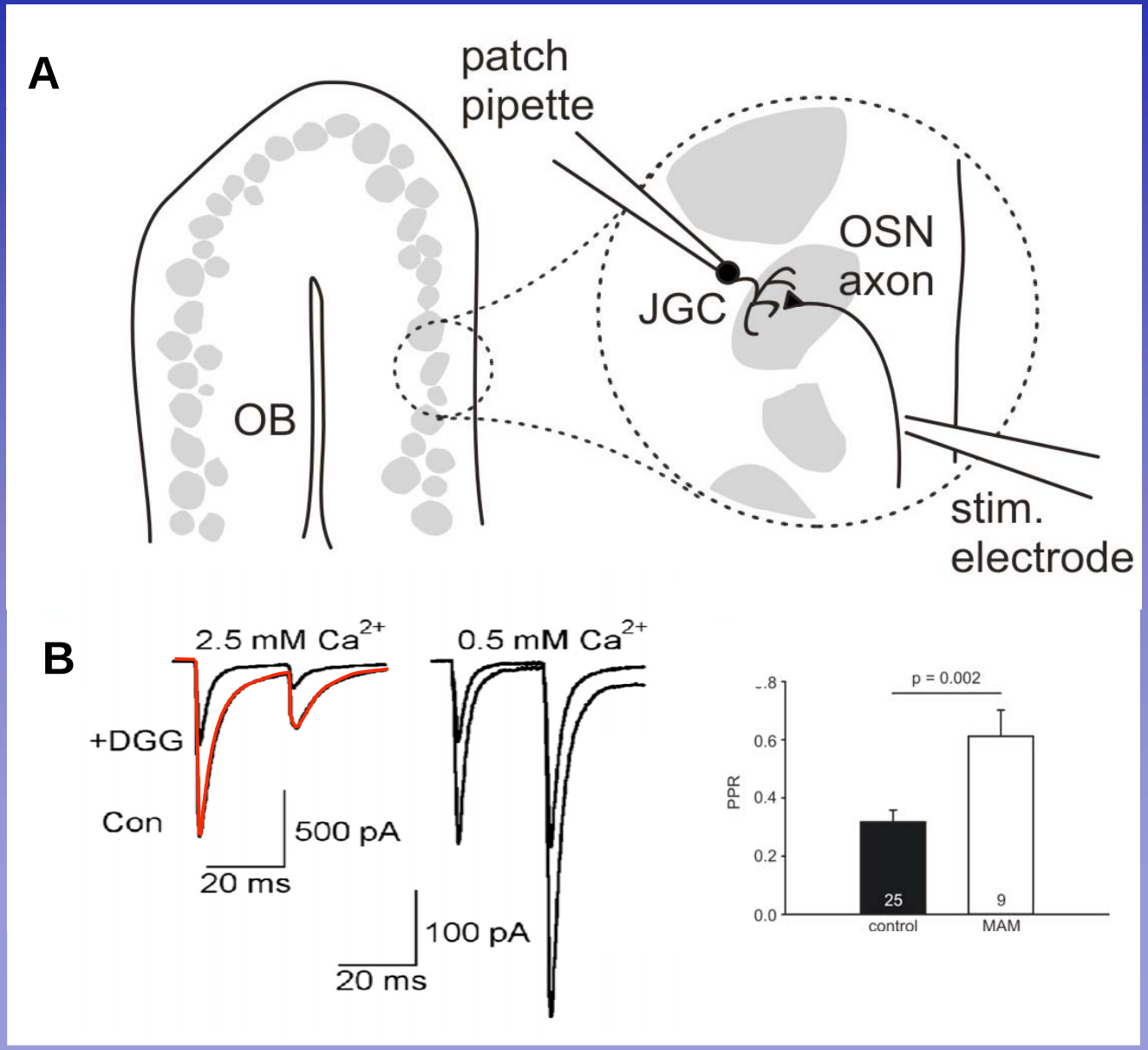
MAM Treatment Reduces Immature OSN



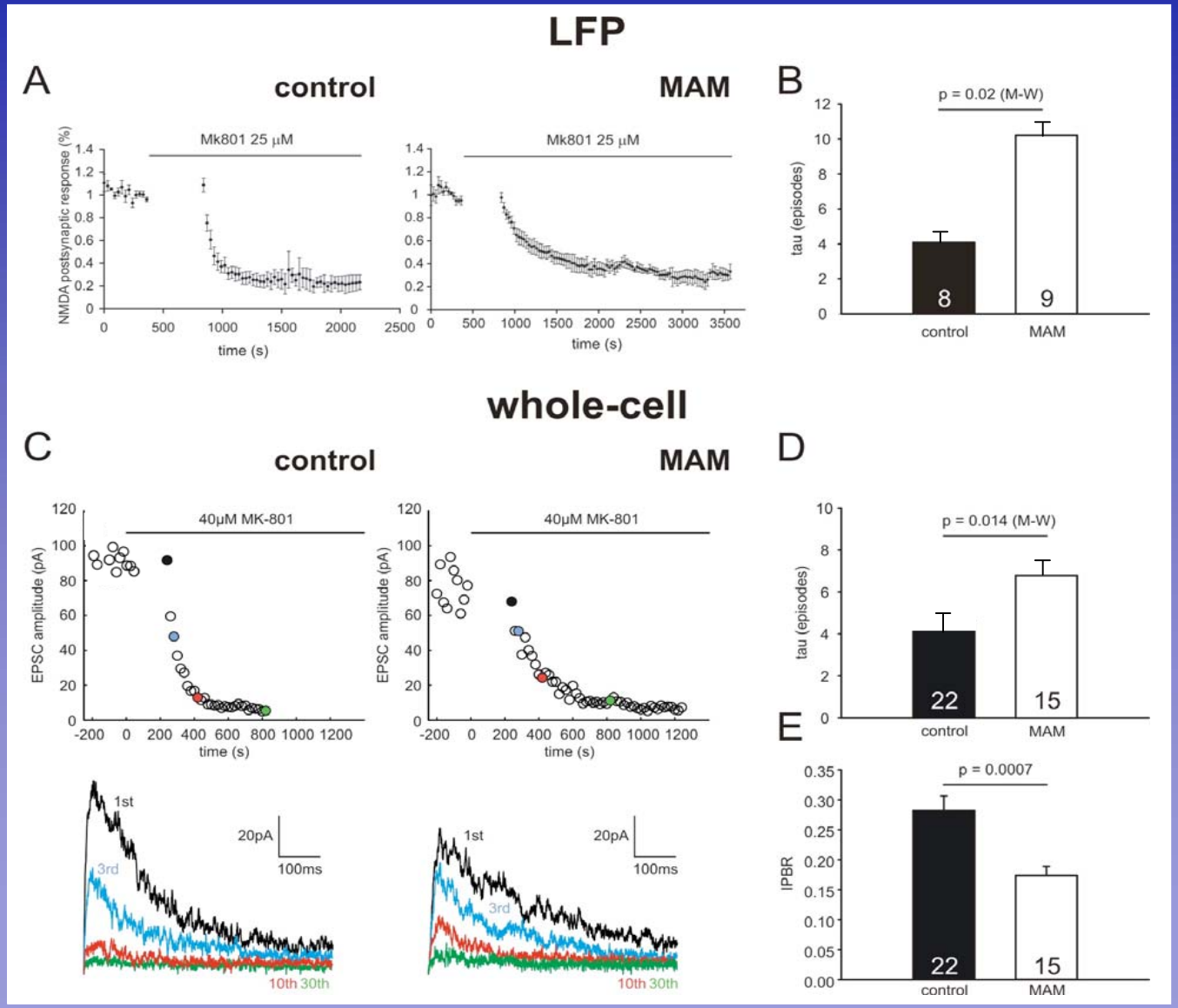
- OMP labels mature OSNs (7d+), while gap43 labels immature OSNs (2-6d)

- Immunohistochemistry in fixed OB slices shows that OMP labelling is unchanged by MAM treatment, but gap43 labelling is significantly reduced

Release Probability I: Paired-Pulse Responses



Release Probability II: MK-801 Experiments



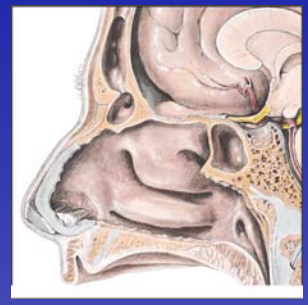
Summary - Part 1

- Reducing the number of immmature sensory neuron inputs to the OB, reduces the overall release probability, but no change in AMPA:NMDA ratio, or quantal size in the projection.

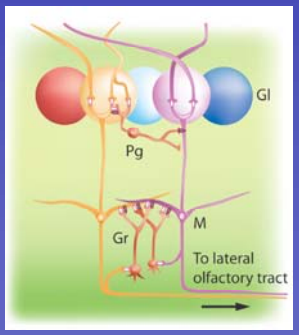
- So, the physiological properties of newborn OSNs are quite different from their more mature counterparts.

Three Main Objectives

(1) Neurogenesis of sensory neurons

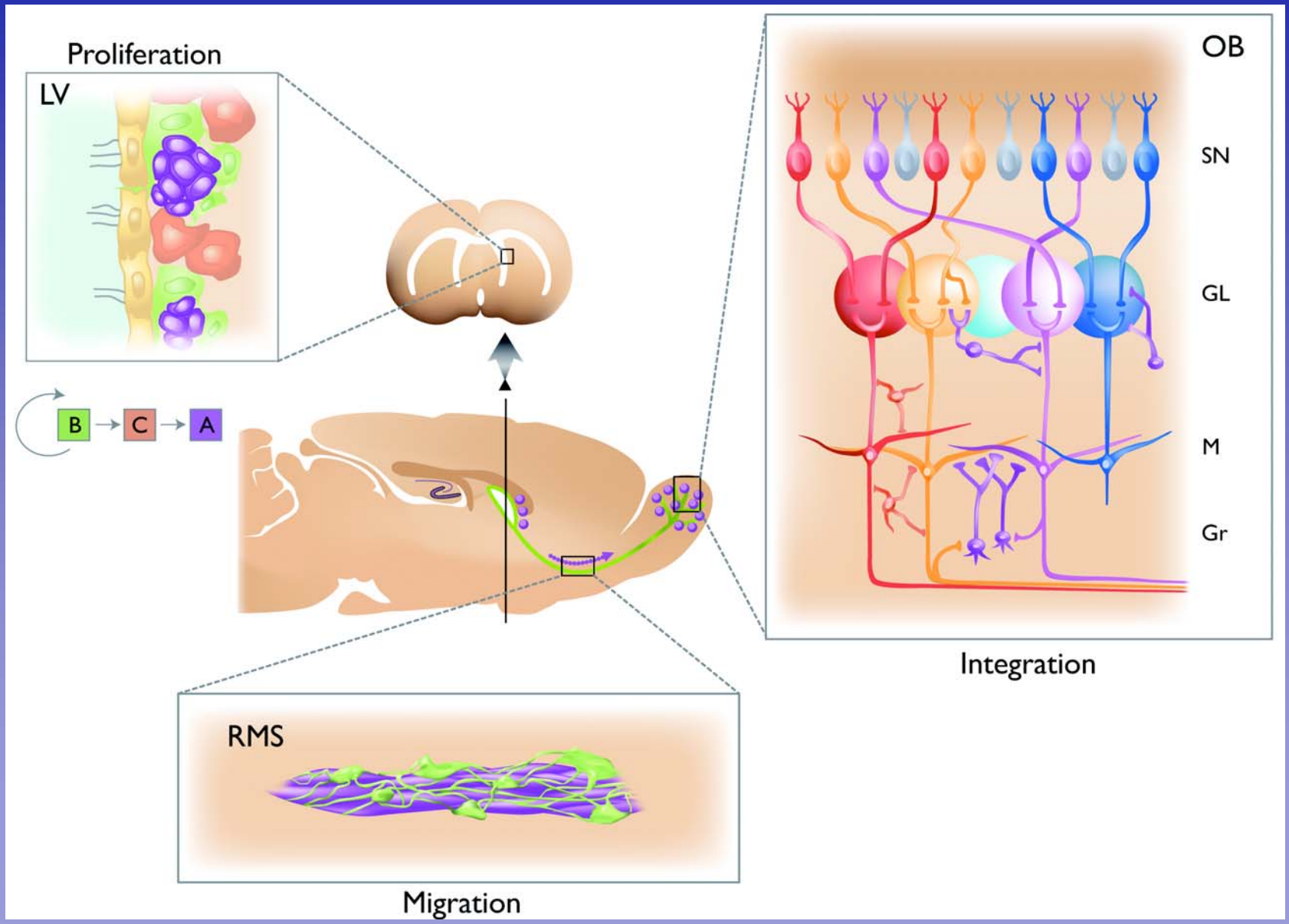


(2) Neurogenesis in the central relay

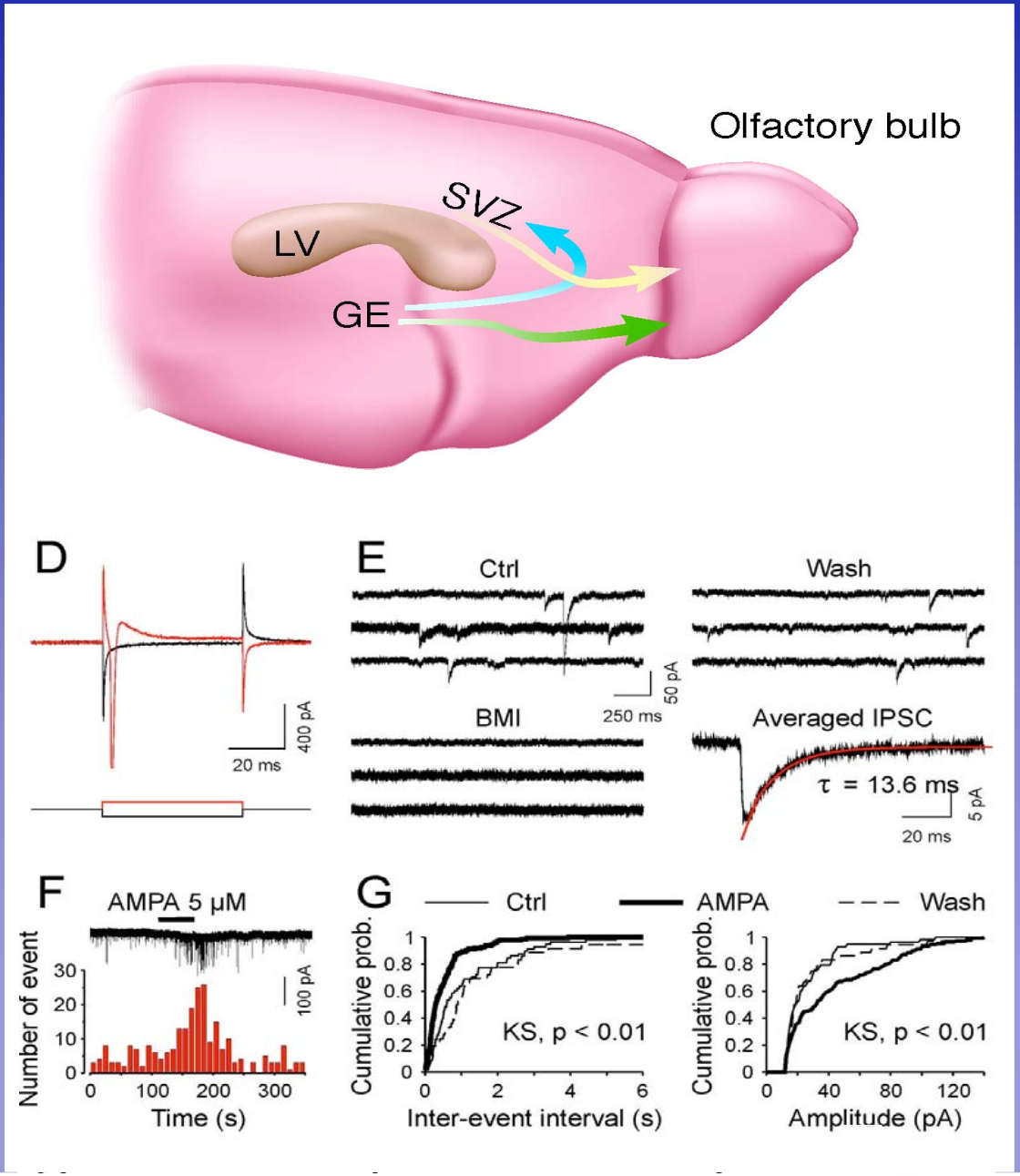


(3) Functional significances

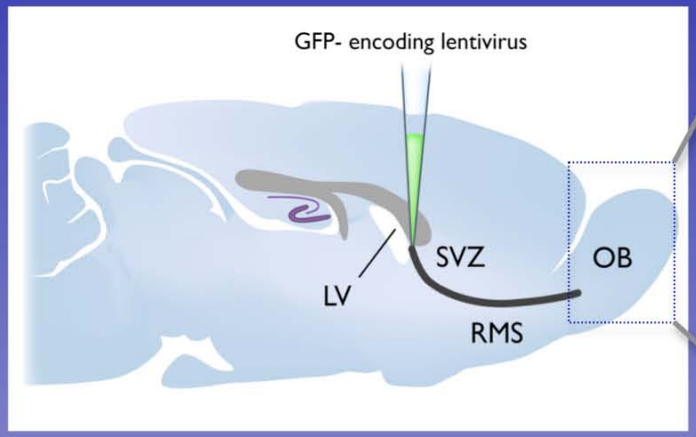
Part II. Bulbar Neurogenesis

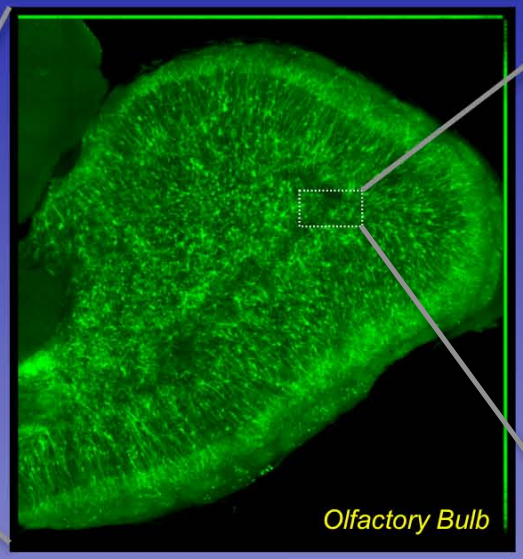


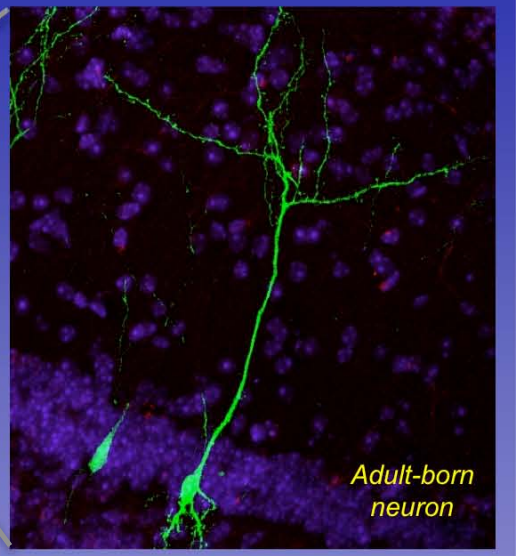
Perinatal Neurogenesis

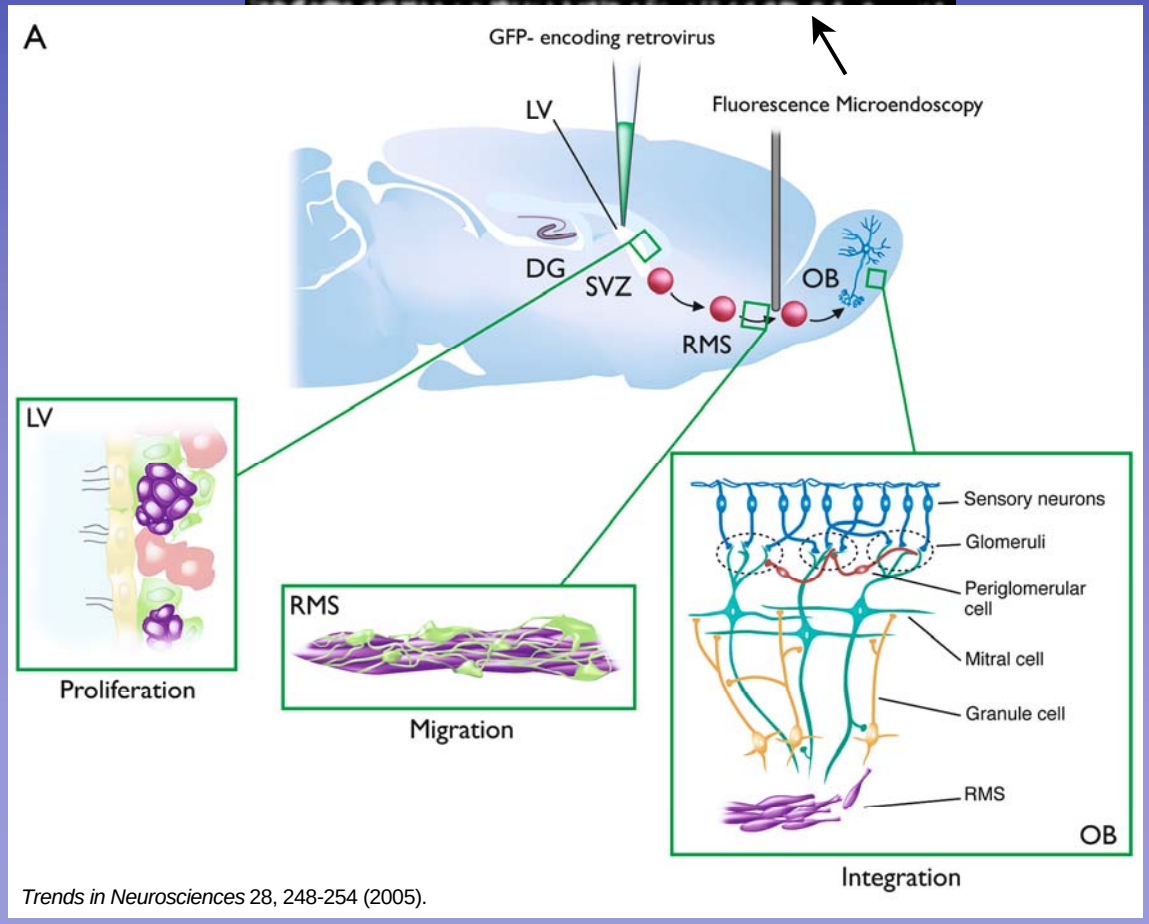


Identifying Newborn Neurons in Adult Olfactory Bulb



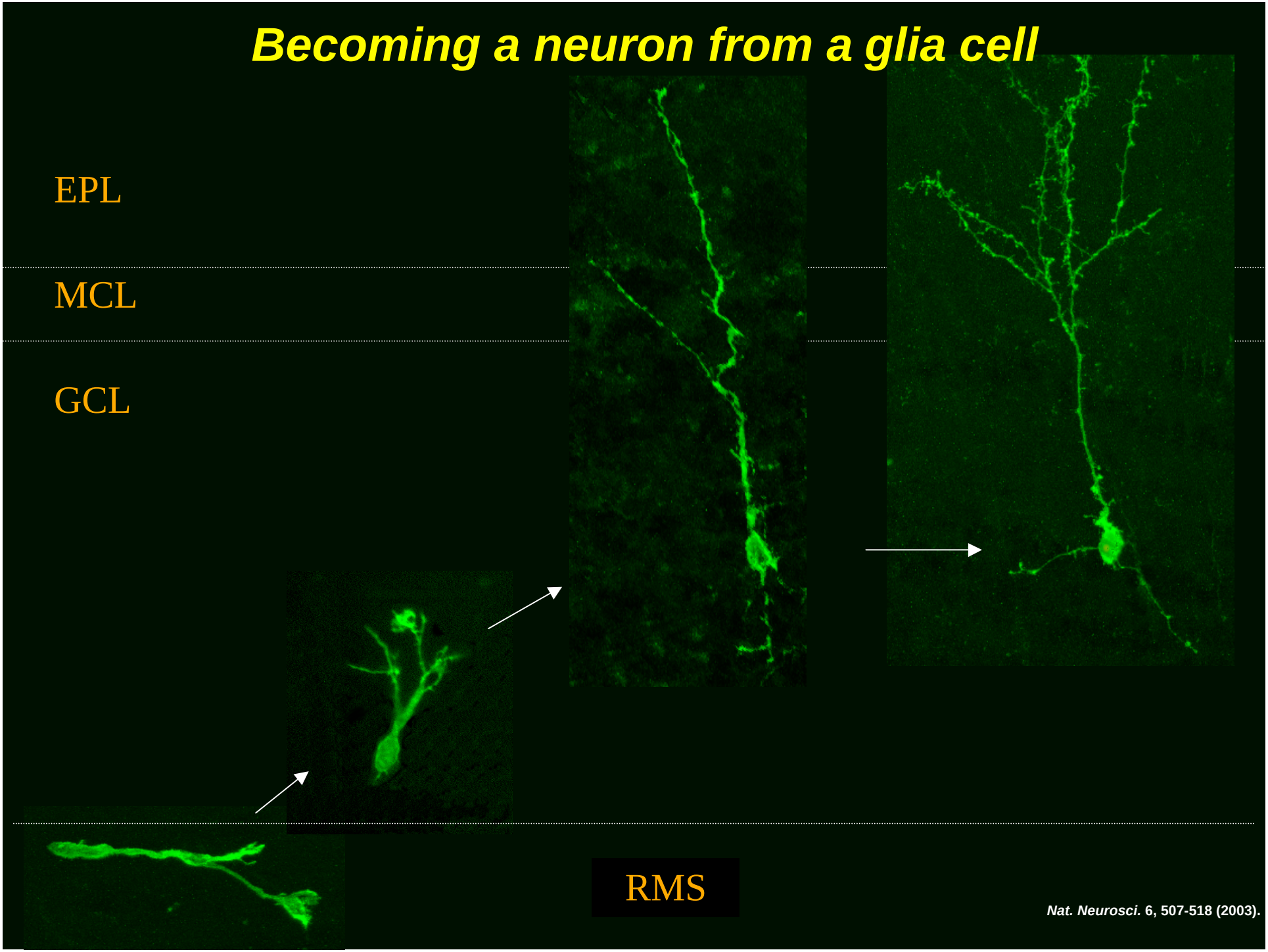






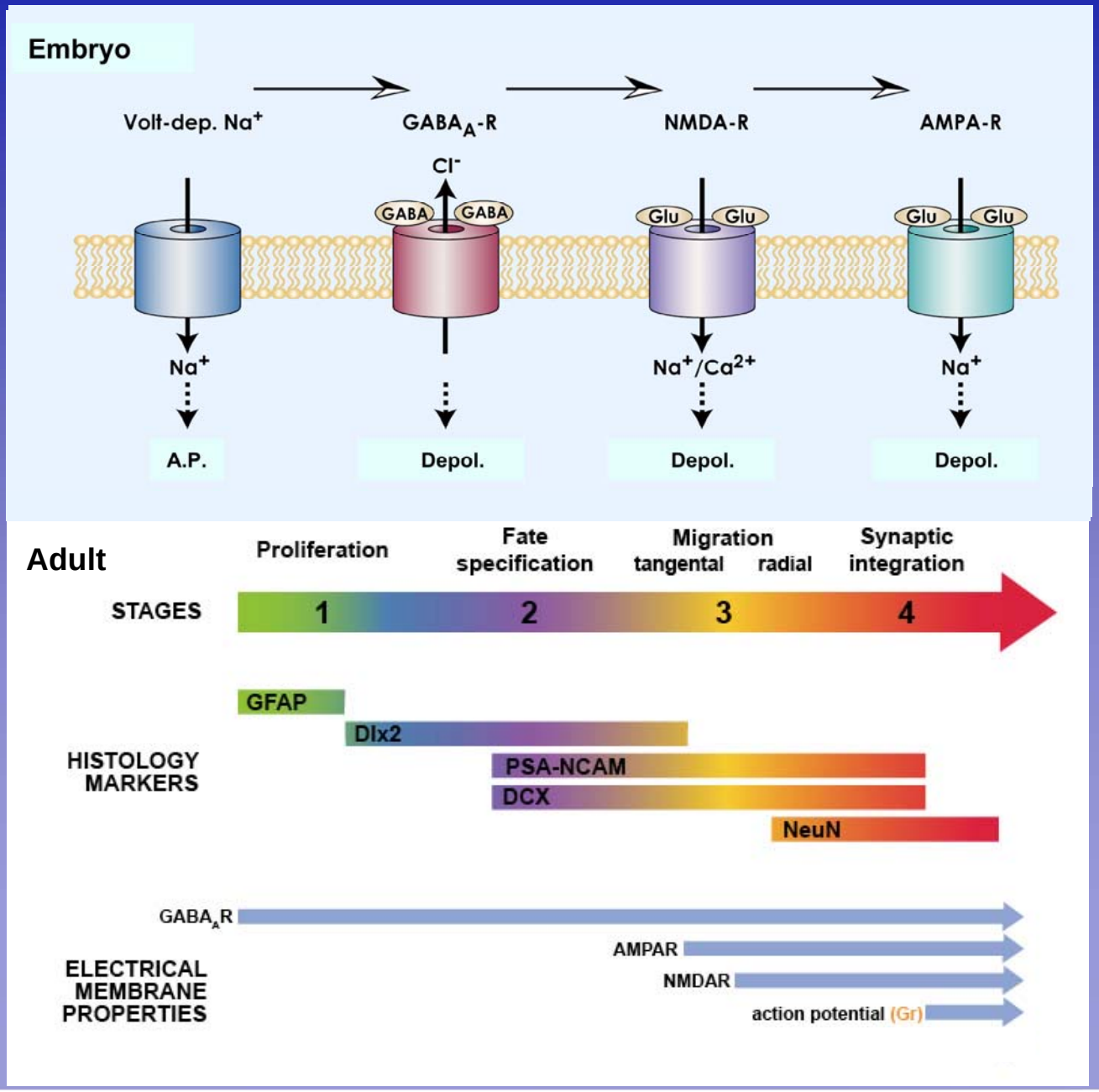
Trends in Neurosciences 28, 248-254 (2005).

Becoming a neuron from a glia cell



Nat. Neurosci. 6, 507-518 (2003).

Early versus *Late Neurogenesis*

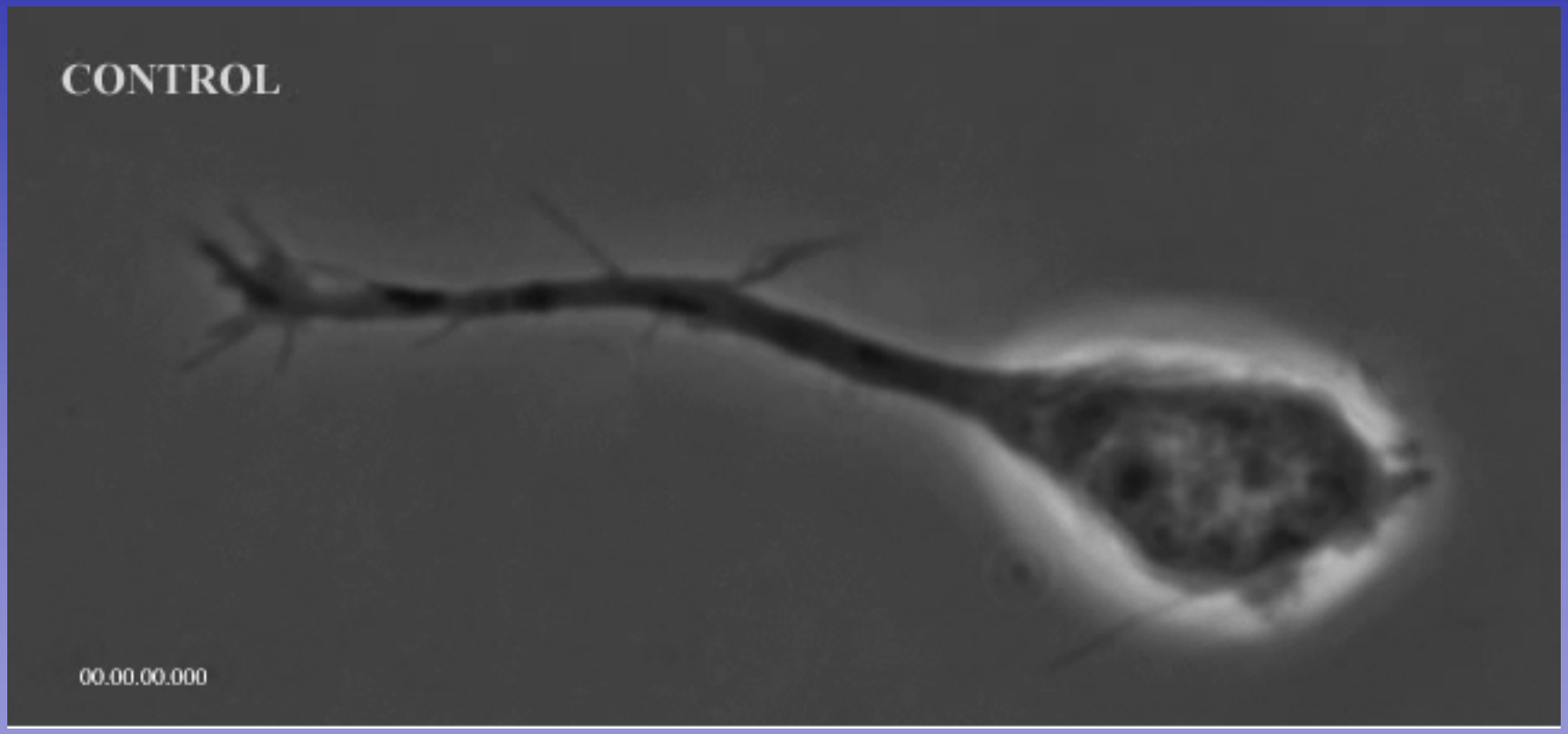


Summary - Part 2

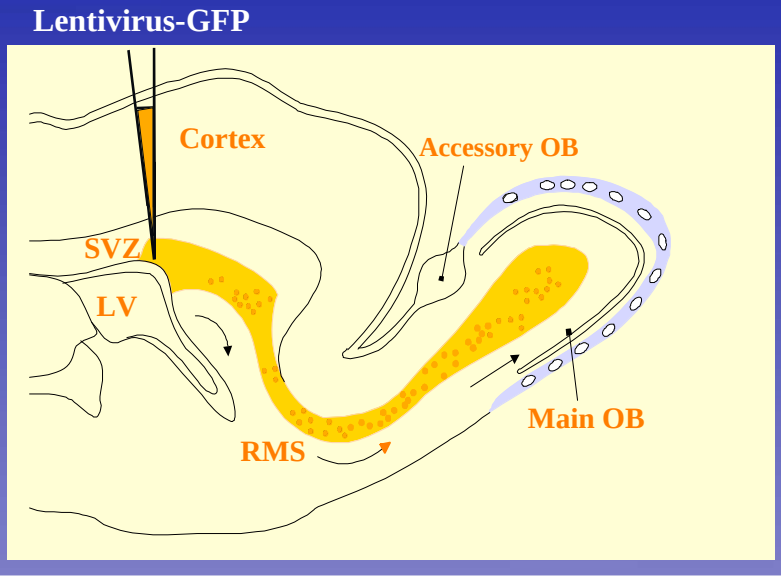
- ***Adult Neurogenesis Does Not Recapitulate Embryogenesis.***

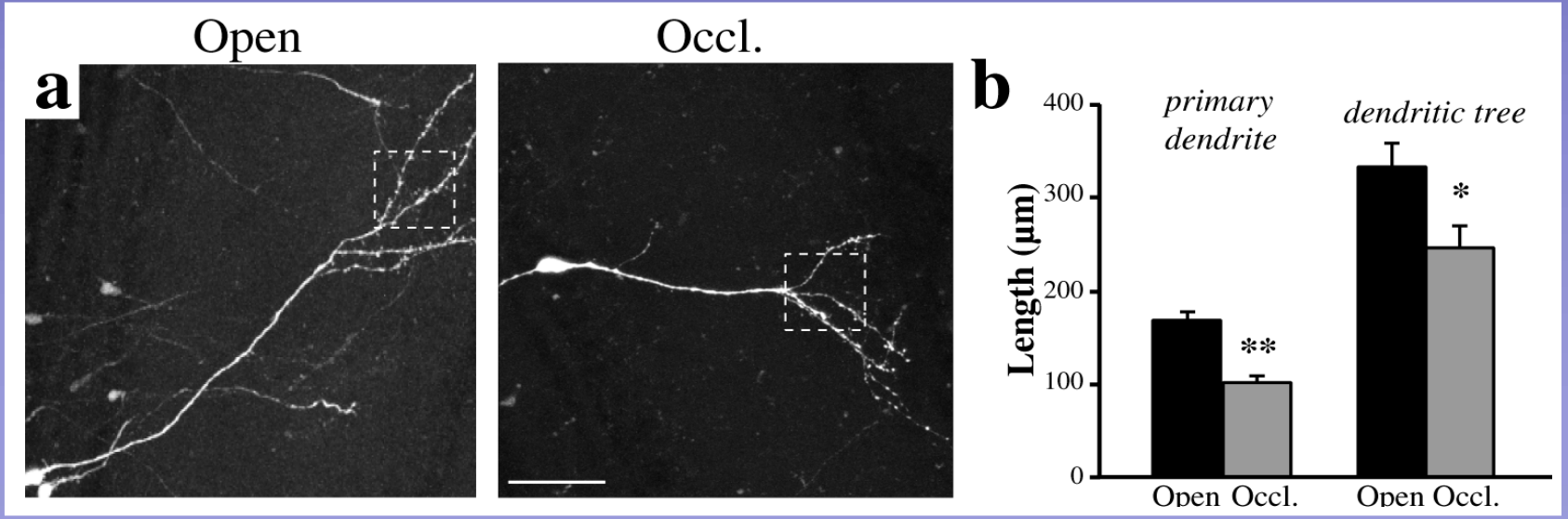
- ***It Offers a Unique Situation in which Epigenetic Regulations May Take Place.***

Activity-depend regulation



Maturation of GABAergic Interneurons

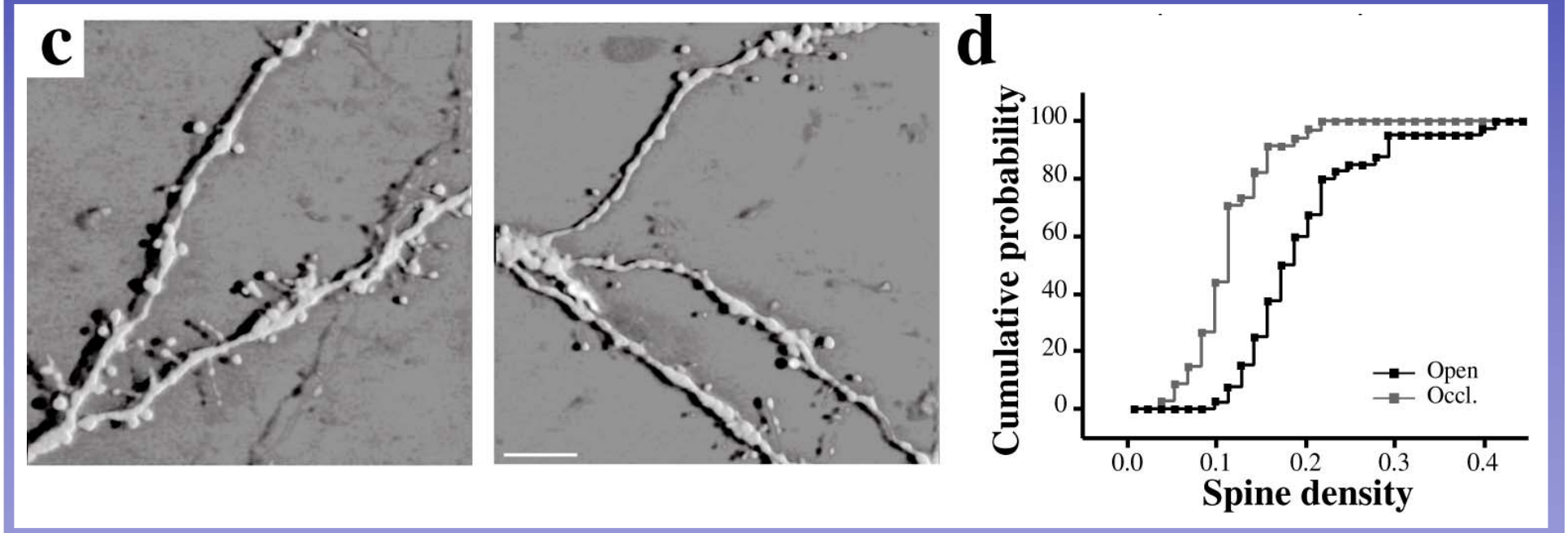




Neuron 46, 103-116 (2005)

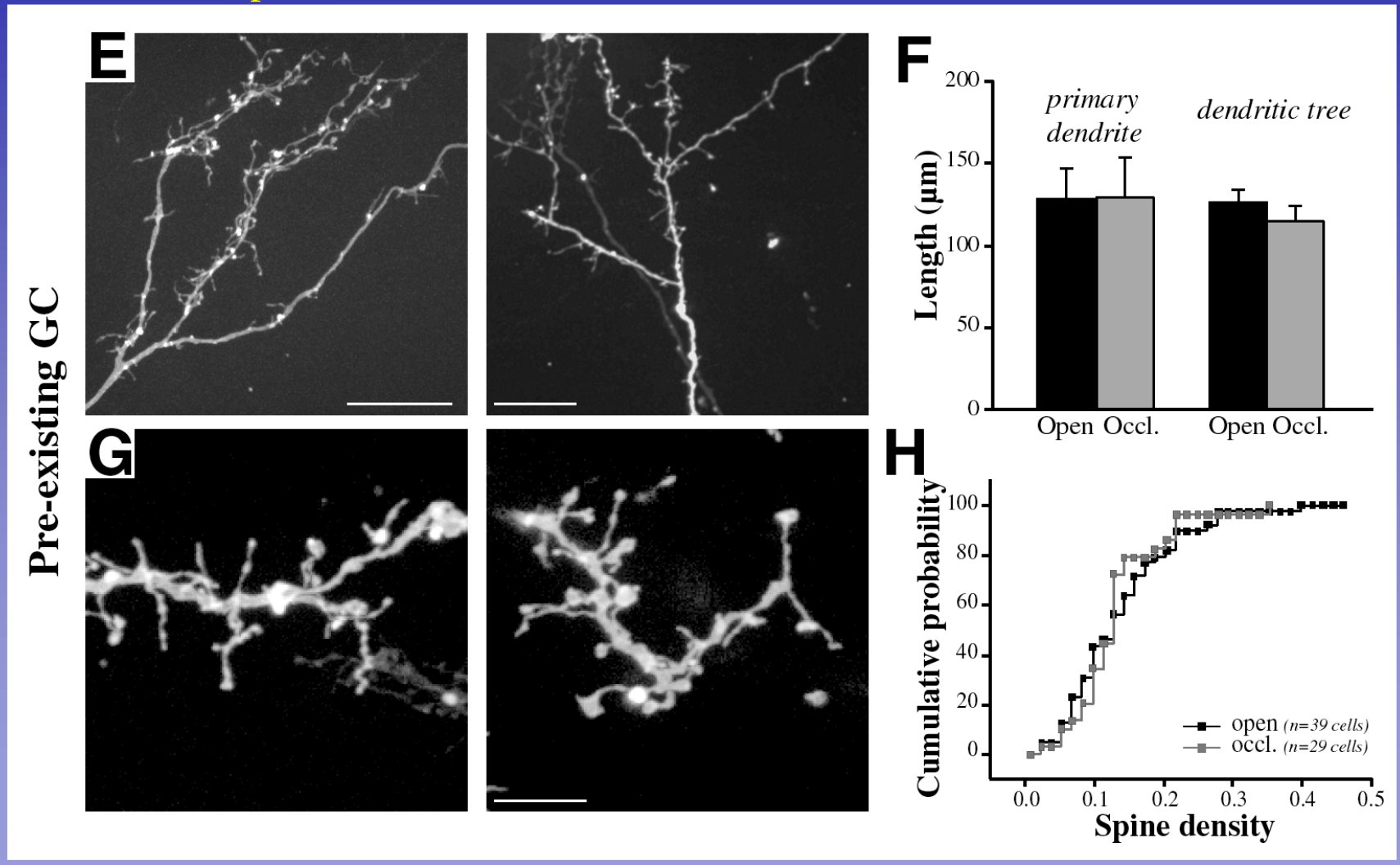
Spine Density of Newborn Neurons

Open Closed



Neuron 46, 103-116 (2005)

Spine Density of Mature Neurons



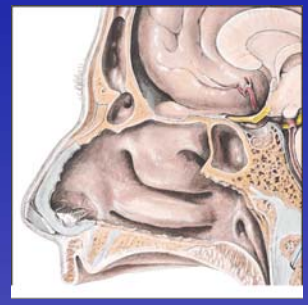
Neuron 46, 103-116 (2005)

Summary - Part 3

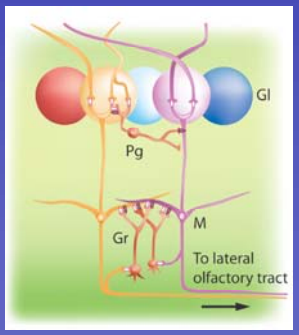
- ***Adult Neurogenesis Offers a Unique Situation in which Activity-Dependent Regulations May Take Place.***

Three Main Objectives

(1) Neurogenesis of sensory neurons



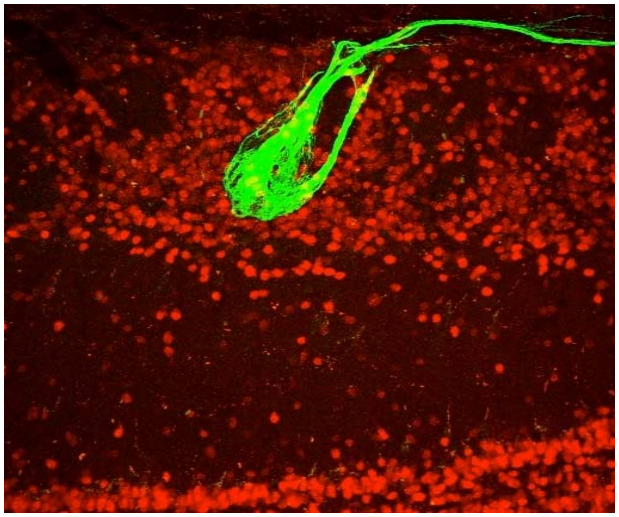
(2) Neurogenesis in the central relay

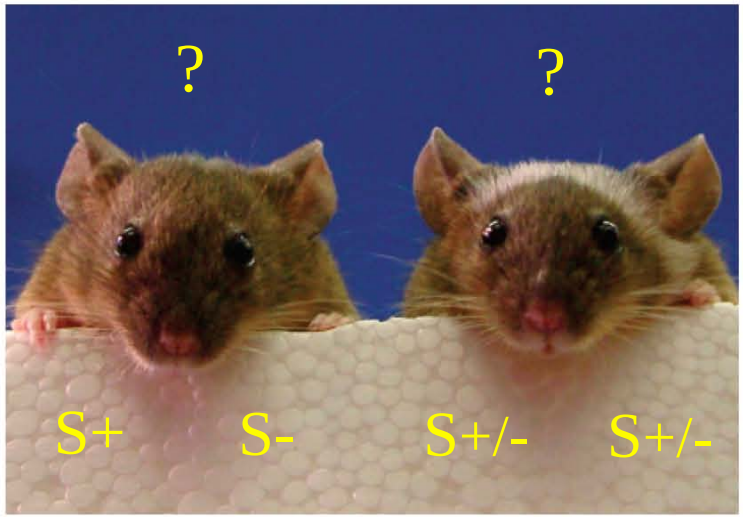


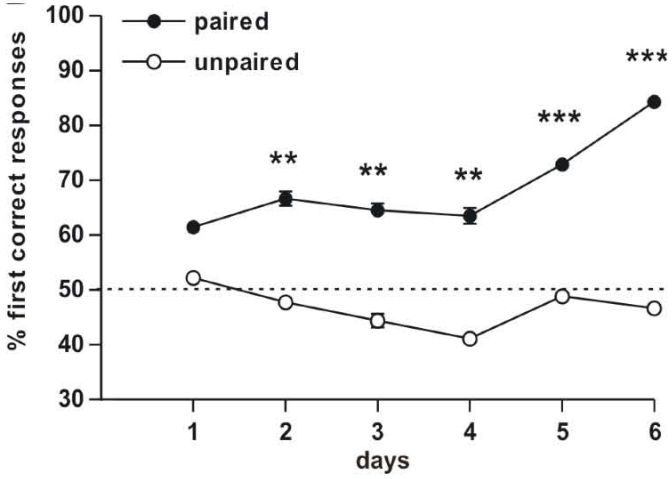
(3) Functional significances

Olfactory Discrimination Learning

MOR23-GFP

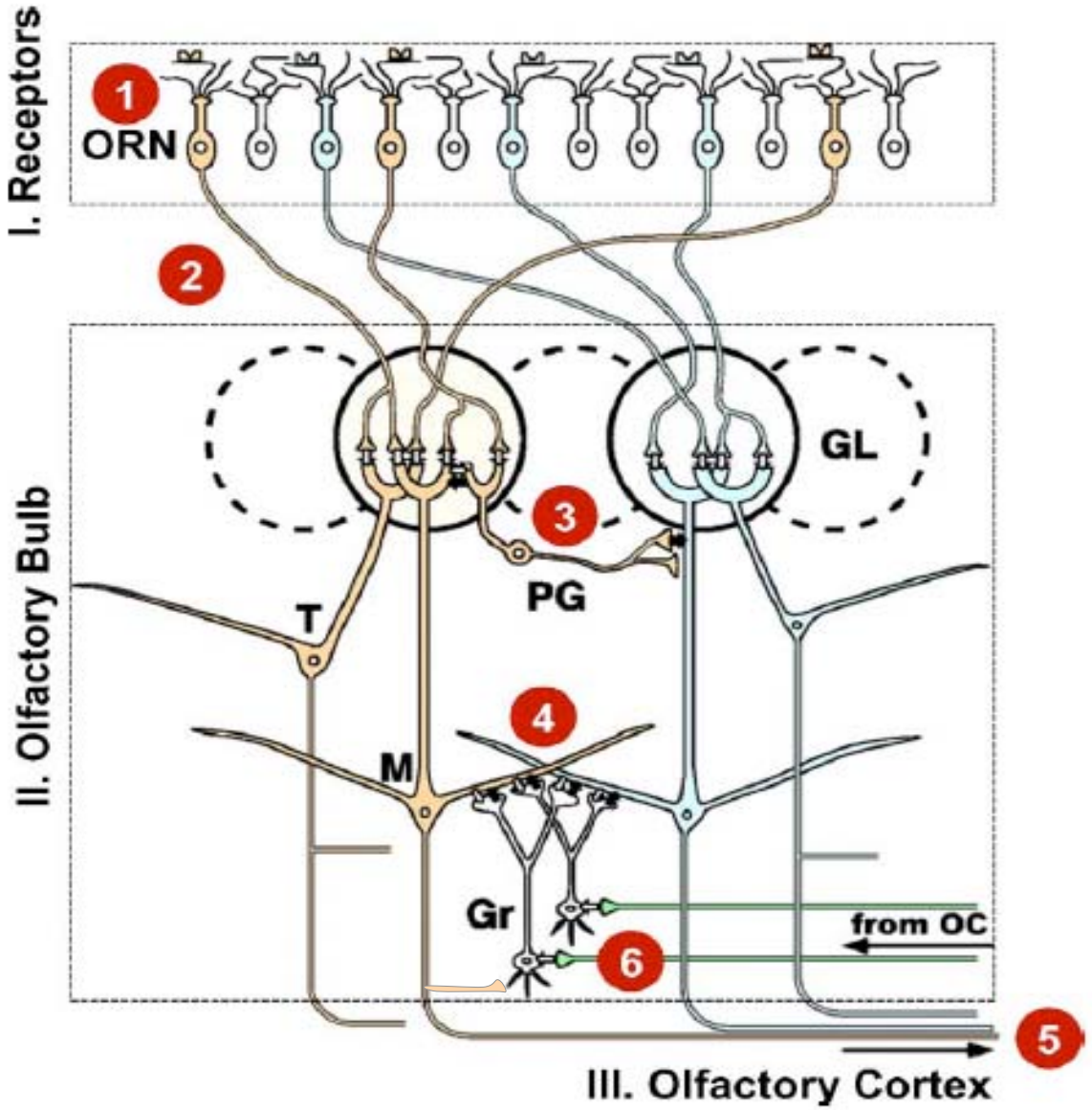




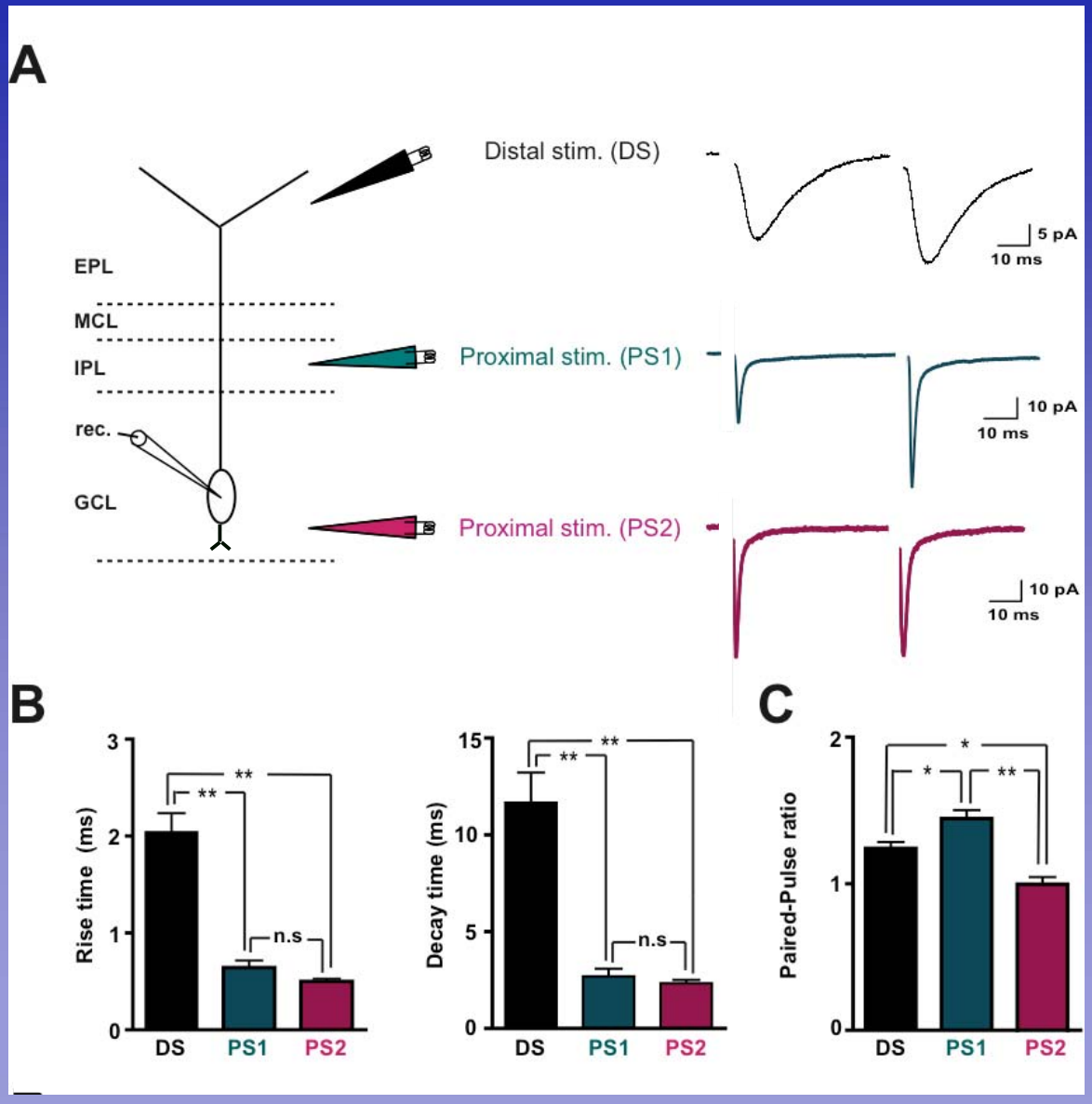


J. Neurosci. 26, 10508-13 (2006)

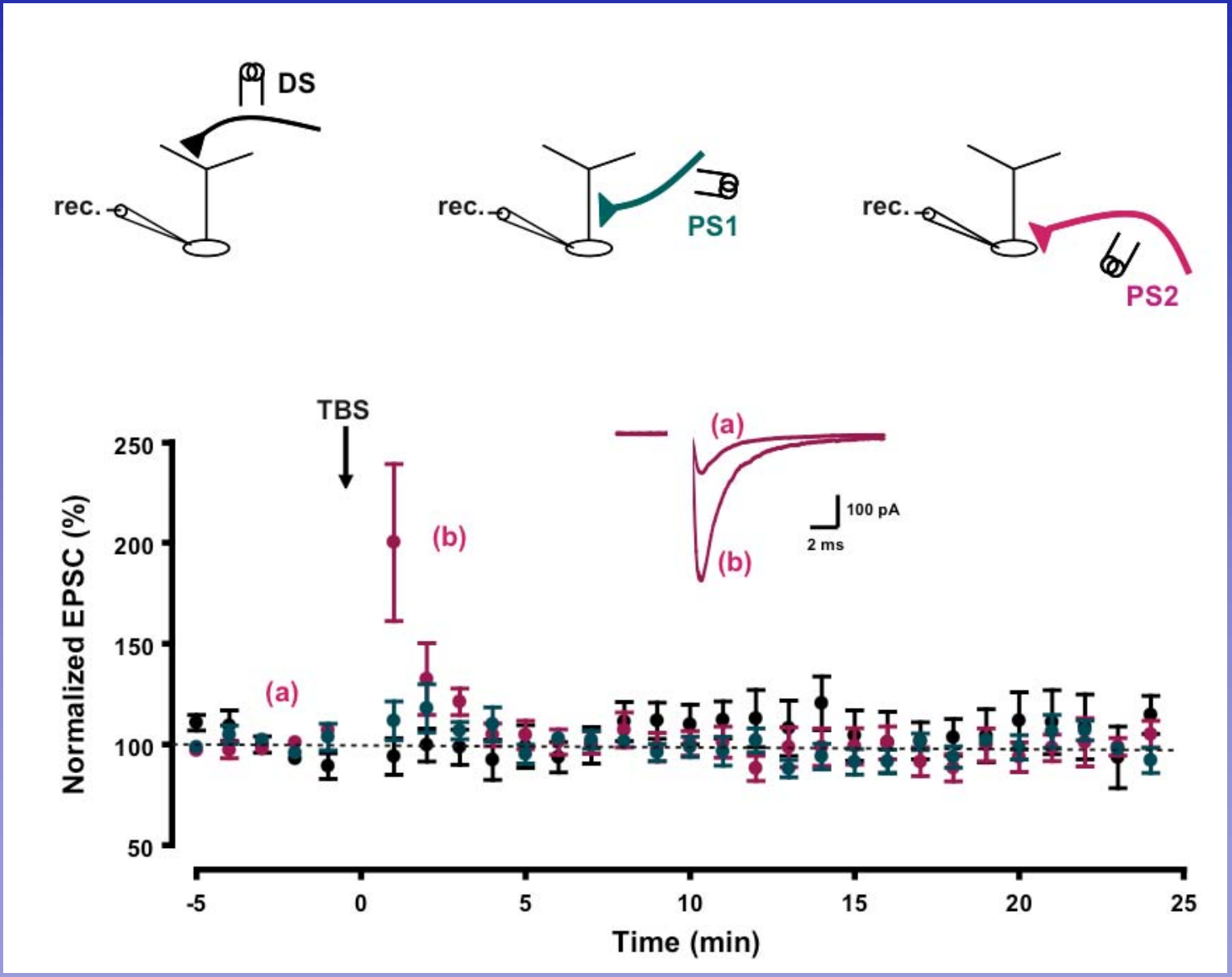
Computational Functions



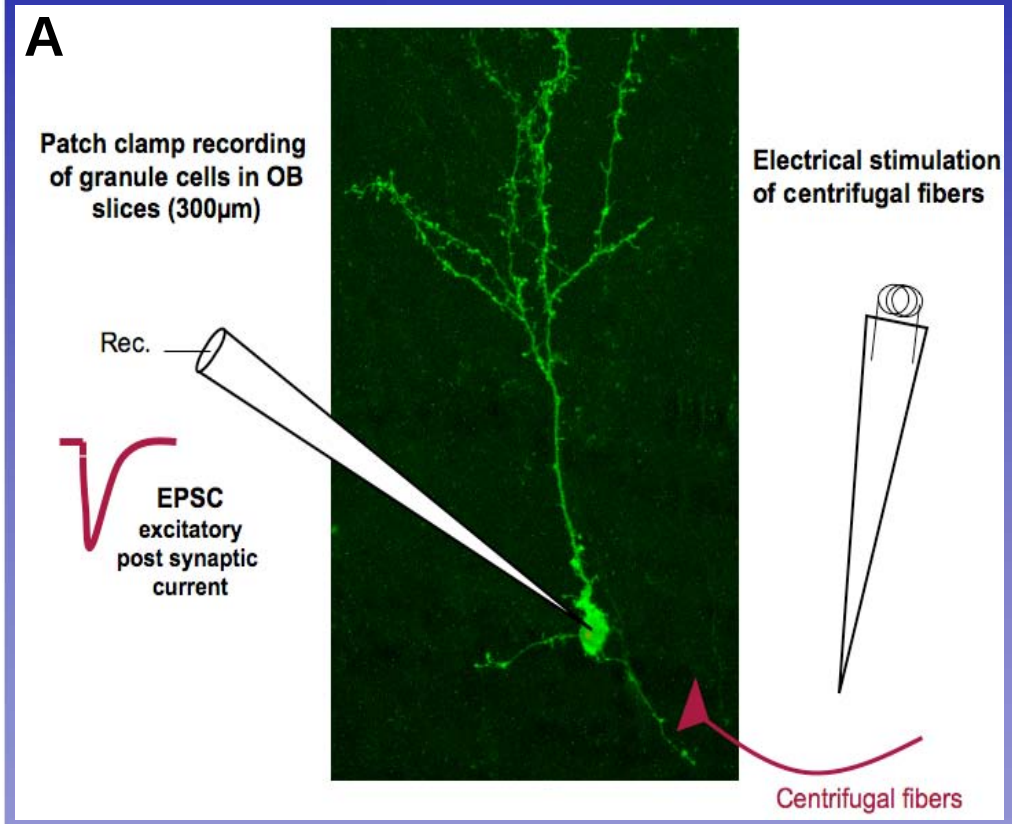
Three Glutamatergic Inputs

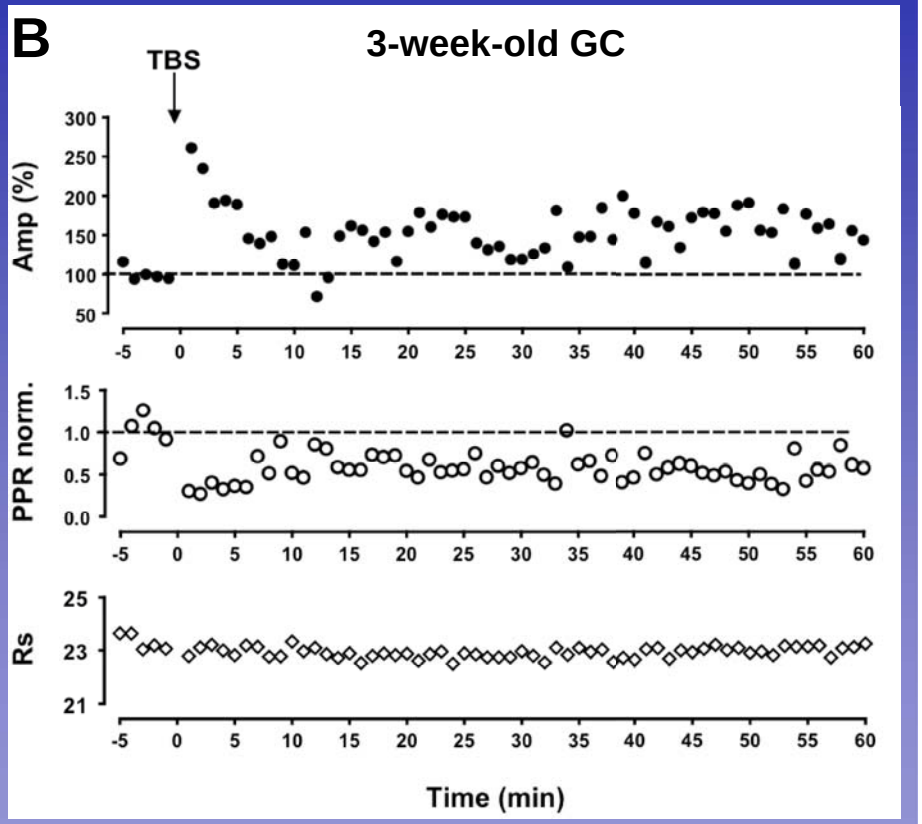


TB Stimulations at Excitatory Synapses



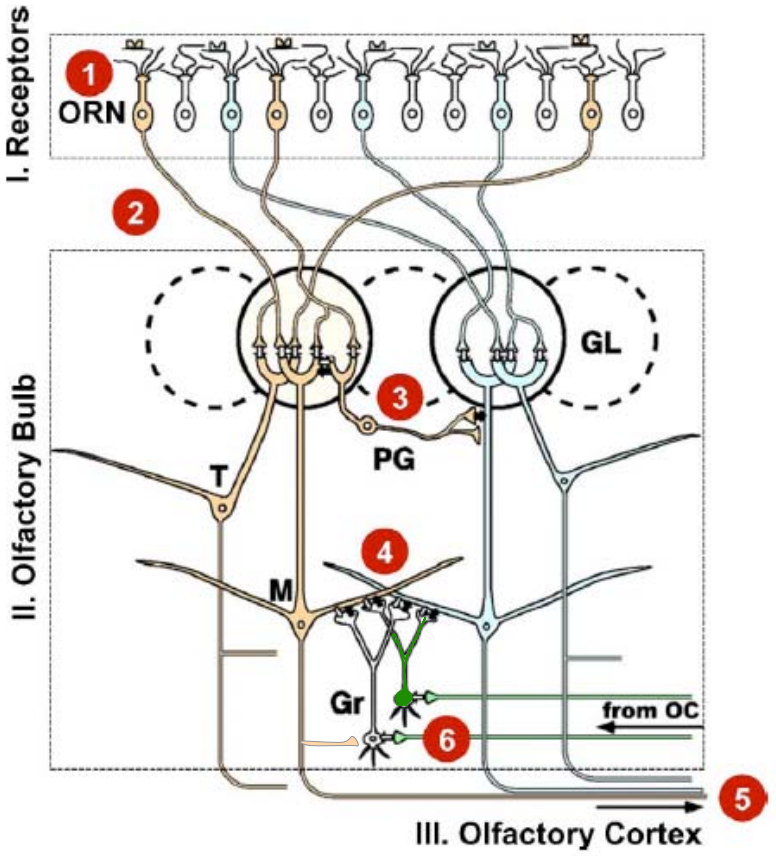
Newborn Interneurons Display LTP



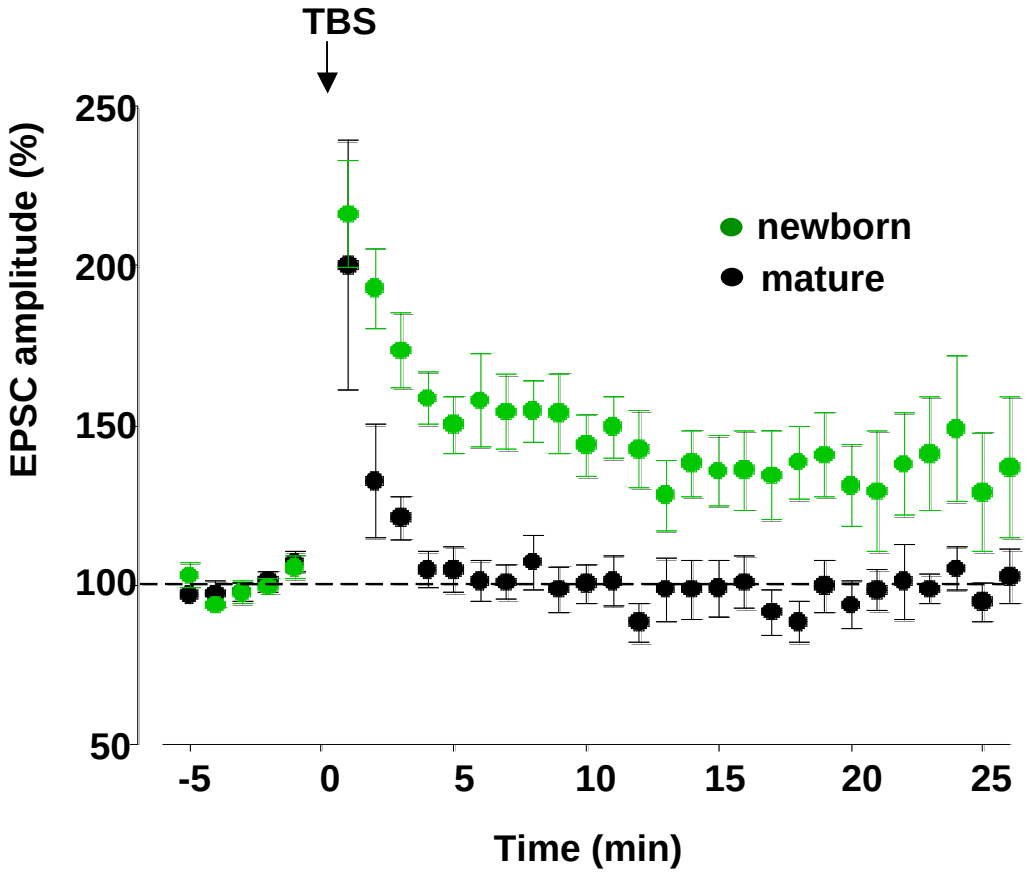


Nat. Neurosci. 12, 728-730 (2009).

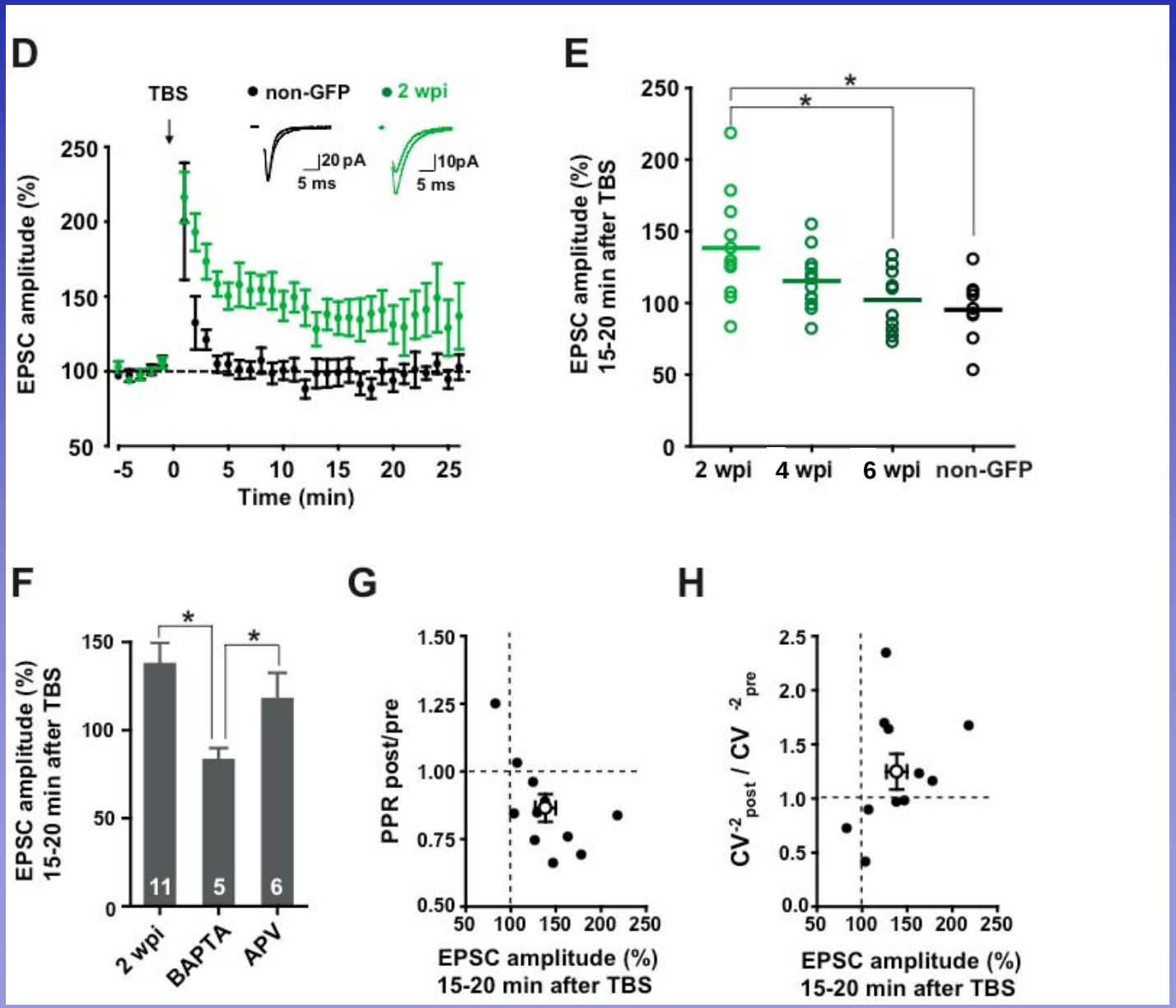
Computational functions



Synaptic plasticity

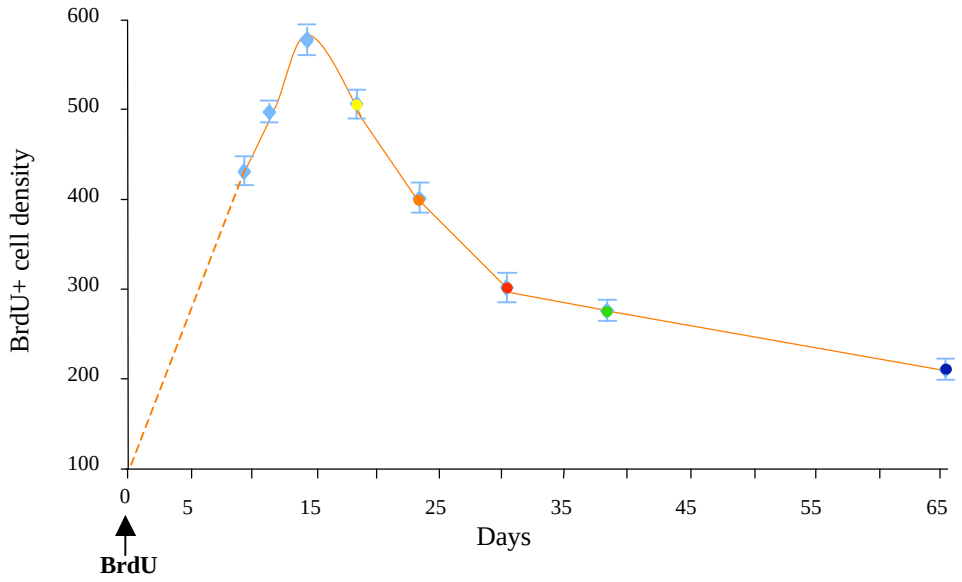


Newborn Interneurons are Transiently Amenable

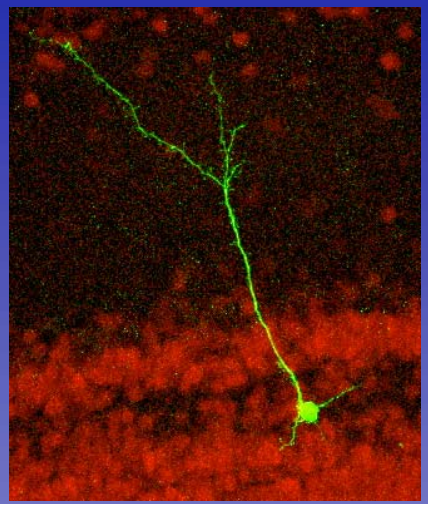


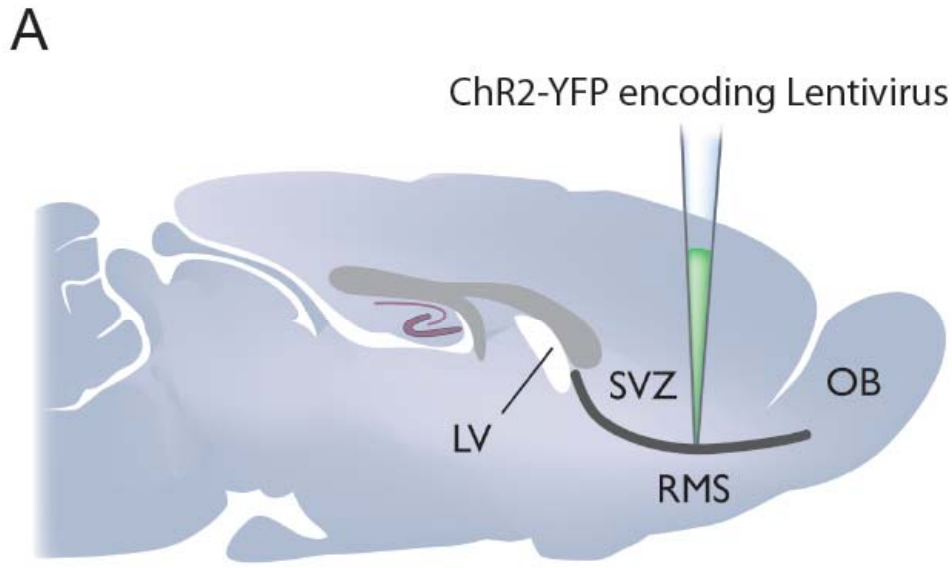
When time matters

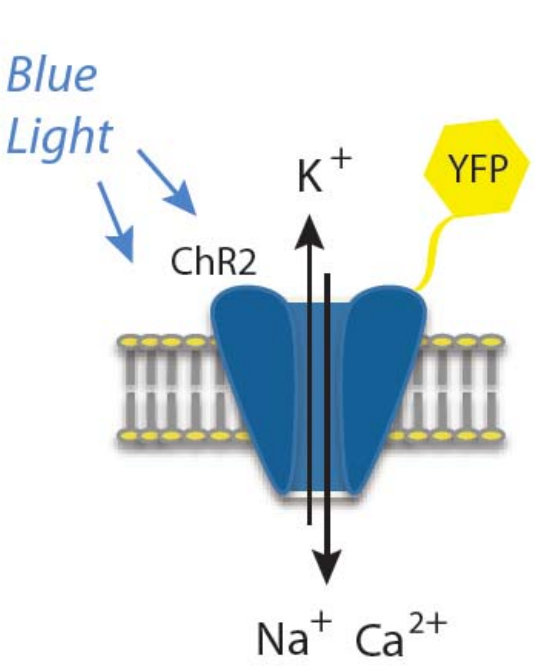
A



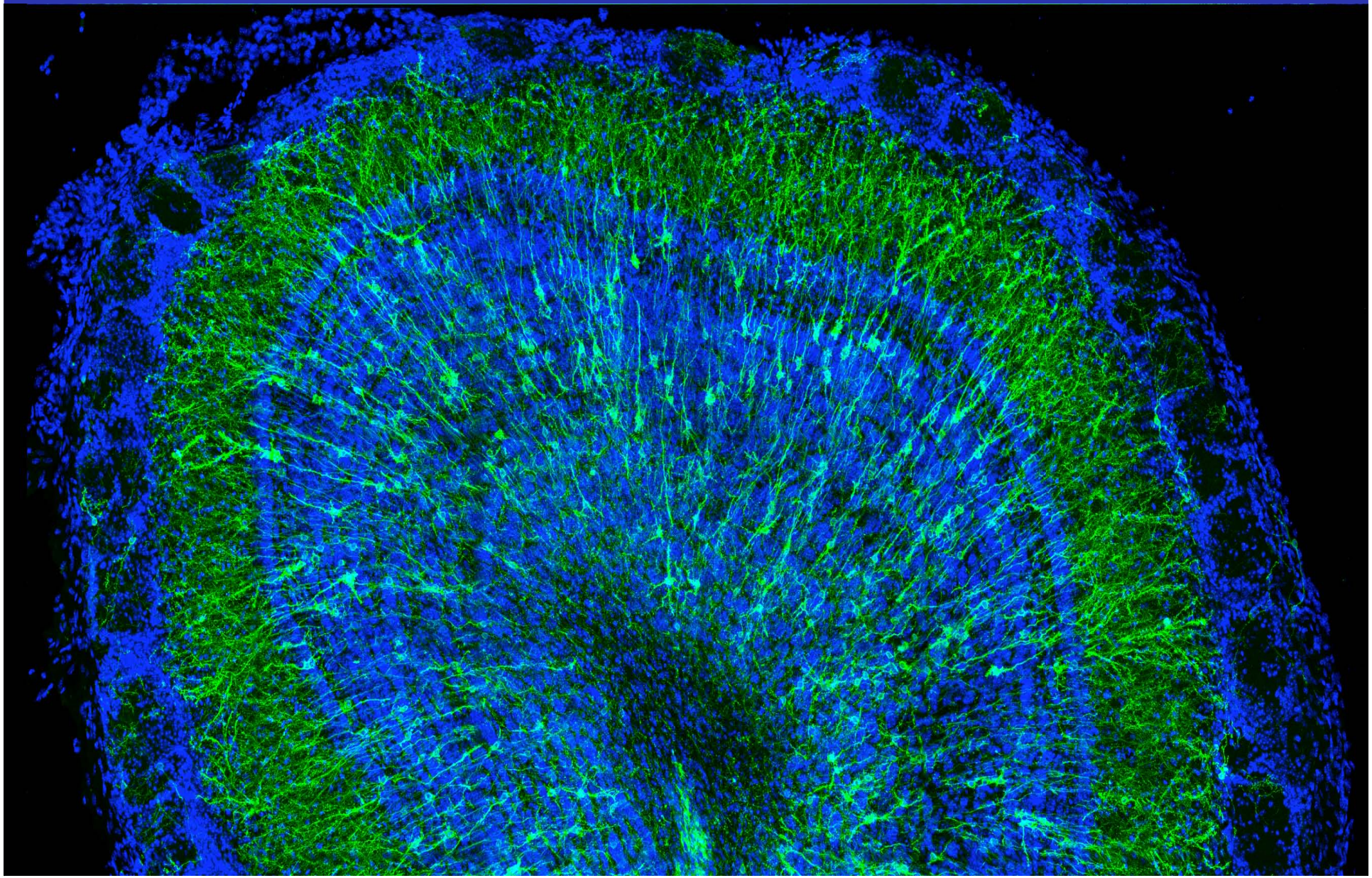
Deciphering the Function of New Neurons



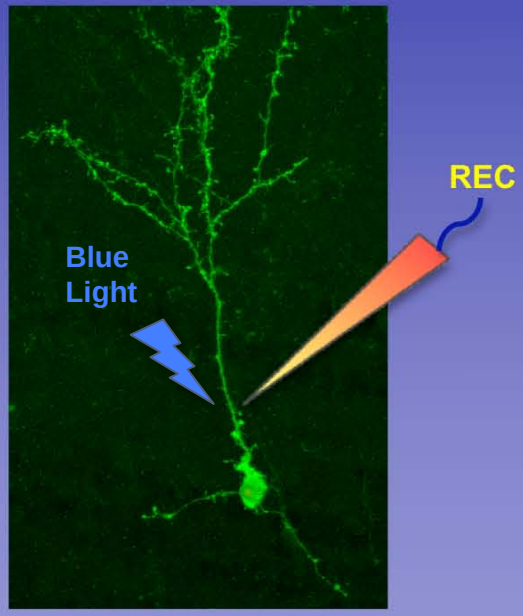


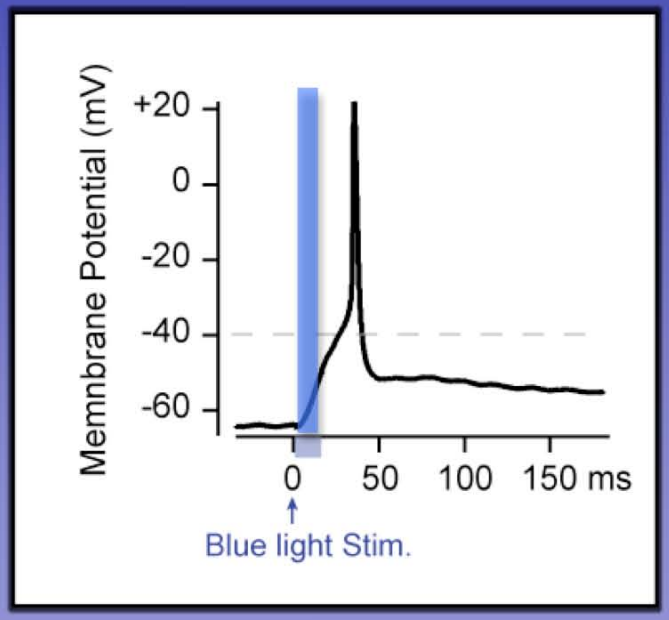


Newborn Interneurons Labeled with YFP



Action Potential Evoked by Flash of Blue Light

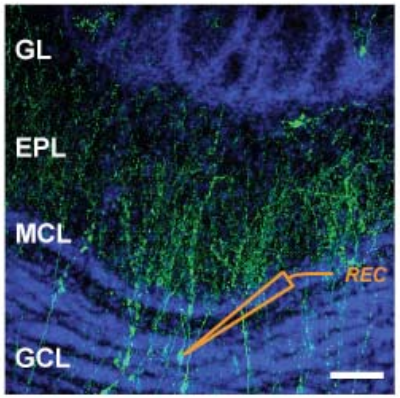




Light-Induced Excitability of Newborn Interneurons

a

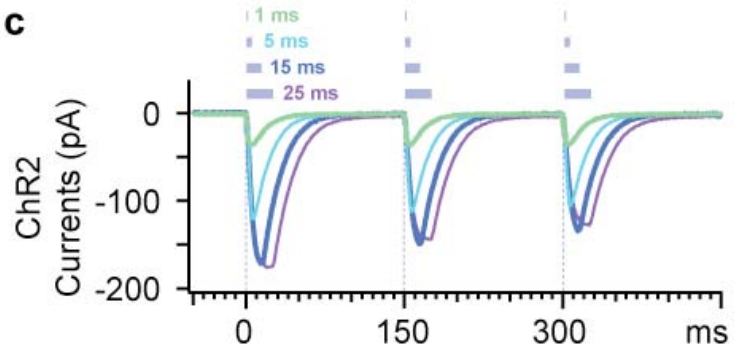
Adult born neurons expressing ChR2-YFP



b

	3 days *n=2*	1 week *n=5*	1 - 4 months *n=7*
VD sodium currents	✓	✓	✓
VD action potentials	0	✓	✓
Light evoked ChR2 currents	✓	✓	✓
Light evoked ChR2 action potentials	0	✓	✓

c



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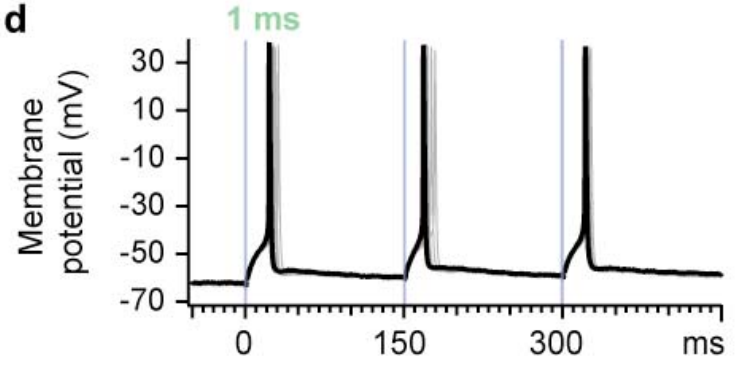

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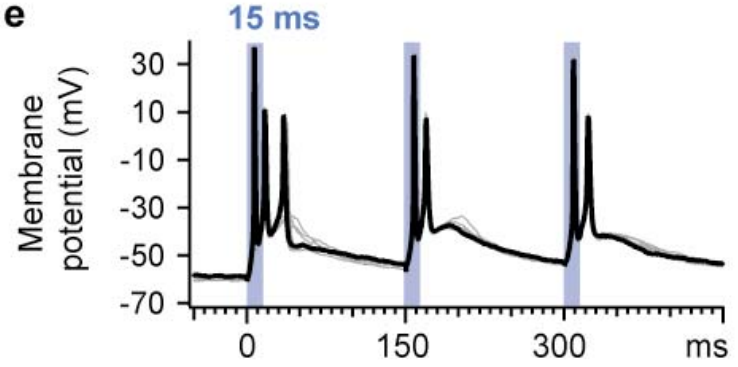
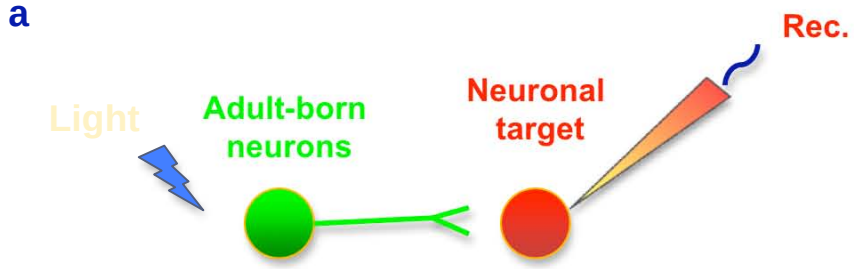
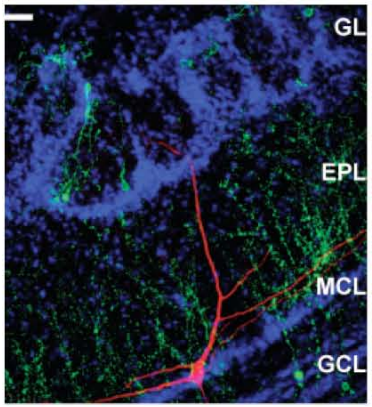
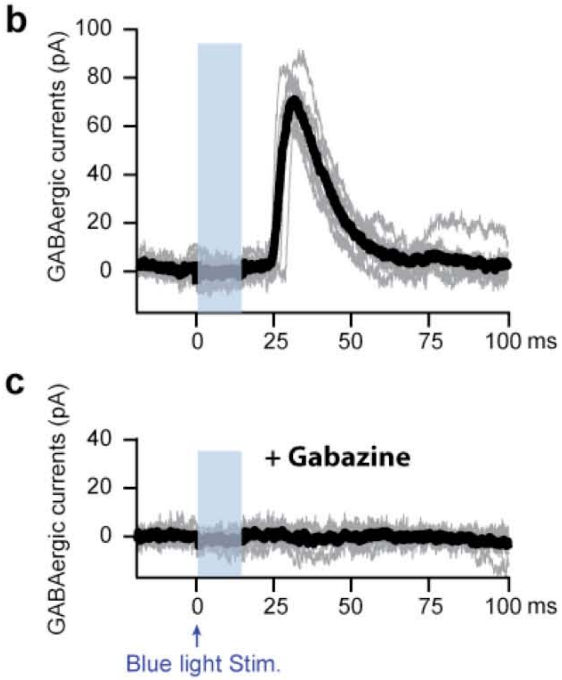


Remote Control of Adult-born Neurons to Inhibit Output Neurons

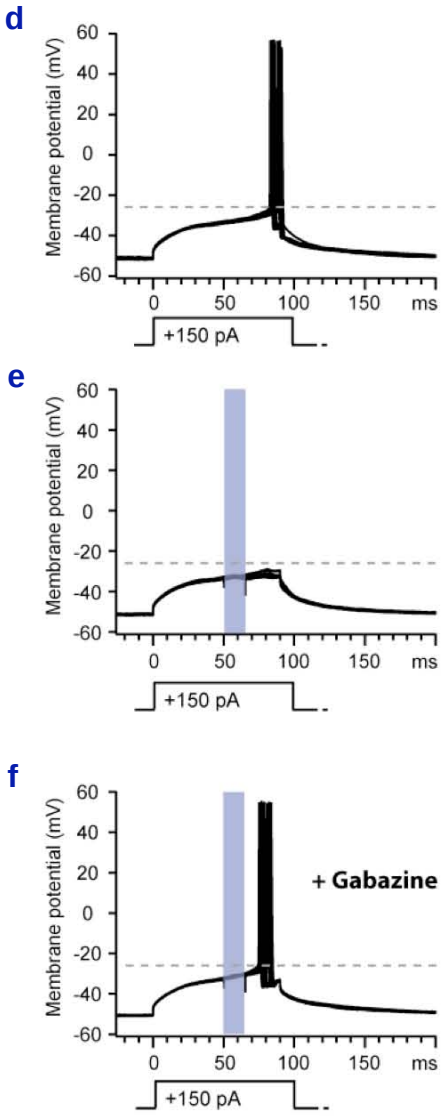




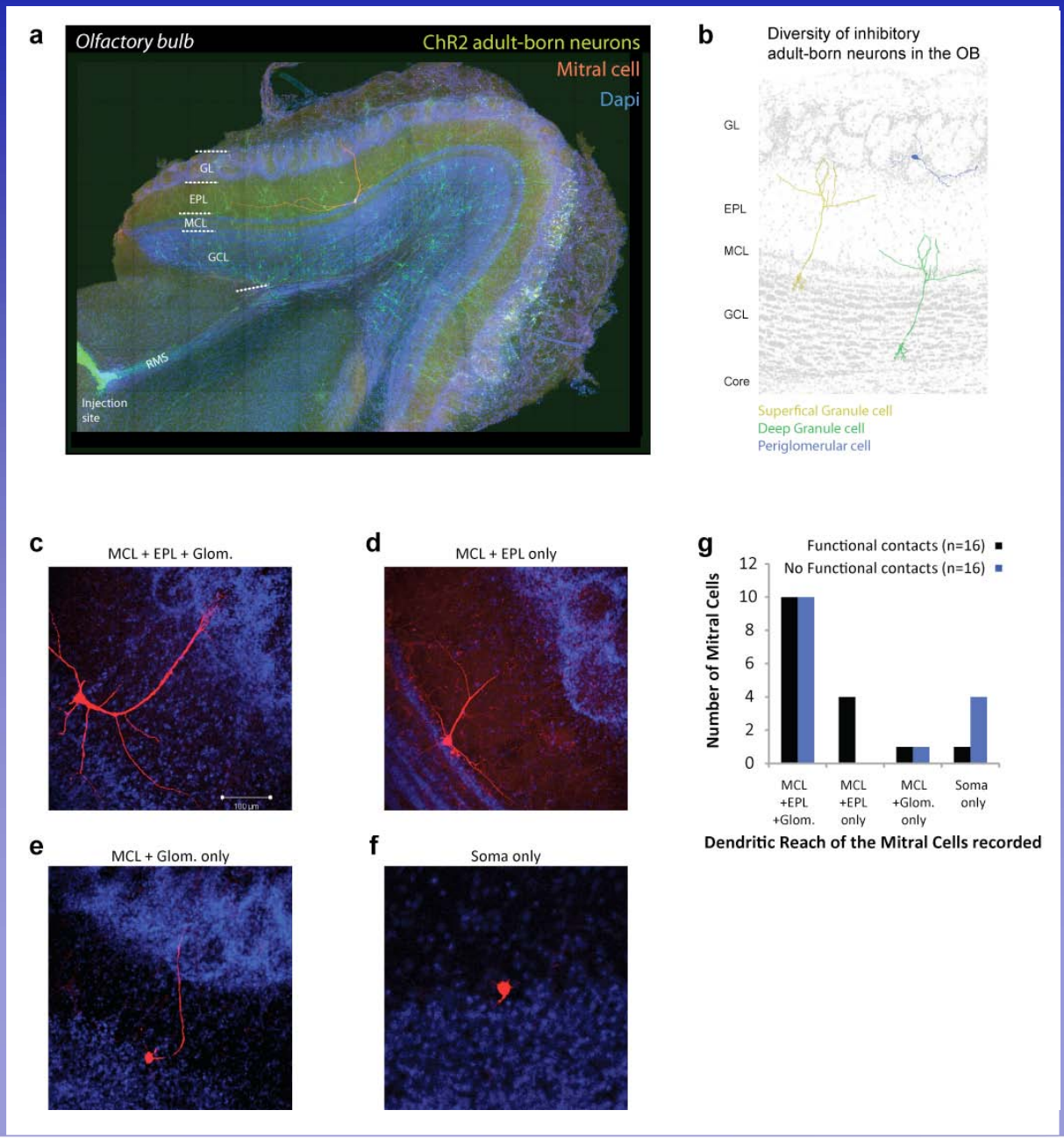
Light evoked GABAergic currents: n = 32



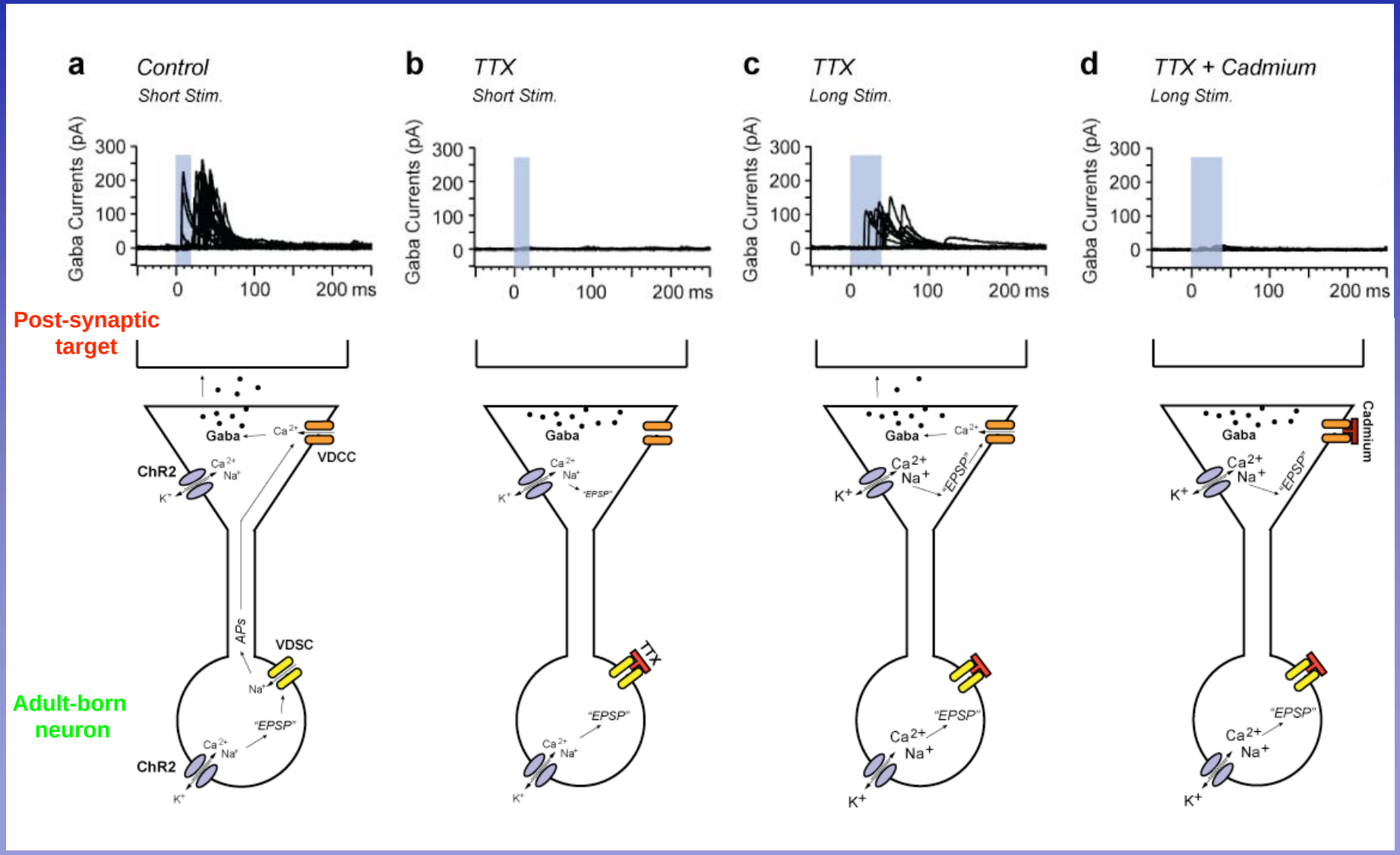
GZ block: n = 7 / 7 cells



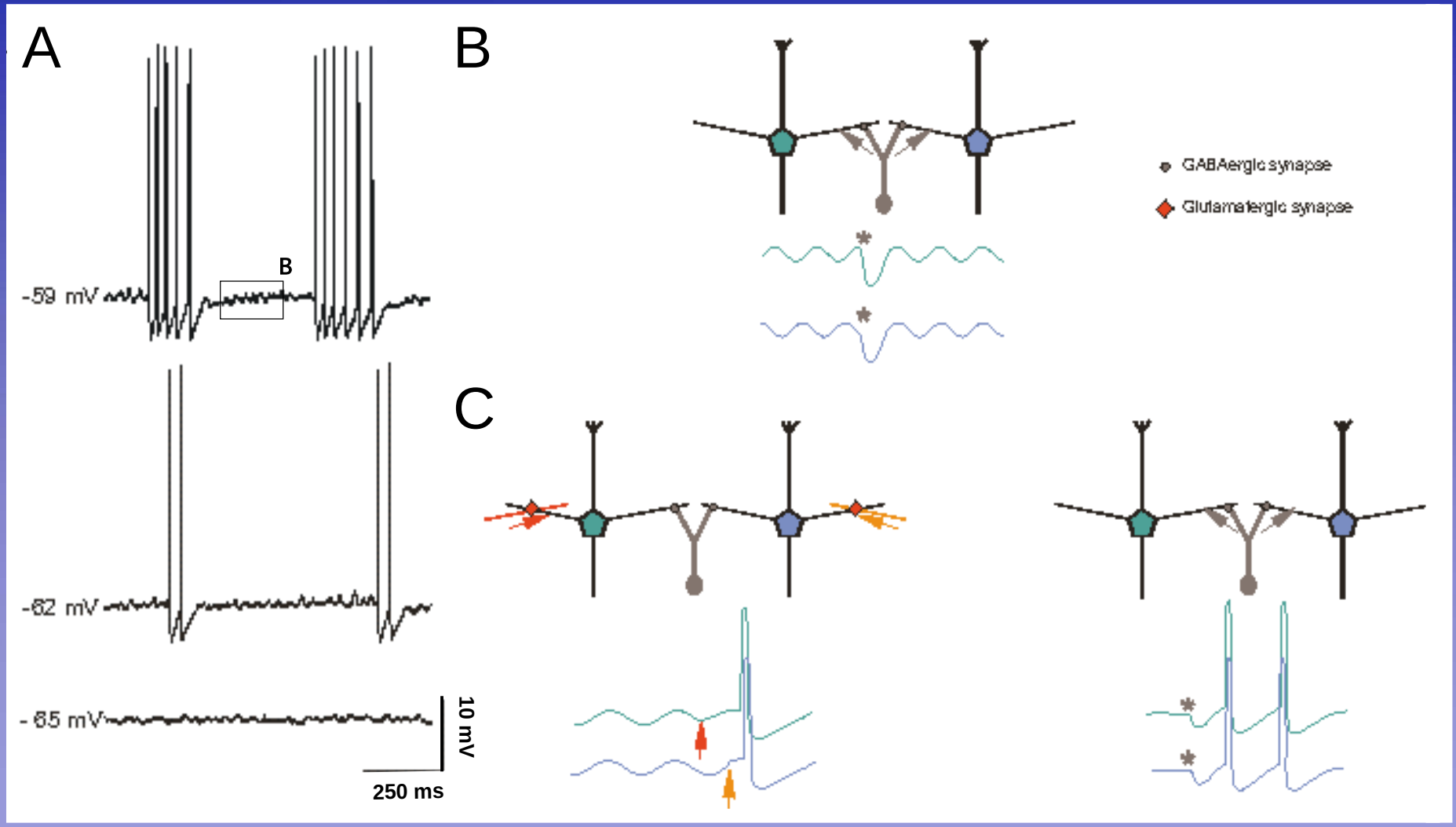
Origin and Location of the Synaptic Contacts from Newborn Neurons



Mechanisms of Light-induced GABA Release

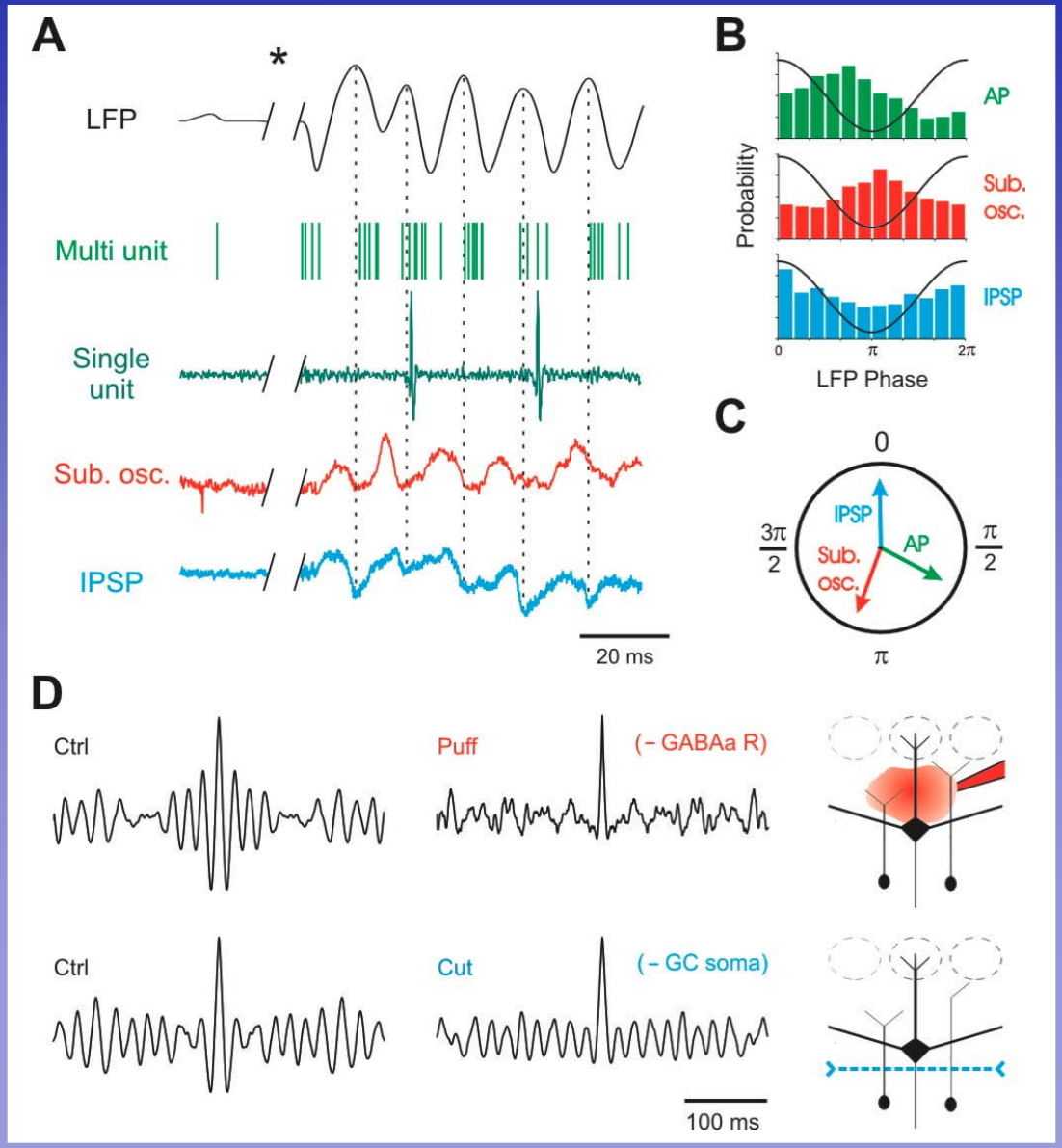


Mature GABAergic interneurons and Synchronization

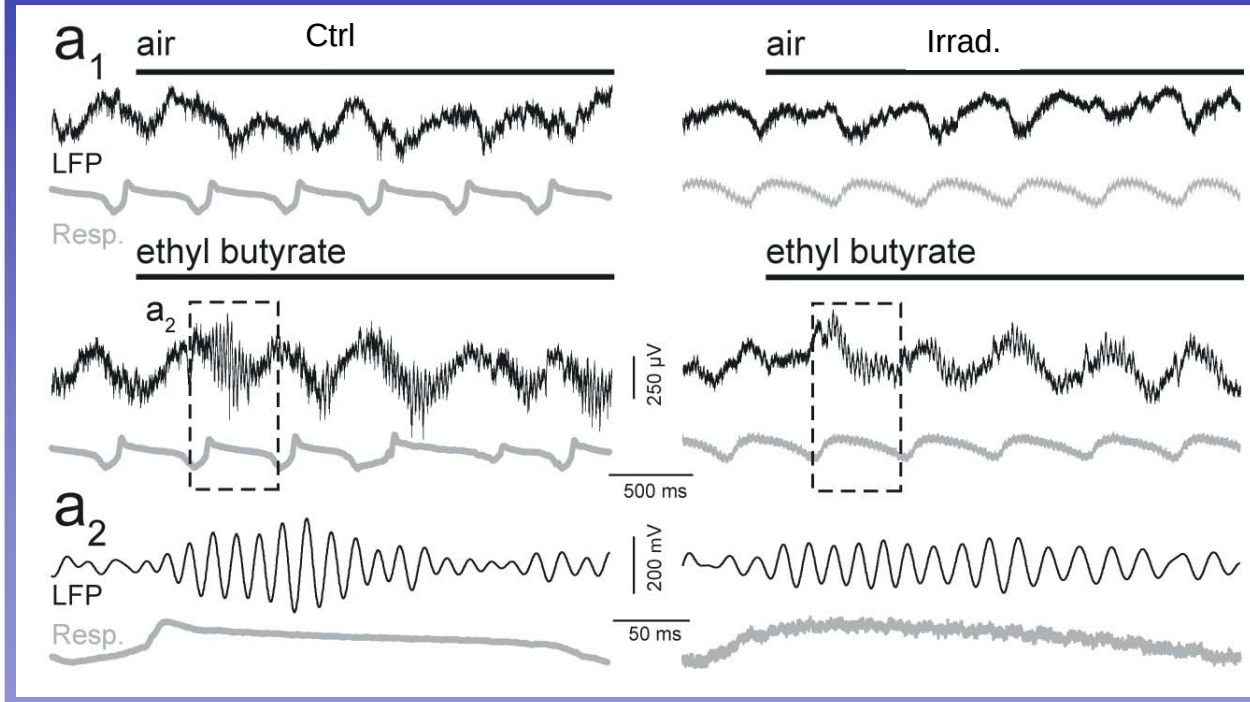


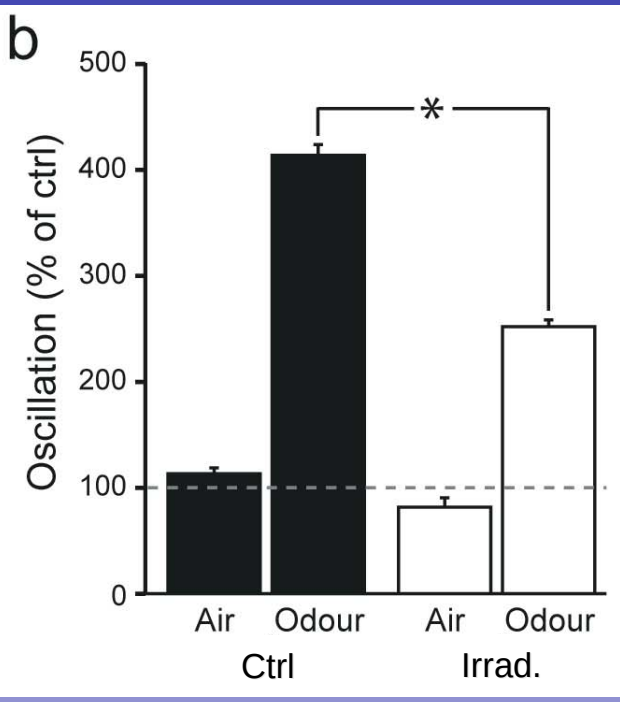
J. Neurosci. 19, 10727 (1999)

Oscillations Depends on Inhibition

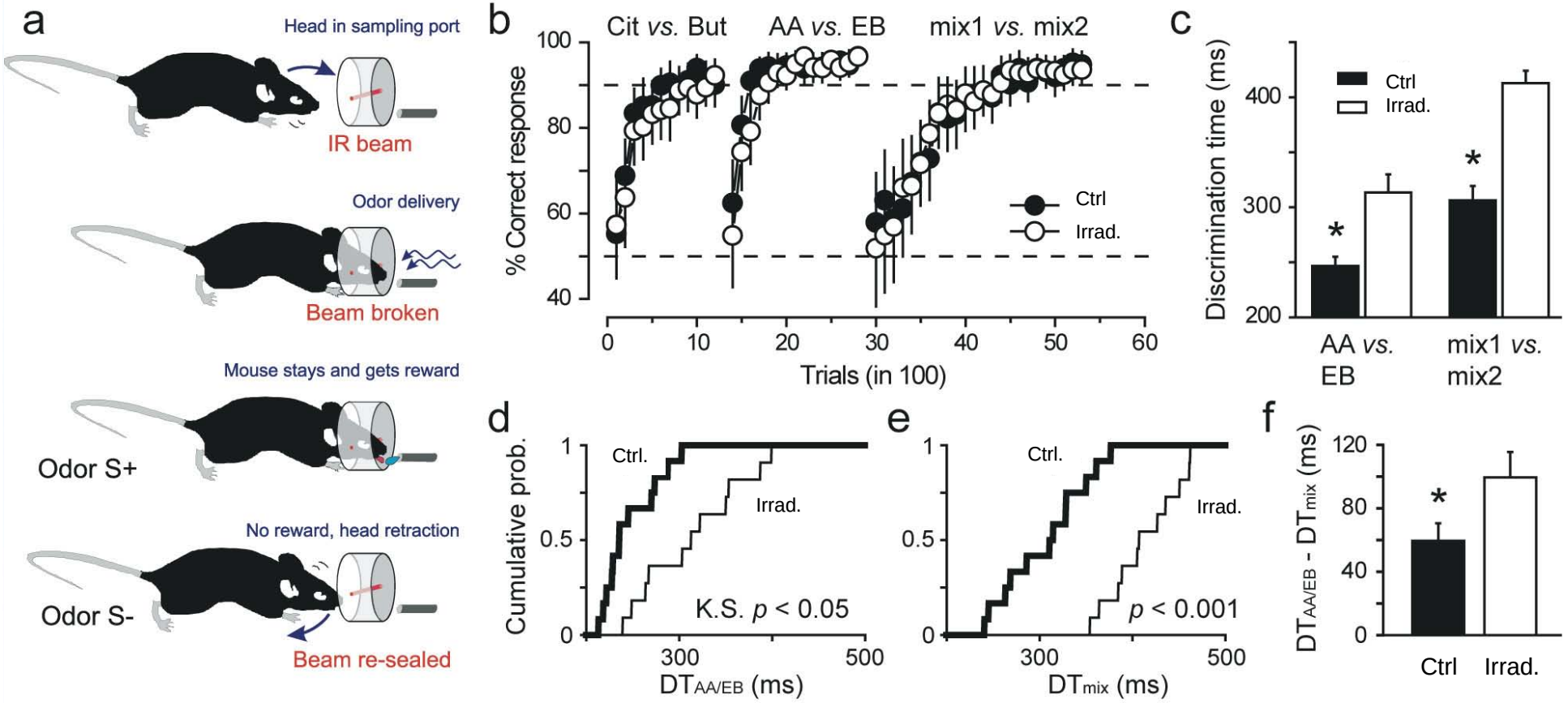


Reducing Neurogenesis Decreases γ oscillations

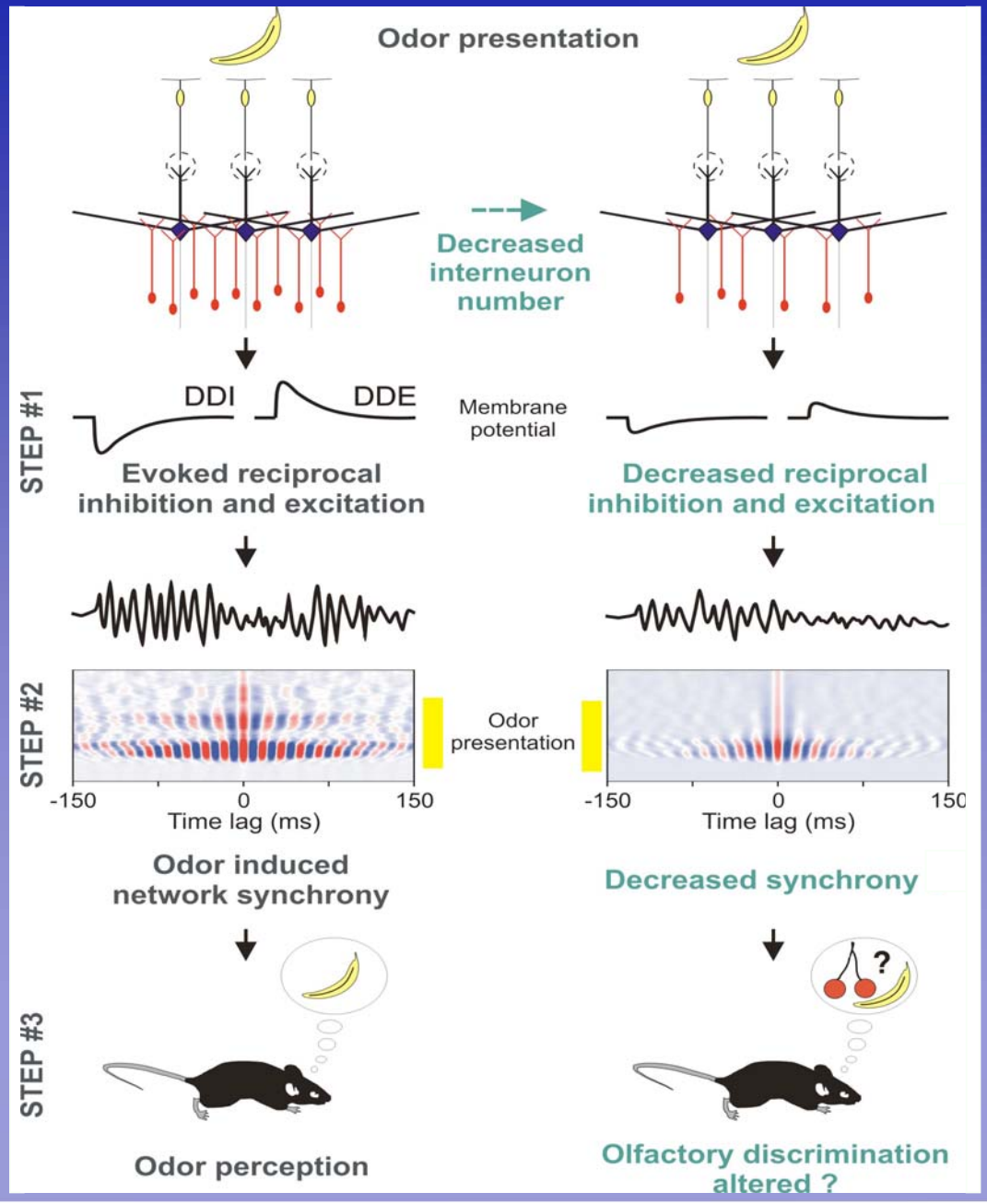




Reducing Neurogenesis Increases Reaction Time



Newborn neurons for discrimination



Conclusions

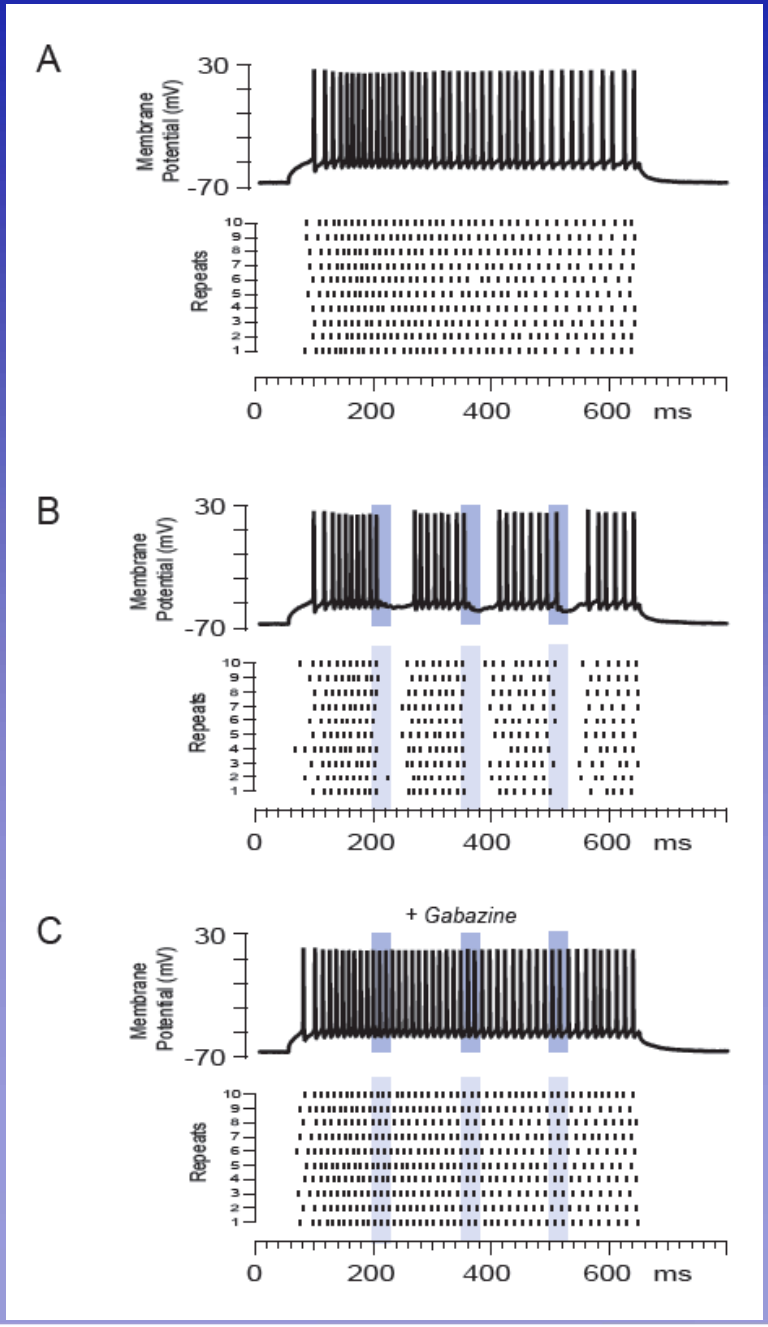
1) New neurons form an integral part of the normal function circuitry.

2) This process is not fixed, and does not recapitulate embryogenesis, it's much more…

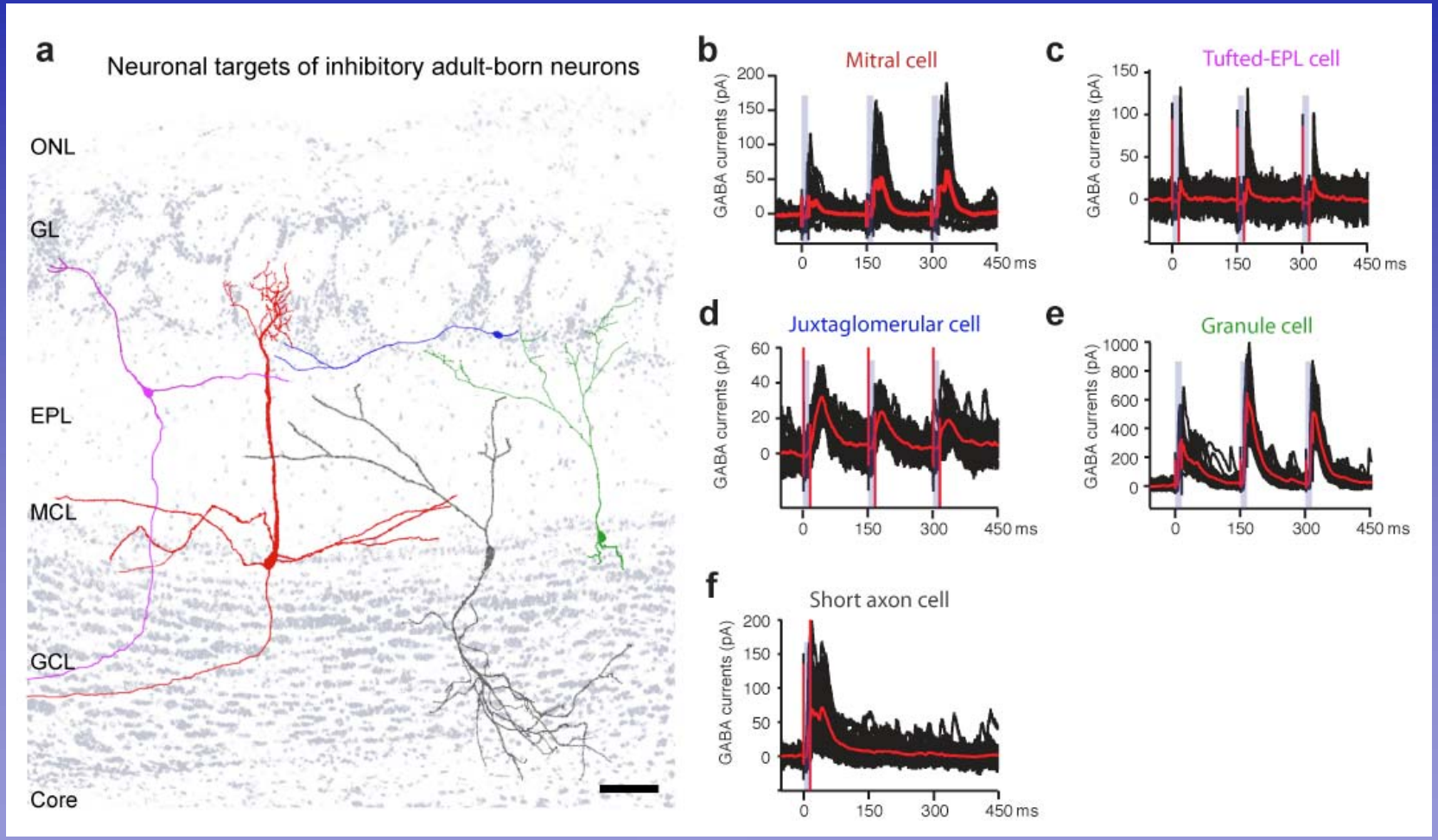
Conclusion

Adult neurogenesis is a form of metaplasticity: a change in the brain facilitating further changes in the brain.

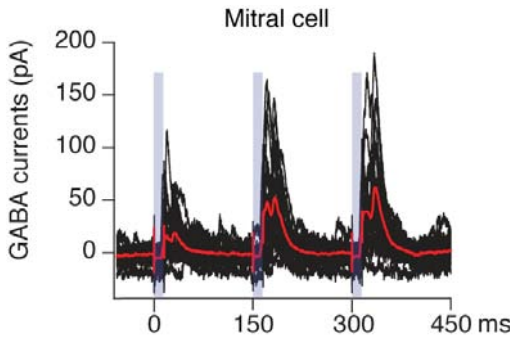
Mature Newborn Interneurons for Decorrelation



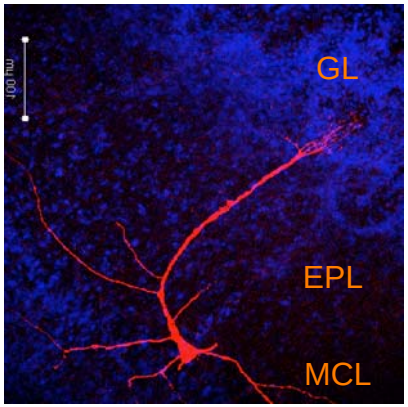
Diversity of targeted cells by adult-born neurons



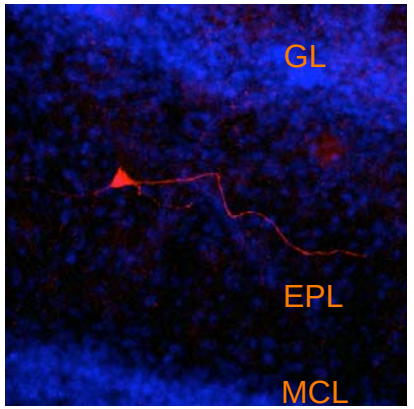
Diversity of targeted cells by adult-born neurons

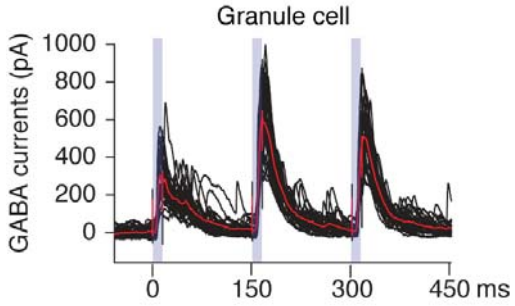


Mitral cell

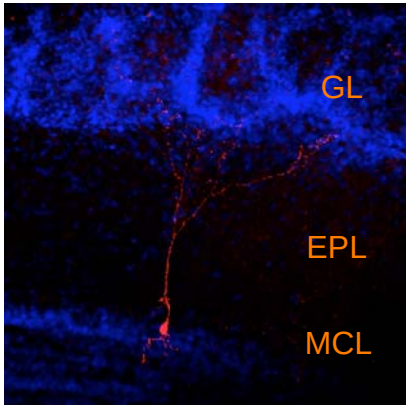


Tufted cell

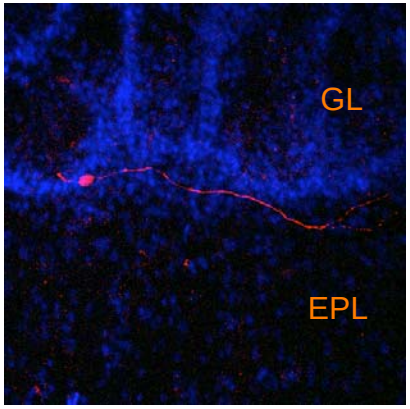




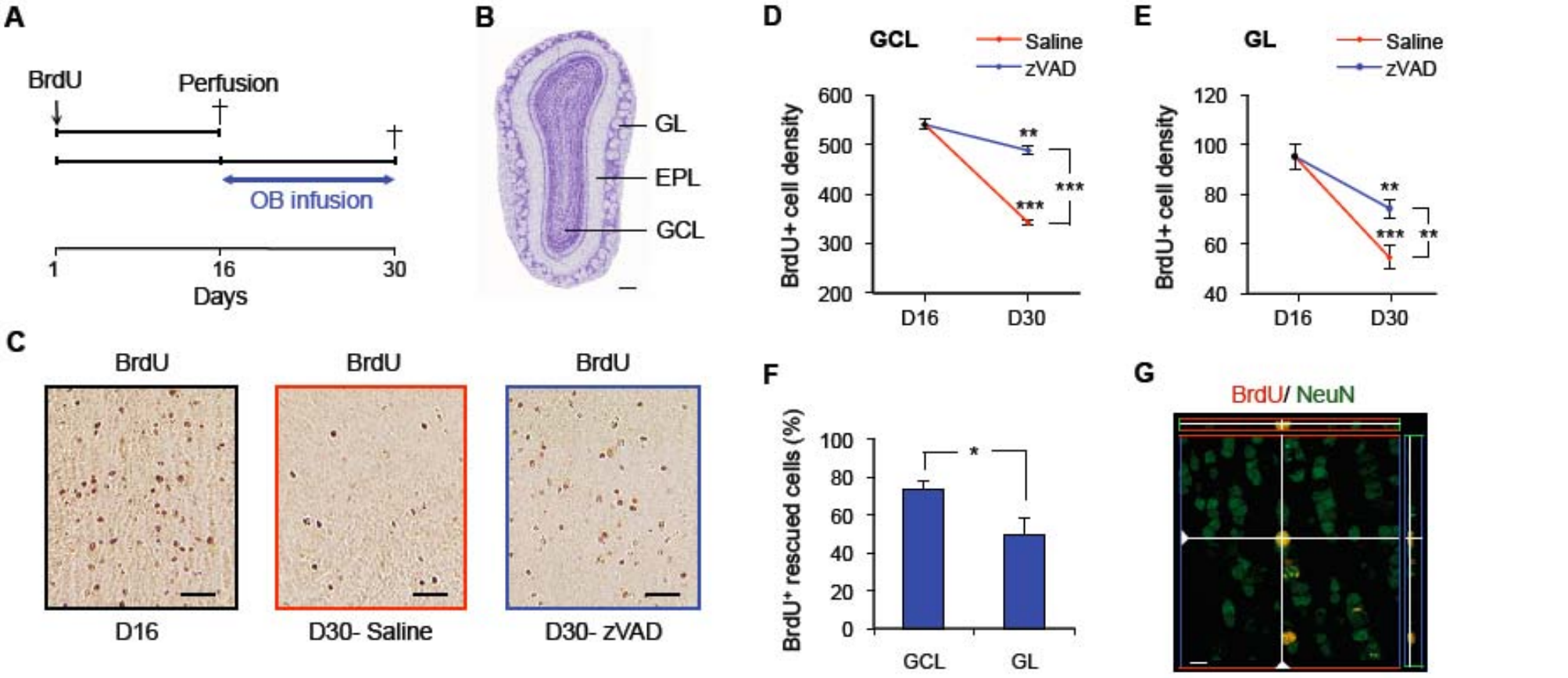
Granule cell



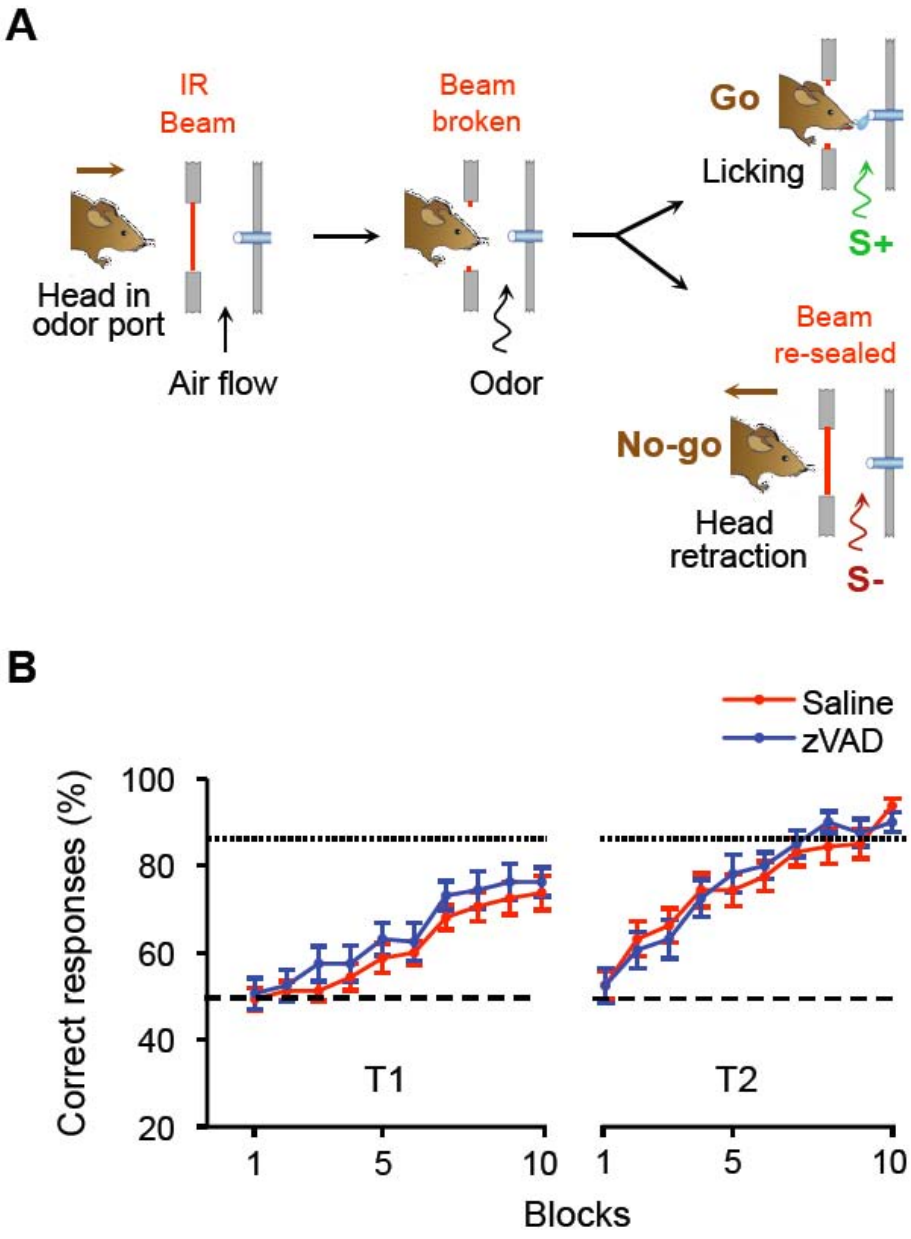
Juxta-glomerular cell



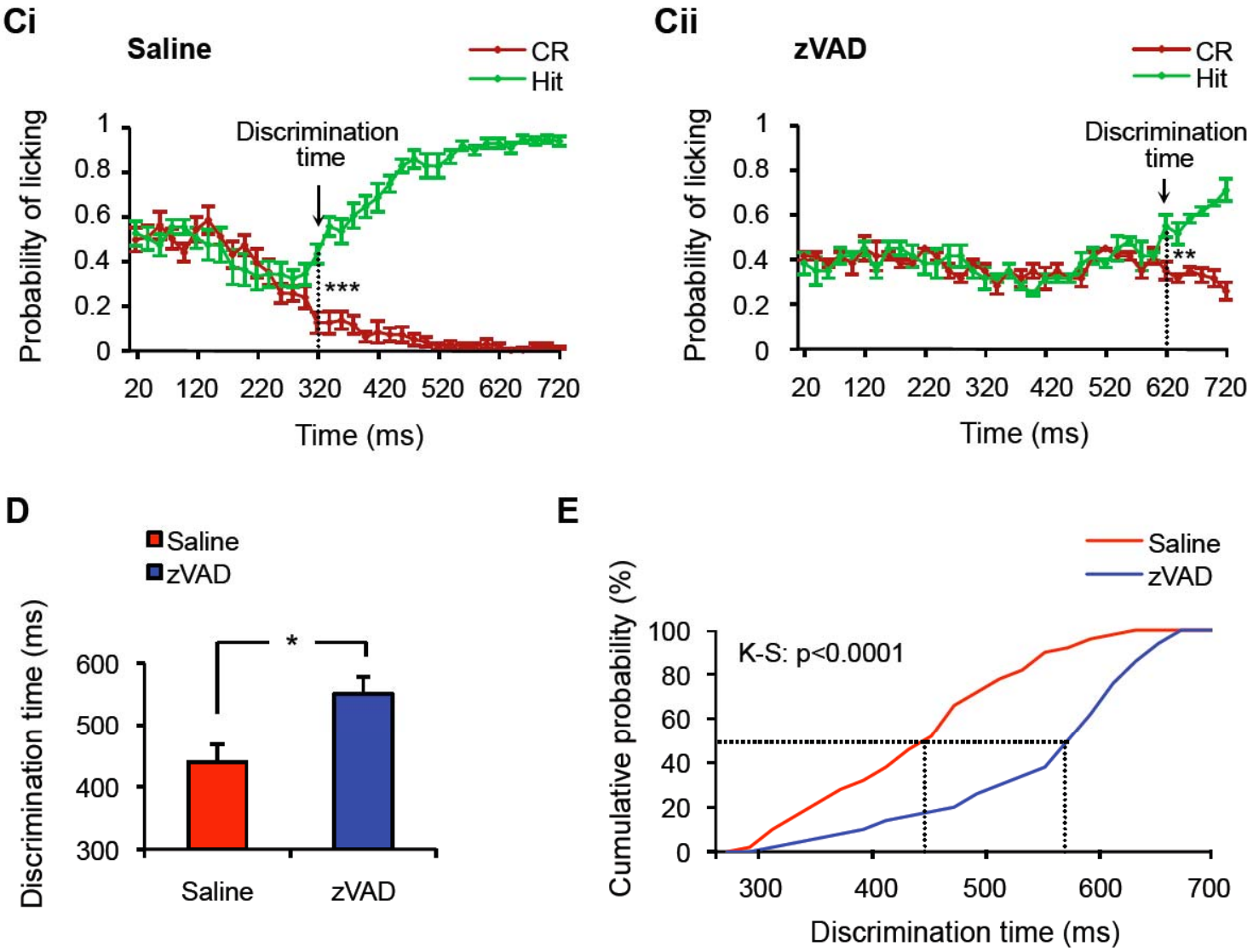
Cell Elimination



Discrimination Learning



Cell Death Impacts the Reaction Time



New Neurons Born to Die