

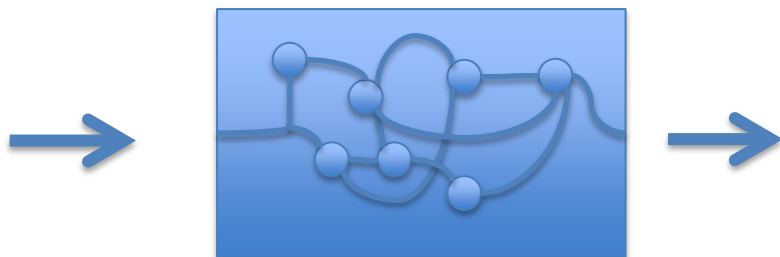
Signal transformation in the olfactory bulb by inhibitory circuits

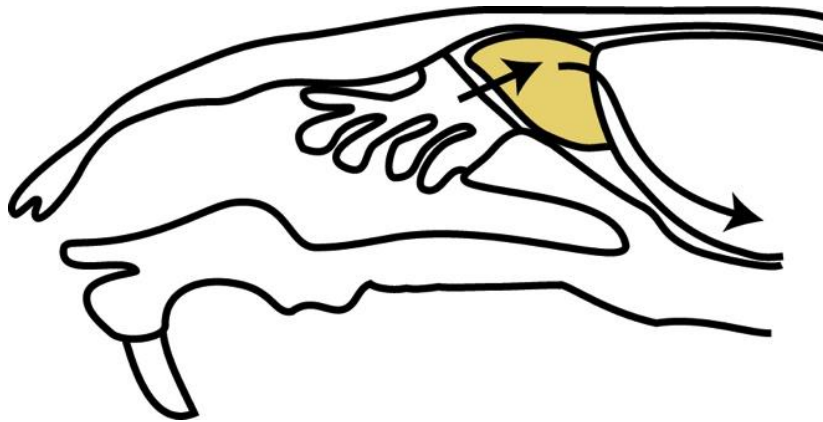
Izumi Fukunaga

Schaefer lab

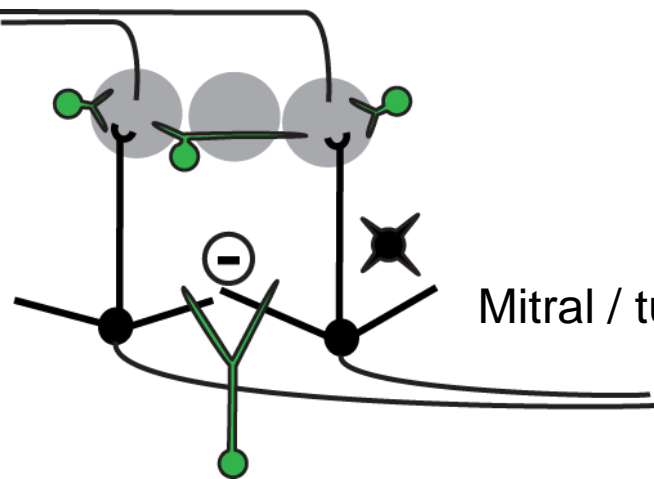
Division of Neurophysiology

The Francis Crick Institute, Mill Hill Laboratory

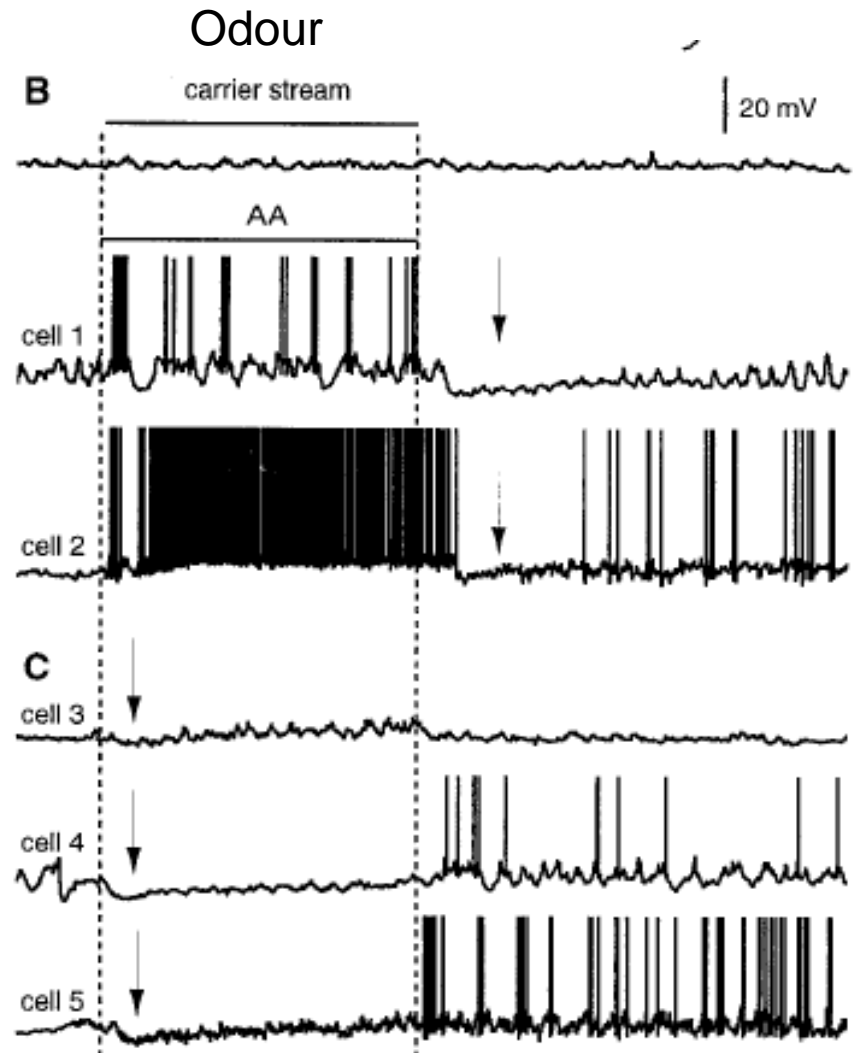
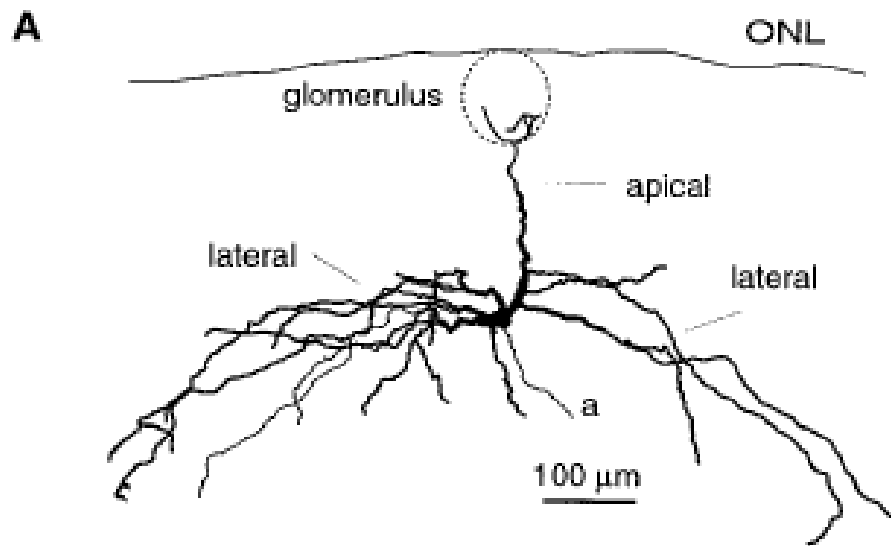




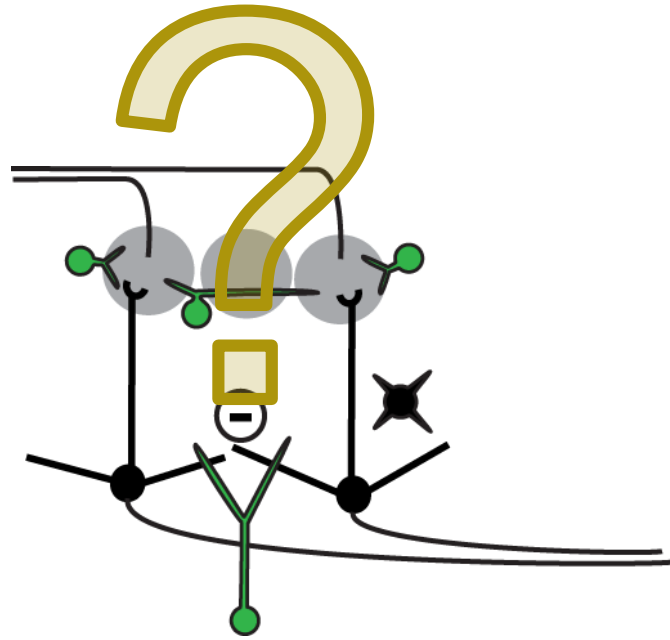
Olfactory nerve



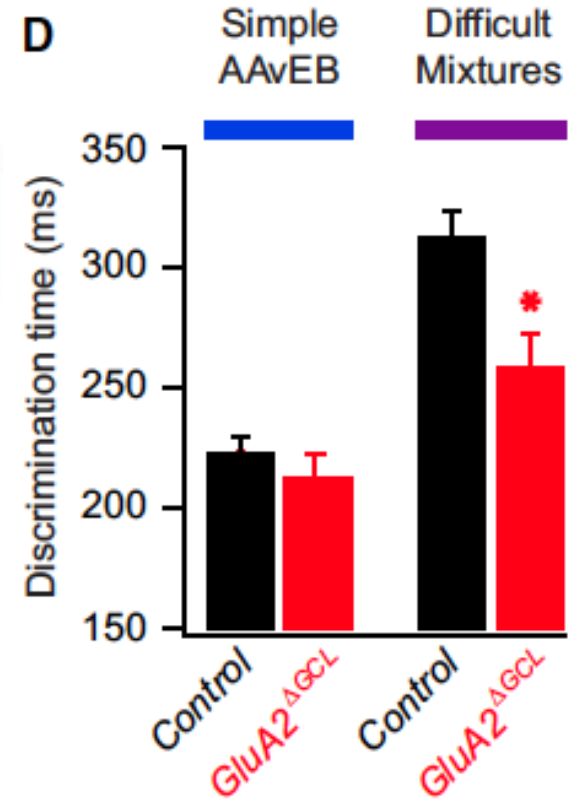
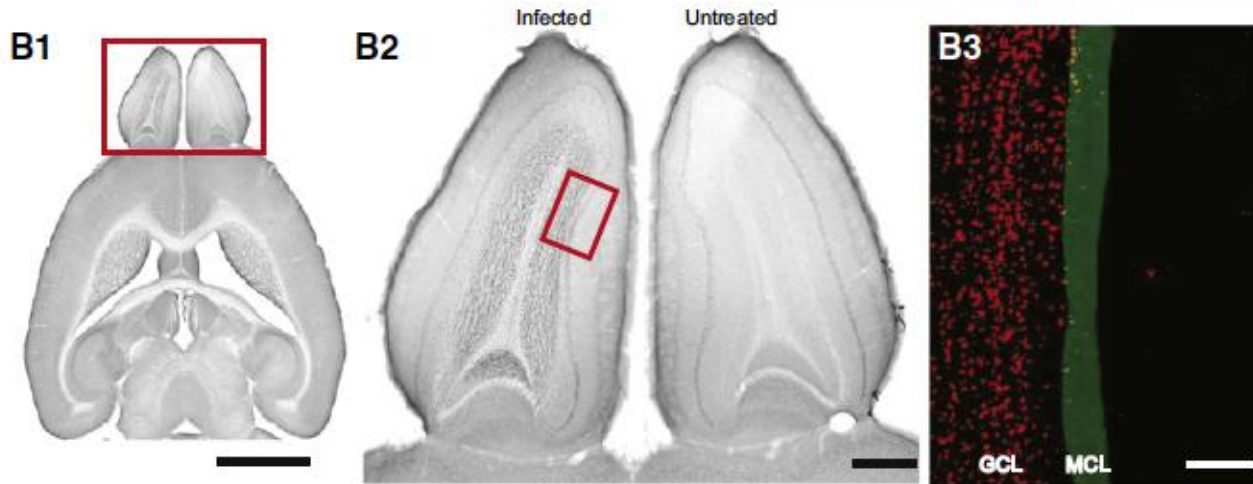
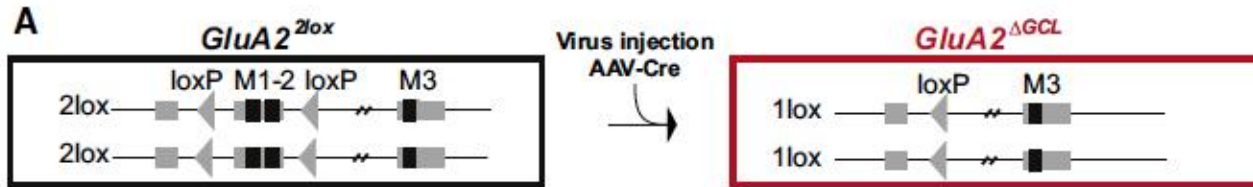
Mitral / tufted cells



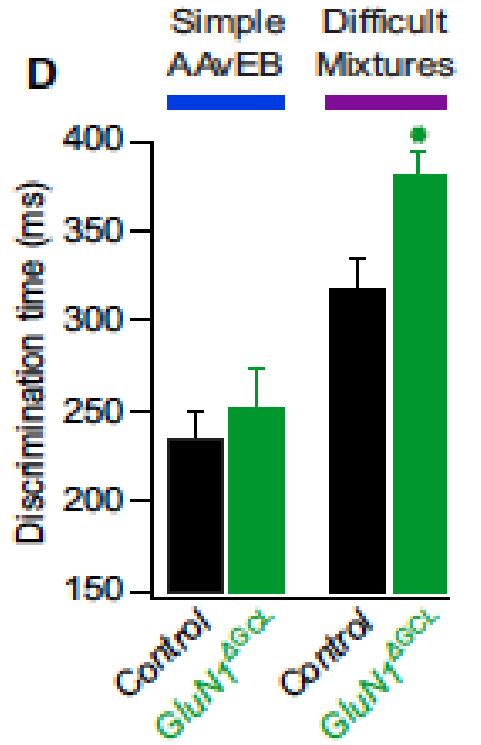
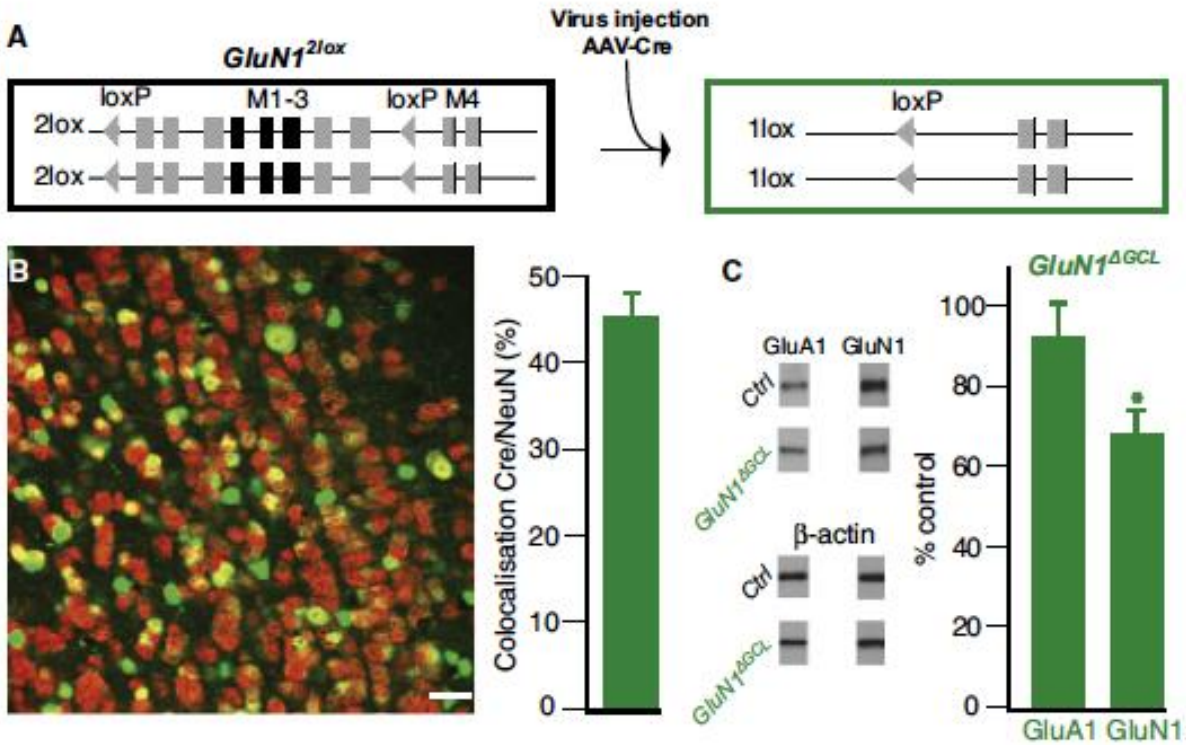
Margrie et al., 2001



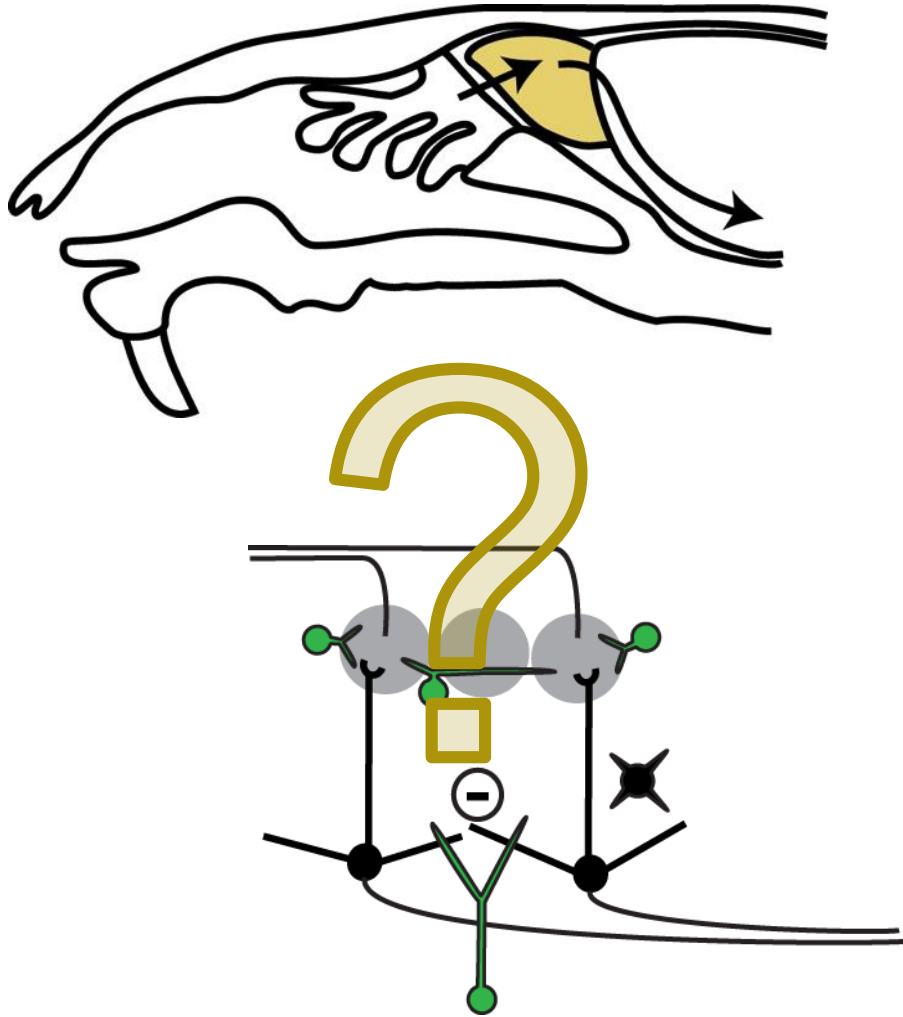
 inhibition



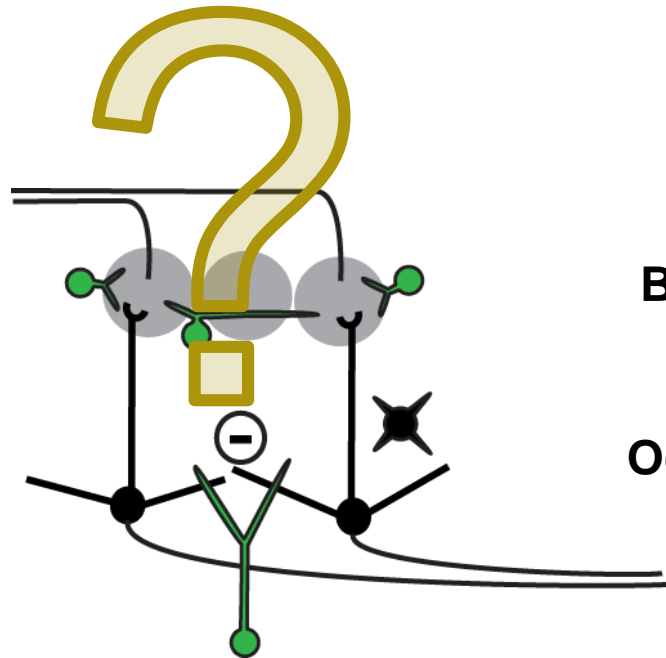
↓ inhibition



Role of inhibition – single cell level?



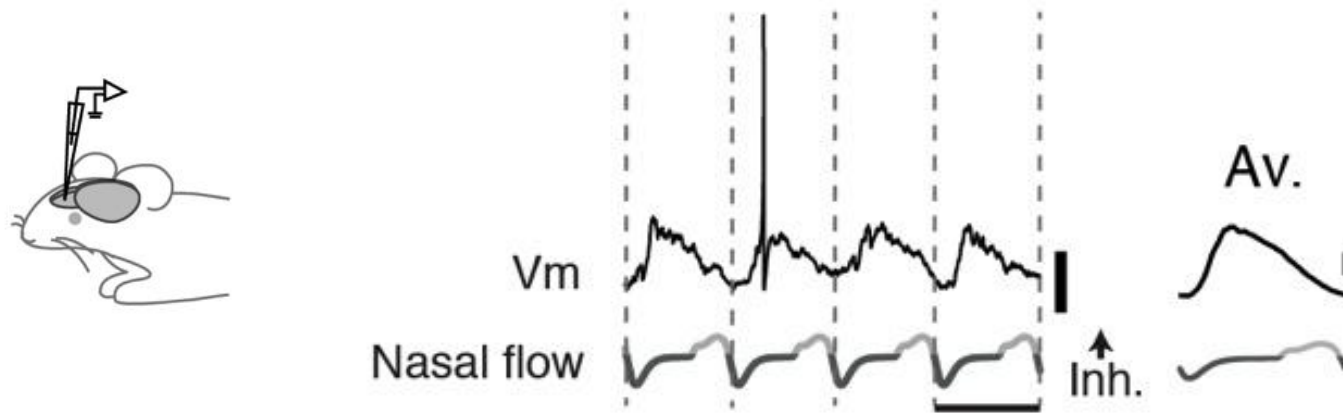
Role of inhibition – single cell level?



Baseline physiology

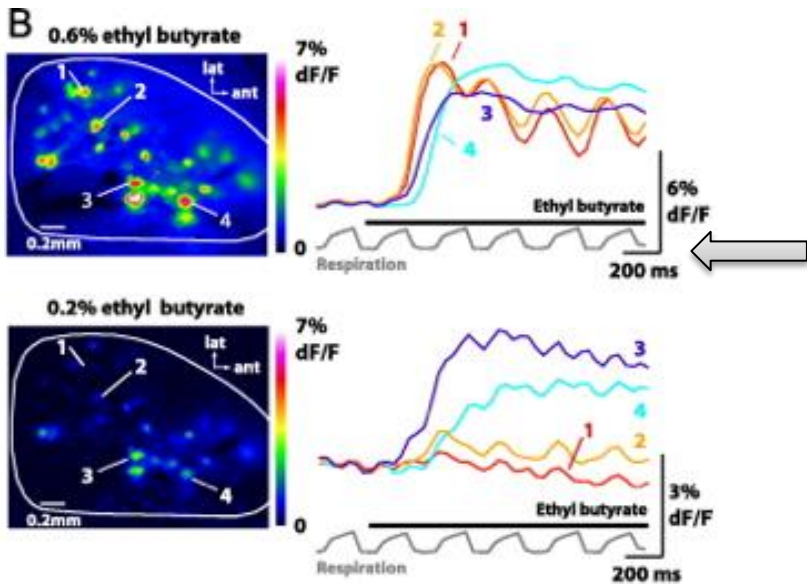
Odour representation

Sniff coupling of M/TCs



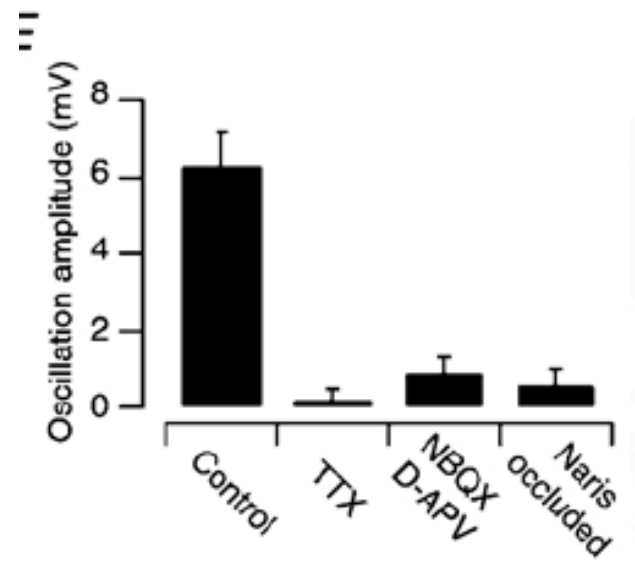
cp. Adrian, 1950; Walsh, 1956; Gault & Coustan, 1965; Macrides & Chorover, 1972; Onoda & Mori, 1980; Chaput & Holley, 1985; Doving, 1987; Ravel & Pager, 1990; Lestienne et al. 1999; Charpak et al. 2001; Luo & Katz, 2001; Belluscio et al. 2002, Margrie & Schaefer 2003, Isaacson 2003, Shusterman et al. 2011; Cury and Uchida 2010; Verhagen et al. 2007 etc etc

Driven by rhythmic, glutamatergic inputs from the OSN



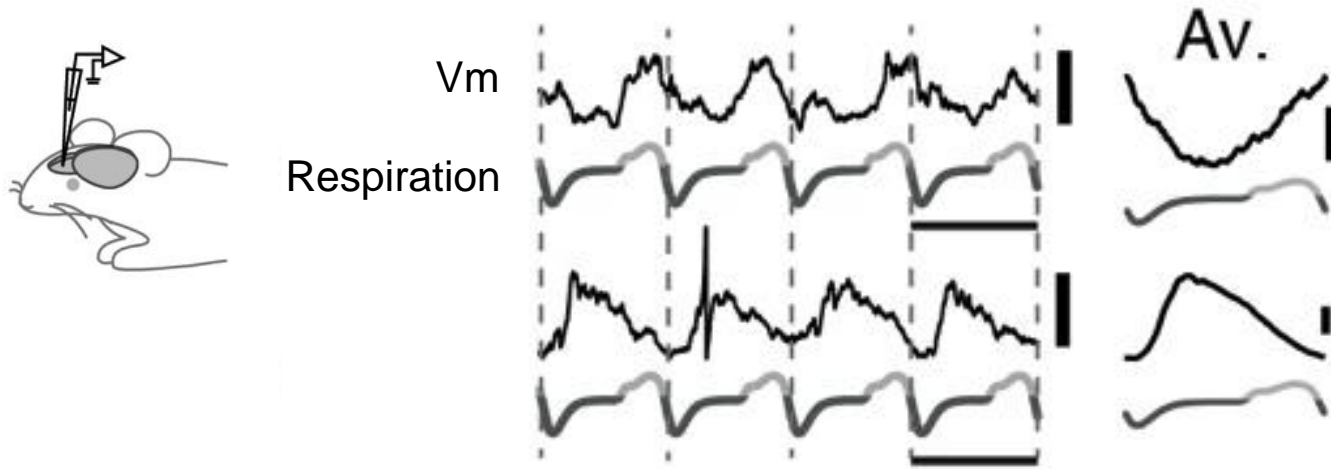
Pressure to upper tracheotomy tube

Spors et al. 2006 *J.Neurosci*

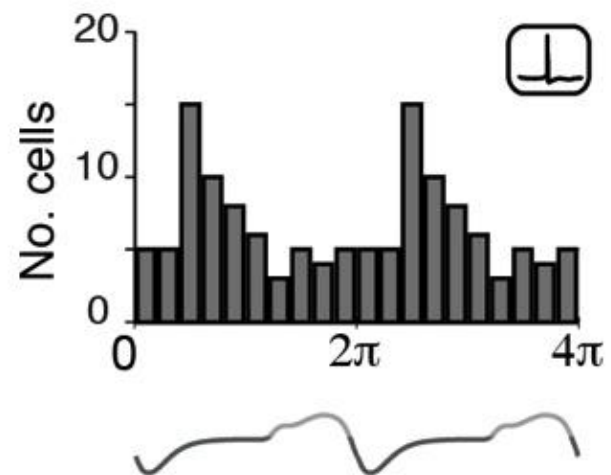
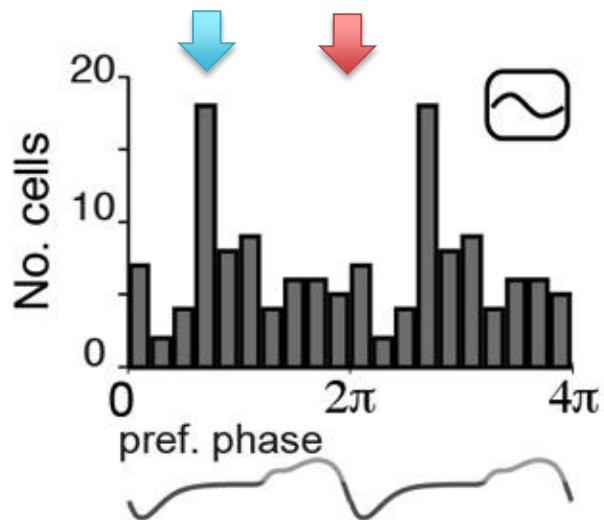
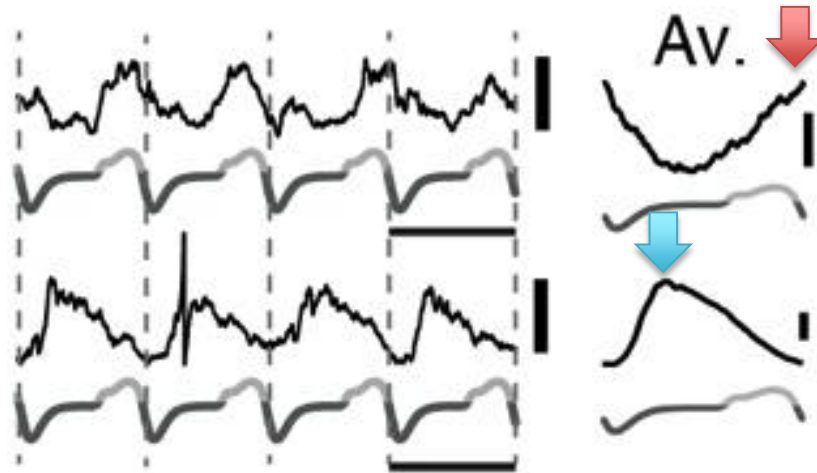


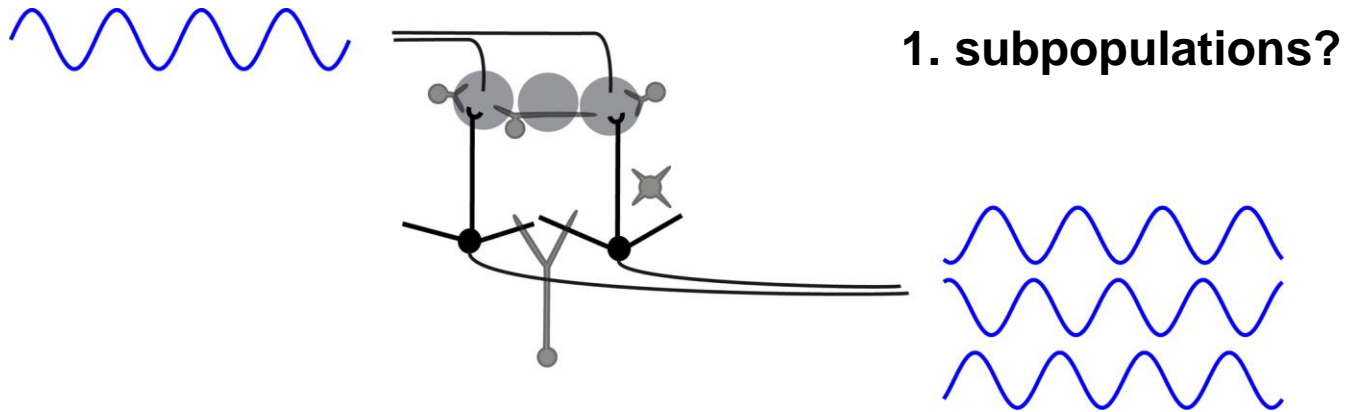
Margrie & Schaefer 2003 *J. Physiol*

Heterogeneous sniff coupling

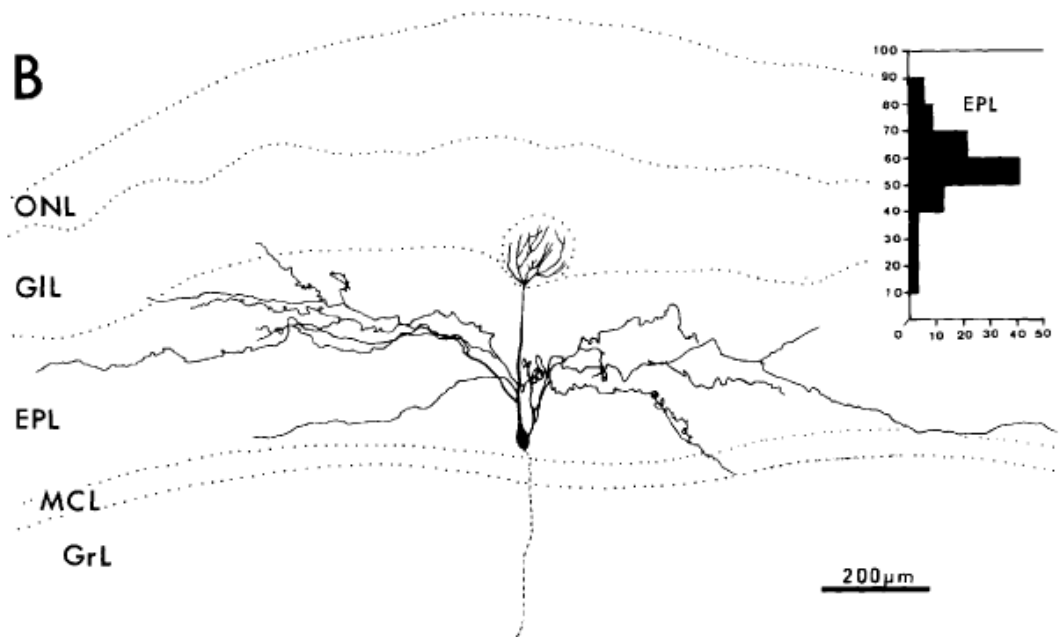
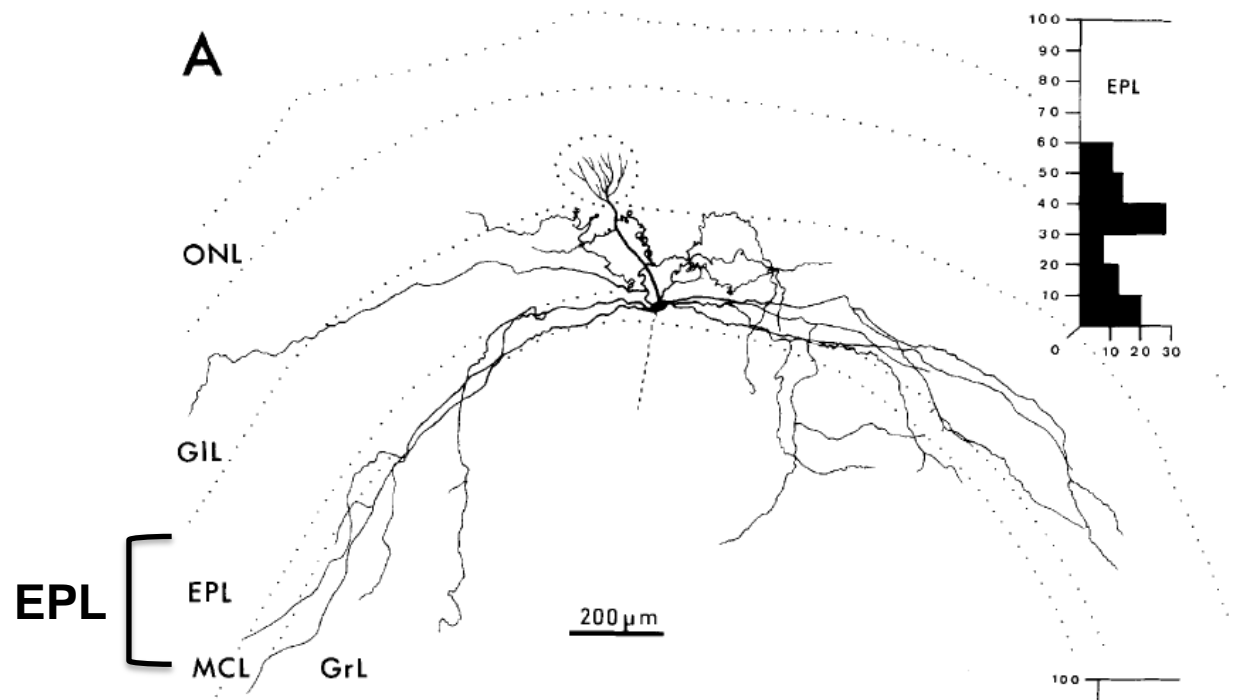


Heterogeneous sniff coupling during baseline periods





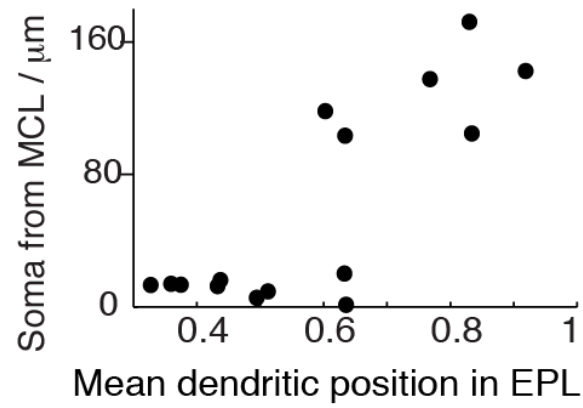
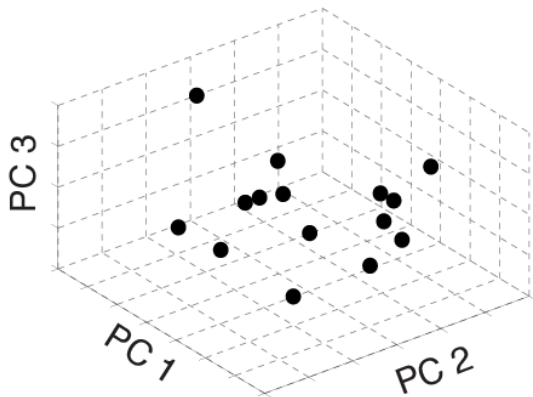
2. Where does the shift come from?



Mori et al., 1983 *J. Comp. Neurol.*

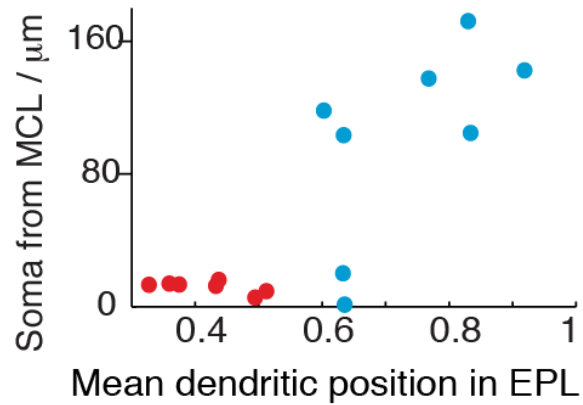
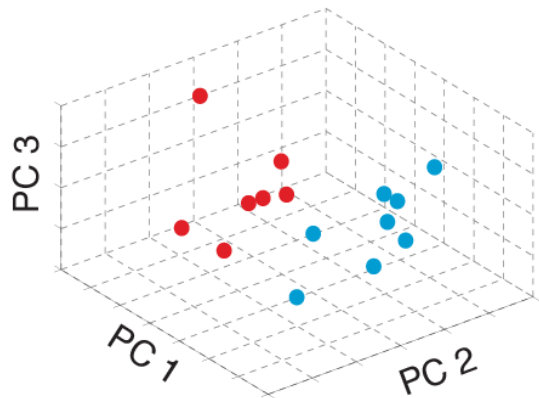
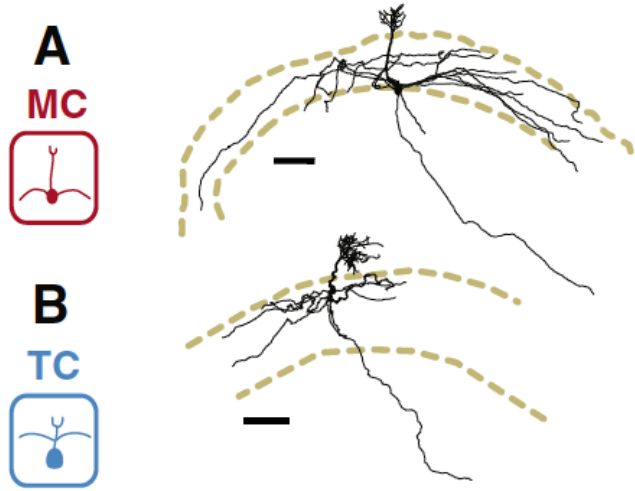


Manuel Berning

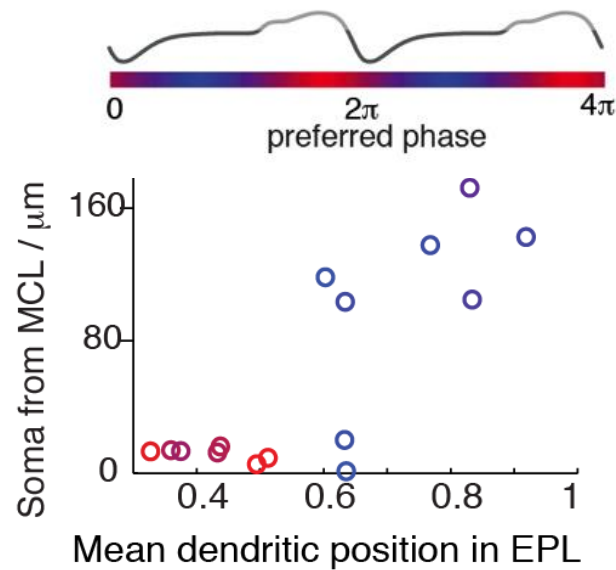
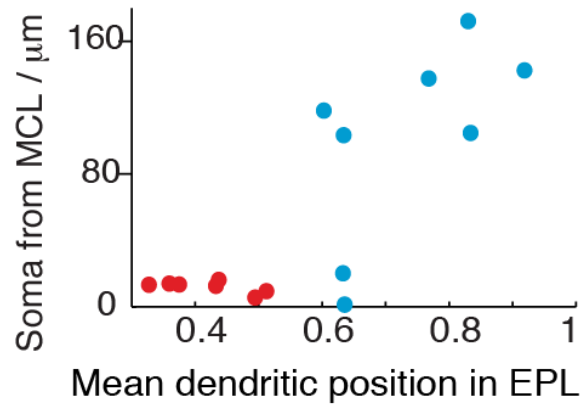
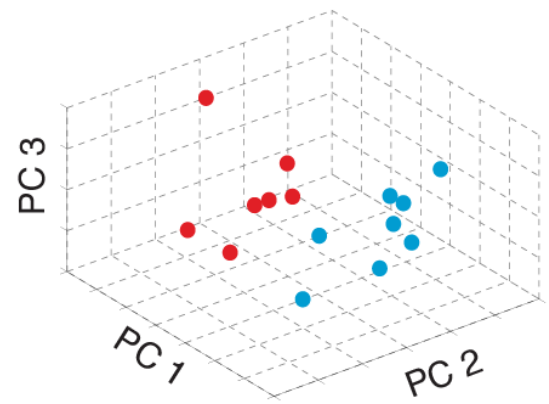
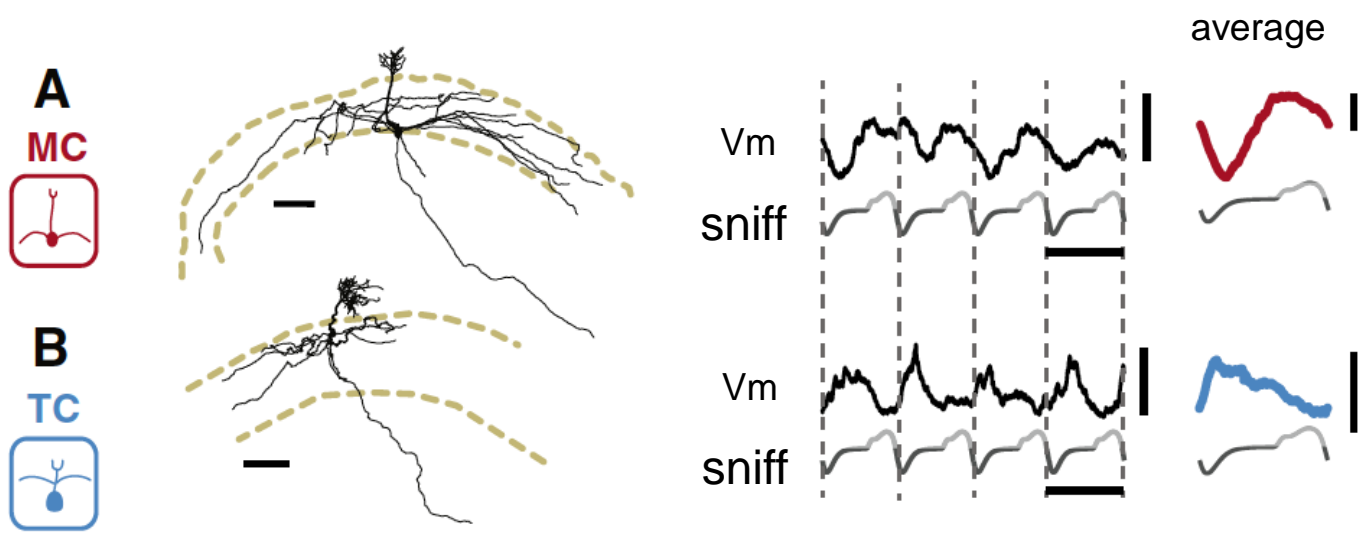


← deeper

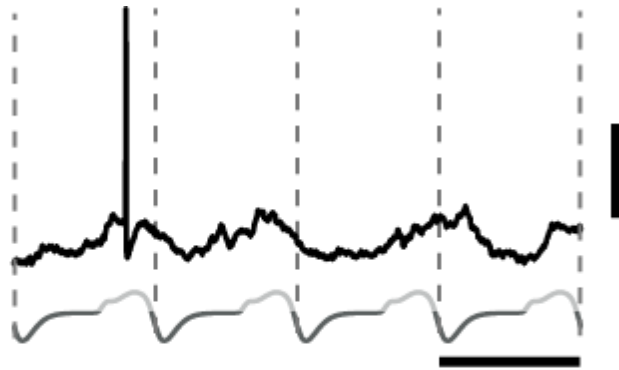
Unbiased classification separates mitral and tufted cells



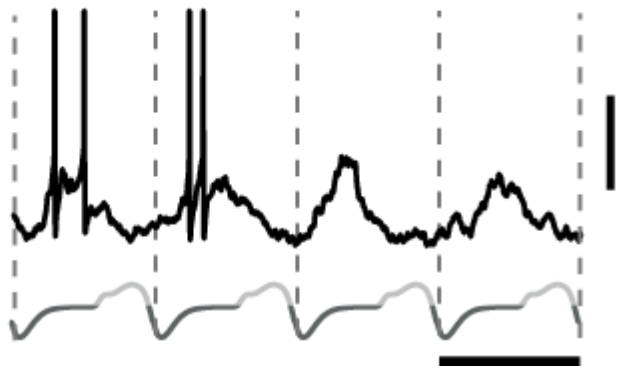
Unbiased classification separates mitral and tufted cells



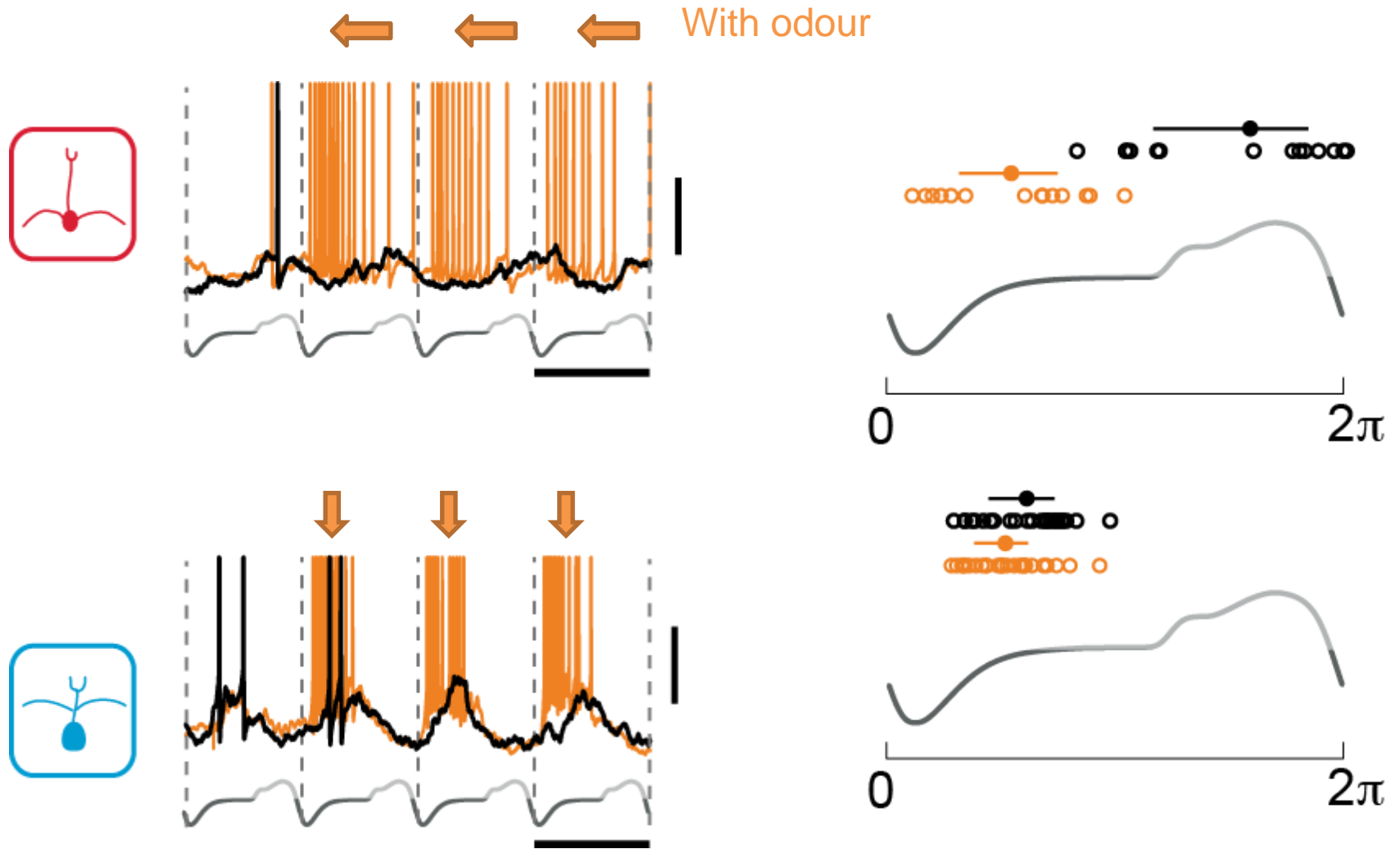
Consequence of different sniff coupling on coding



baseline



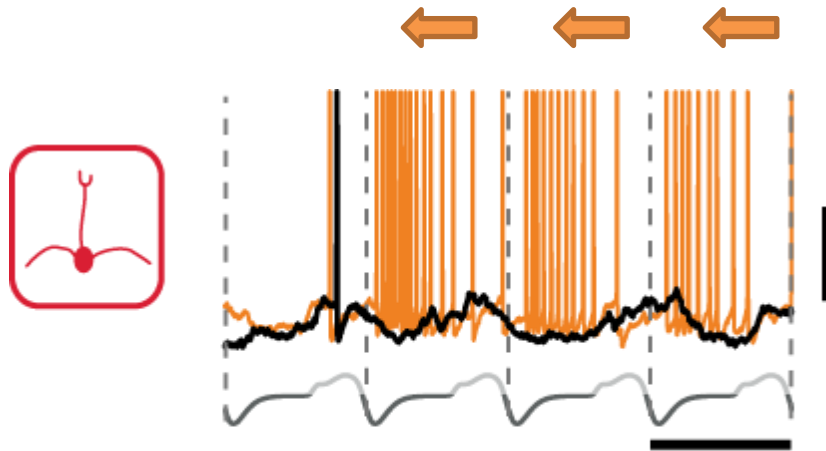
Consequence of different sniff coupling on coding



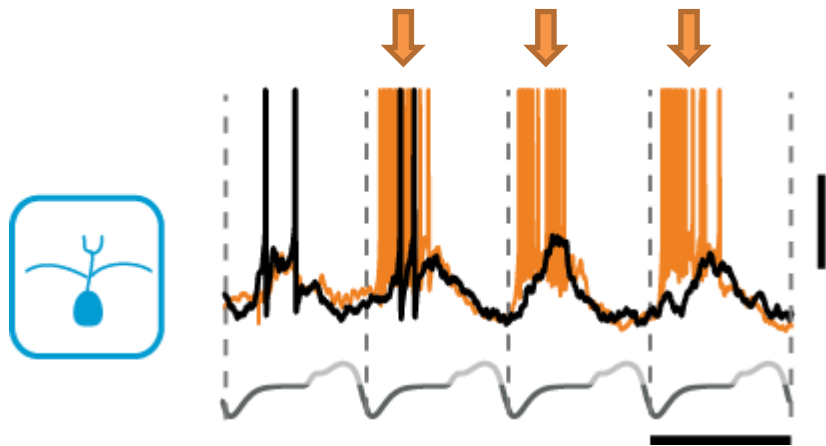
Fukunaga et al 2012 *Neuron*

Also see Igarashi et al., 2012 *J. Neurosci.*

Consequence of different sniff coupling on coding



Phase/latency



Firing rate modulation

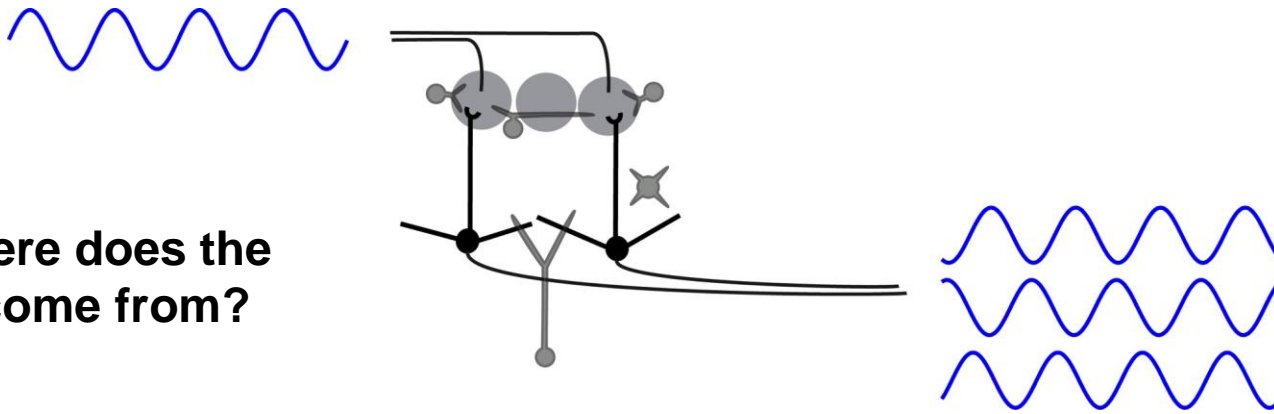
Fukunaga et al 2012 *Neuron*

Also see Igarashi et al., 2012 *J. Neurosci.*

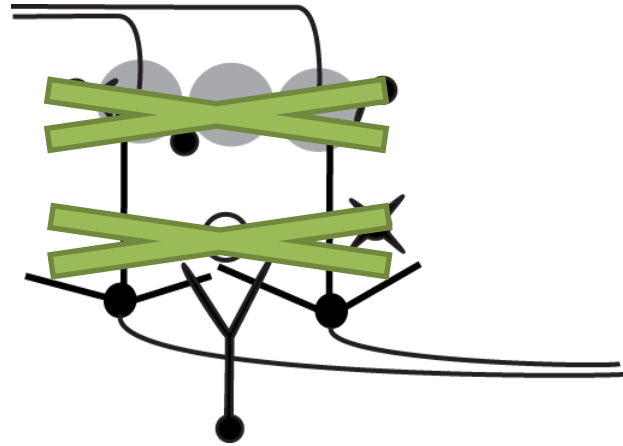
1. Heterogeneity corresponds to cell identity



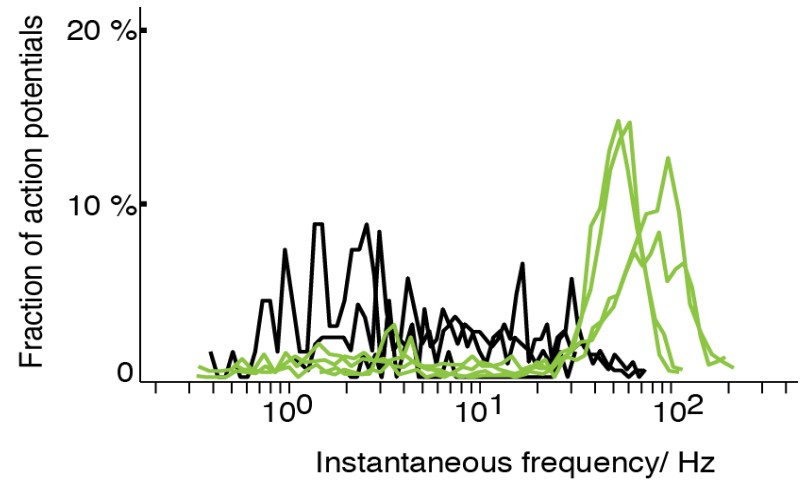
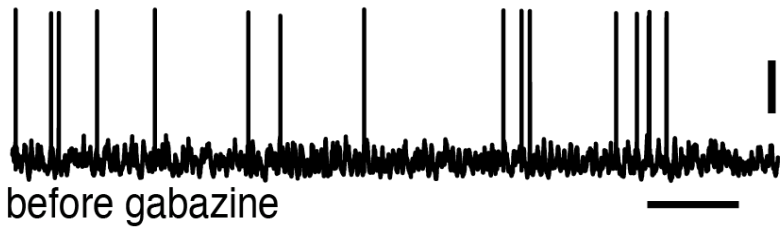
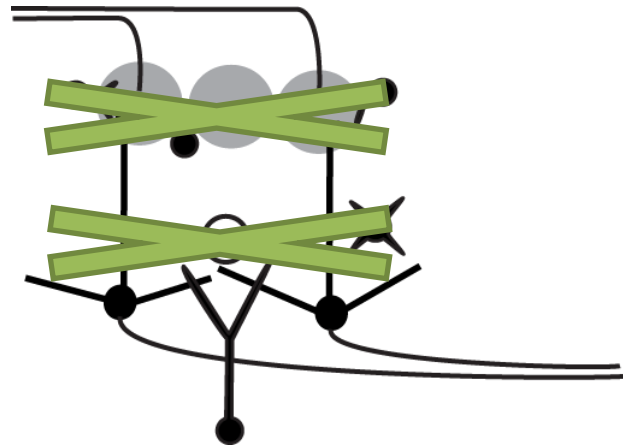
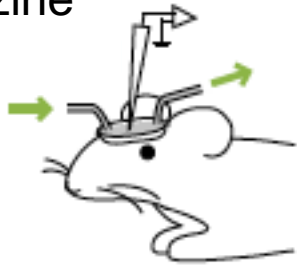
2. Where does the shift come from?



Pharmacological block of inhibition *in vivo*

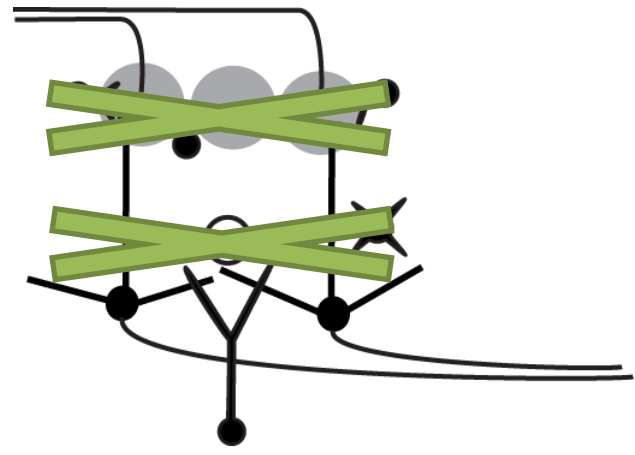
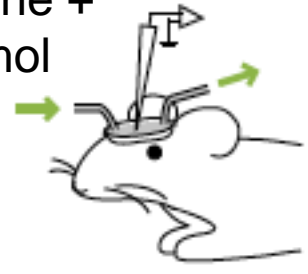


Gabazine
only

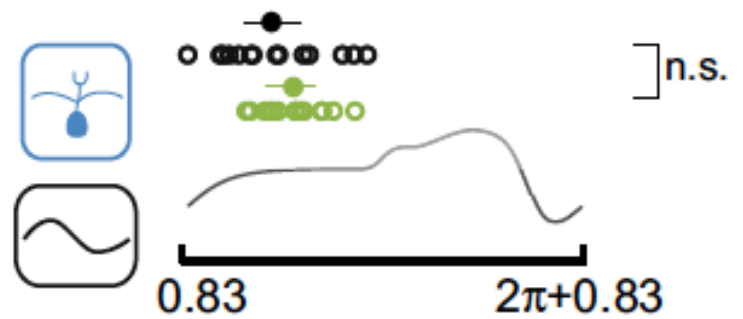
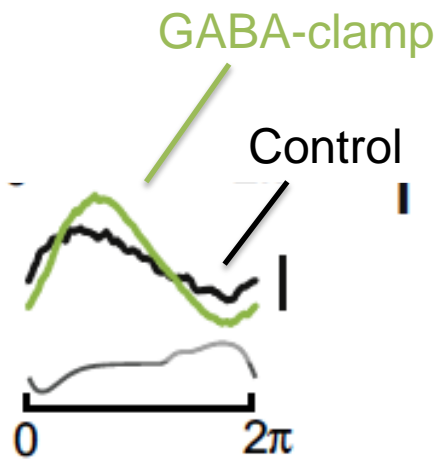
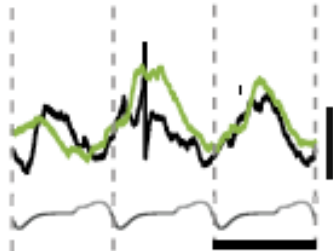
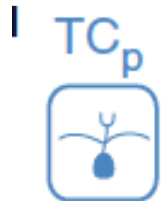
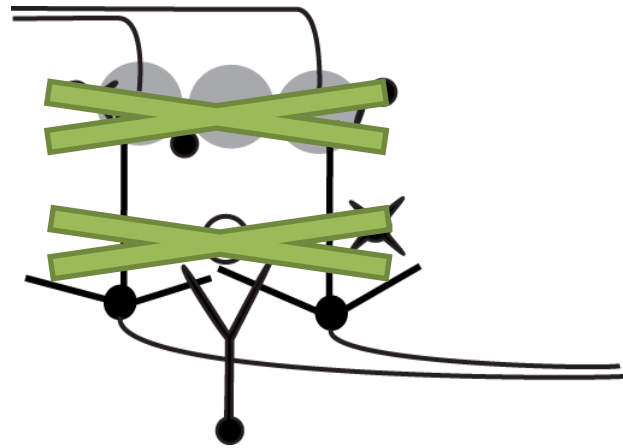
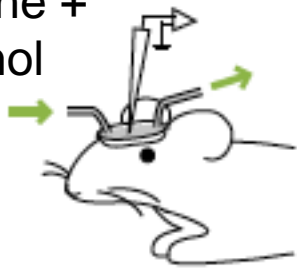


“GABA_A-clamp”

Gabazine +
muscimol

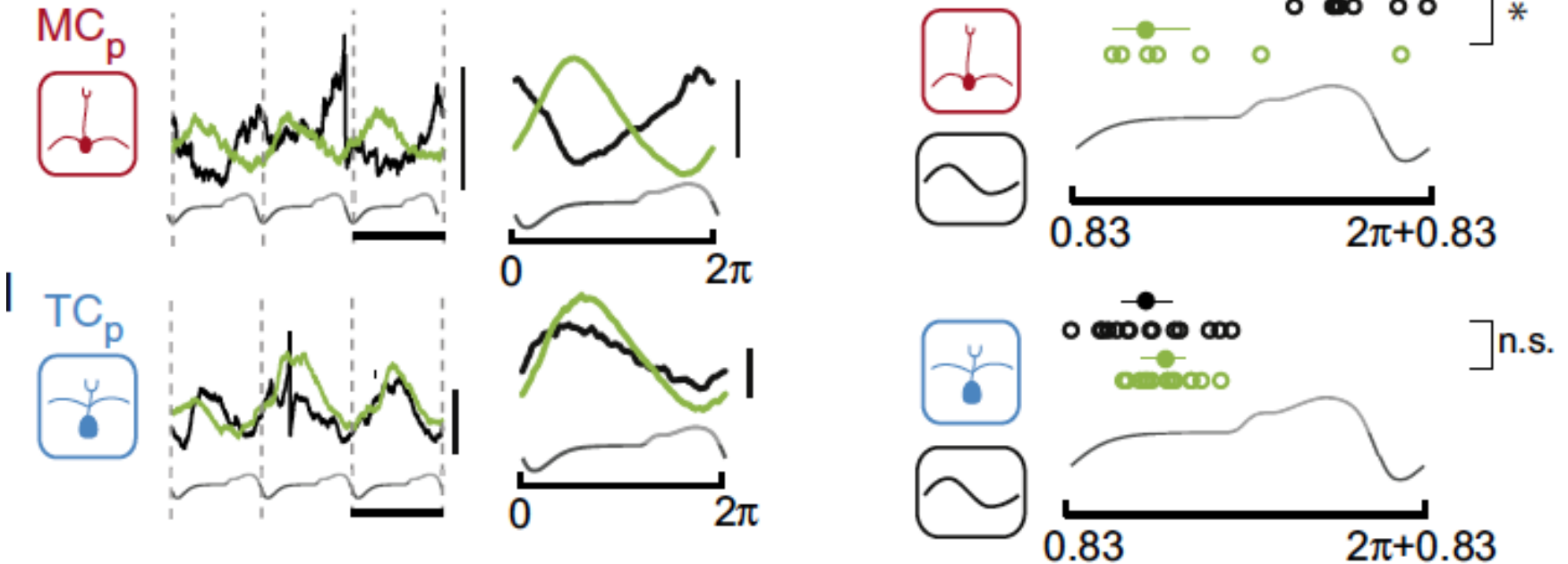
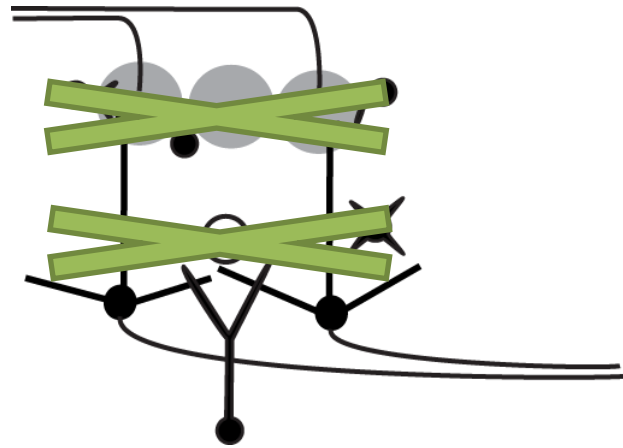
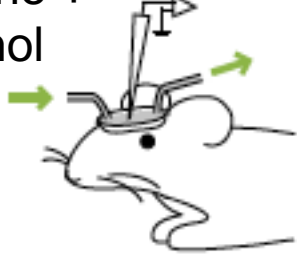


Gabazine +
muscimol

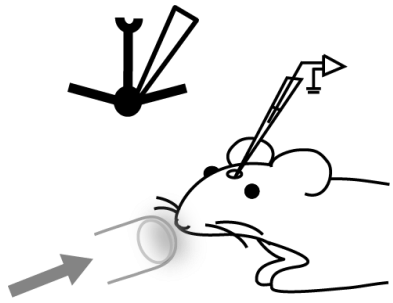


Role of inhibition in the OB

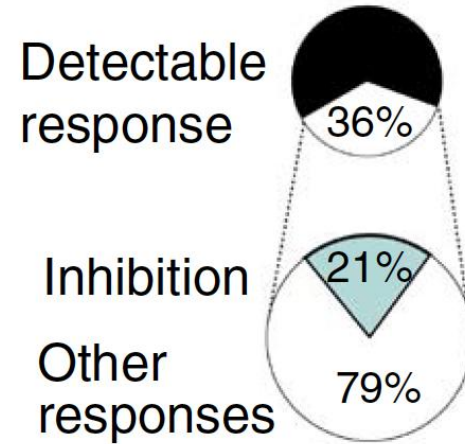
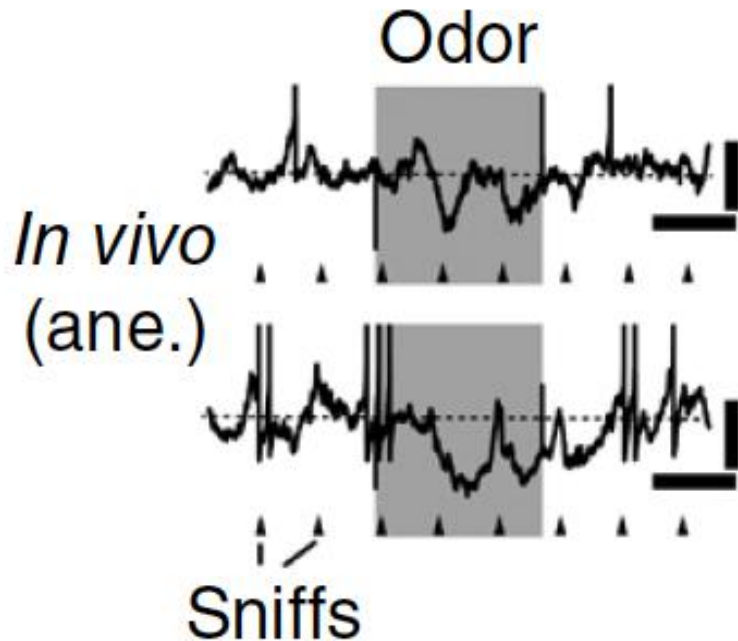
Gabazine + muscimol



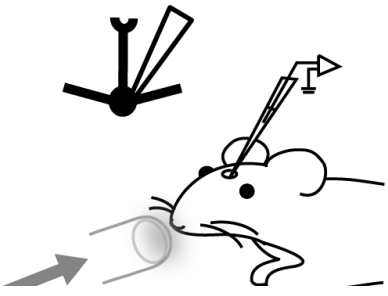
Transformation of odour-related inputs



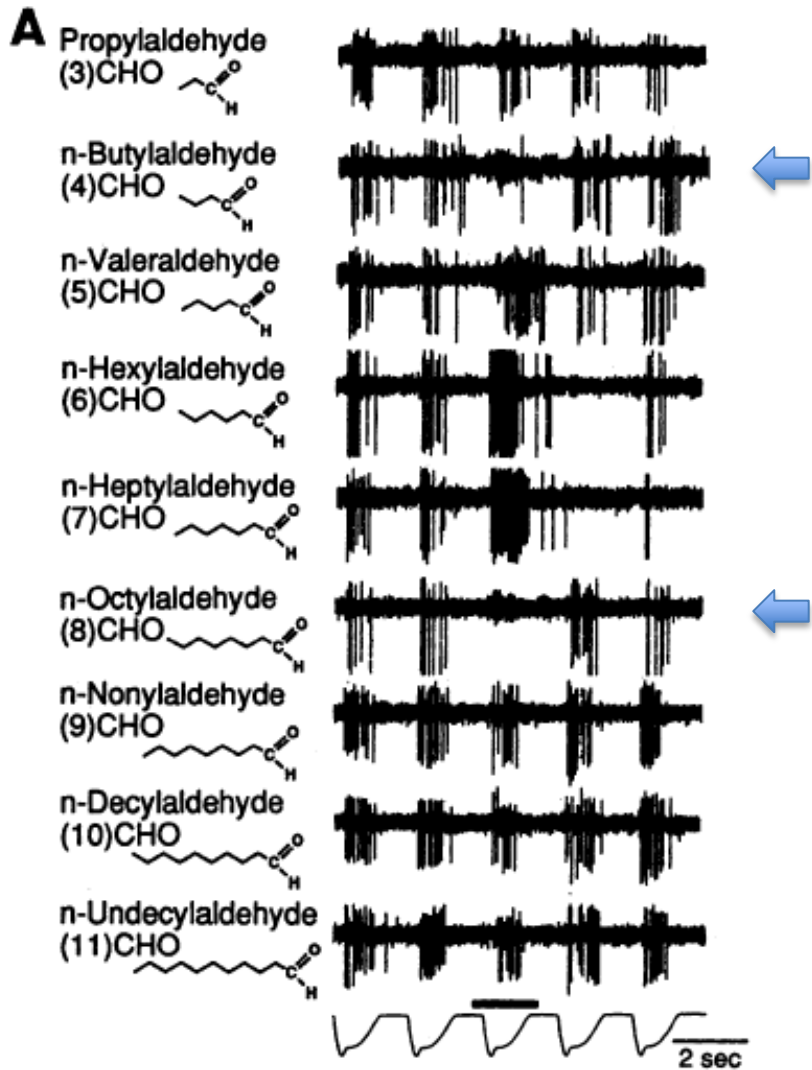
Sniff-coupled inhibitory responses



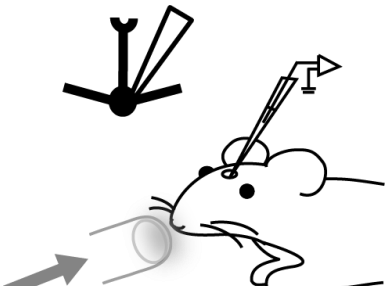
Also: Hamilton & Kauer 1989, Margrie et al., 2001, Luo & Katz 2007



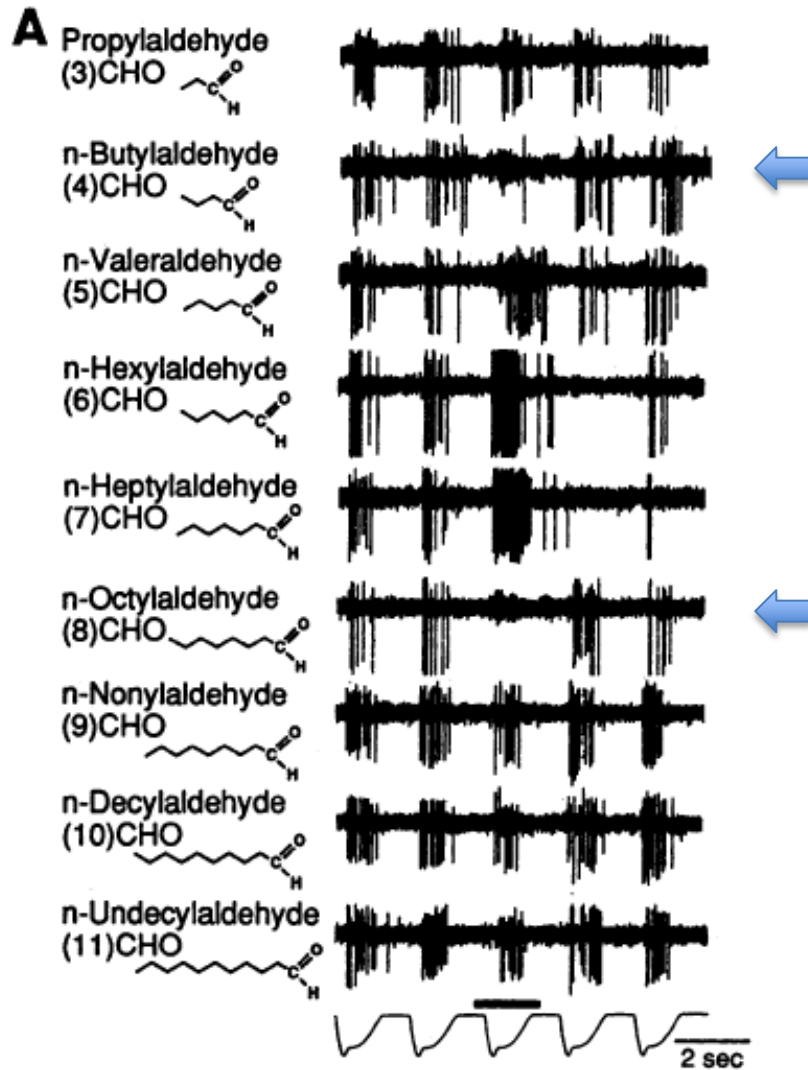
Evoked pauses as contrast enhancement



Yokoi et al., 1995 *Proc. Nat. Acad. Sci. USA*

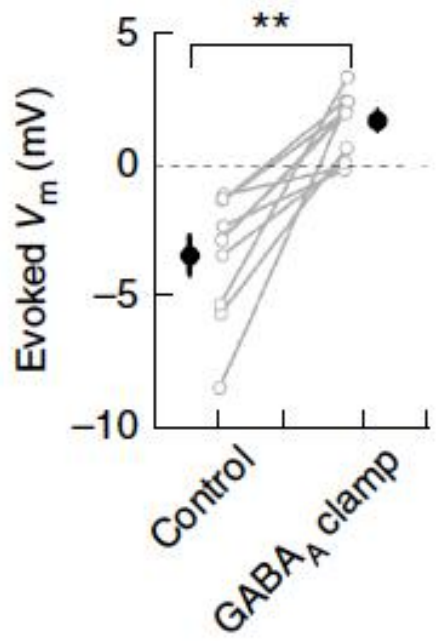
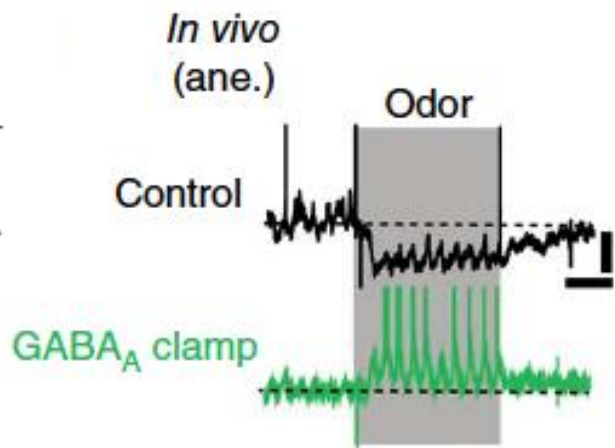


Evoked pauses as contrast enhancement

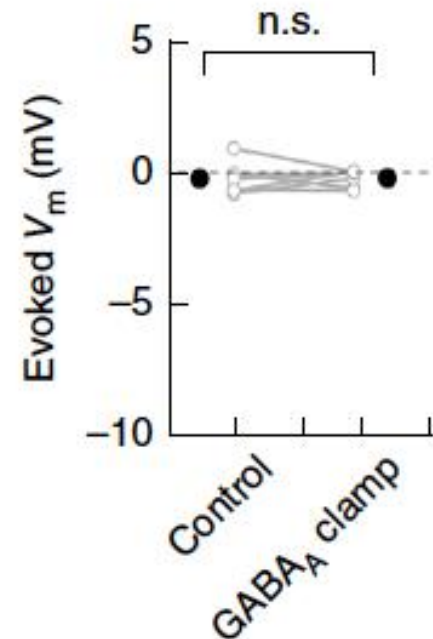
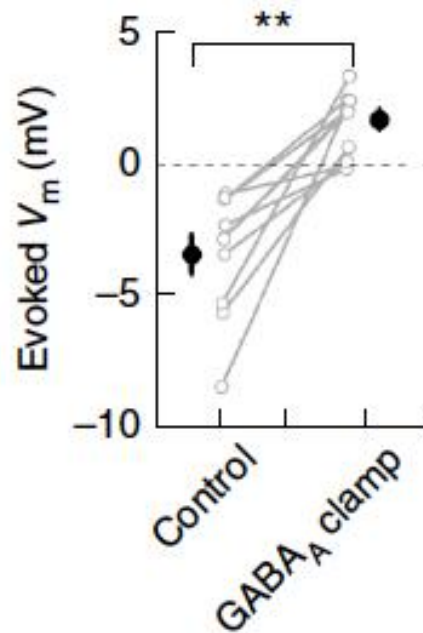
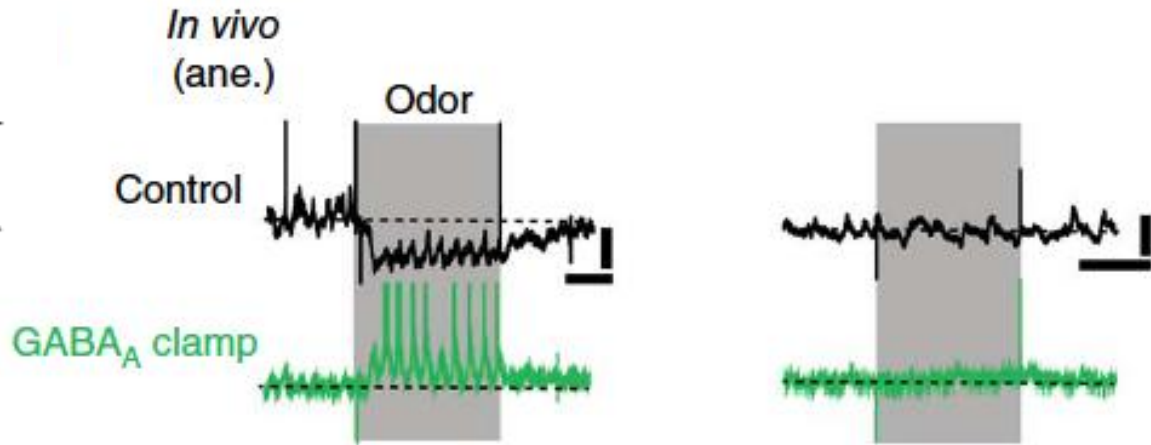


Inhibition in the OB?

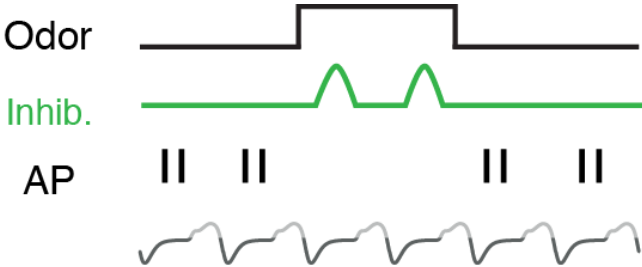
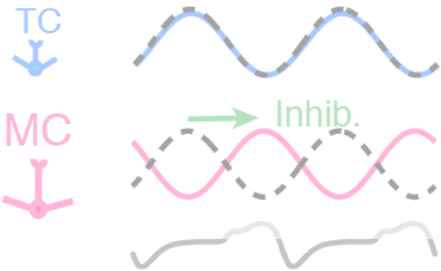
Yokoi et al., 1995 *Proc. Nat. Acad. Sci. USA*

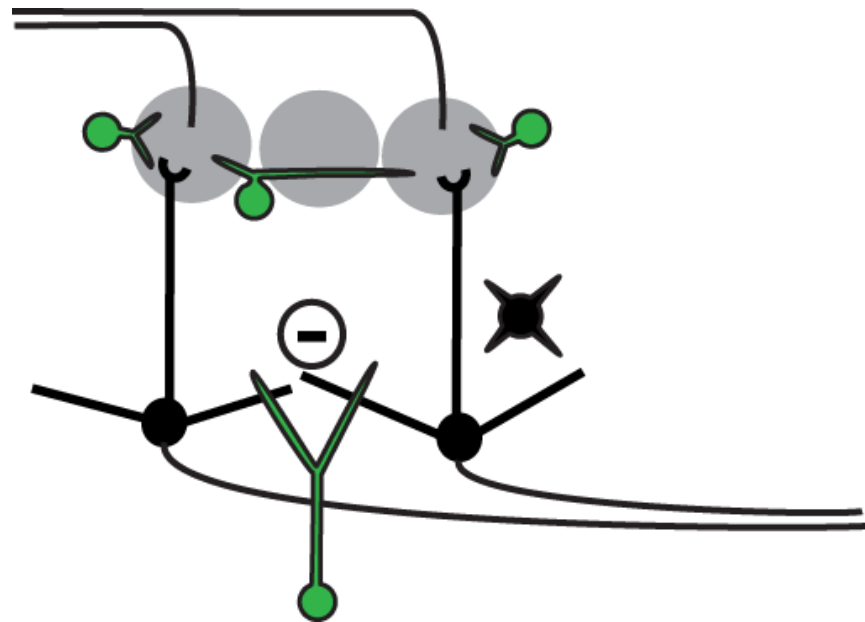
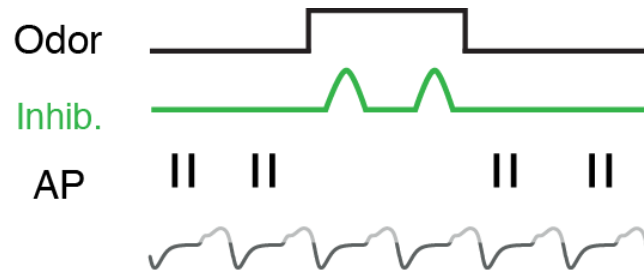
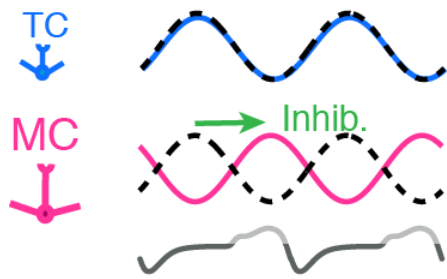


Unmasking is odour-specific

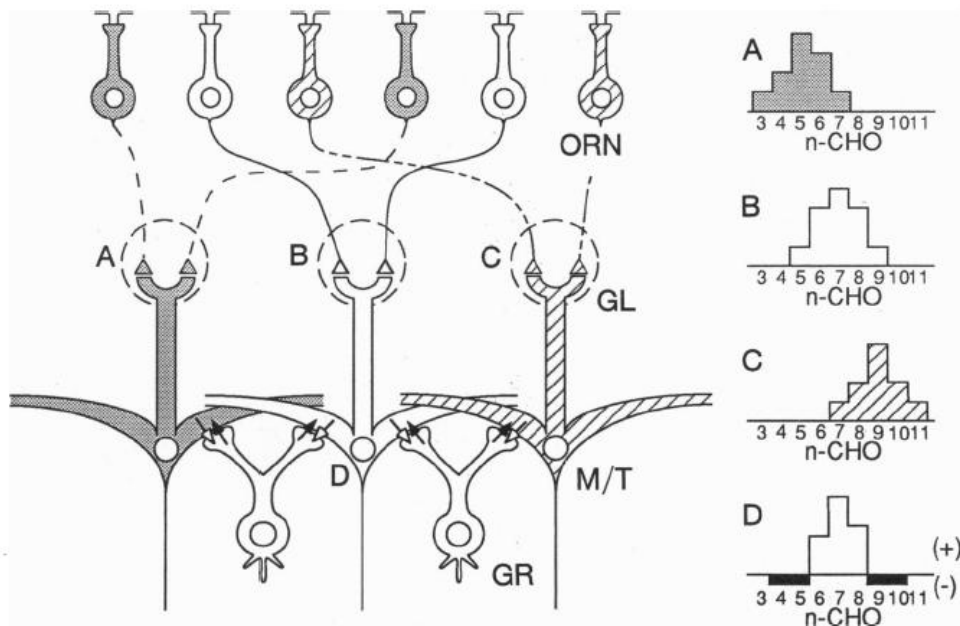


Transformation 2: inhibition inverts signal

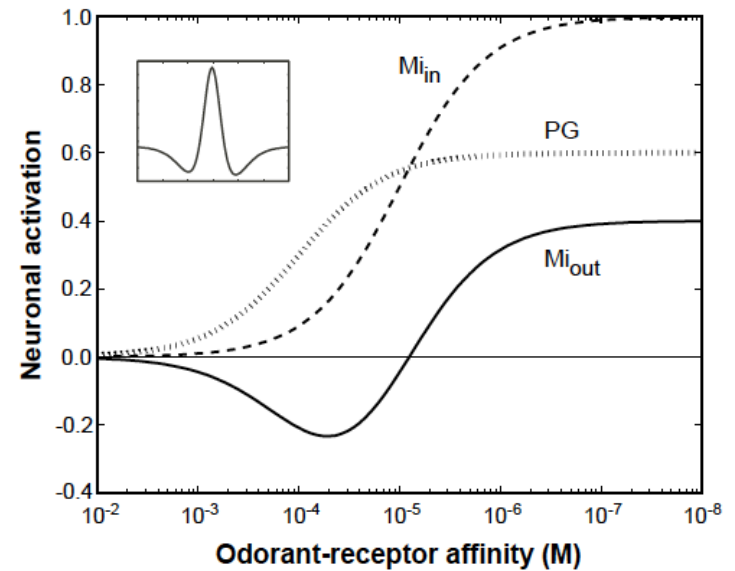
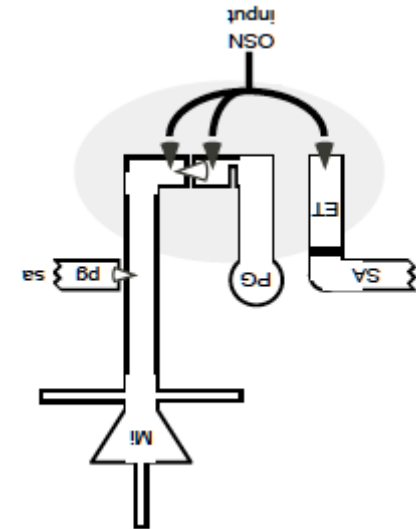




Models for contrast enhancement in the olfactory bulb

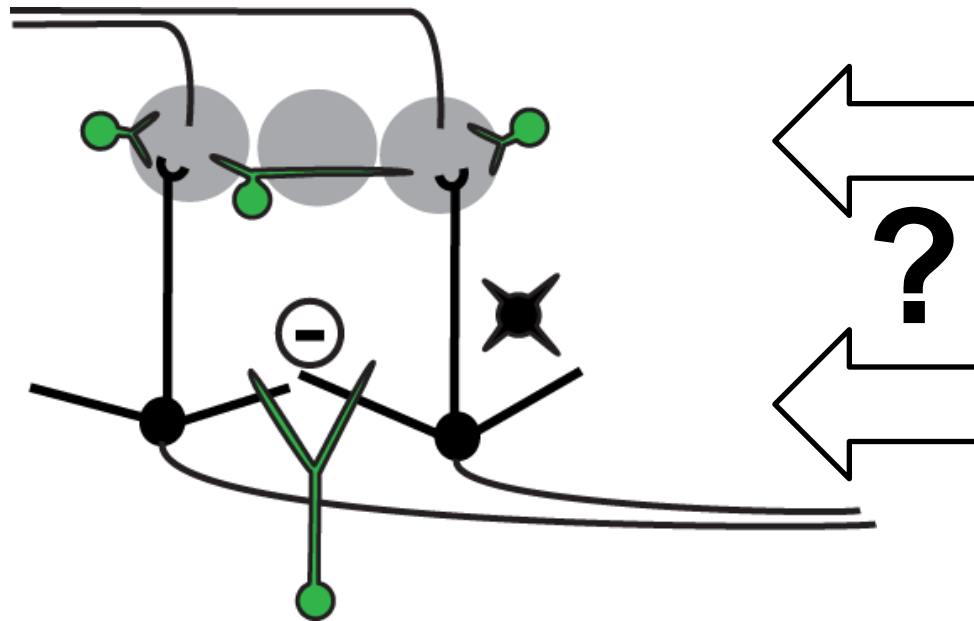


Yokoi et al., 1995; also see Luo & Katz 2007
Shepherd 2007



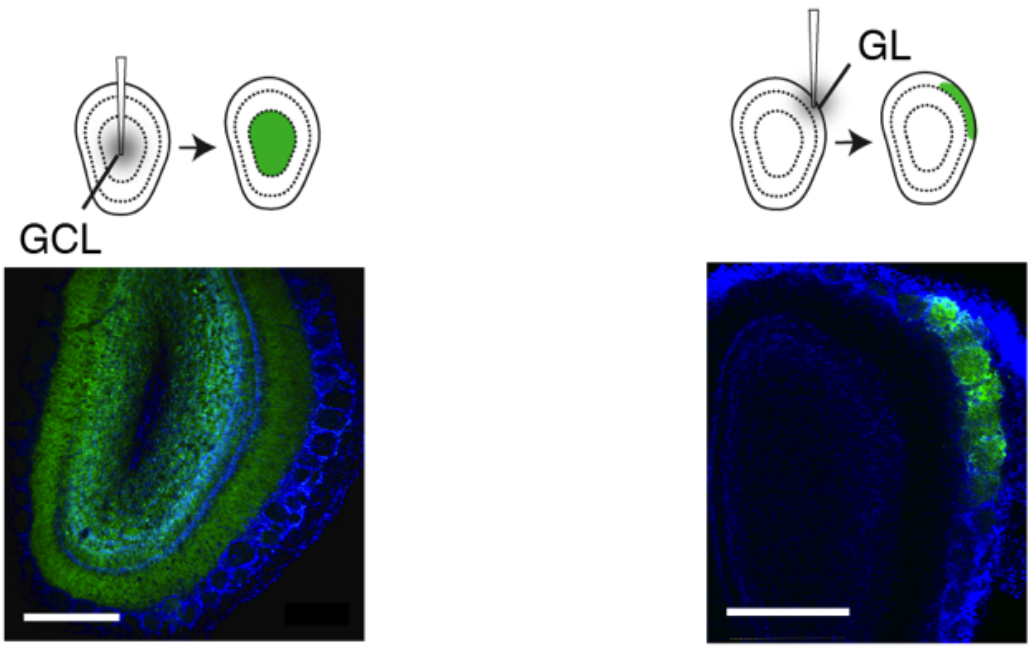
Cleland and Sethupathy 2006 *BMC Neurosci.*

Ambiguity in the source of inhibition





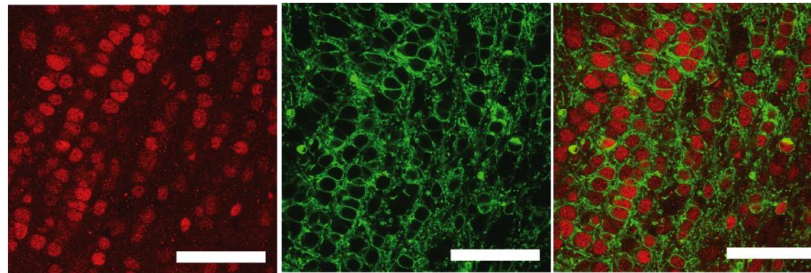
In *Gad2*-ires-Cre (Taniguchi et al.,)
 or
Vgat-ires-Cre mice (Vong et al.,)



Fukunaga et al., 2014 *Nat. Neurosci.*

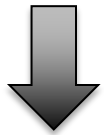
Efficient and selective silencing

GFP
Anti-cre
> 90%

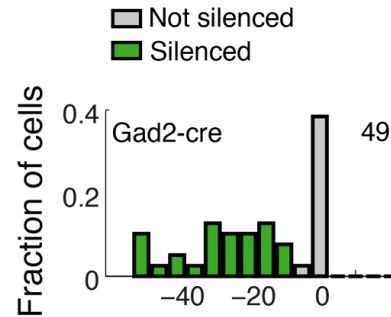
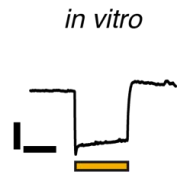


Jan Herb

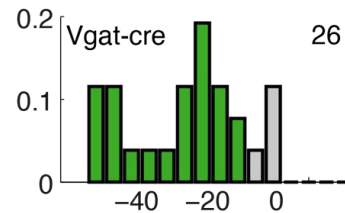
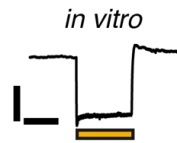
GC injection



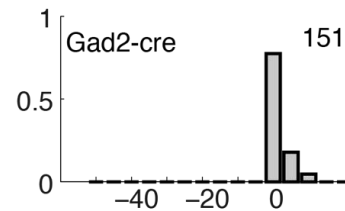
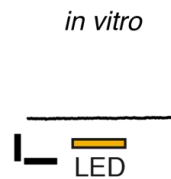
In vitro recording



59%

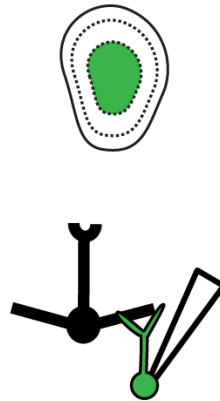
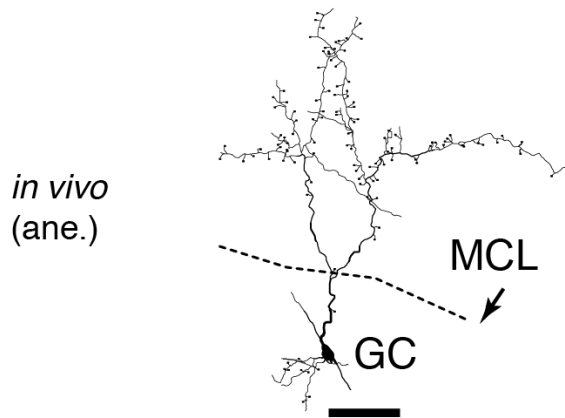


85%

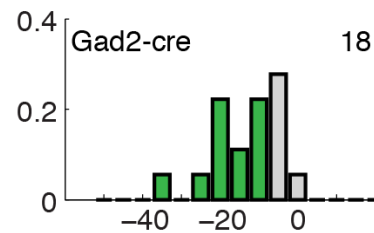
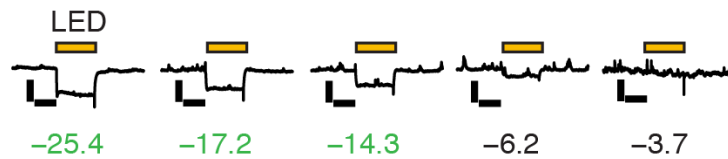


0%

Works efficiently in vivo

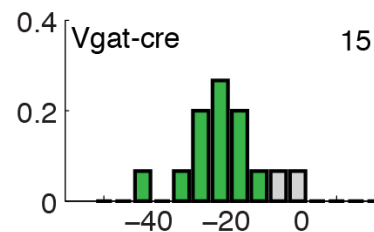
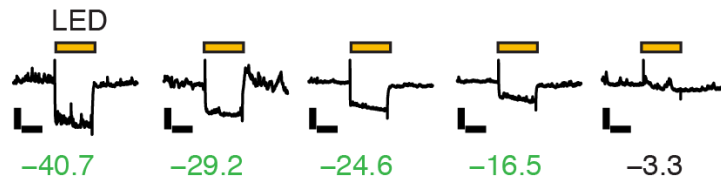


in vivo
(anaesthetised)



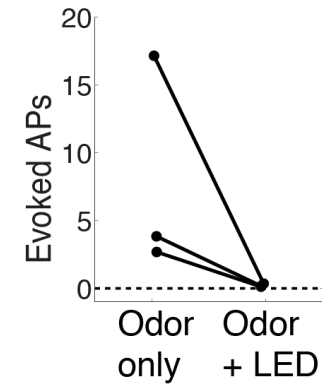
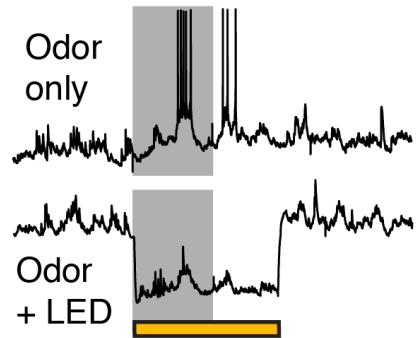
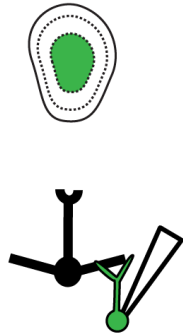
50%

in vivo
(awake, head-fixed)

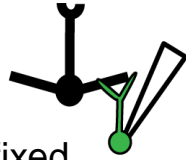


87%

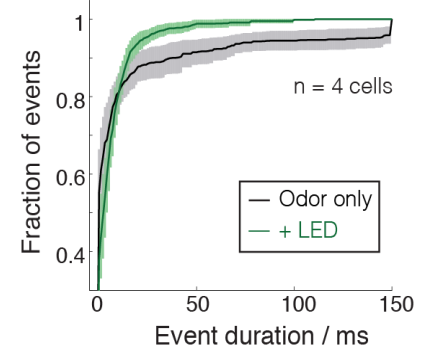
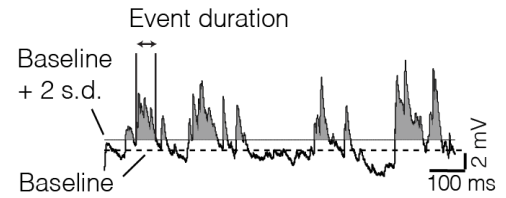
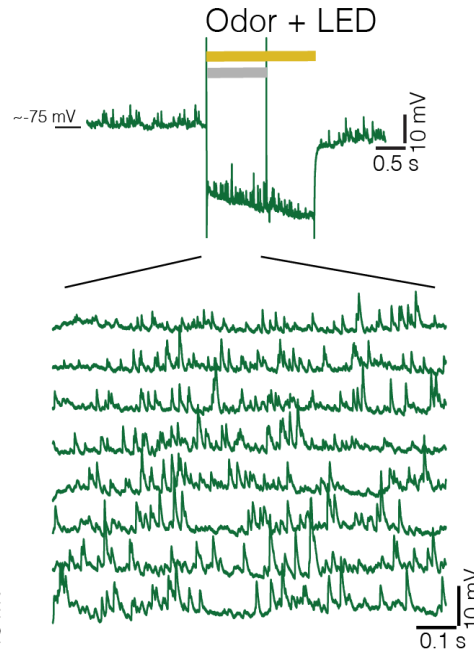
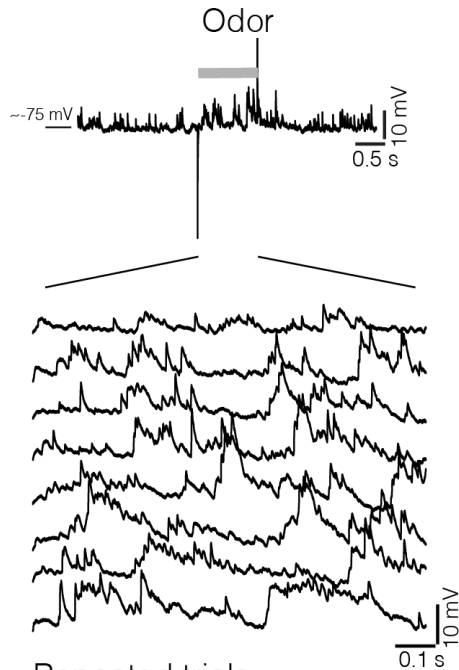
Odour-evoked APs are silenced

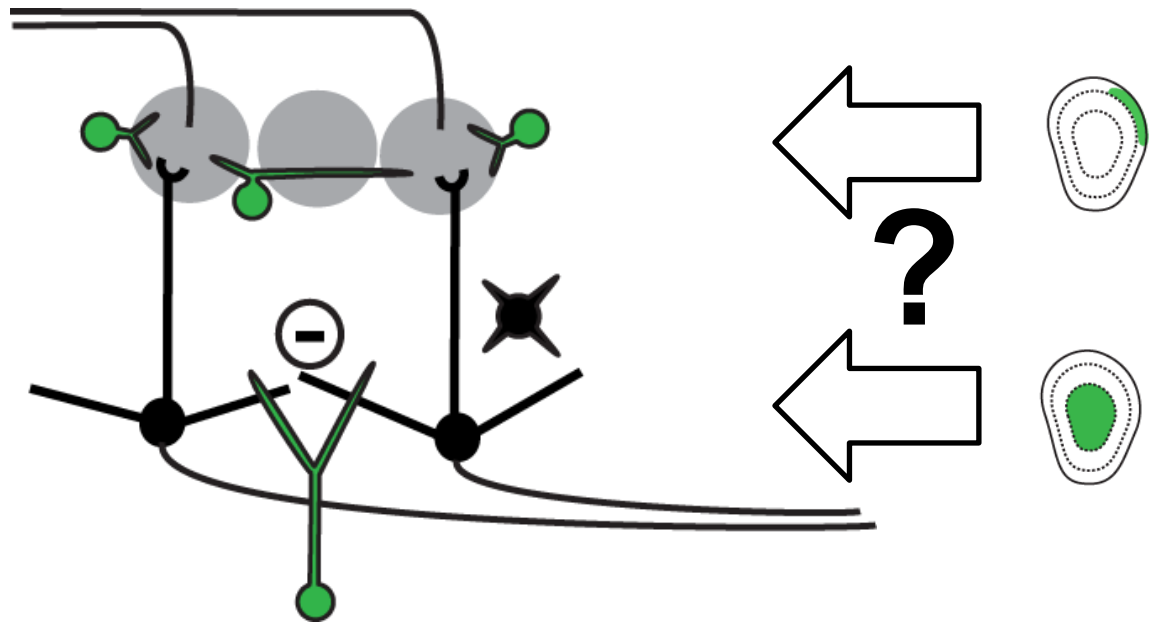
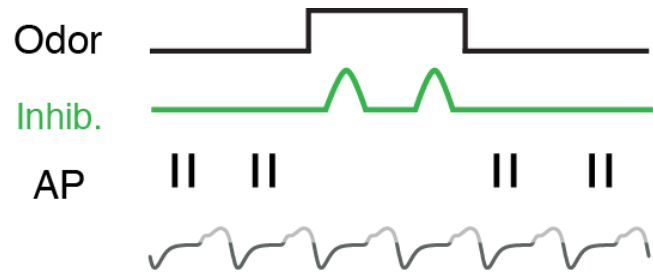
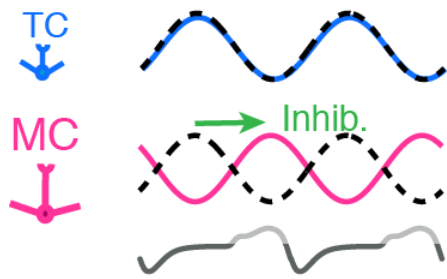


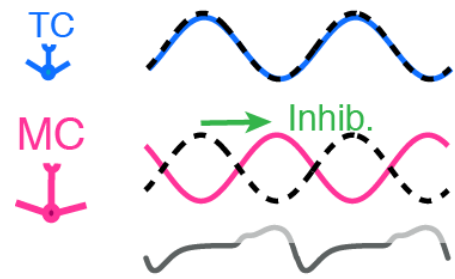
Broad events are absent during silencing



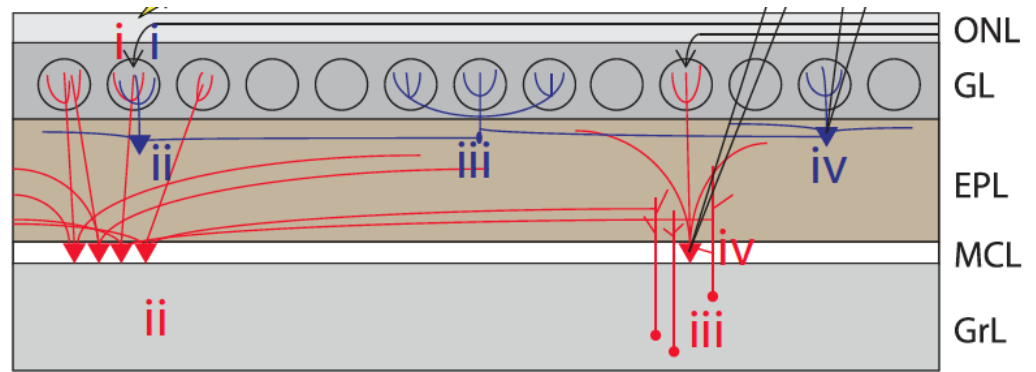
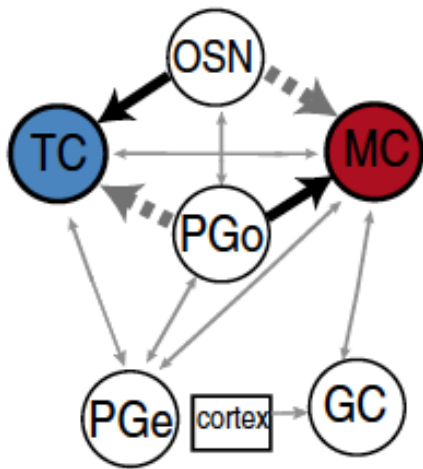
Awake, head-fixed







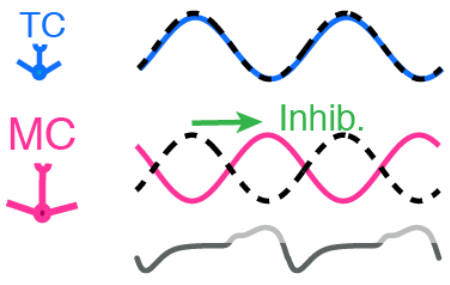
Alternative hypotheses of sniff phase separation

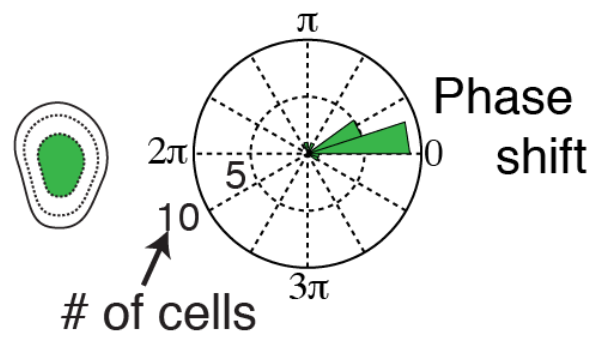
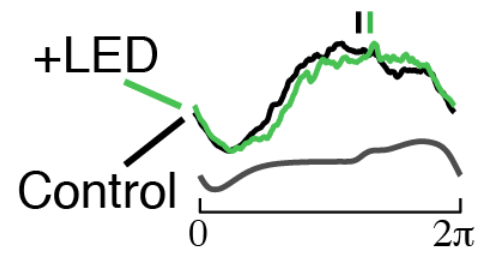
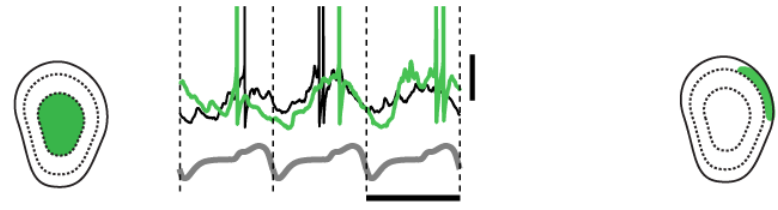
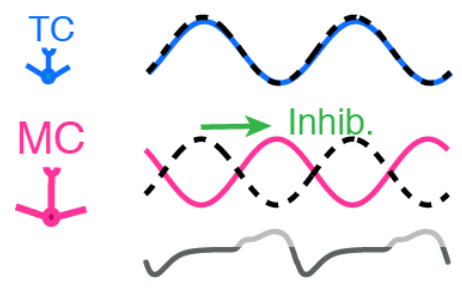


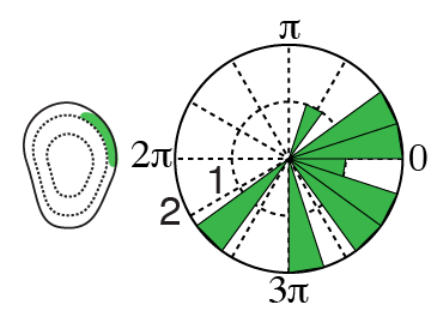
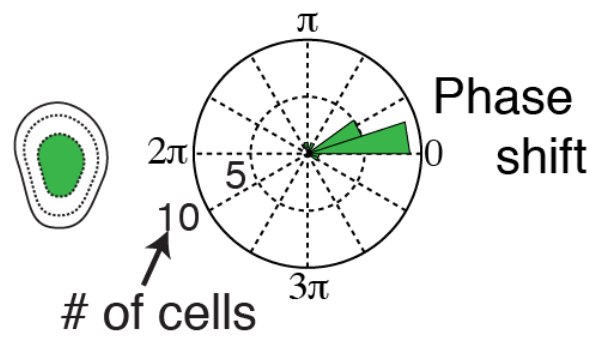
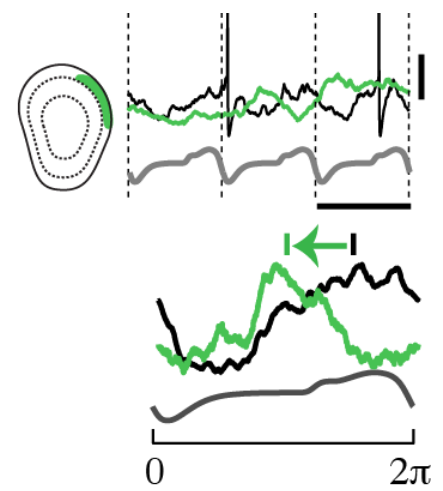
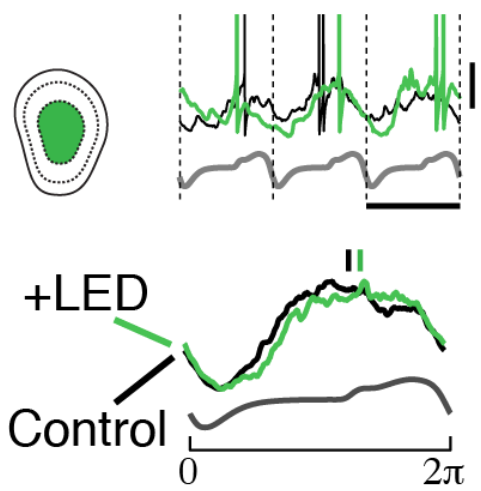
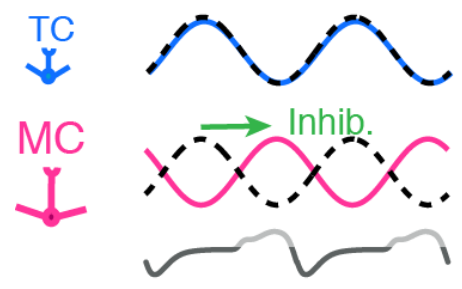
Manuel Berning

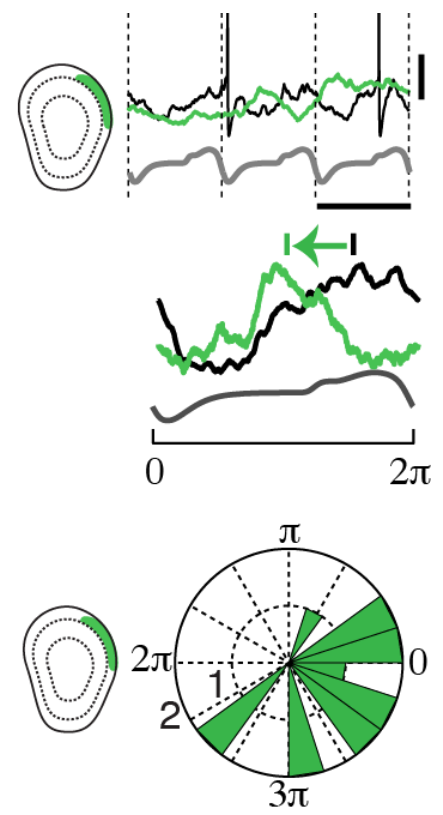
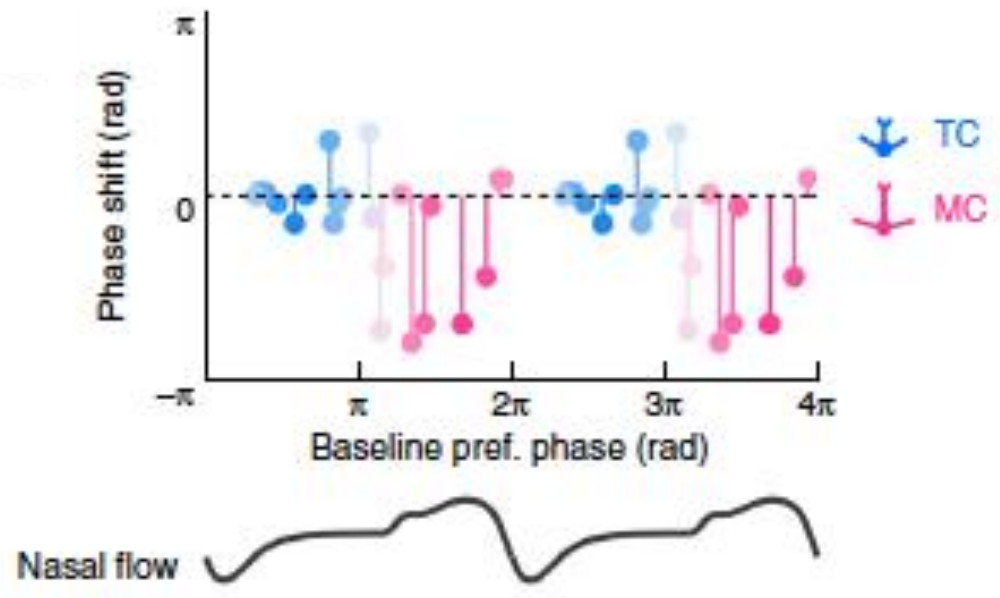
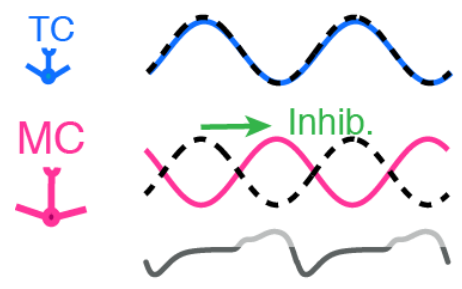
In Fukunaga et al., 2012 *Neuron*

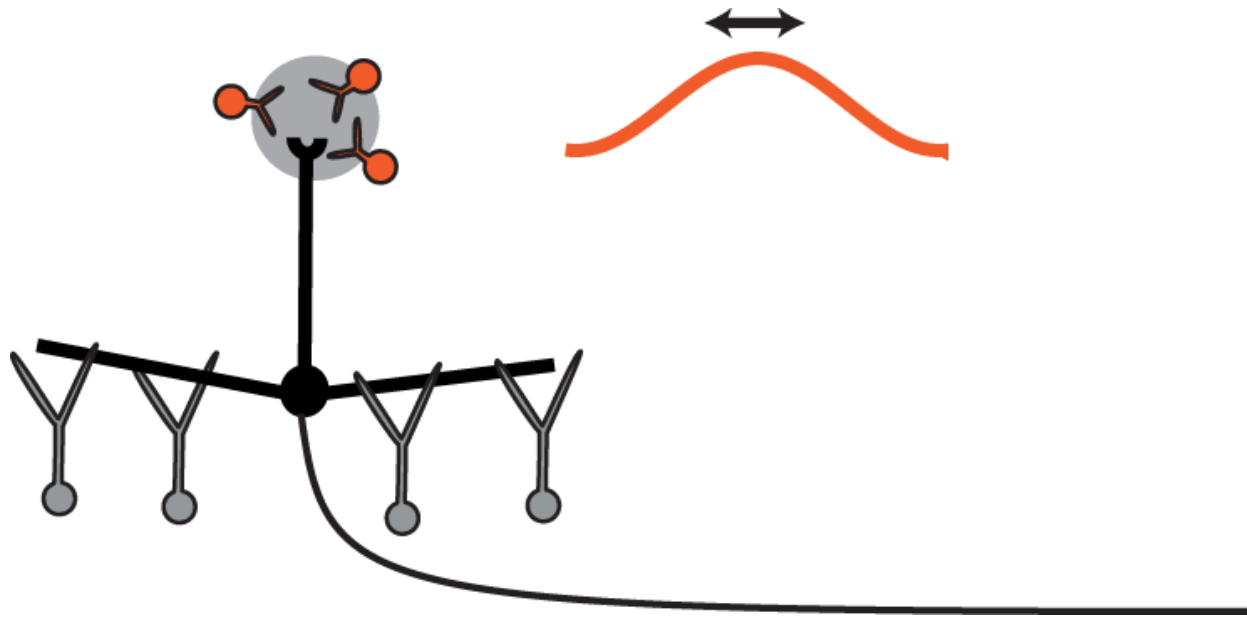
Phillips et al., 2011 *J. Neurosci*

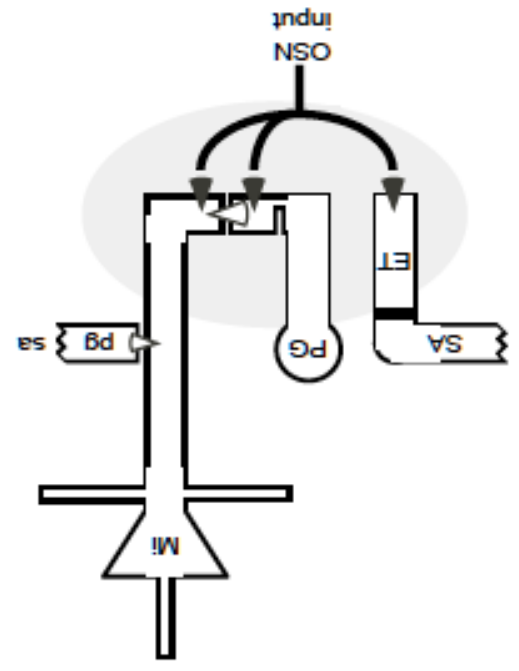
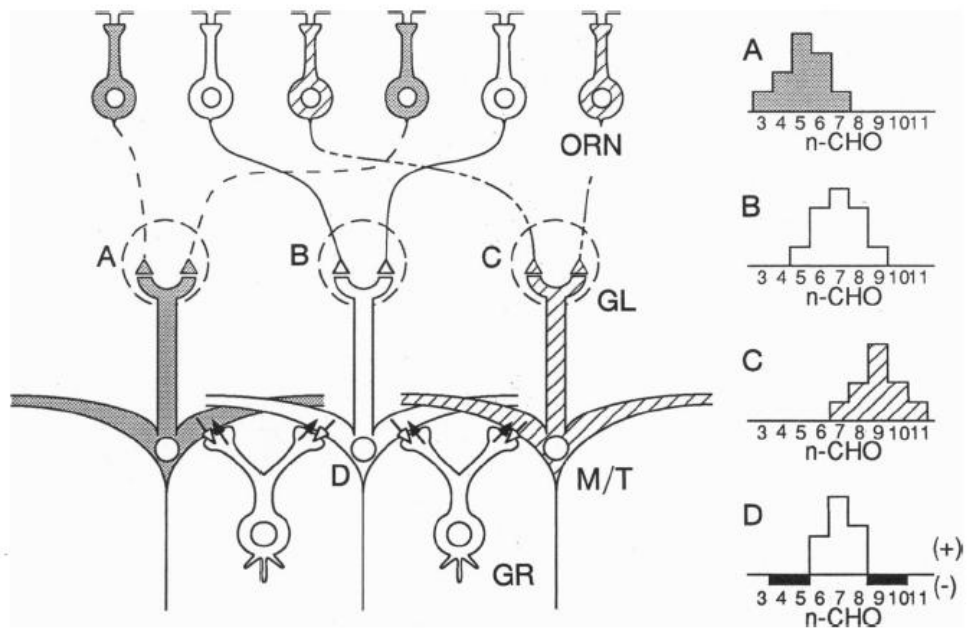
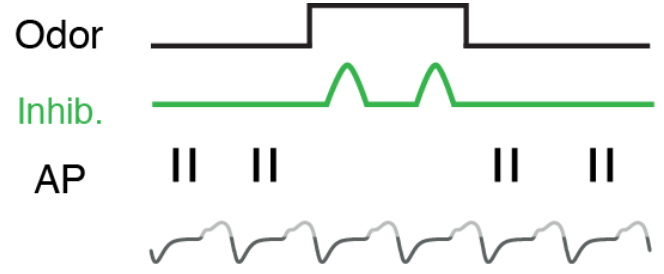
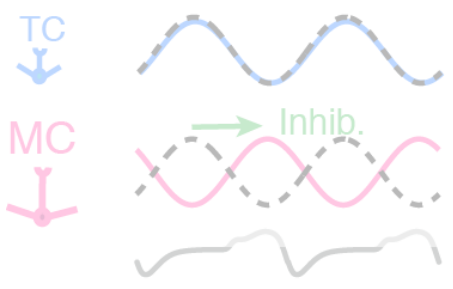


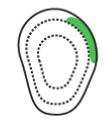
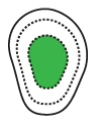
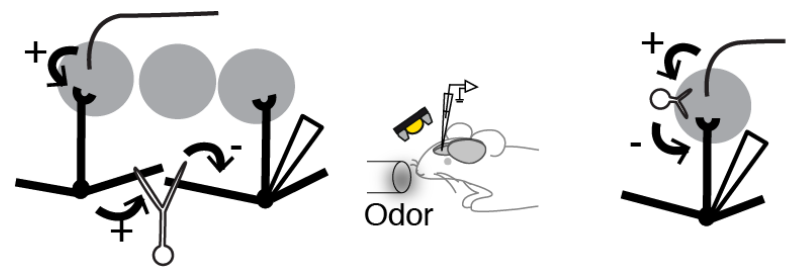
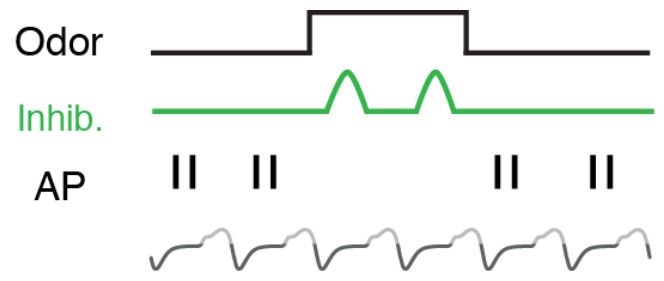
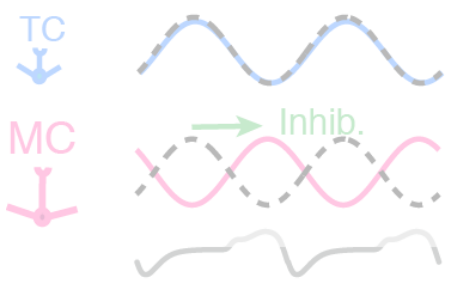


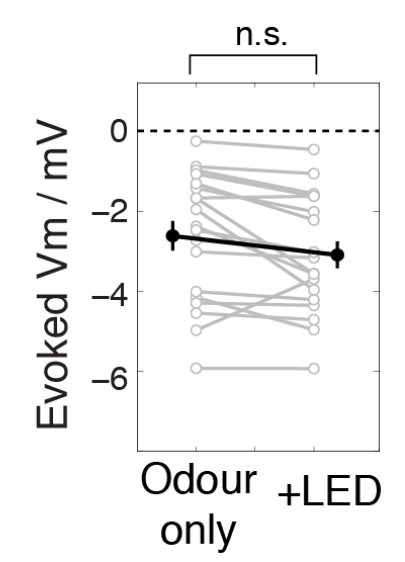
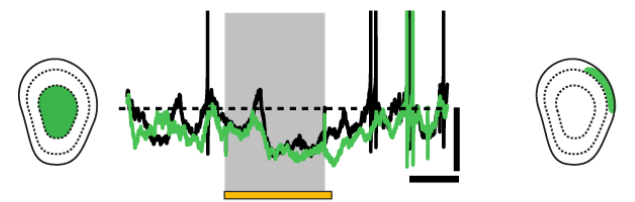
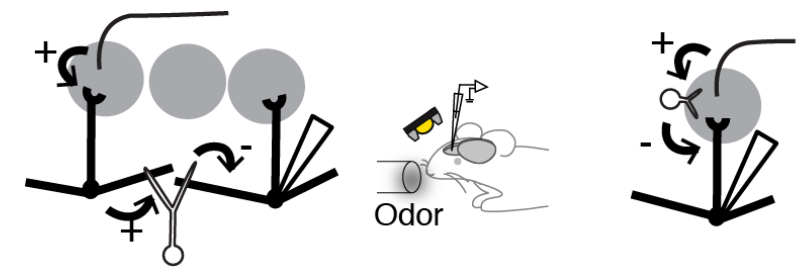
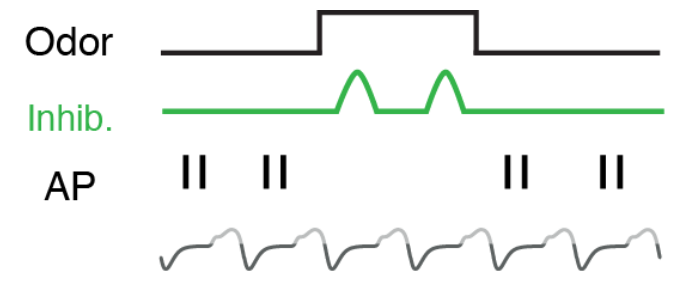
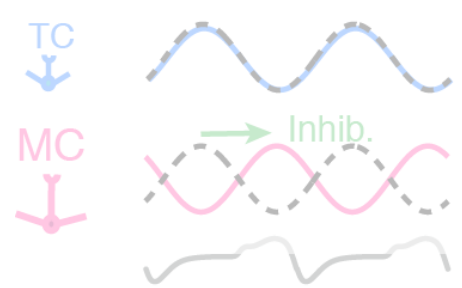


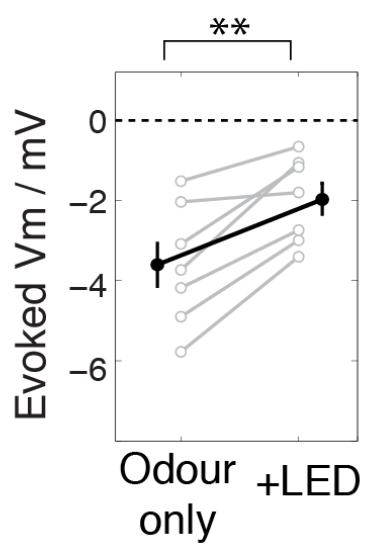
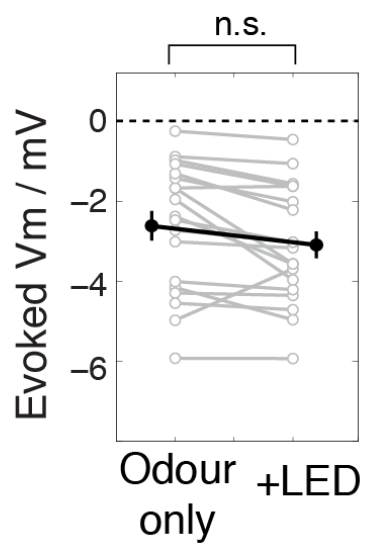
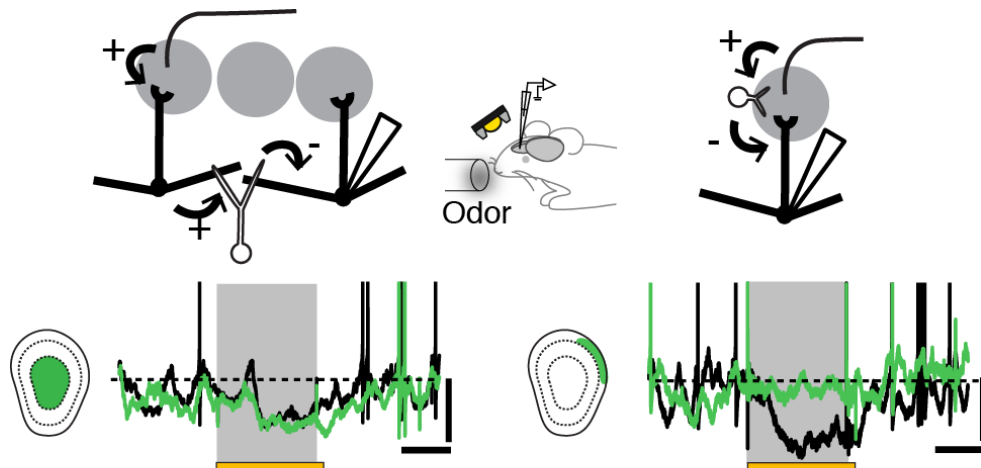
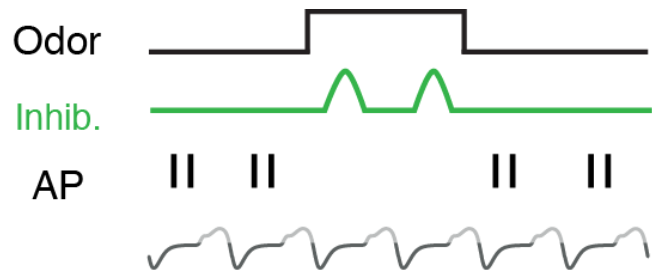
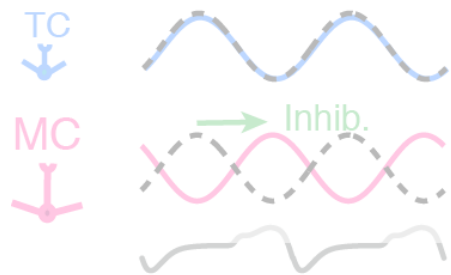


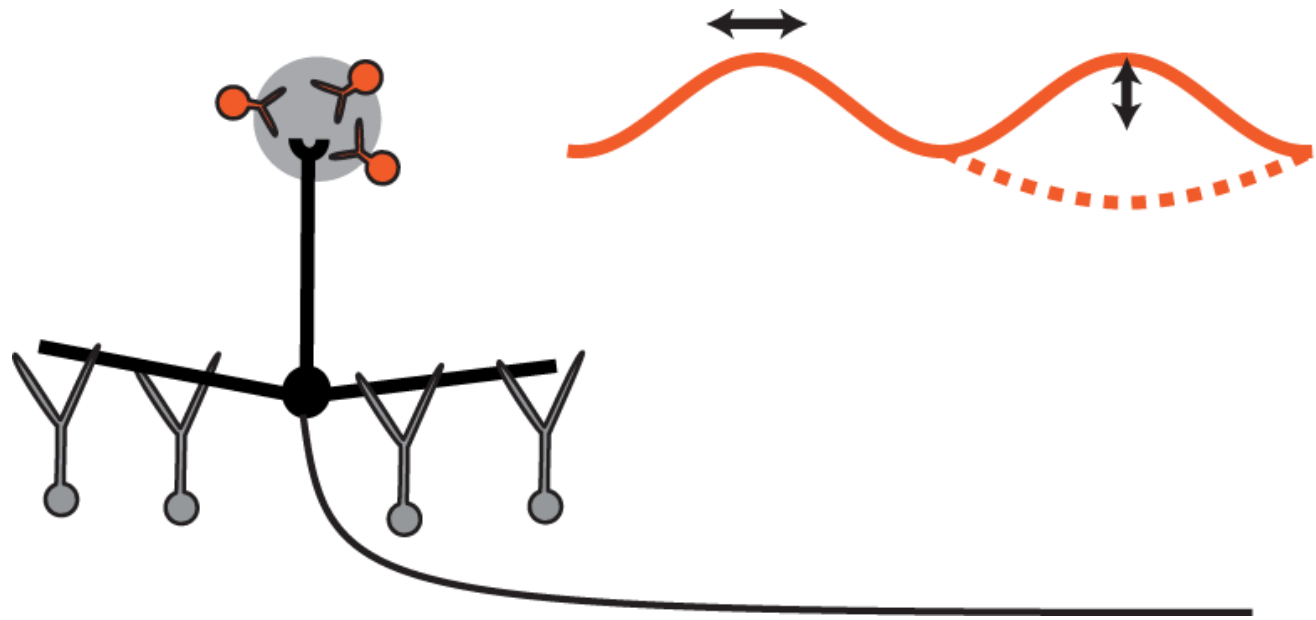


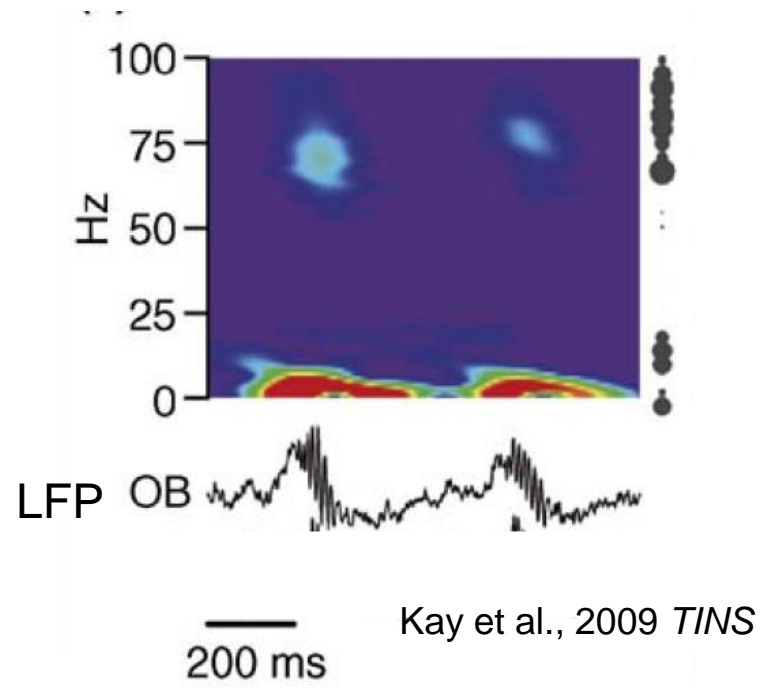


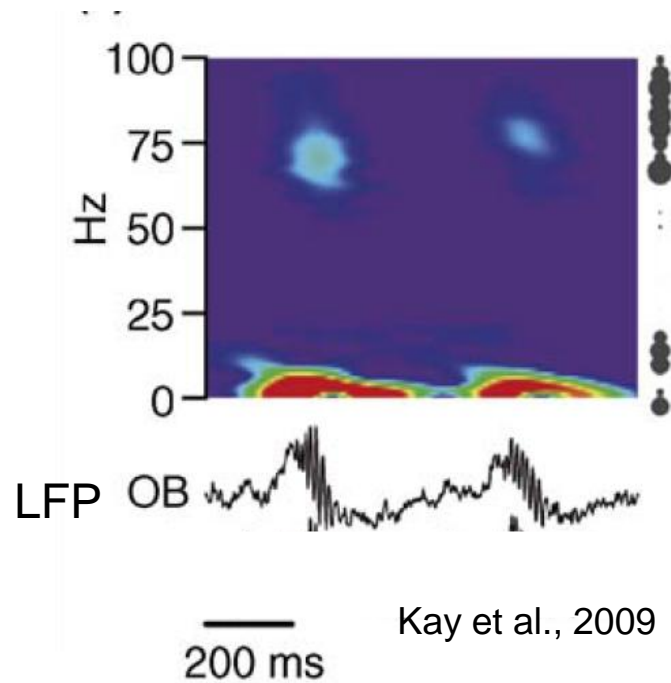




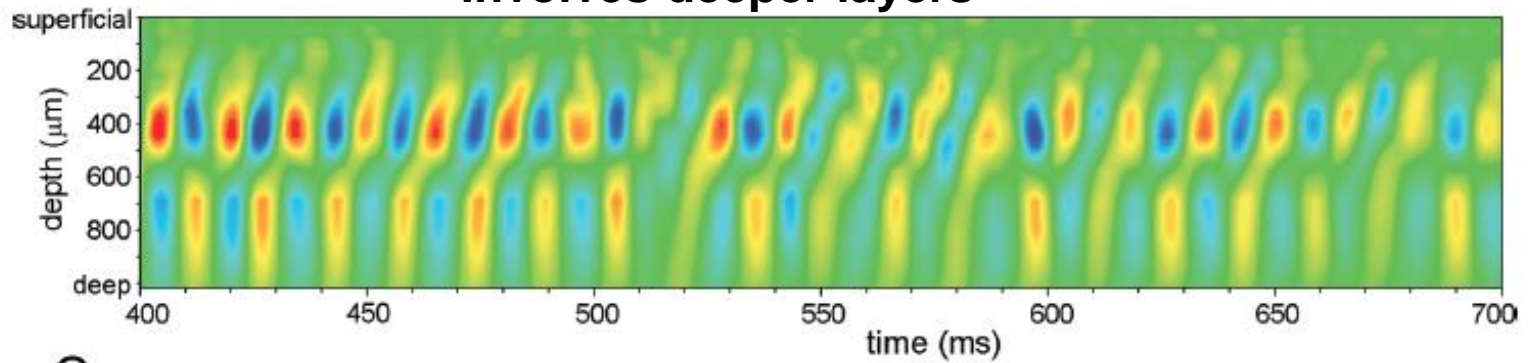




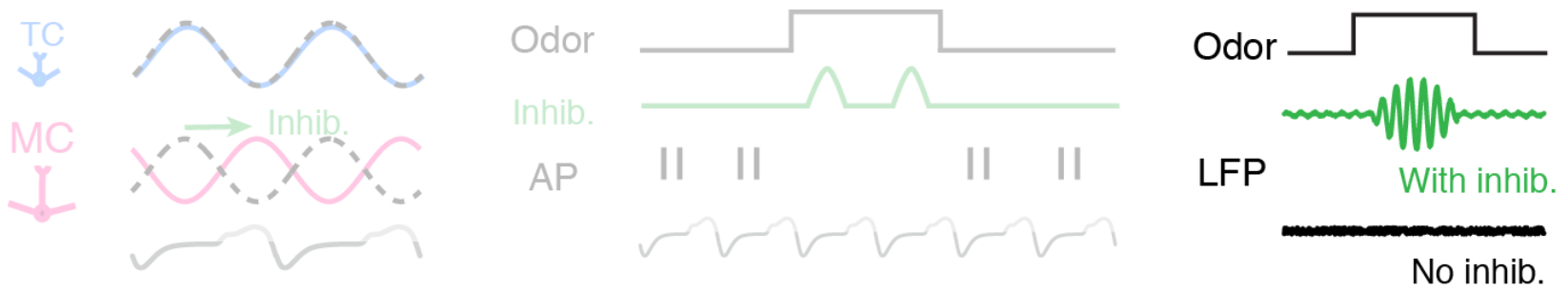




Involves deeper layers

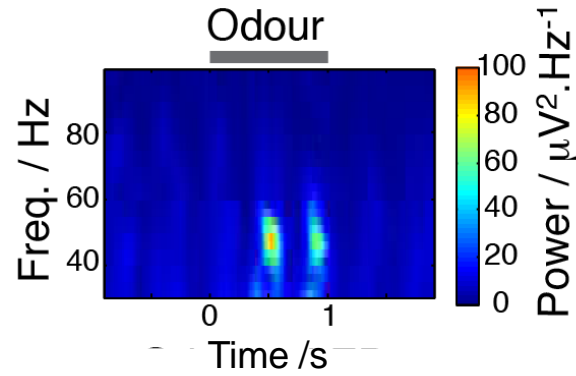
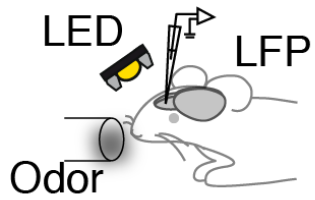
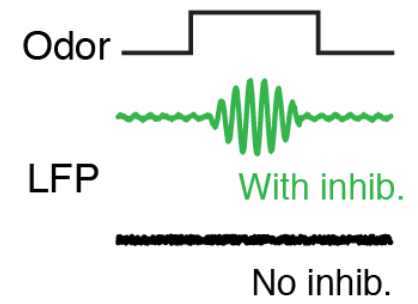
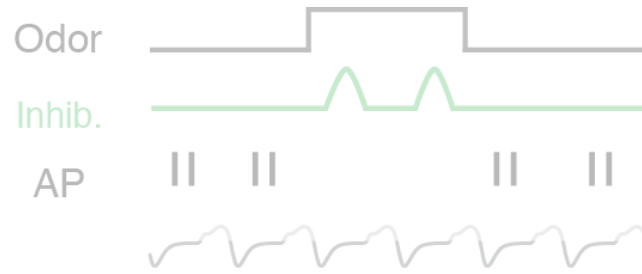
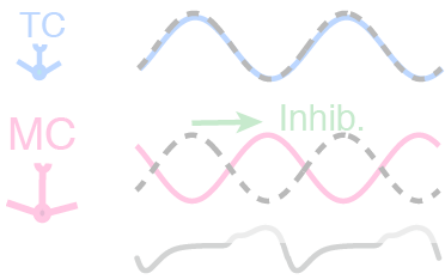


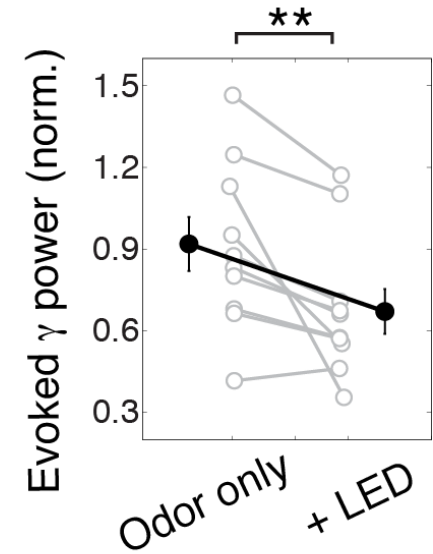
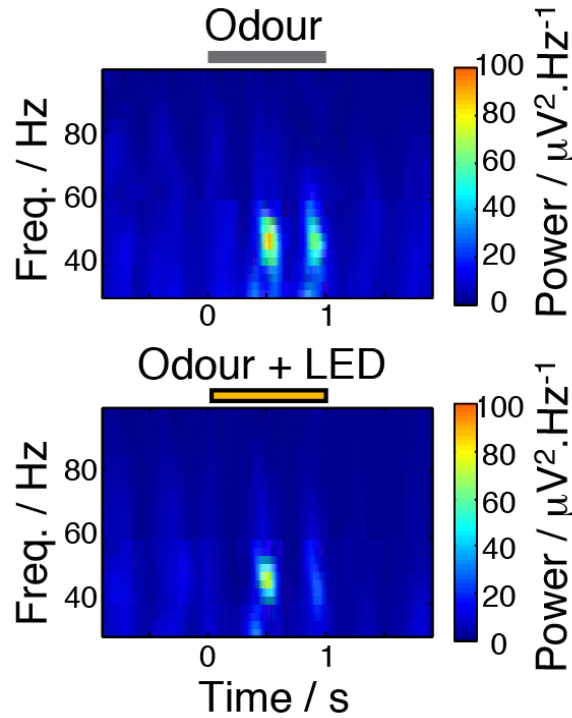
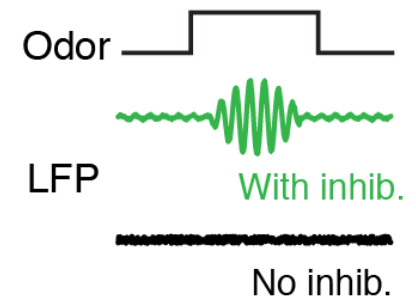
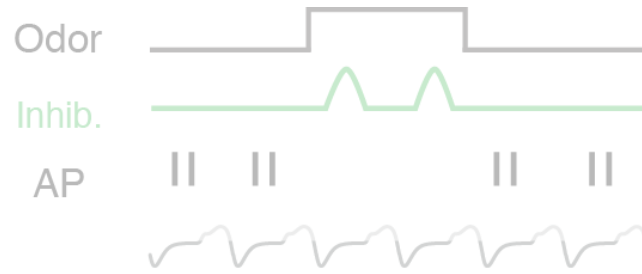
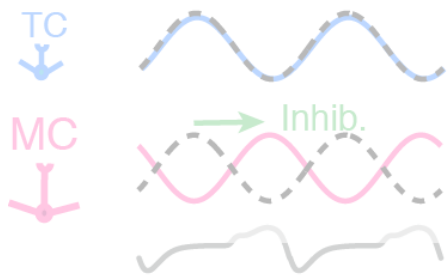
Neville & Haberly, 2003 *J. Neurophysiol.*



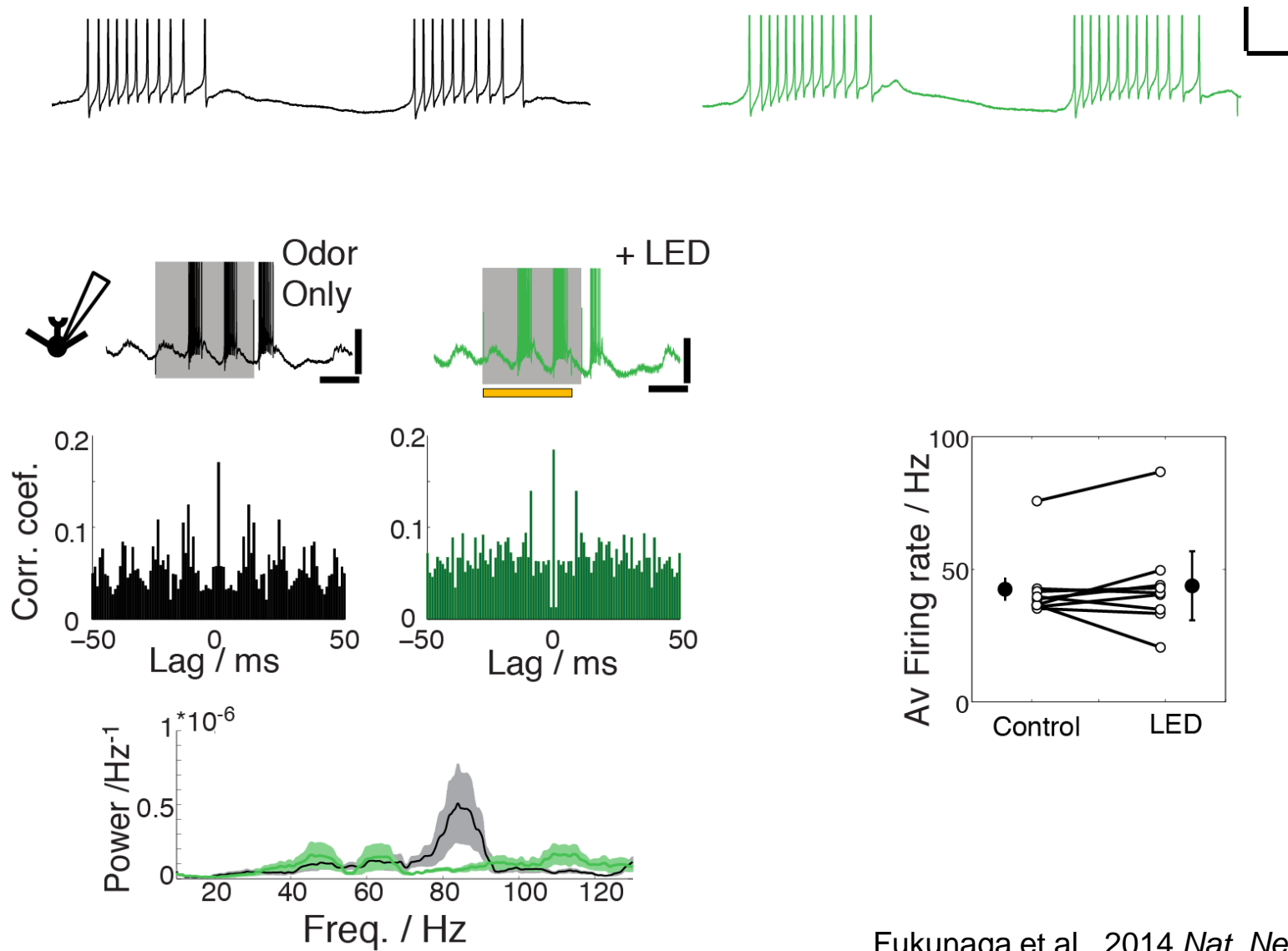
Inhibition is crucial for gamma oscillations

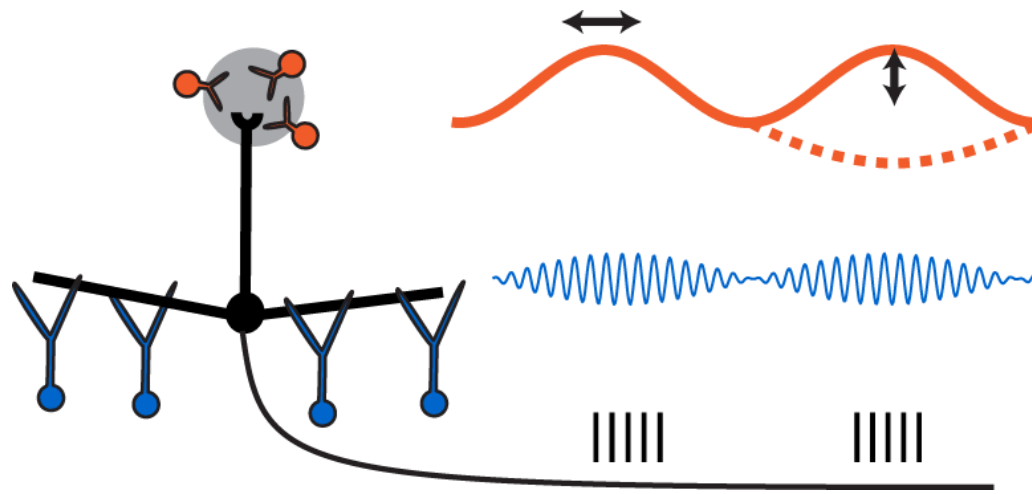
Nusser et al., 2001 *J. Neurophysiol*
 Halabisky & Strowbridge 2003 *J. Neurophysiol*
 Lepoussez & Lledo 2013 *Neuron*



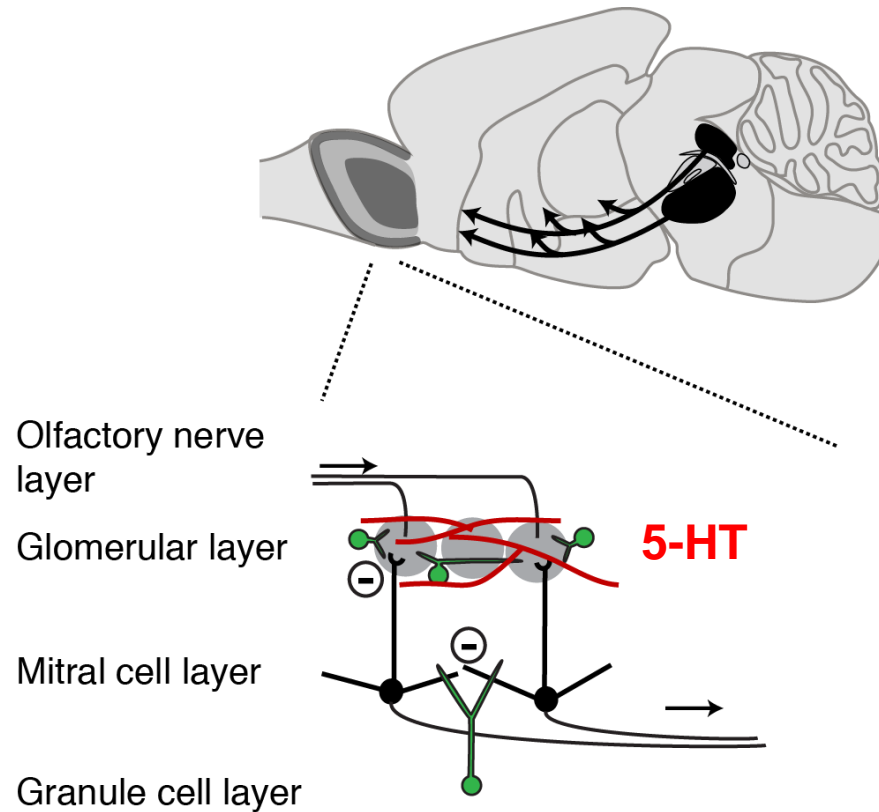


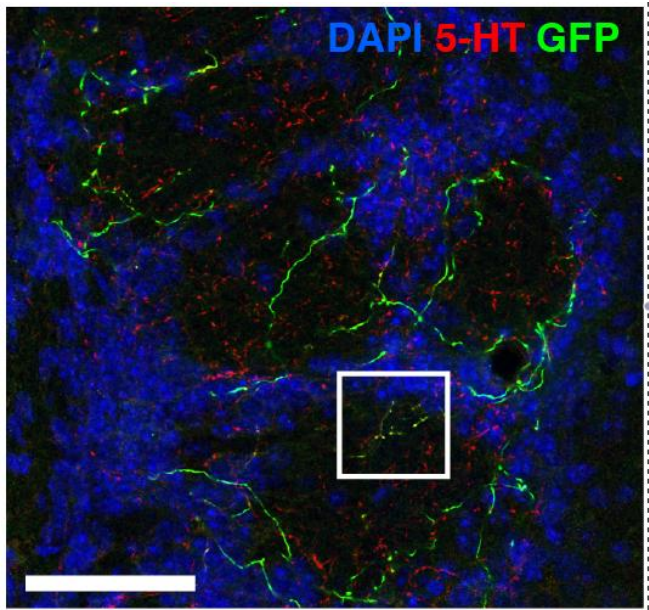
Spike precision at gamma frequencies





Differential neuromodulation of fast and slow activity?

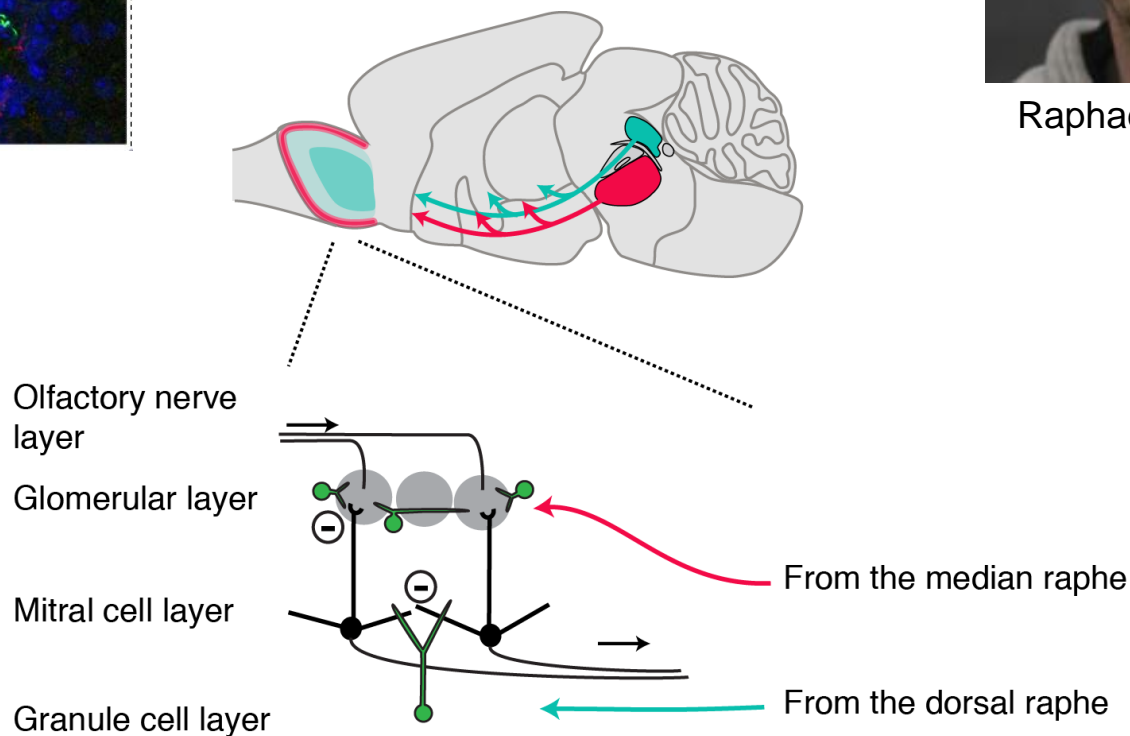




Layer specific projection from the raphe nuclei



Raphael Steinfeld



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