Intrinsic and synaptic inhibition for odor coding in the early olfactory system

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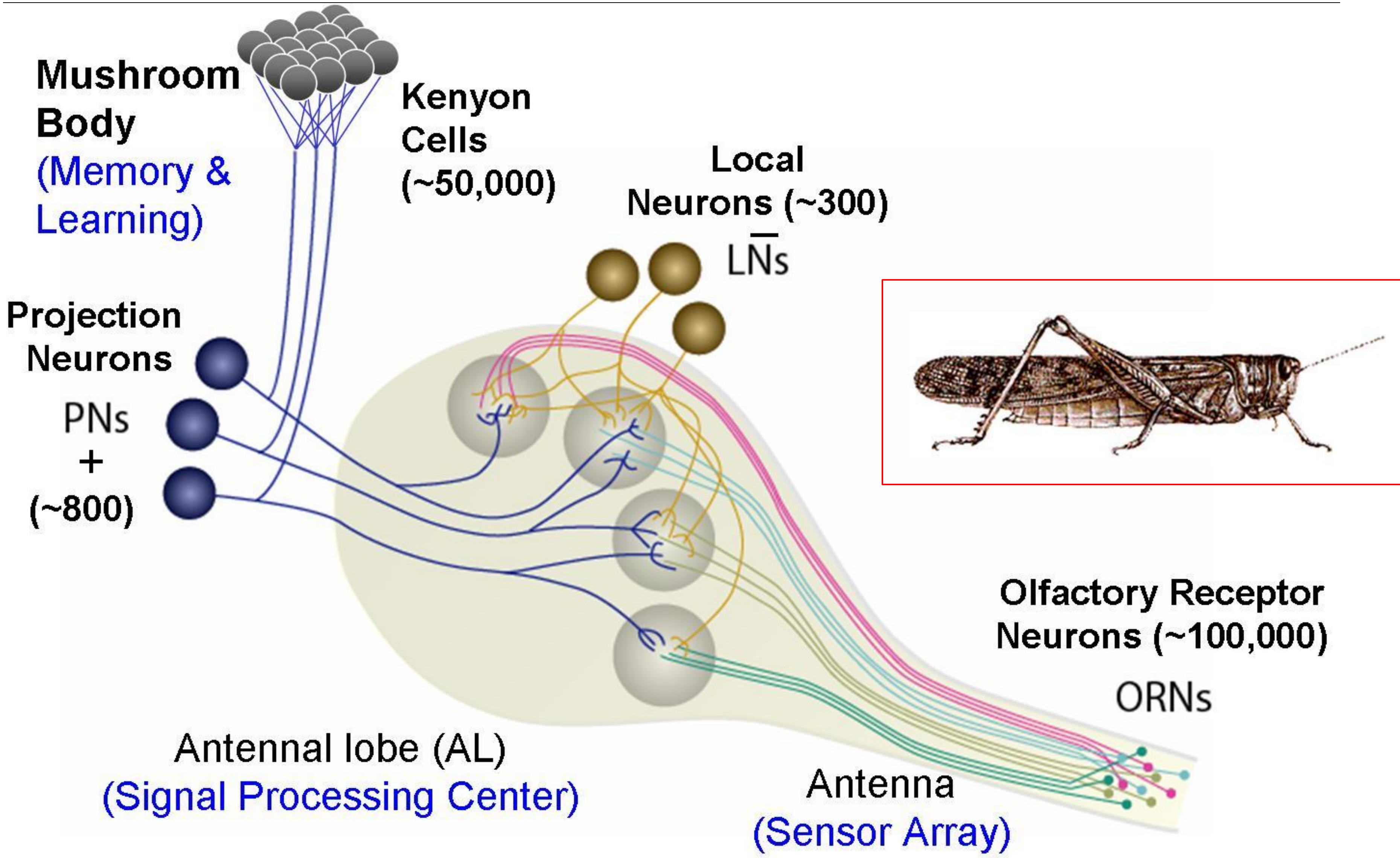
A “typical” overview of the insect olfactory system



Source: http://labs.seas.wustl.edu/bme/raman/research.html

Outlines

- Synaptic inhibition in the AL and MB for odor coding
- ORN adaptation for background-invariant odor recognition

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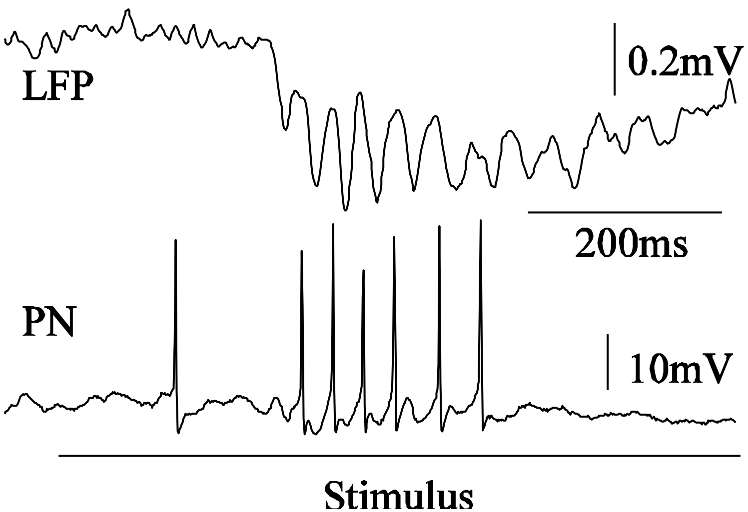
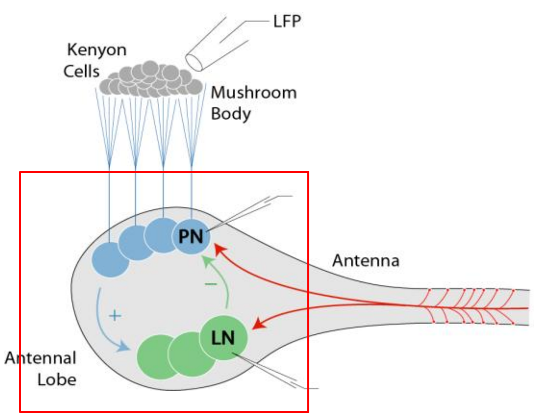
- ORN adaptation for background-invariant odor recognition

Odor triggers oscillatory responses in the AL

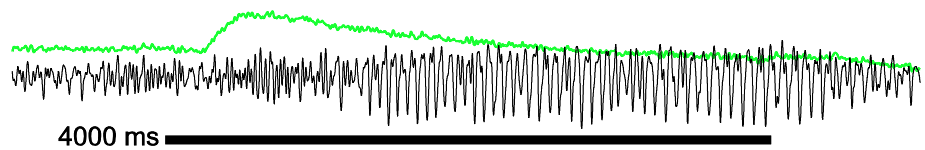
Locust



Bazhenov, et al., Neuron, 2000

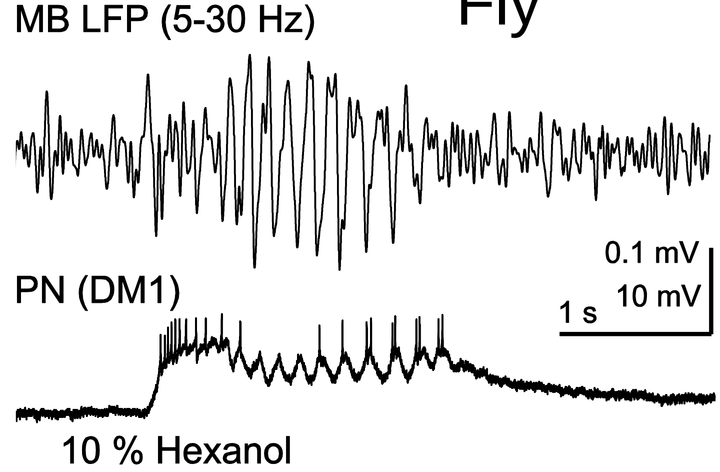


Moth



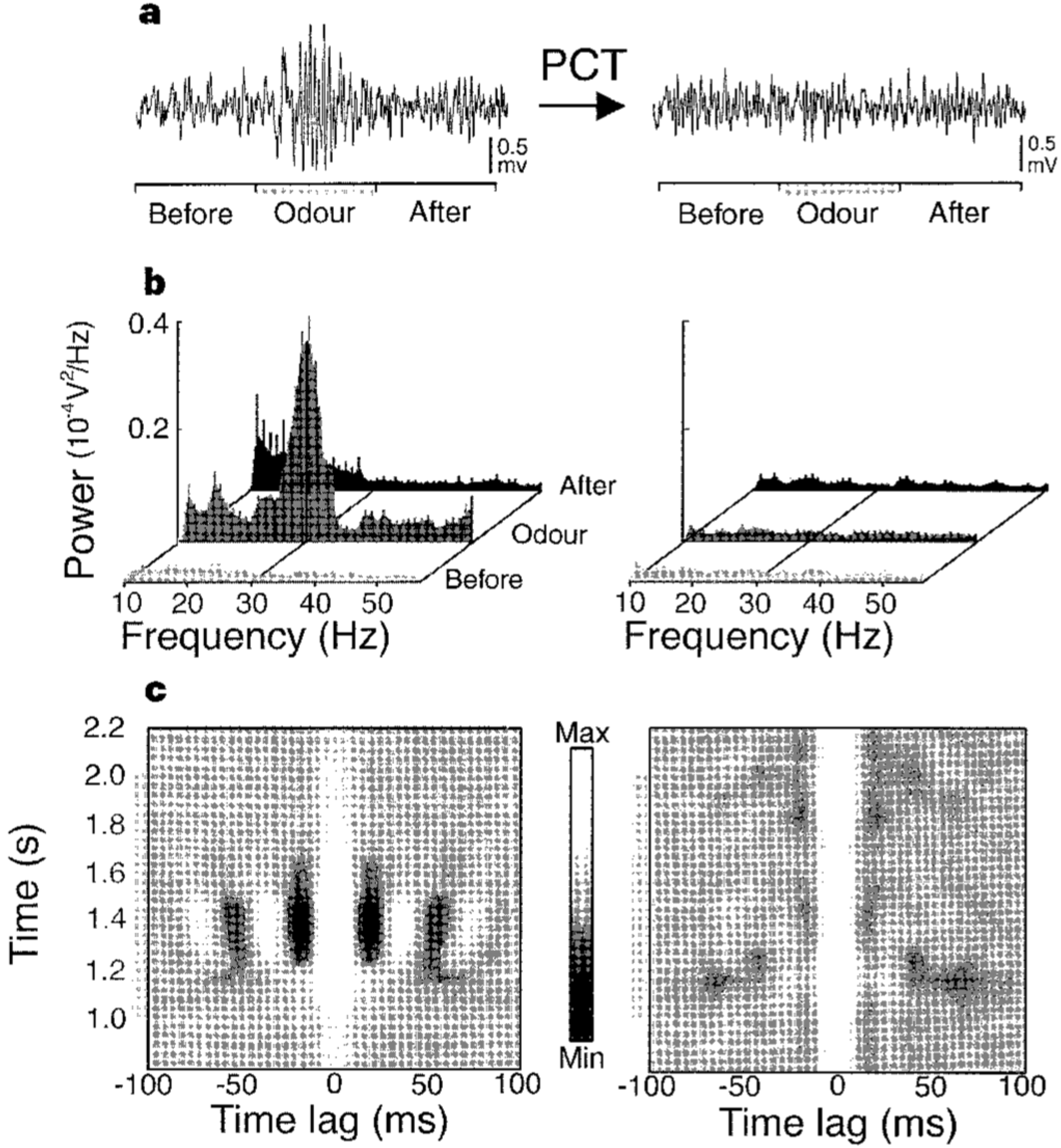
Ito et al., 2008

Fly



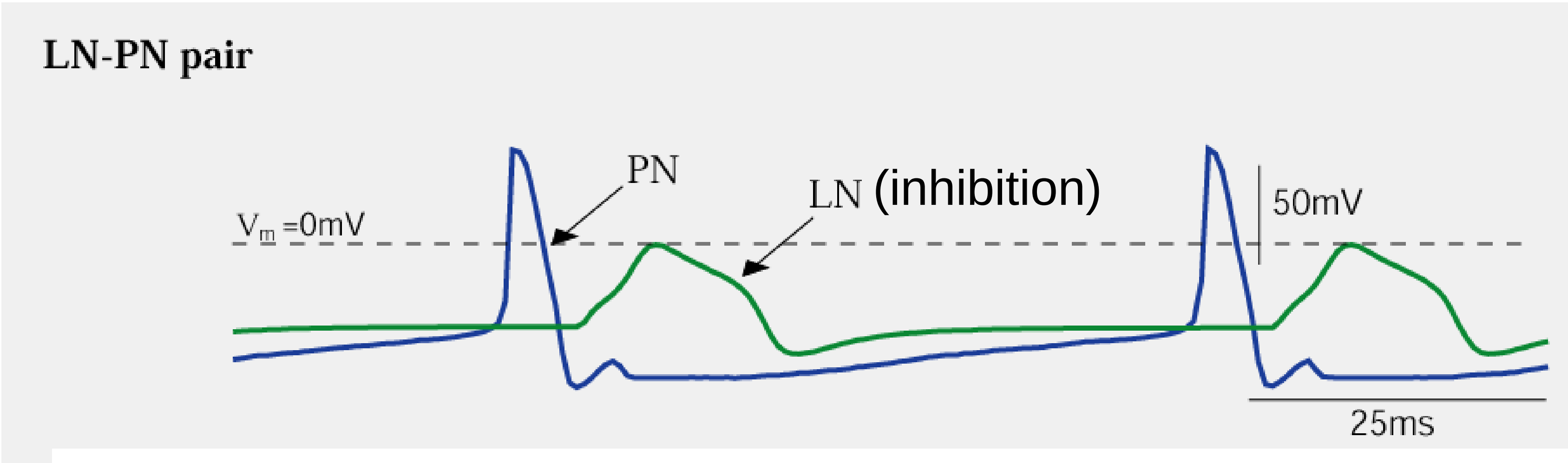
Tanaka and Stopfer 2009

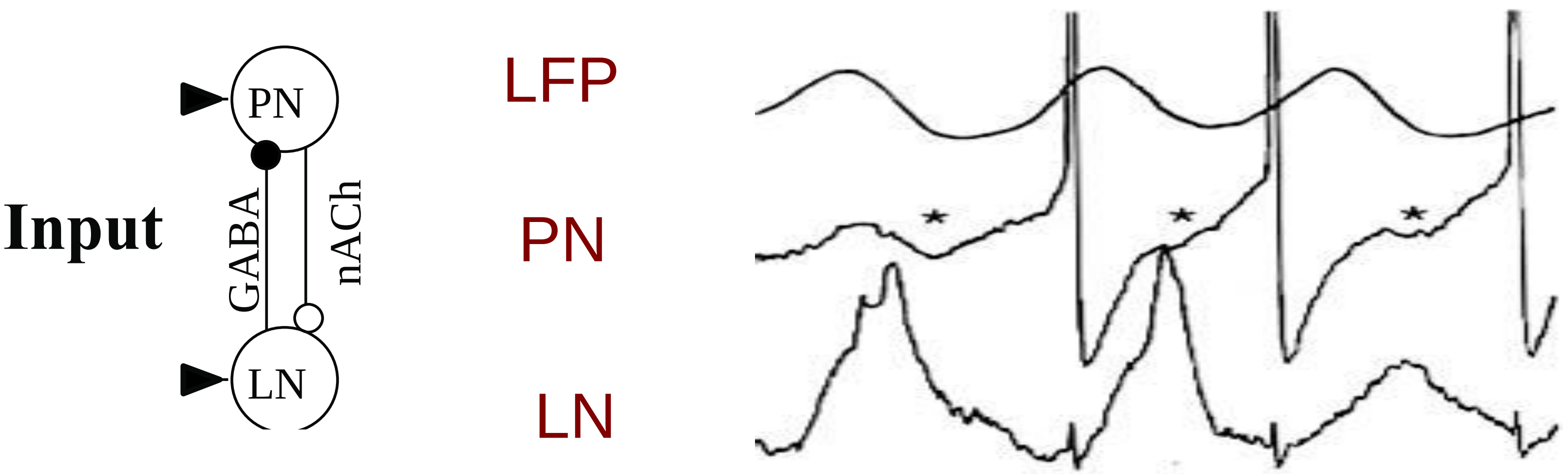
Odor triggered AL oscillations depend on inhibition



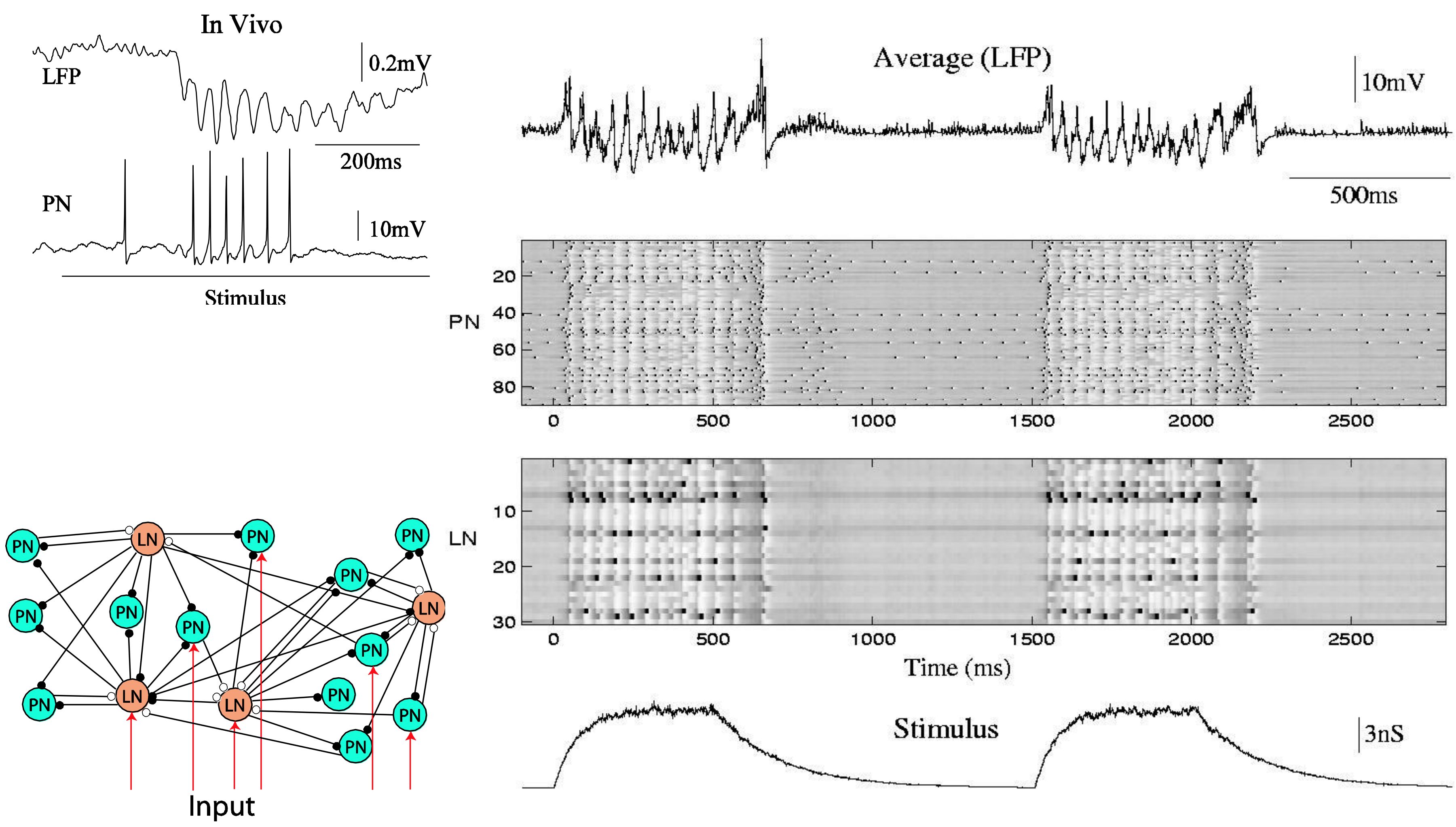
Stopfer et al, 1997

Feedback inhibition by LN provides a mechanism of PNs phase-locking



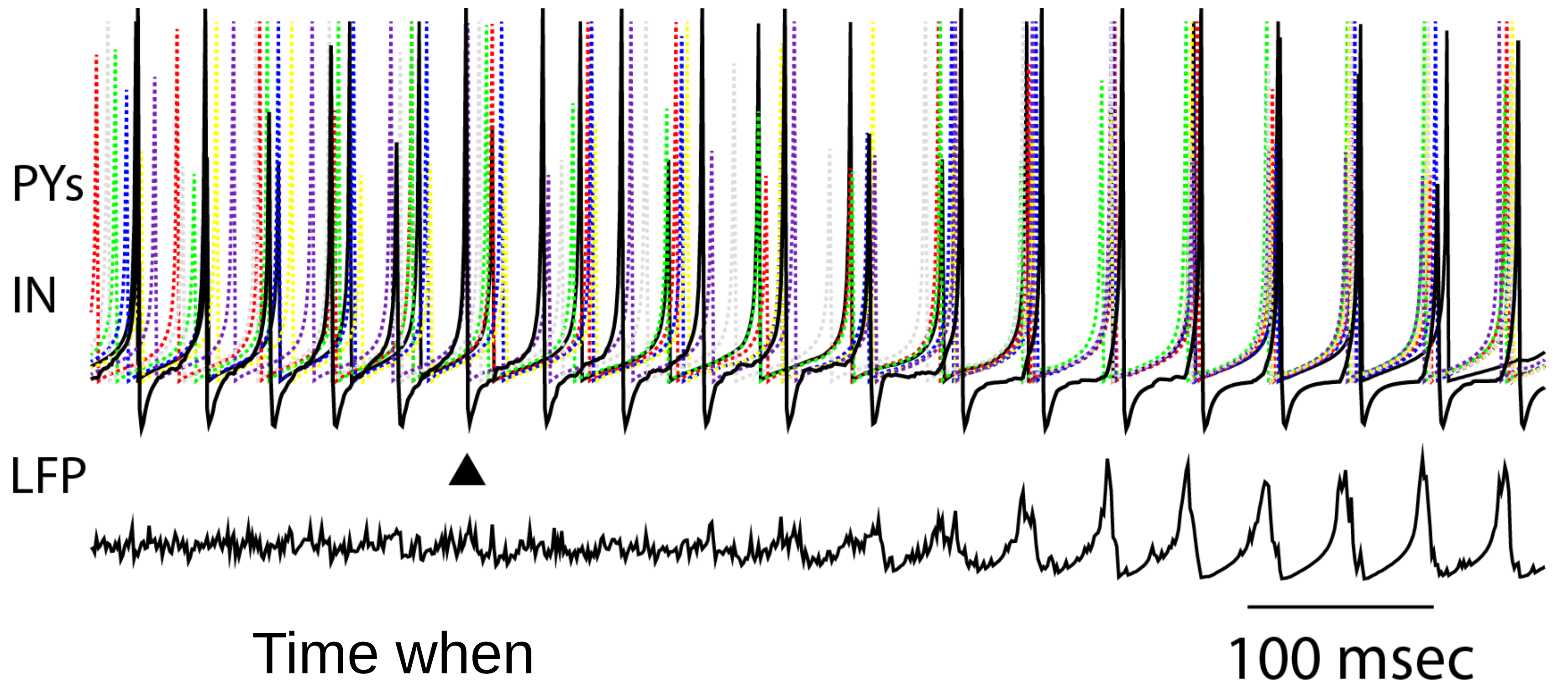


In the AL network model feedback inhibition by local LNs is responsible for odor triggered oscillations



Bazhenov, et al., Neuron, 2000

Feedback inhibition is a very common mechanisms of synchronization in neural circuits.

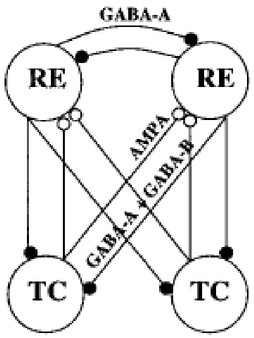


Time when inhibition is turned on

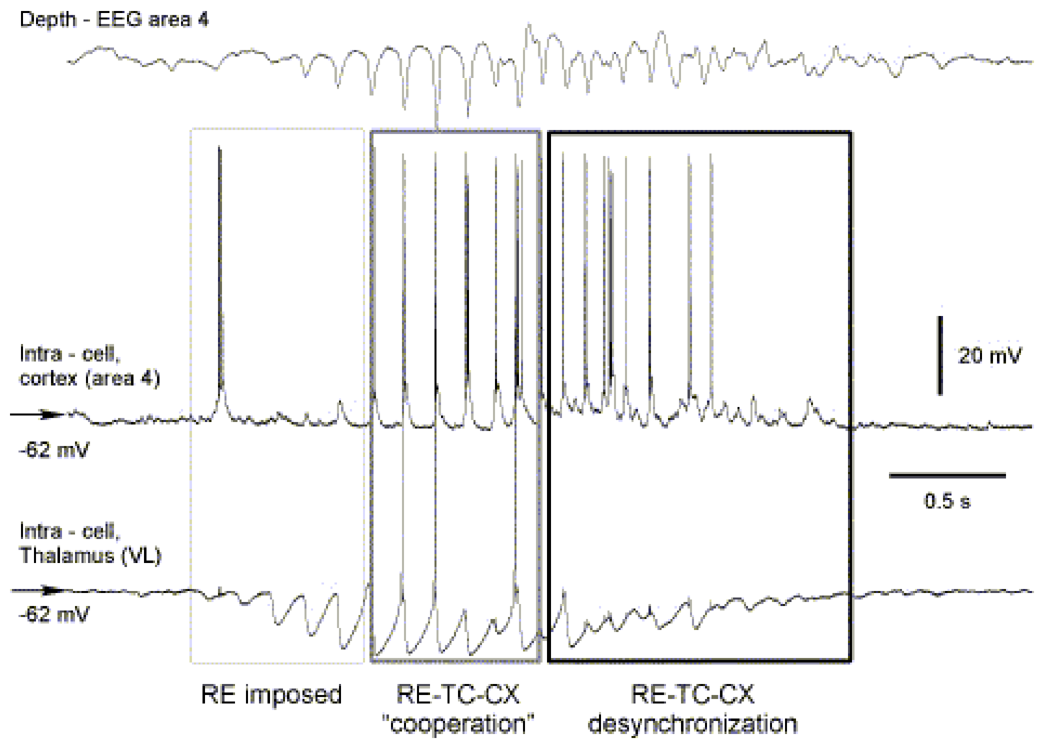
For example, in the neocortex, feedback inhibition by interneurons synchronizes principal neurons

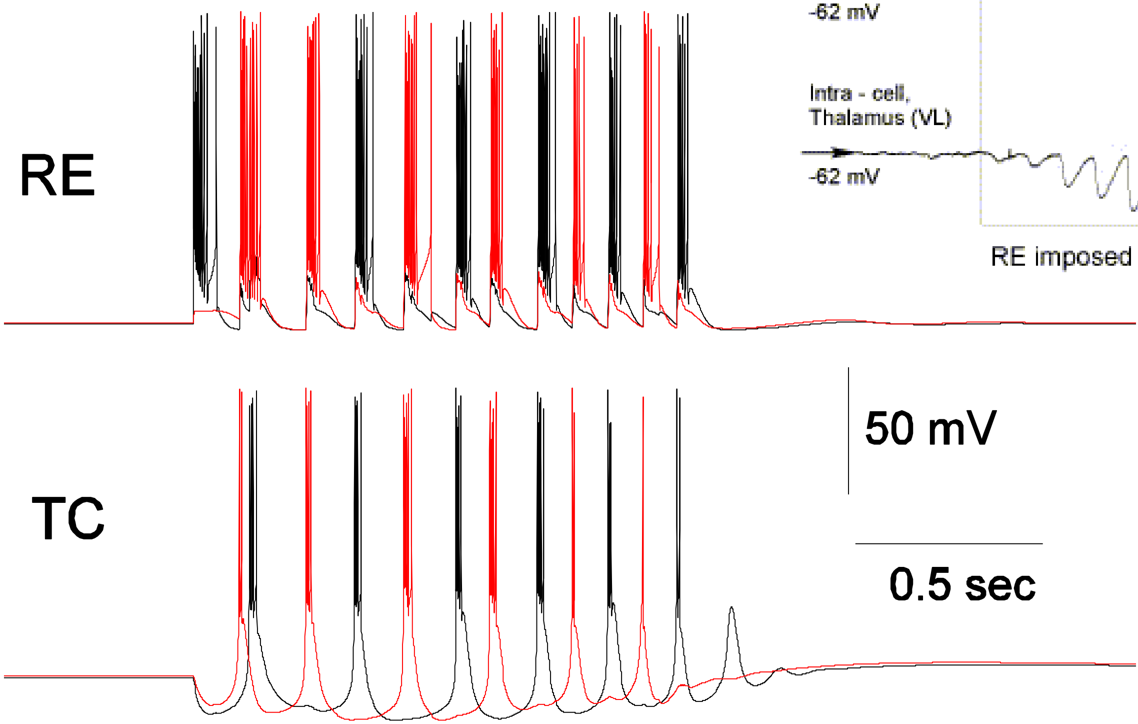
Timofeev, Bazhenov, Seigneur, Sejnowski, Jasper's basic mechanisms of the epilepsies, 2012

Sleep spindle oscillations



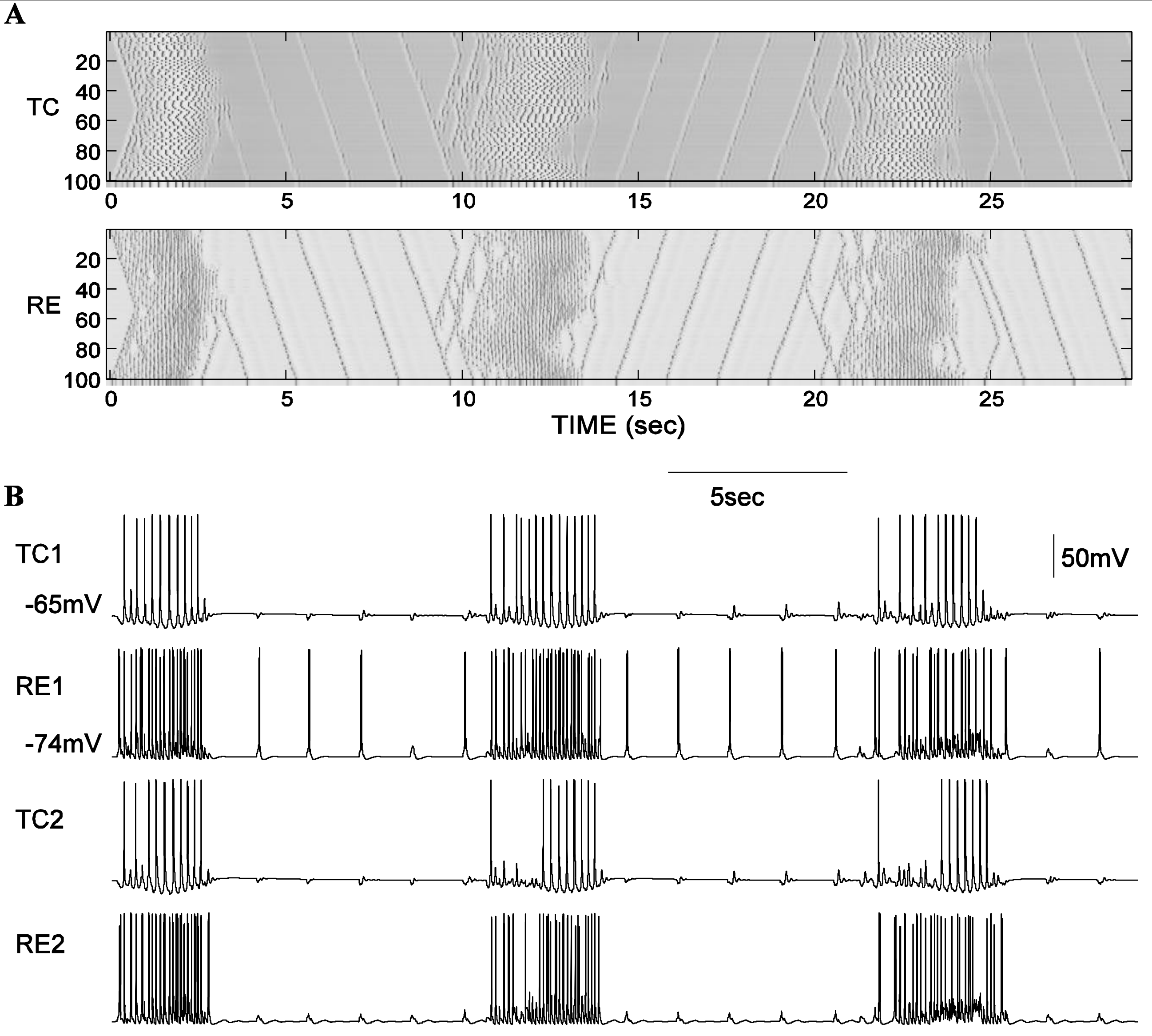
Inhibitory cells





Timofeev and Bazhenov, 2005

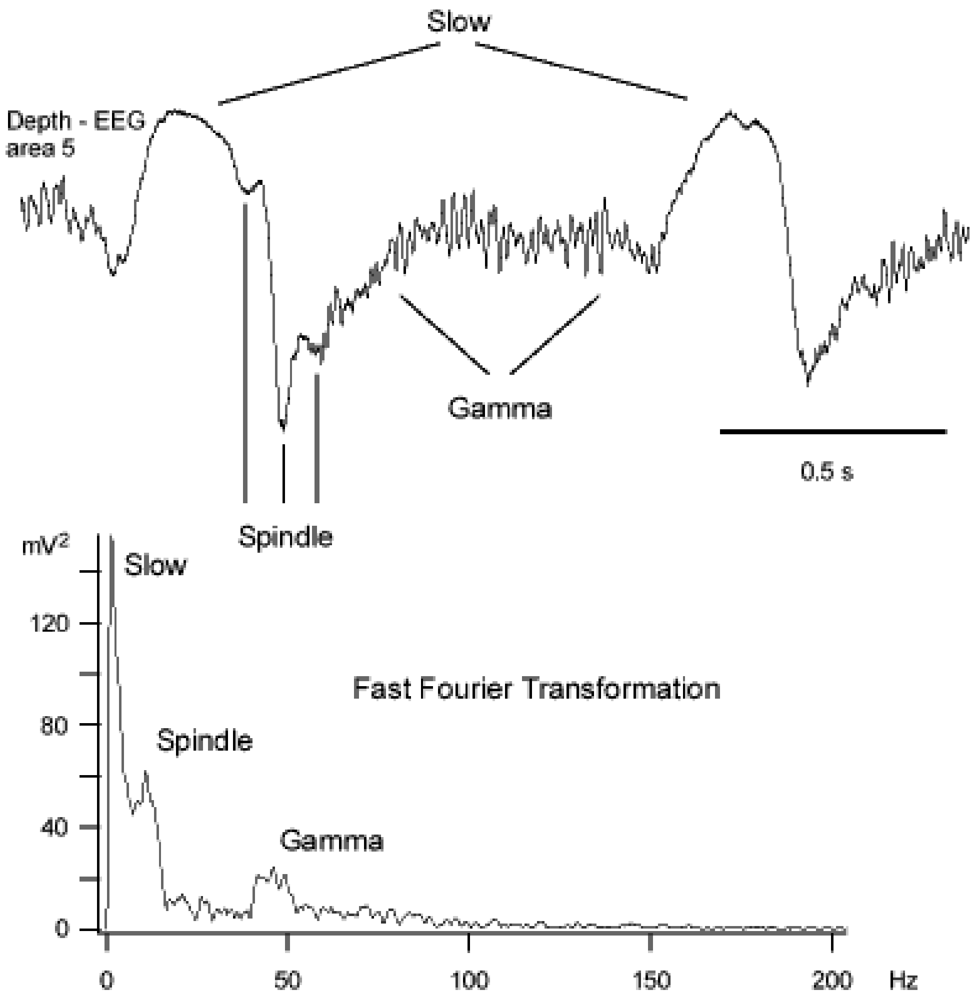
Spindle sequences in RE-TC network



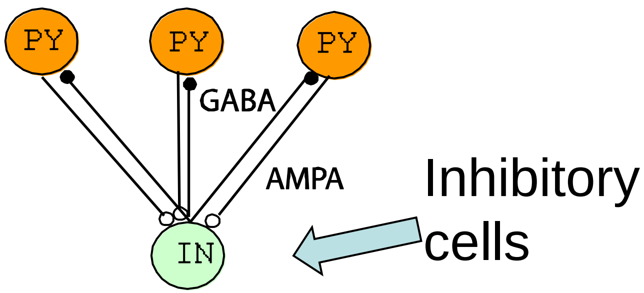
Bazhenov et al, J Neurophys, 2000;
Bonjean at al., J Neurosci 2011, 2012

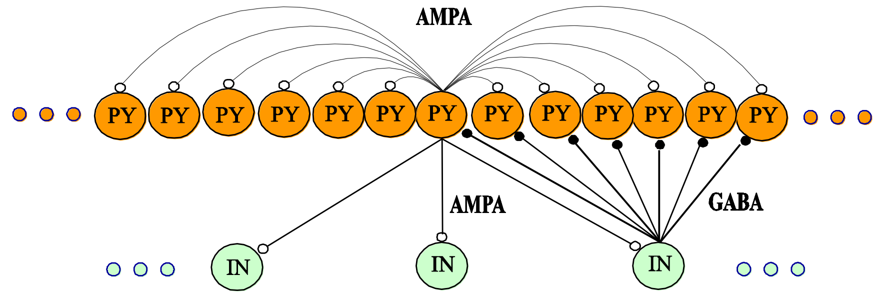
Beta-gamma oscillation

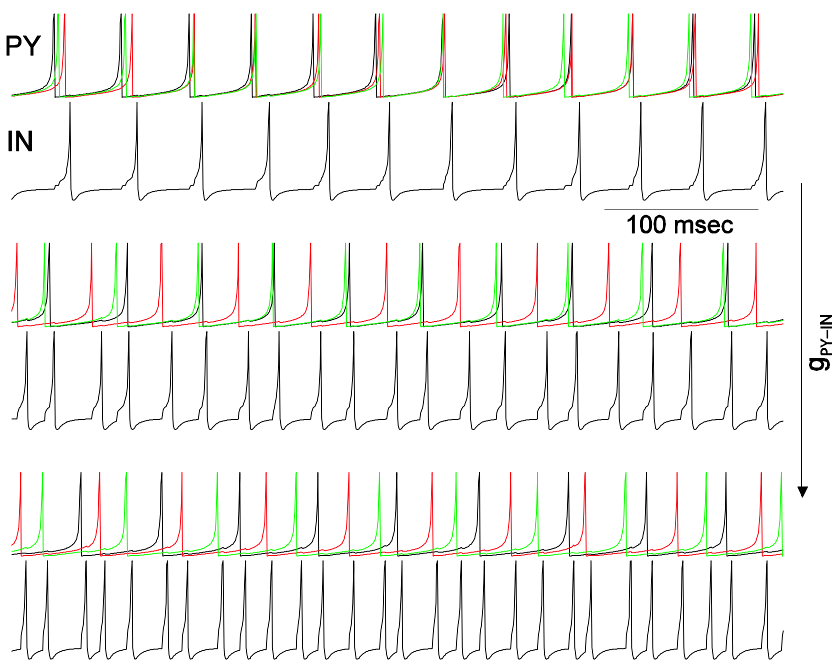
The waking state of the mammalian brain is characterized by the predominance of frequencies in the beta (15-30 Hz) and gamma (30-80 Hz) ranges. During slow-wave sleep the fast rhythms follow the onset of depth-negative EEG wave.

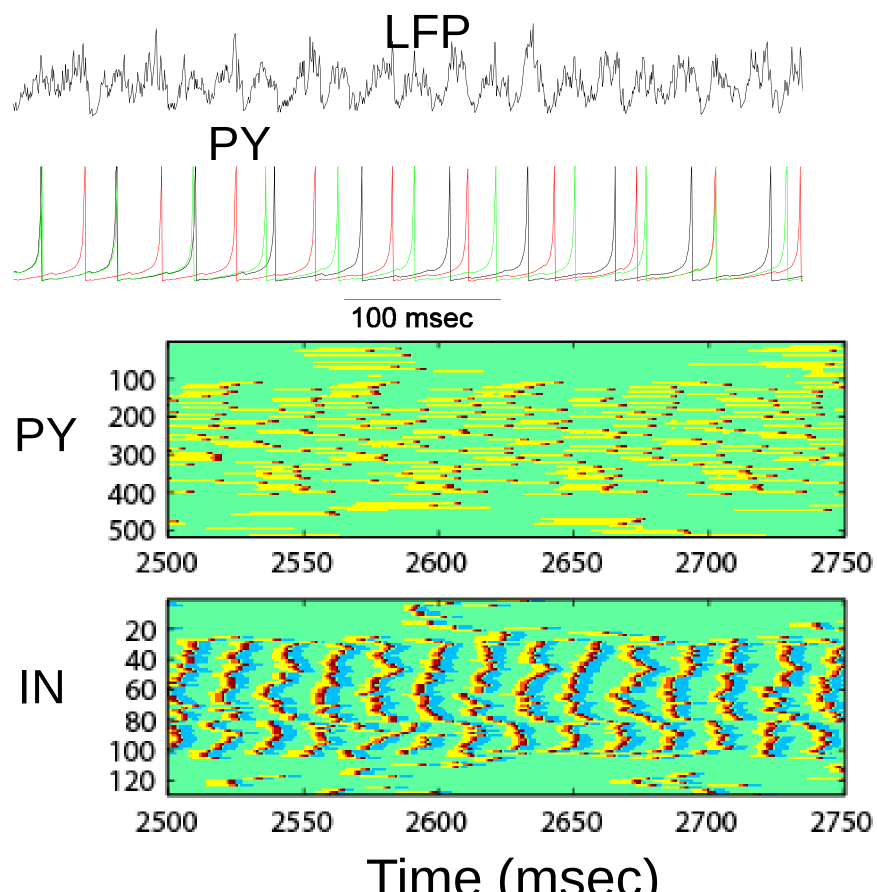


Mechanisms of persistent gamma



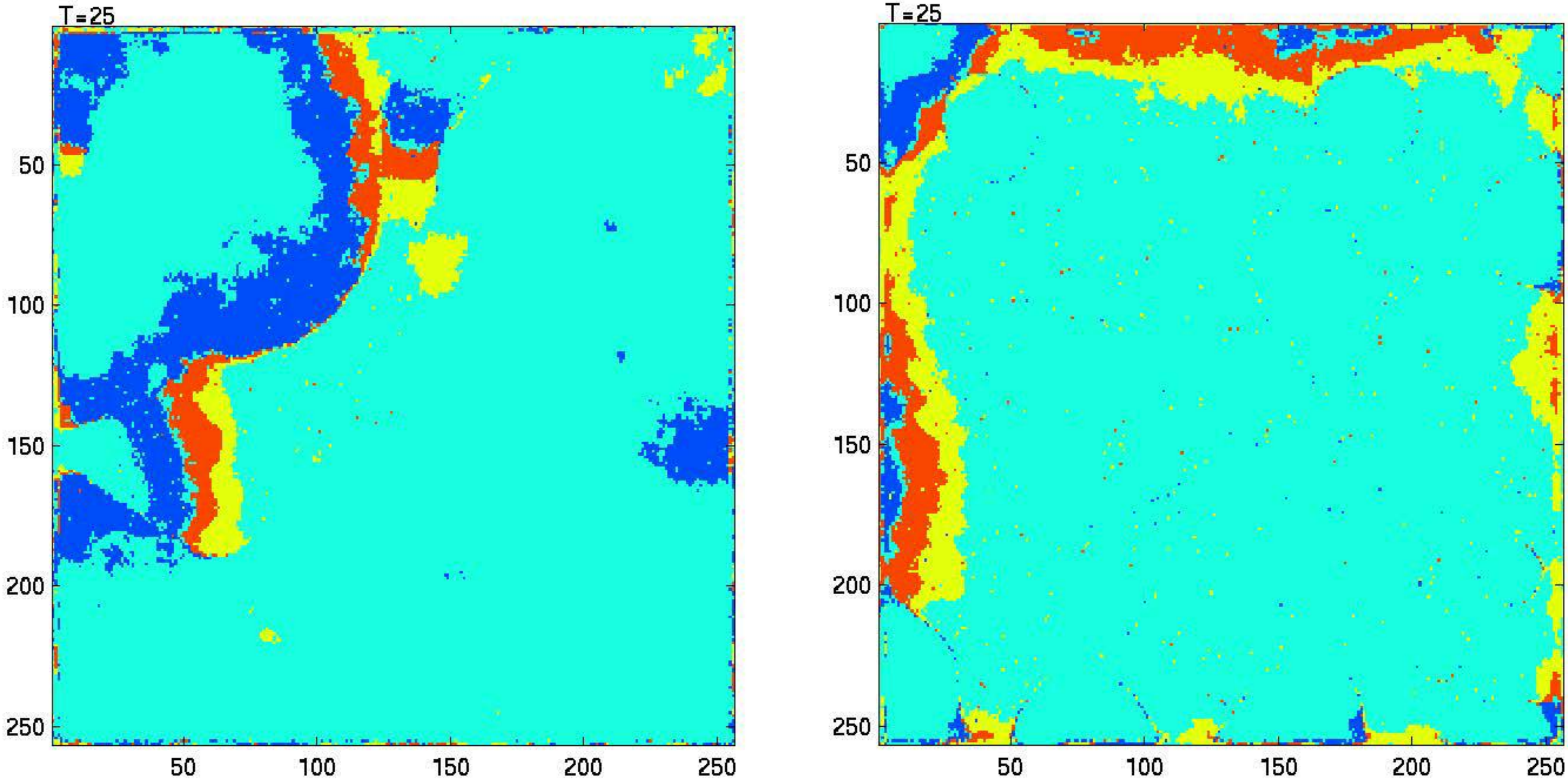






Bazhenov & Rulkov, 2006

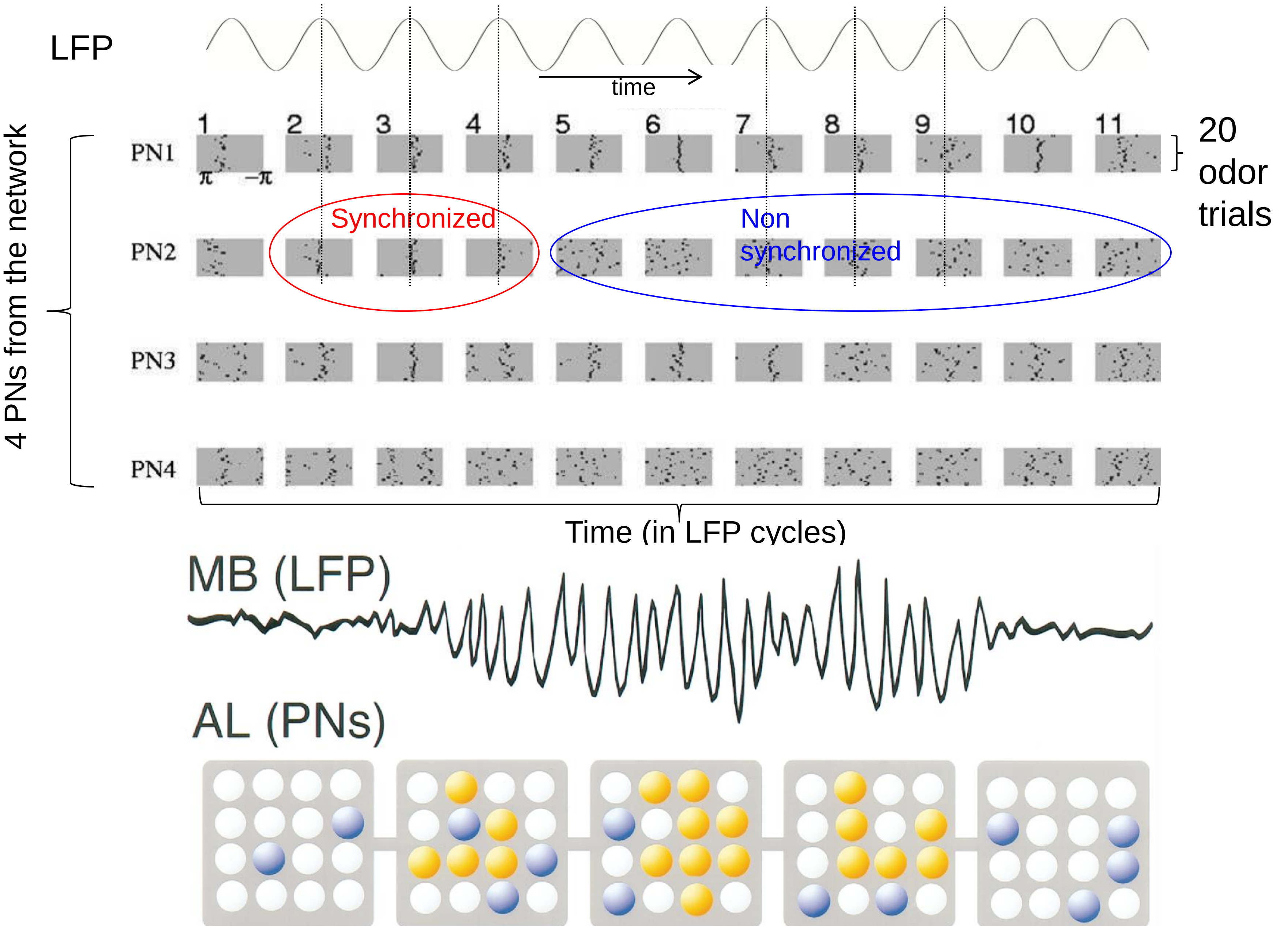
Network dynamics can be quite complex



In many systems feedback inhibition can synchronize spike timing of postsynaptic cells.

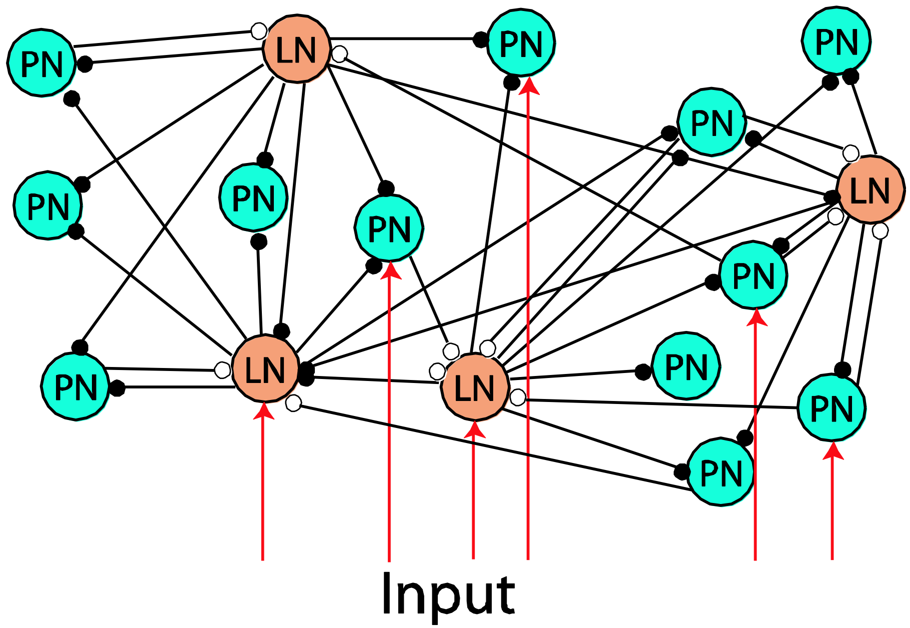
What is happening in the locust AL seems to be more complex: Different PNs become synchronized at specific times during odor stimulation – transient PN synchronization

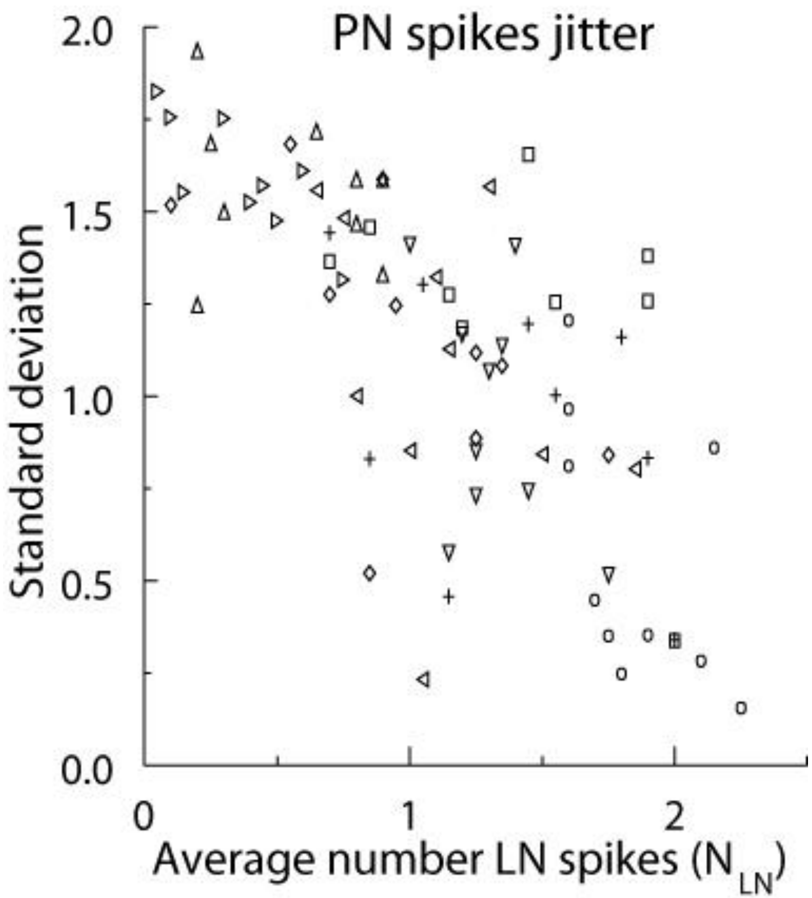
Transient synchronization of olfactory neurons



In the locust AL different PNs become synchronized at different times during odor stimulation – transient PN synchronization

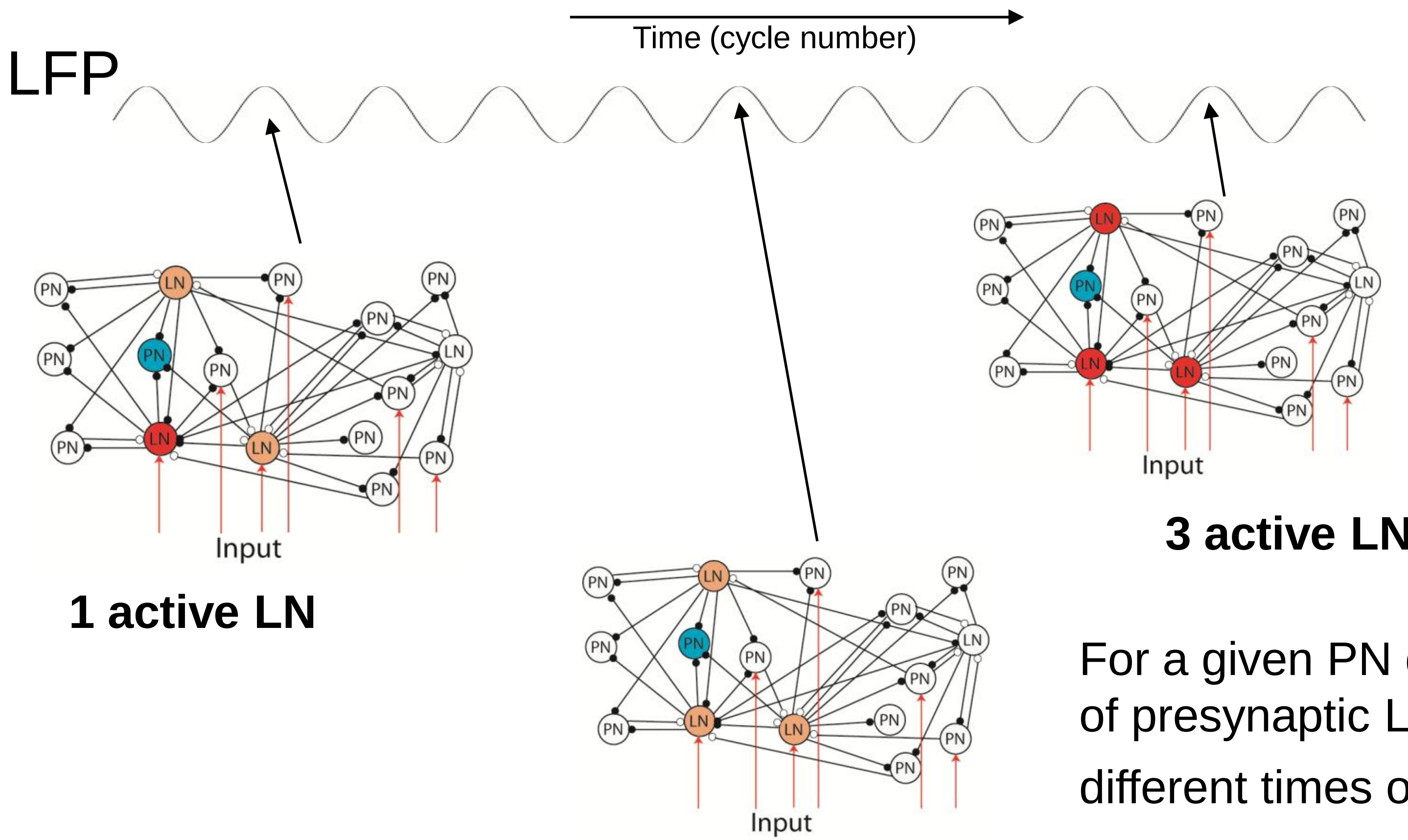
PNs are synchronized when they receive strong enough inhibition from their LNs. The strength of inhibition may changes over time.





Different PNs receive input from different subsets of LNs

LN-mediated inhibition to specific PN changes over time mediating transient PN synchronization



1 active LN

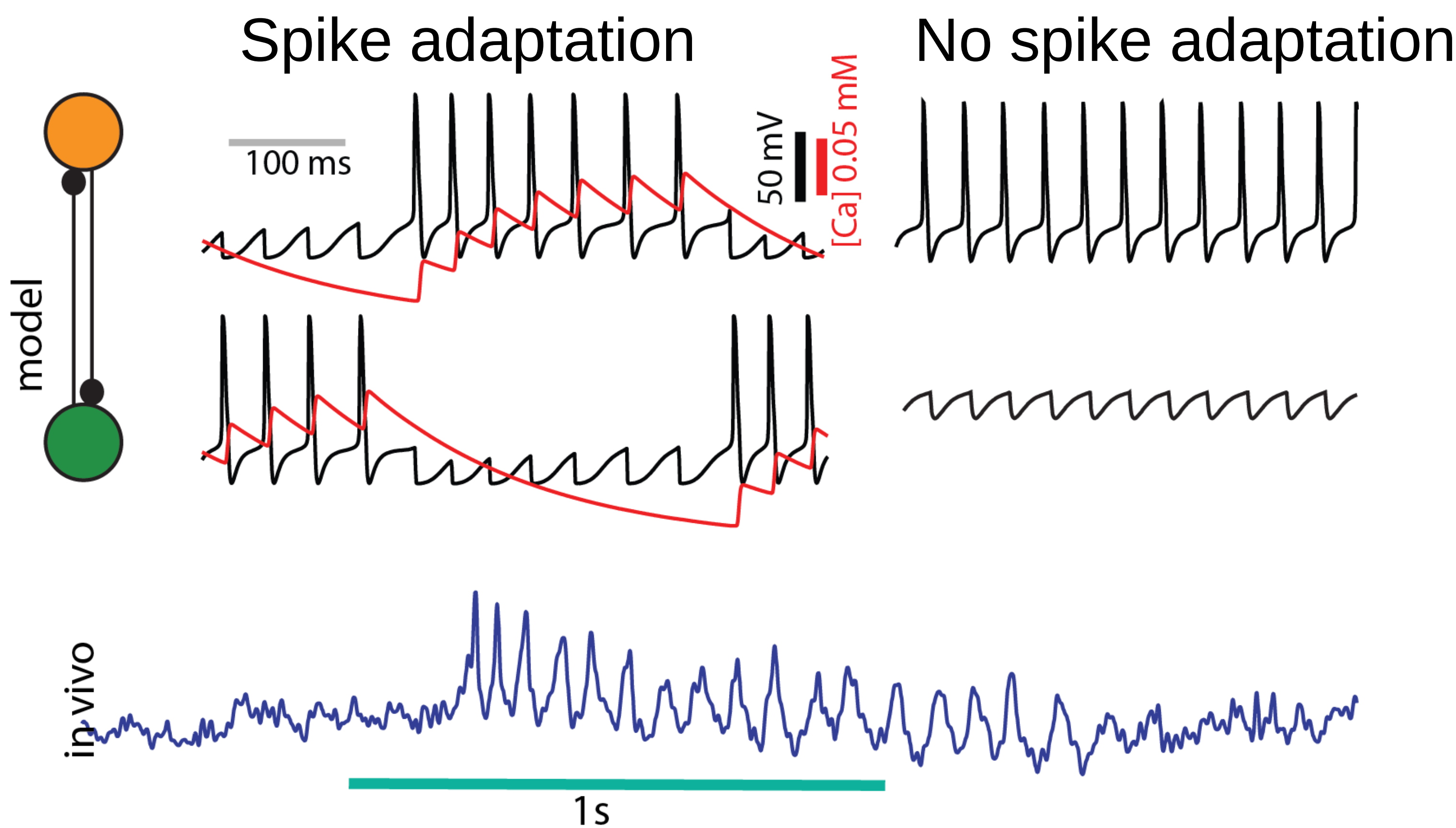
No active LNs

3 active LNs

For a given PN different number of presynaptic LNs is active at different times of odor stimulation

GABAergic input mediated by local interneurons (LNs) mediates PN synchronization and the transient nature of PN synchronization is linked to variations in inhibitory drive from LNs over the duration of a response.

Simple network with 2 inhibitory neurons



Spike adaptation is responsible for active states alternation

Assisi, Stopfer, Bazhenov Neuron, 2010

Dimensionality reduction

$$\tau \frac{dA_i}{dt} = c \cdot f_i - A_i,$$

$$f_i = F_0\left(I_i^{ext} - \sigma A_i\right),$$

$$\tau \frac{dA_j}{dt} = - A_j,$$

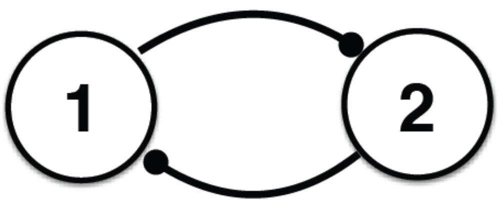
$$f_j = 0,\ j = 1,..,N,\ j \neq i$$

To describe dynamics of the inhibitory network, we can define low-dimensional phenomenological system for a network of globally pulse-coupled oscillators

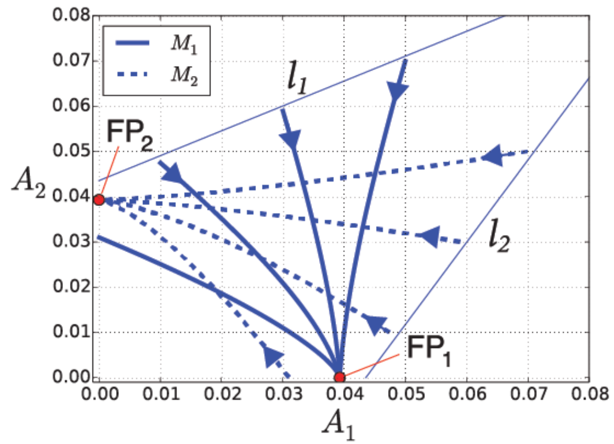
$$A(t) = T_{isi}^{-1}(t) \int_{t-T_{isi}(t)/2}^{t+T_{isi}(t)/2} g^K(t')\,dt'$$

Komarov and Bazhenov, in preparation

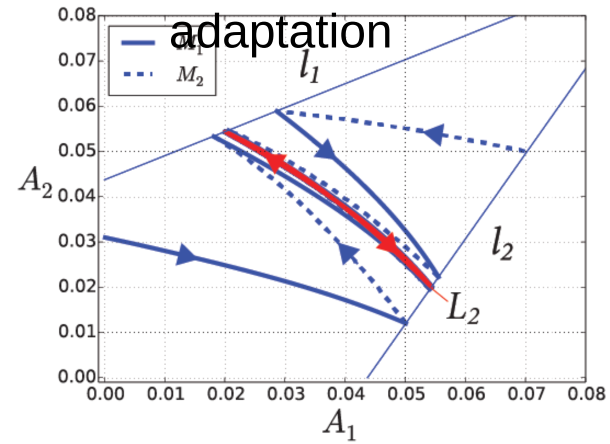
Phase space of 2 neuron model

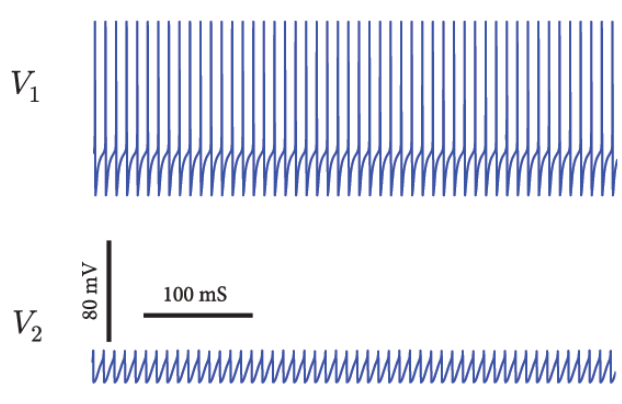


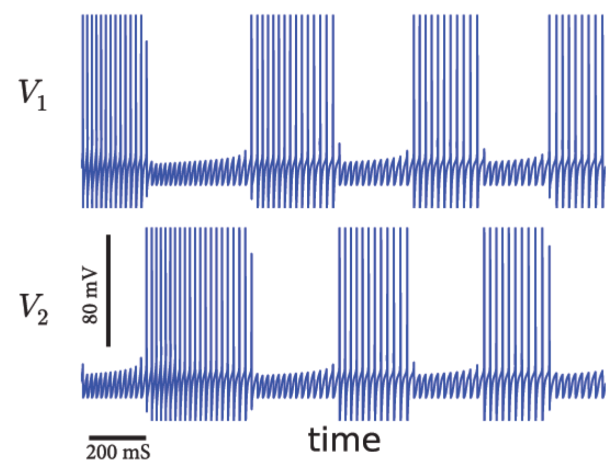
Weak adaptation



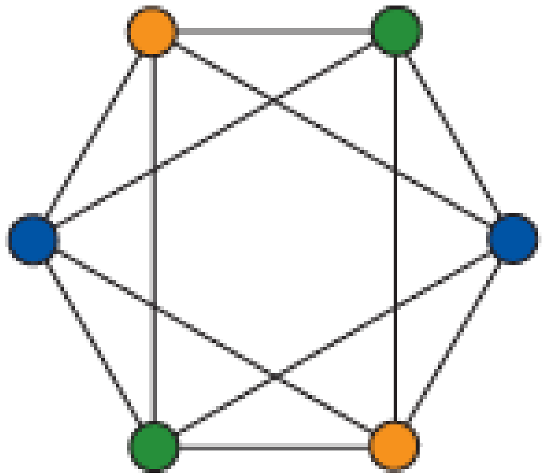
Strong adaptation

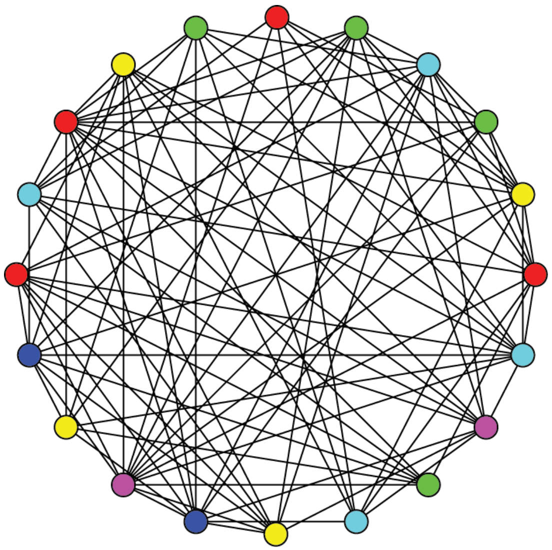






Graph coloring provides an efficient tool to describe dynamics of the inhibitory network



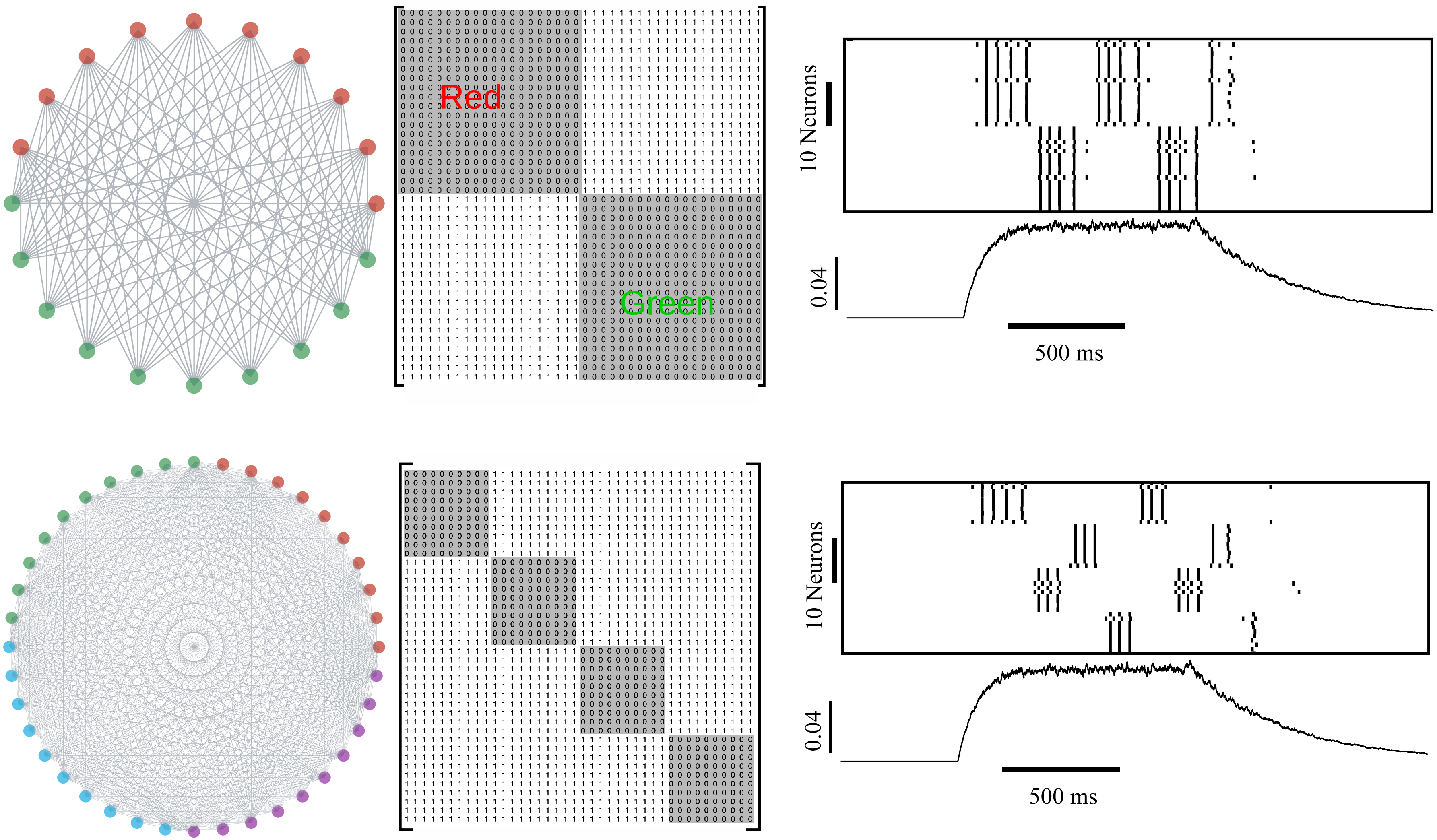


Definition

Graph coloring, specifically, vertex coloring of a graph is the assignment of colors to the nodes of a graph such that no two nodes that share an edge are assigned the same color.

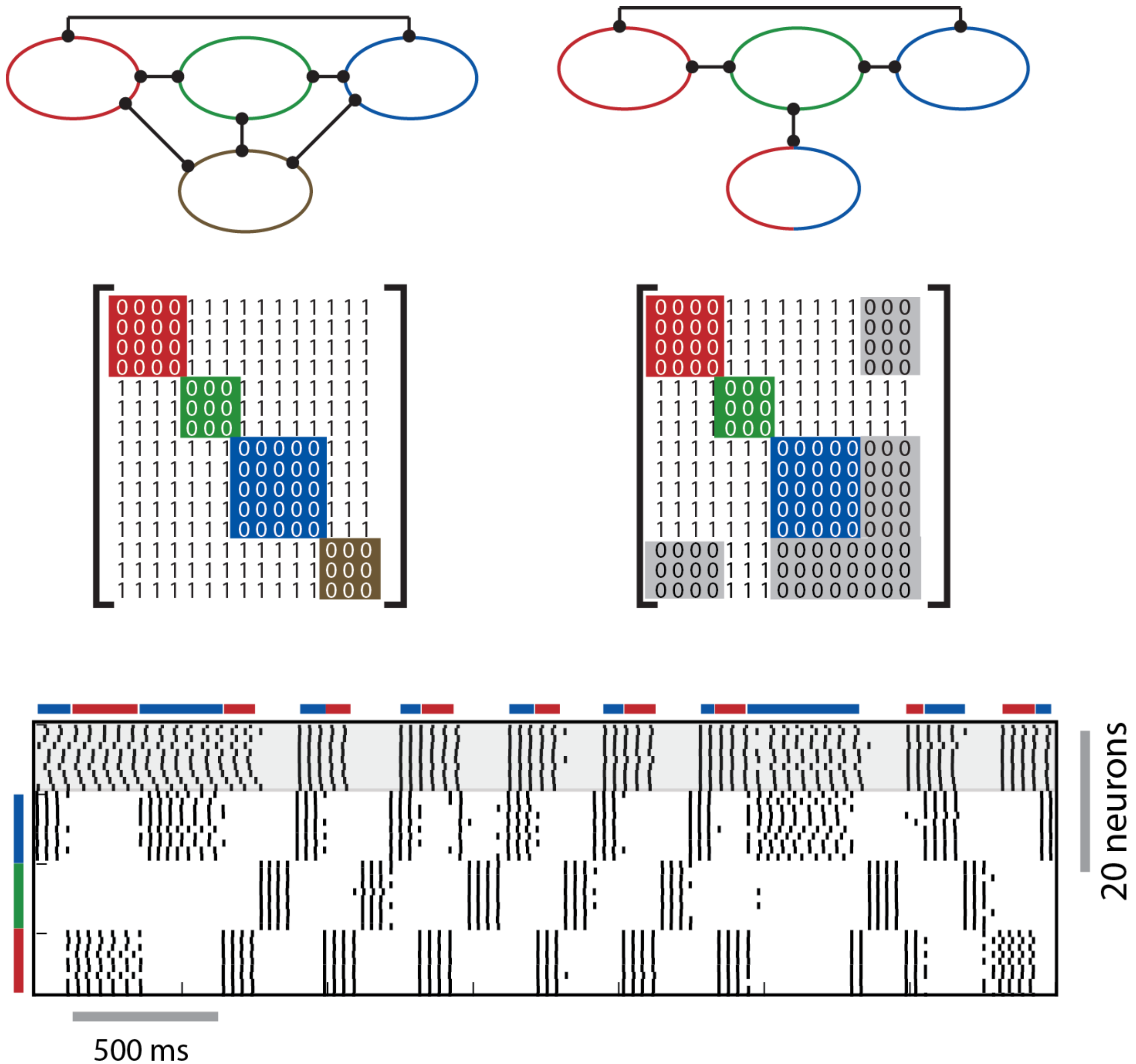
Increasing number of colors preserves the network dynamics

Connectivity matrix



Assisi and Bazhenov, Front Neuroeng, 2012

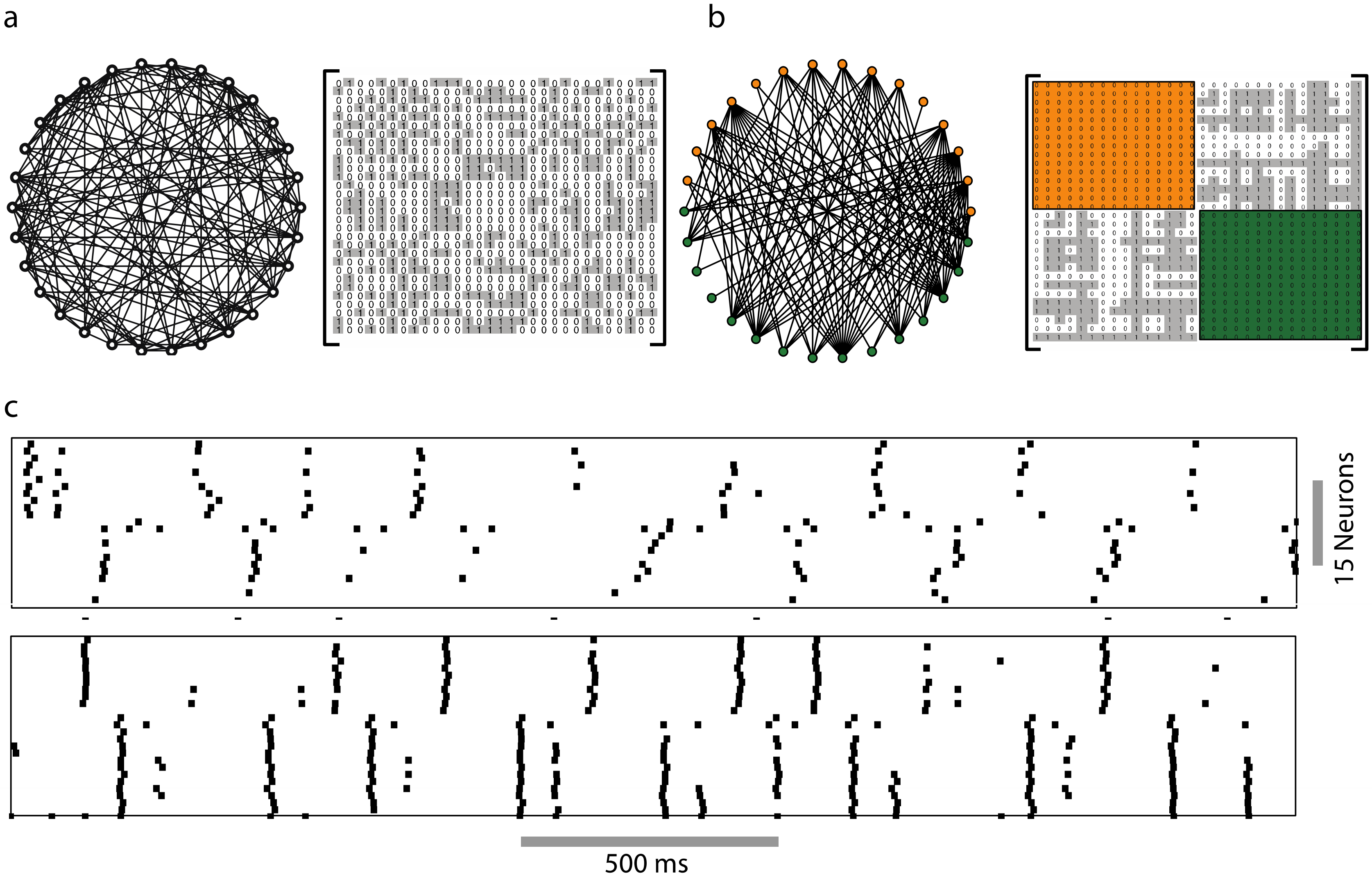
Transient activity in the network with non-unique coloring



When multiple colorings are possible a group of neurons (highlighted) may switch allegiance from one synchronous ensemble (blue) to another (red).

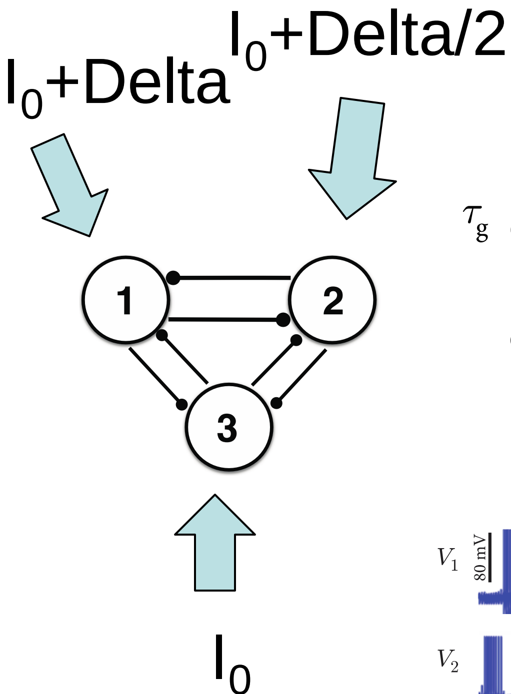
Assisi, et al., Neuron, 2010

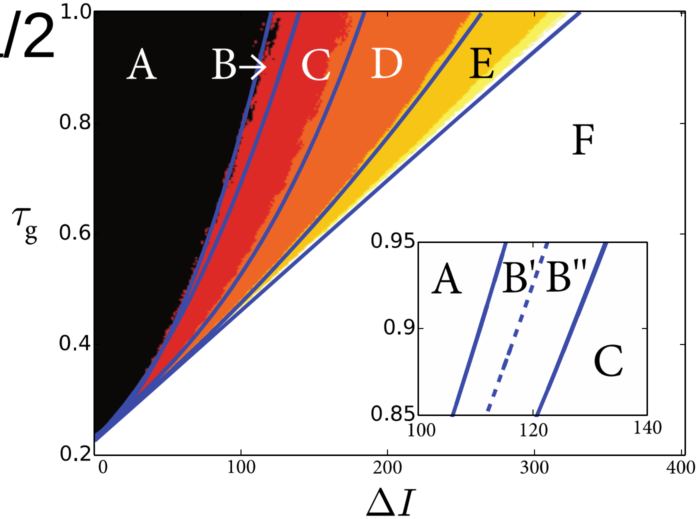
Coloring–based dynamics in “random” neural networks

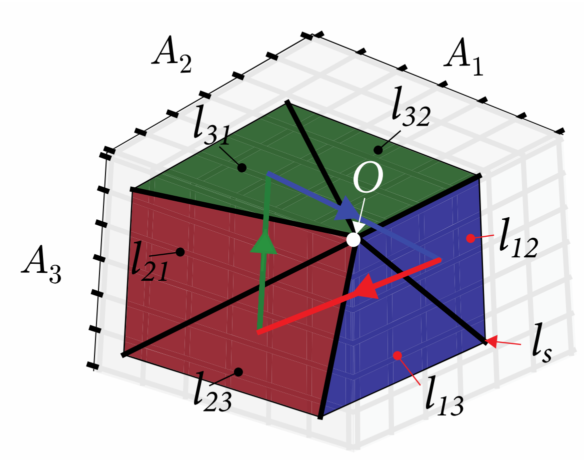


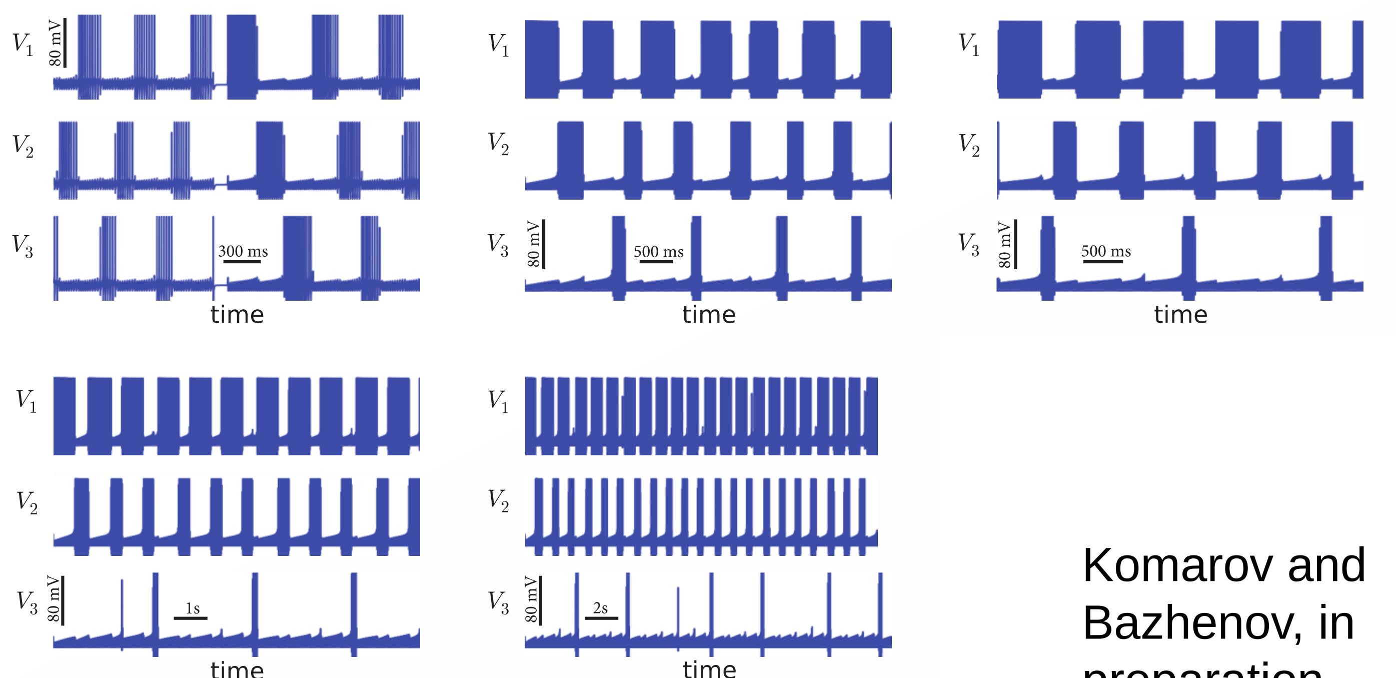
Assisi, et al., Neuron, 2010

Difference in the input to individual LNs leads to different oscillatory patterns



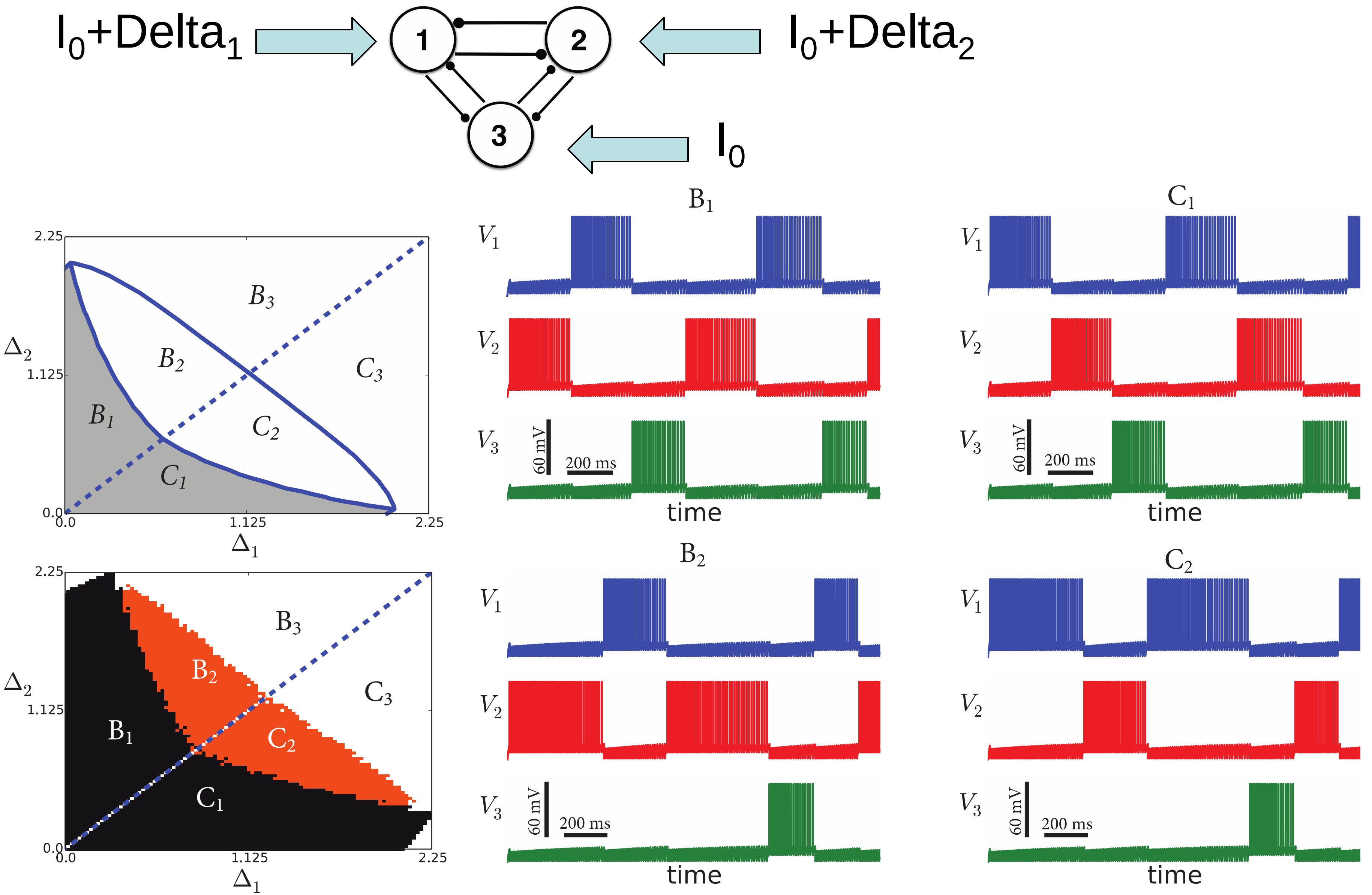




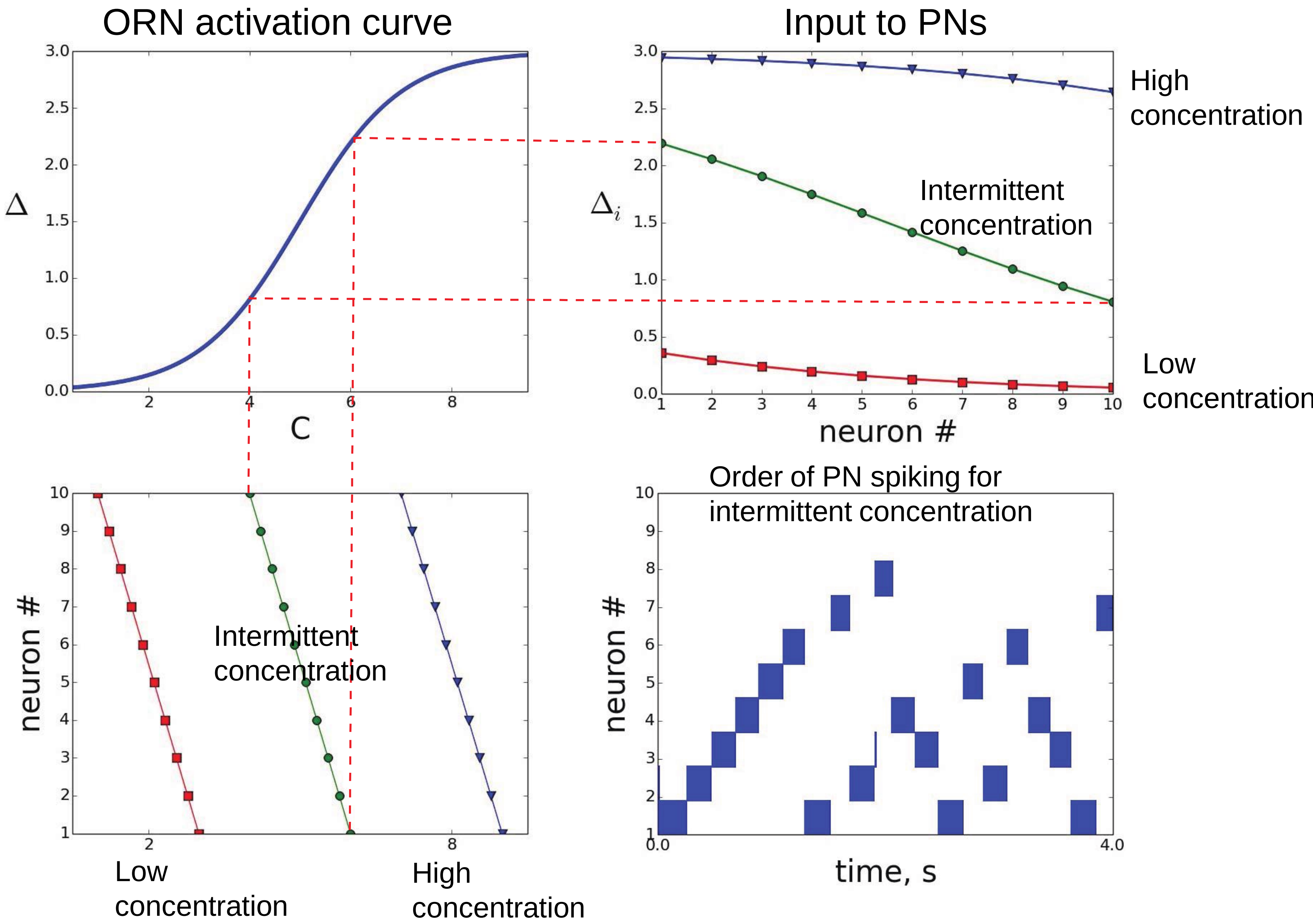


Komarov and Bazhenov, in preparation

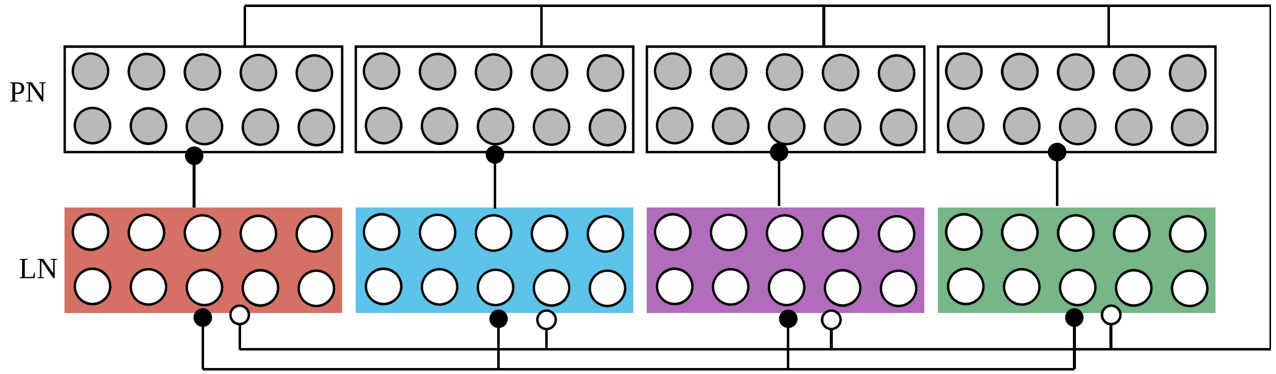
Ranking of the inputs to the circuits predicts order of firing within a sequence



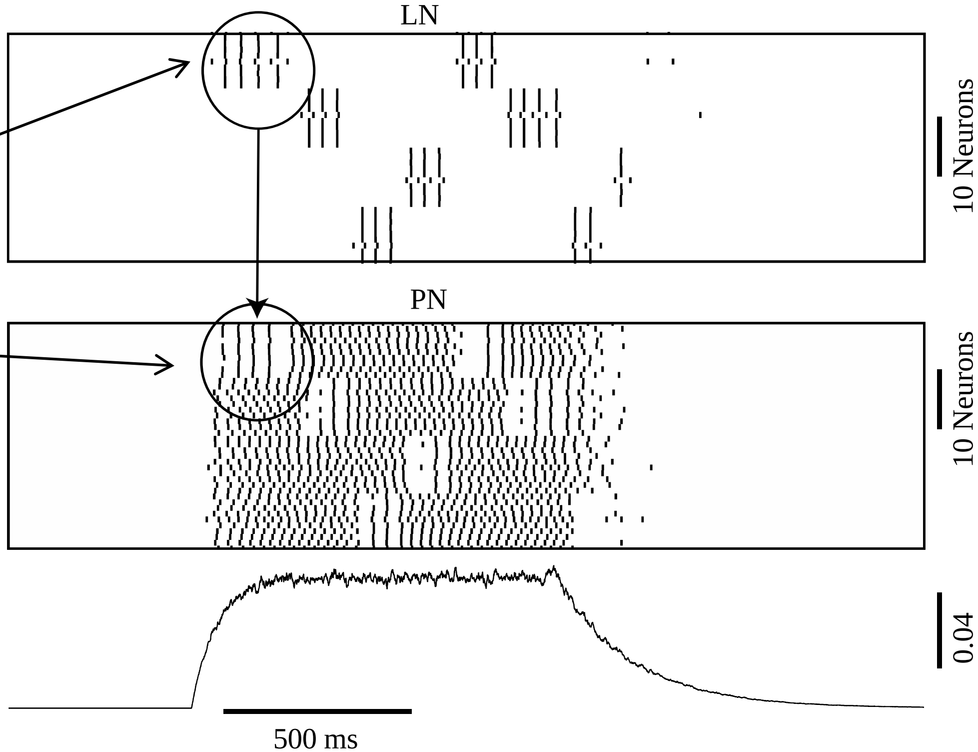
For a given odor concentration different ORNs would show different response intensity



Active LNs synchronize postsynaptic PN at specific times providing a mechanisms of transient PN synchronization



During active phase of presynaptic LNs, a group of postsynaptic PNs is synchronized



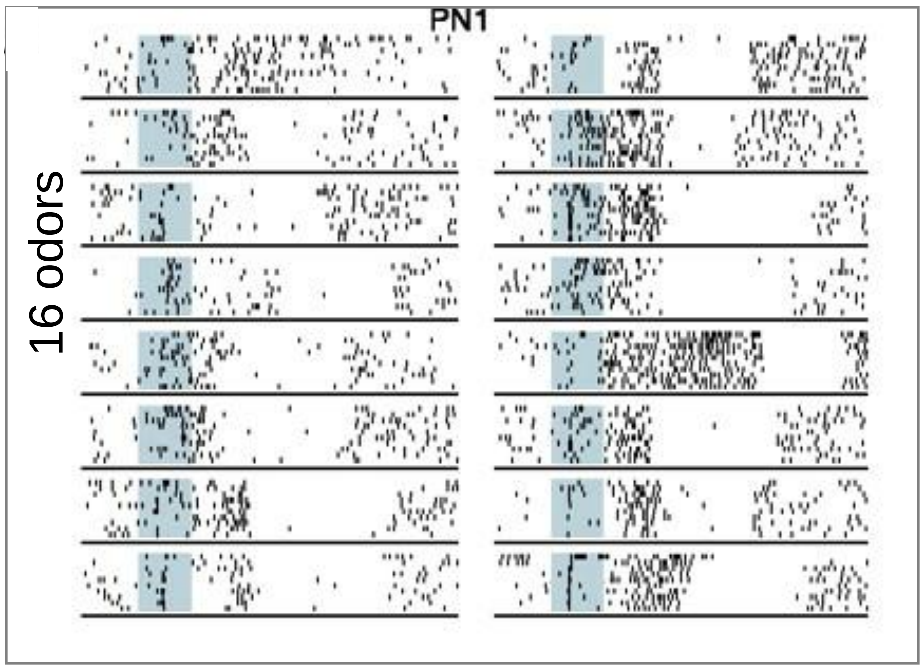
Conclusions

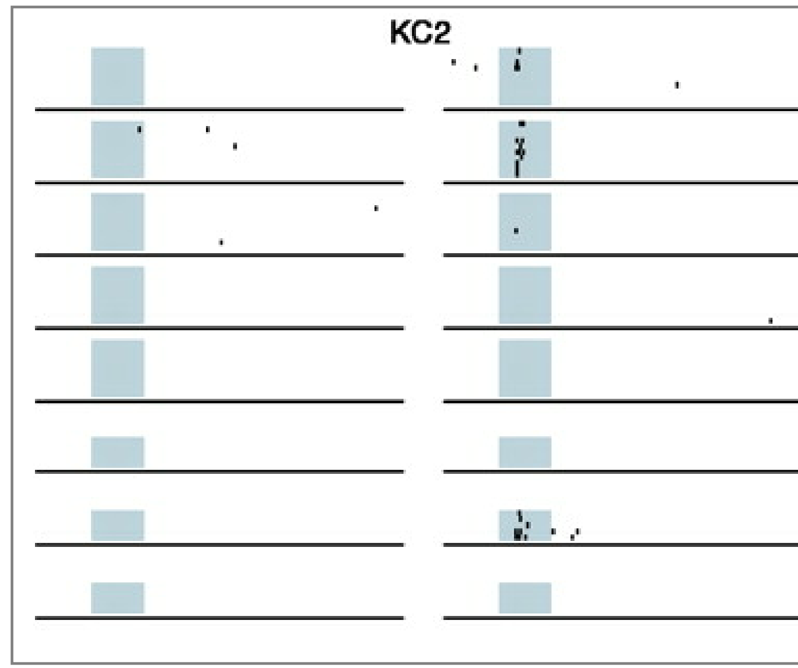
- Feedback inhibition mediated by local interneurons (LNs) provides a mechanism for PN synchronization. Transient nature of PN synchronization is linked to variations in inhibitory drive from LNs over the duration of a response.
- Lateral inhibitory connections between LNs in the AL are responsible for complexity of LN responses during odor stimulation.
- Inhibitory networks with spike-frequency adaptation are able to discriminate different external stimuli configurations.

PNs and KCs odor responses *in vivo*

AL: Individual PNs

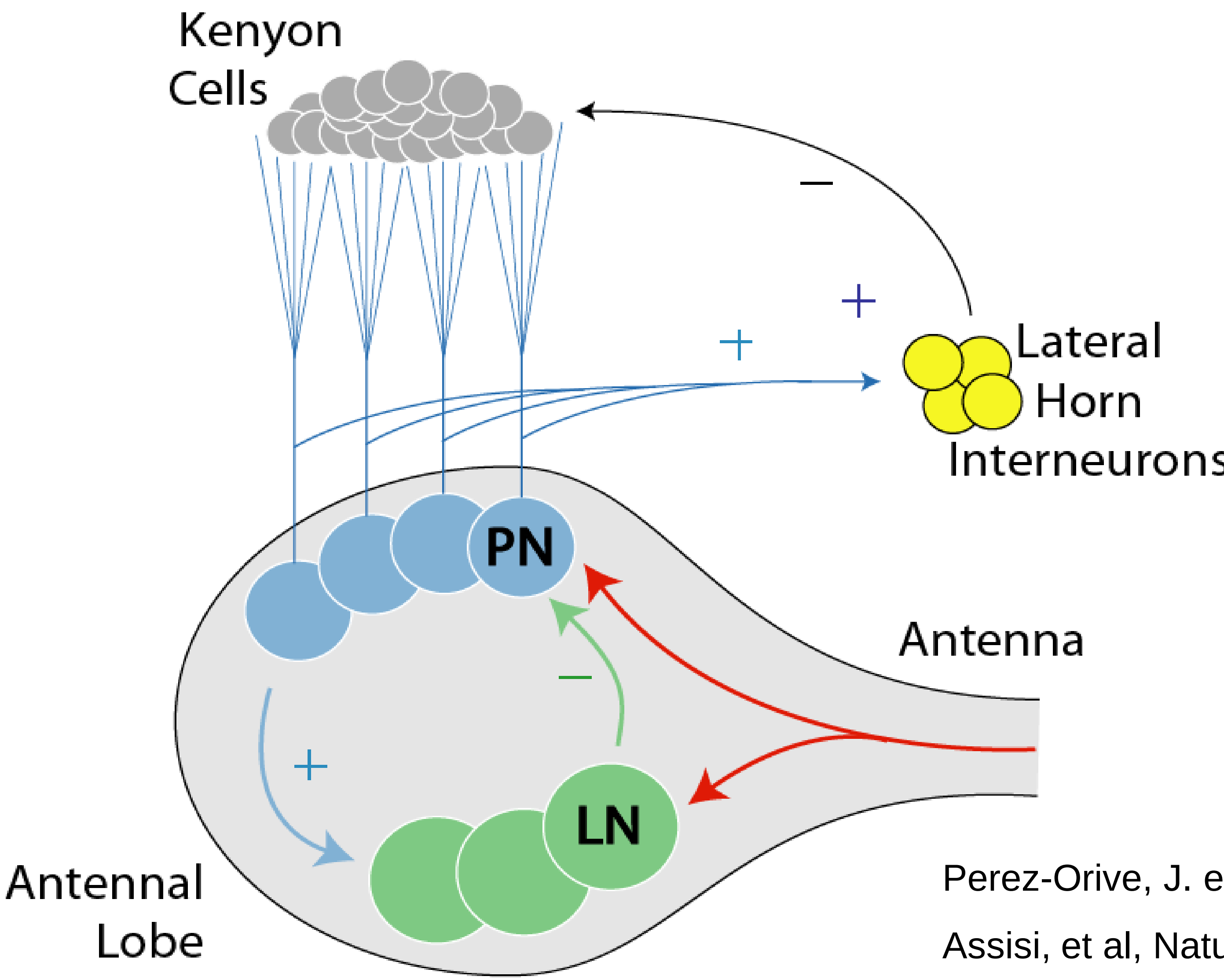
MB: Individual KCs





Perez-Orive et al., *Science* 2002

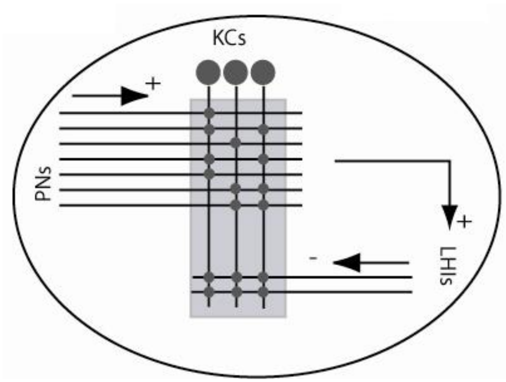
We previously proposed that feed-forward inhibition from LH to MB mediates sparseness of KCs responses



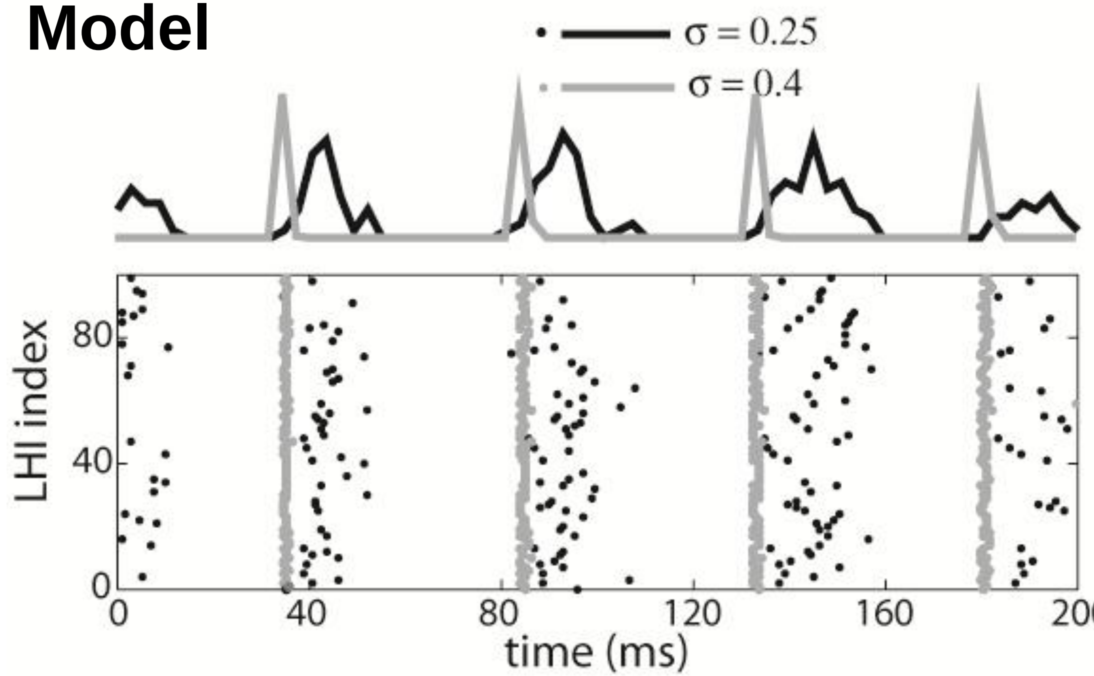
Perez-Orive, J. et al. Science 2002

Assisi, et al, Nature Neurosci, 2007

LH neurons receive PN input and their activity depends on odor concentration



Model

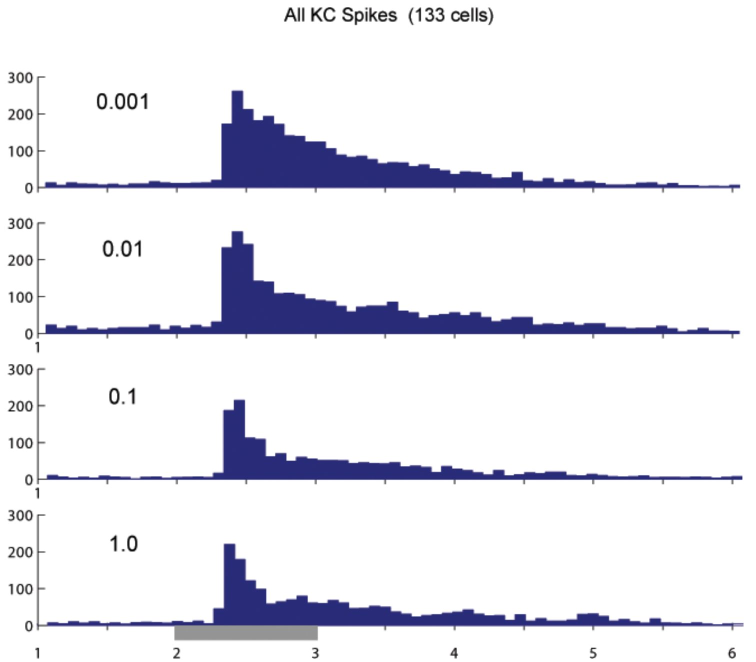


Prediction: As odor concentration increases it advances the timing of the peak of the LHI-mediated inhibitory input thus effectively **reducing the integration window** of the KCs.

Assisi, at al, *Nature Neurosci*, 2007

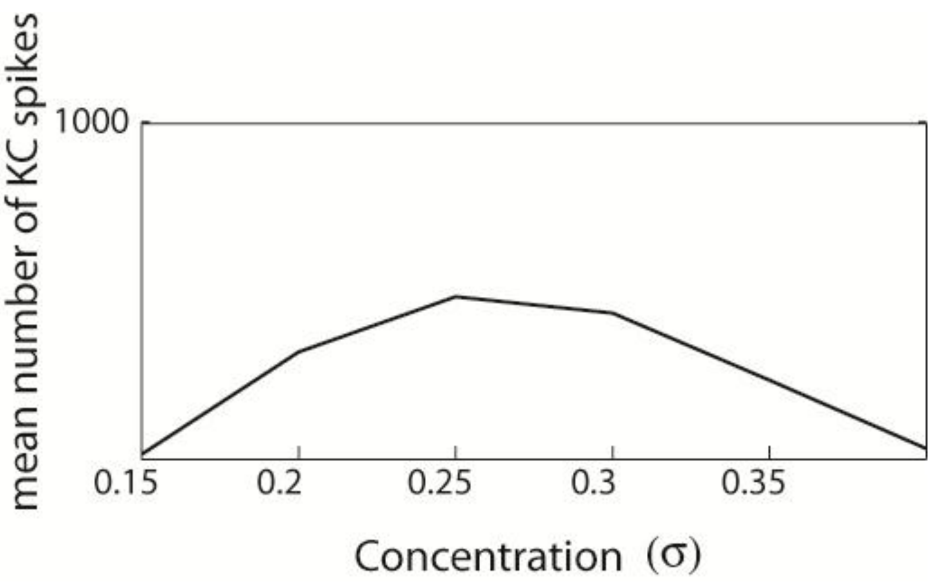
Adaptive inhibition limits MB response at high concentrations

In vivo



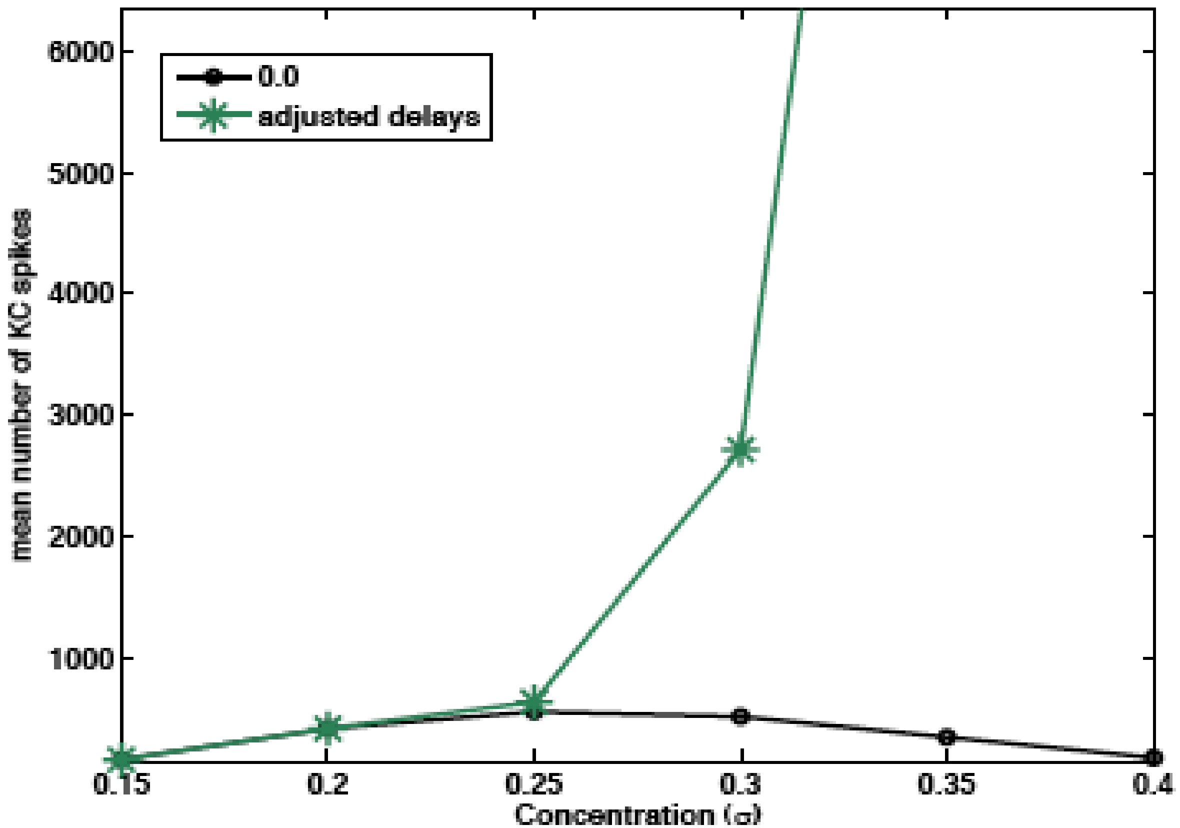
<- In vivo increase of odor concentration leads to decrease of KCs spiking

Model



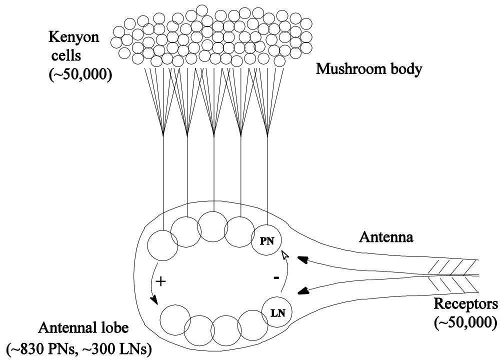
In the model adaptive **->** feedforward inhibition reduces KCs spiking at high concentrations

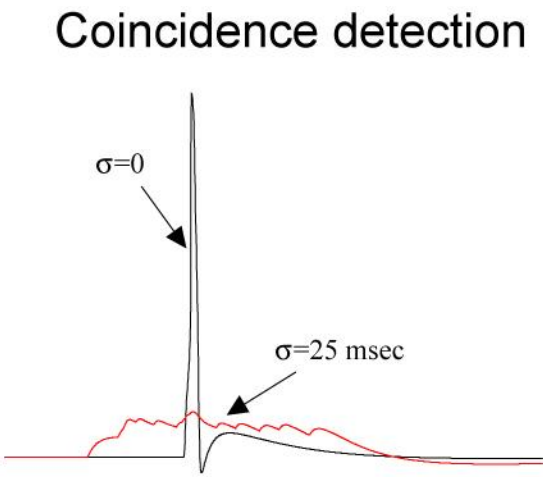
Fixed size integration window does not support sparseness

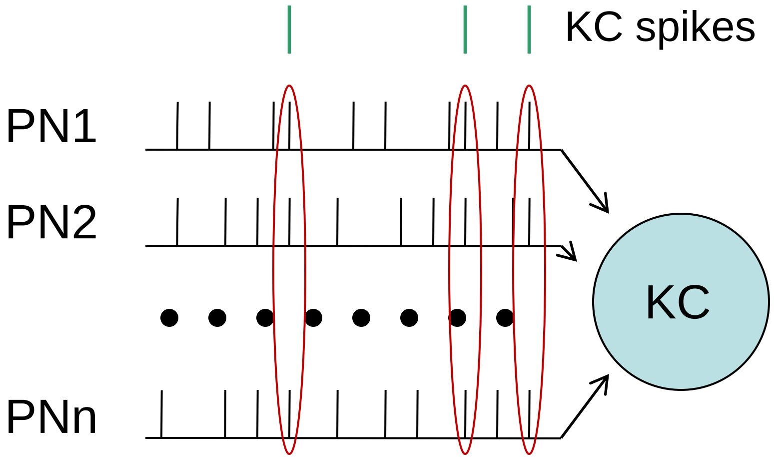


The LHI phase advances as a function of increasing concentration thus controlling the sparseness of KC activity.

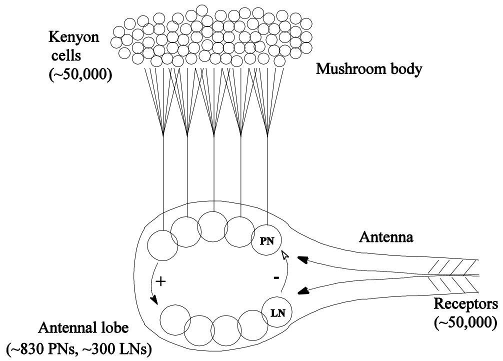
KCs operate as coincidence detectors for **high** odor concentrations

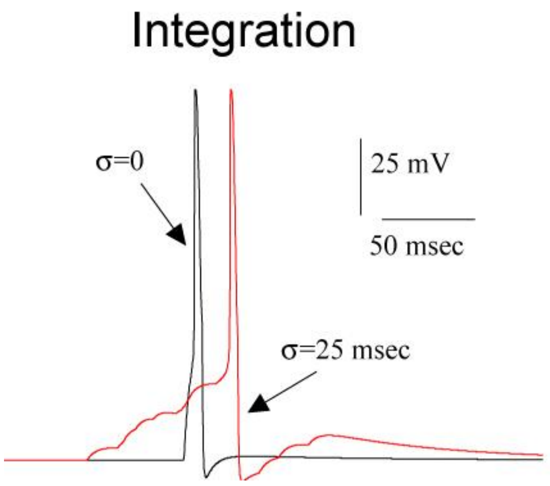


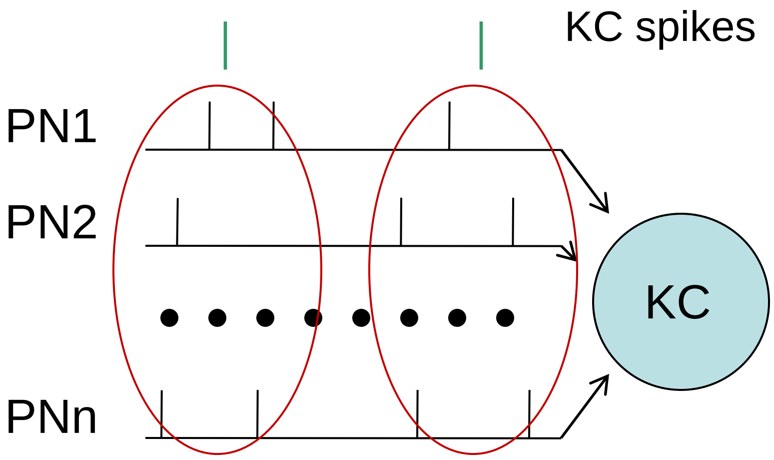




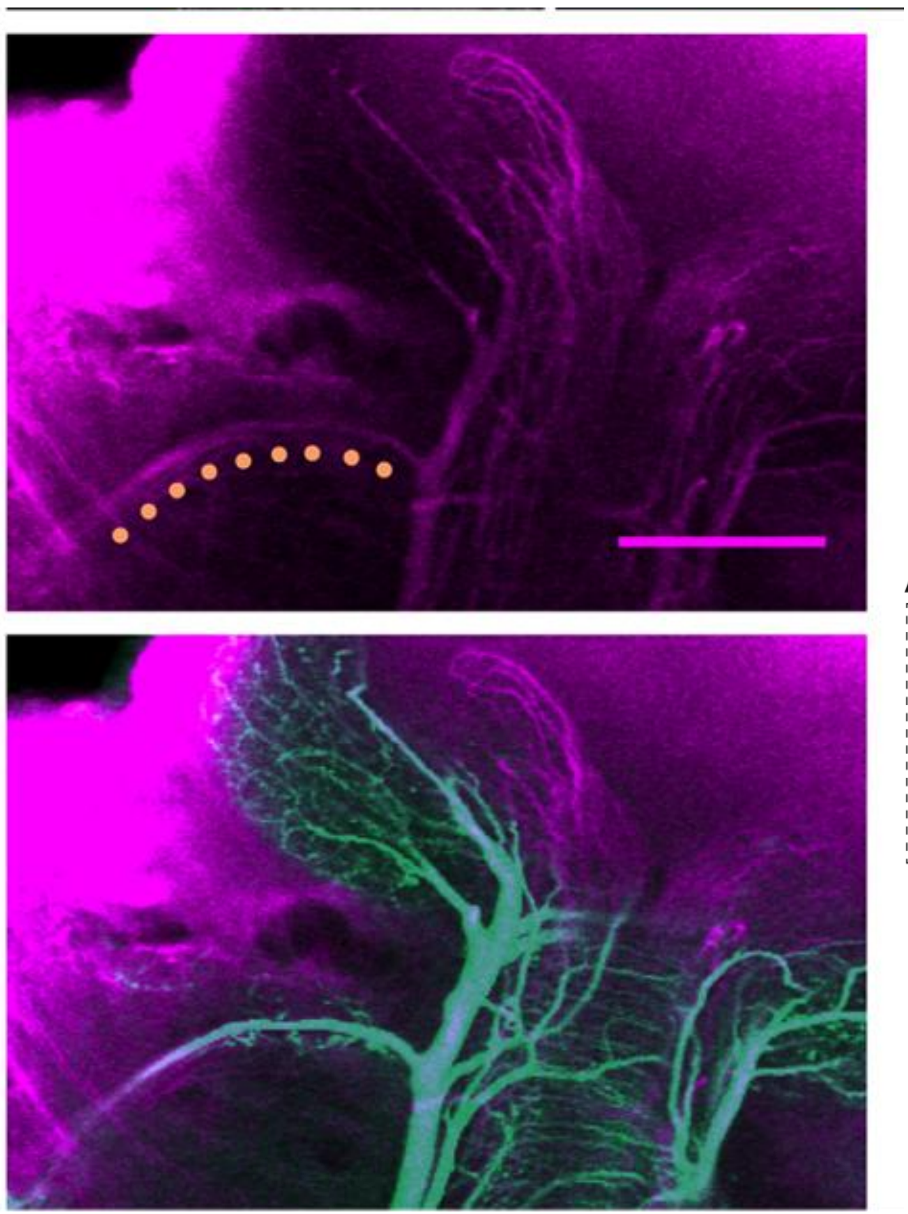
KCs operate as temporal integrators for **low** odor concentrations



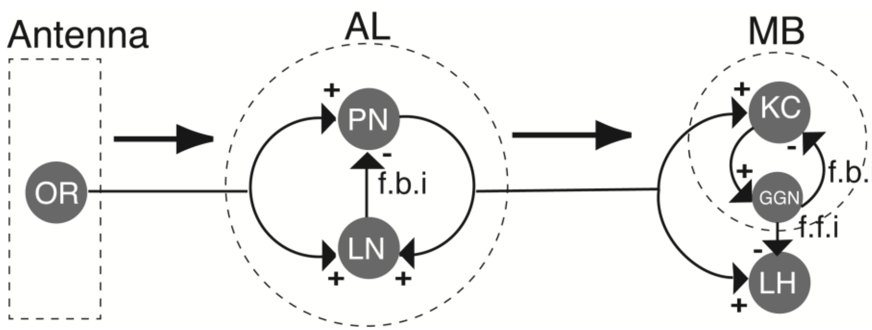




Source of GABAergic inhibition to the MB calyx

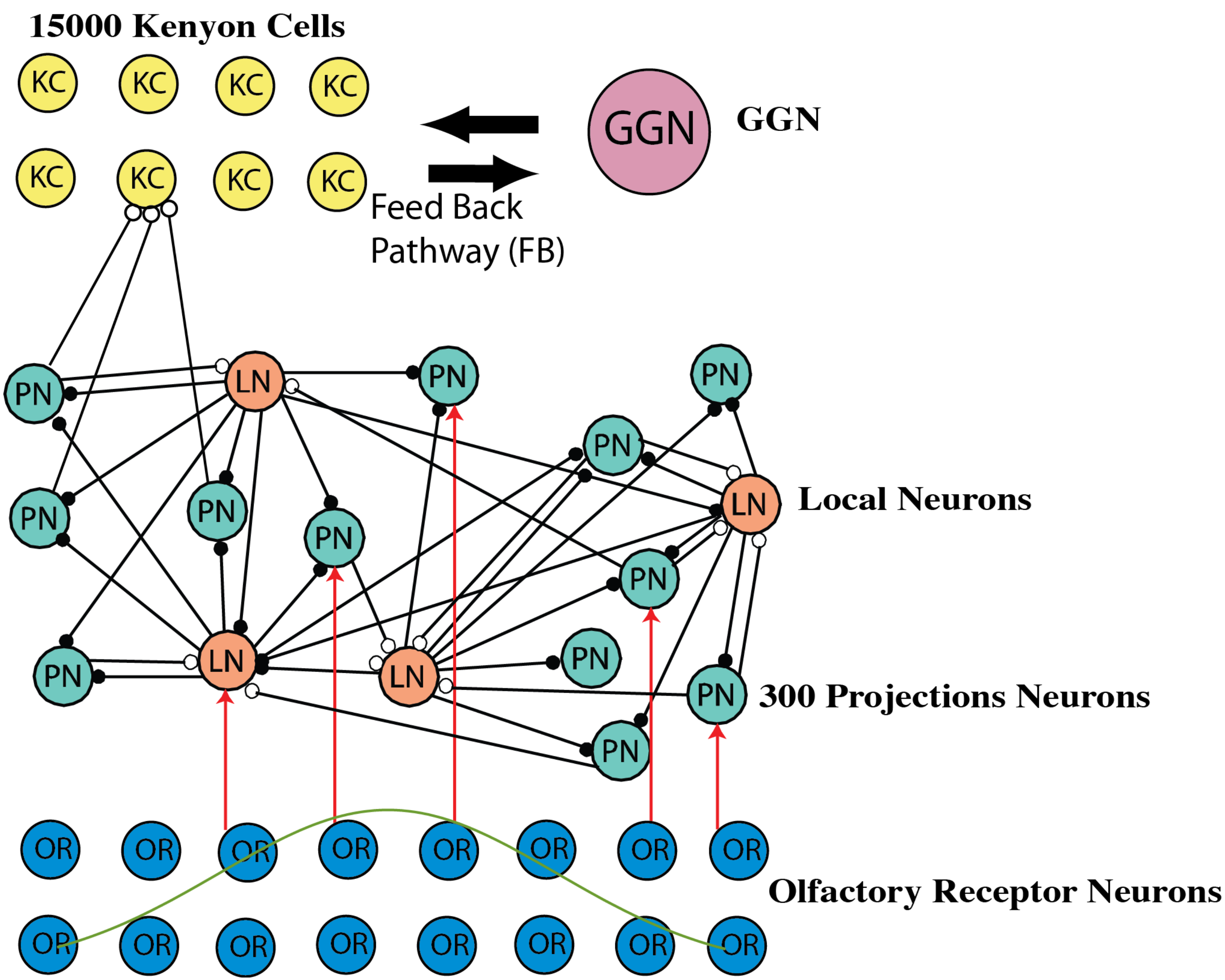


Intracellular fill of GGN shows that GABAergic tract between LH and MB calyx is a branch of GGN

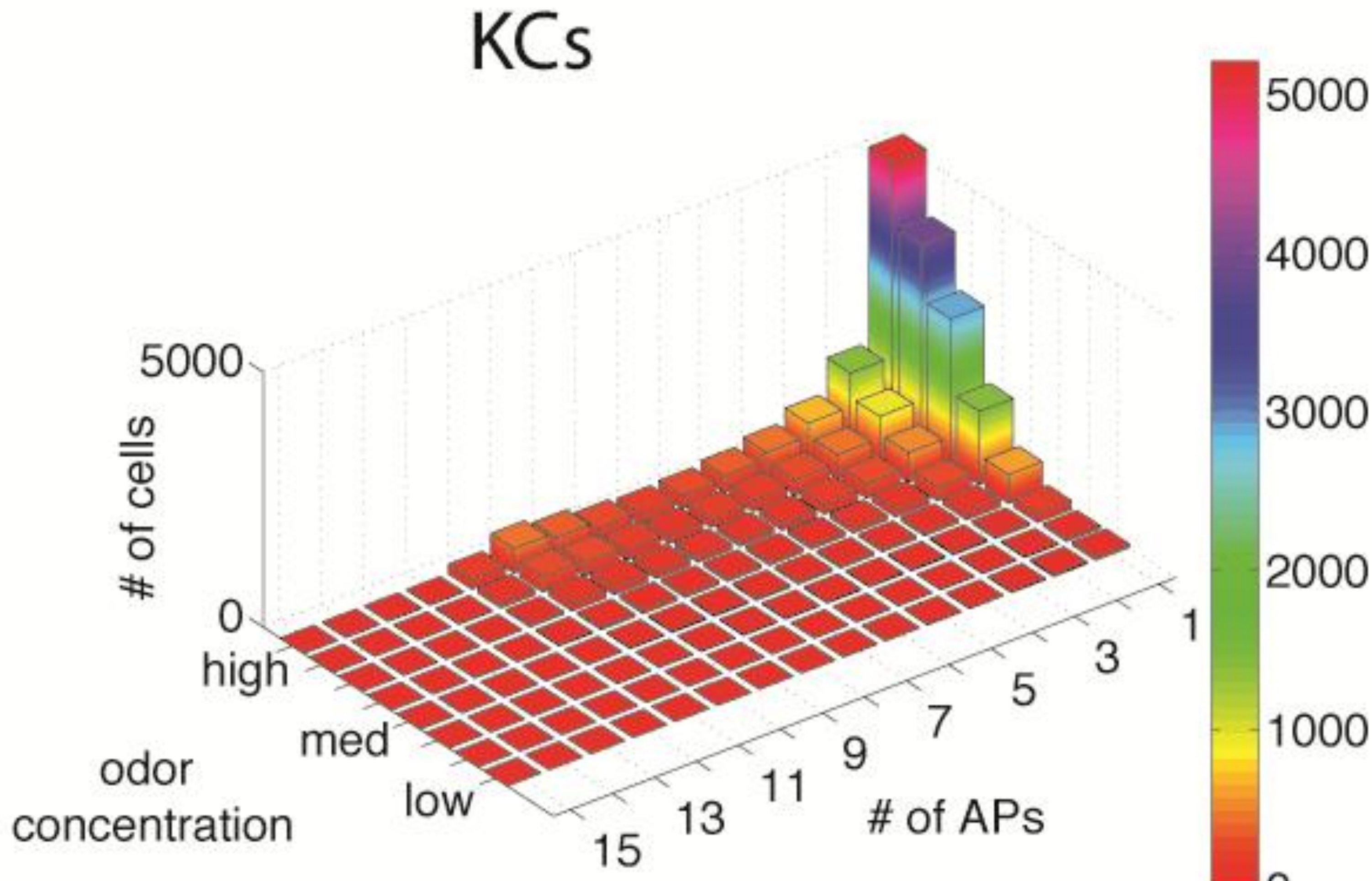


Gupta and Stopfer, J Neurosci, 2012

GGN provides feedback inhibition to KCs that controls sparseness of the odor representation

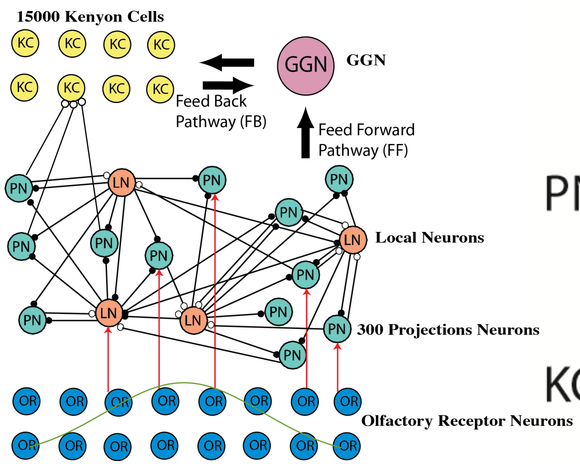


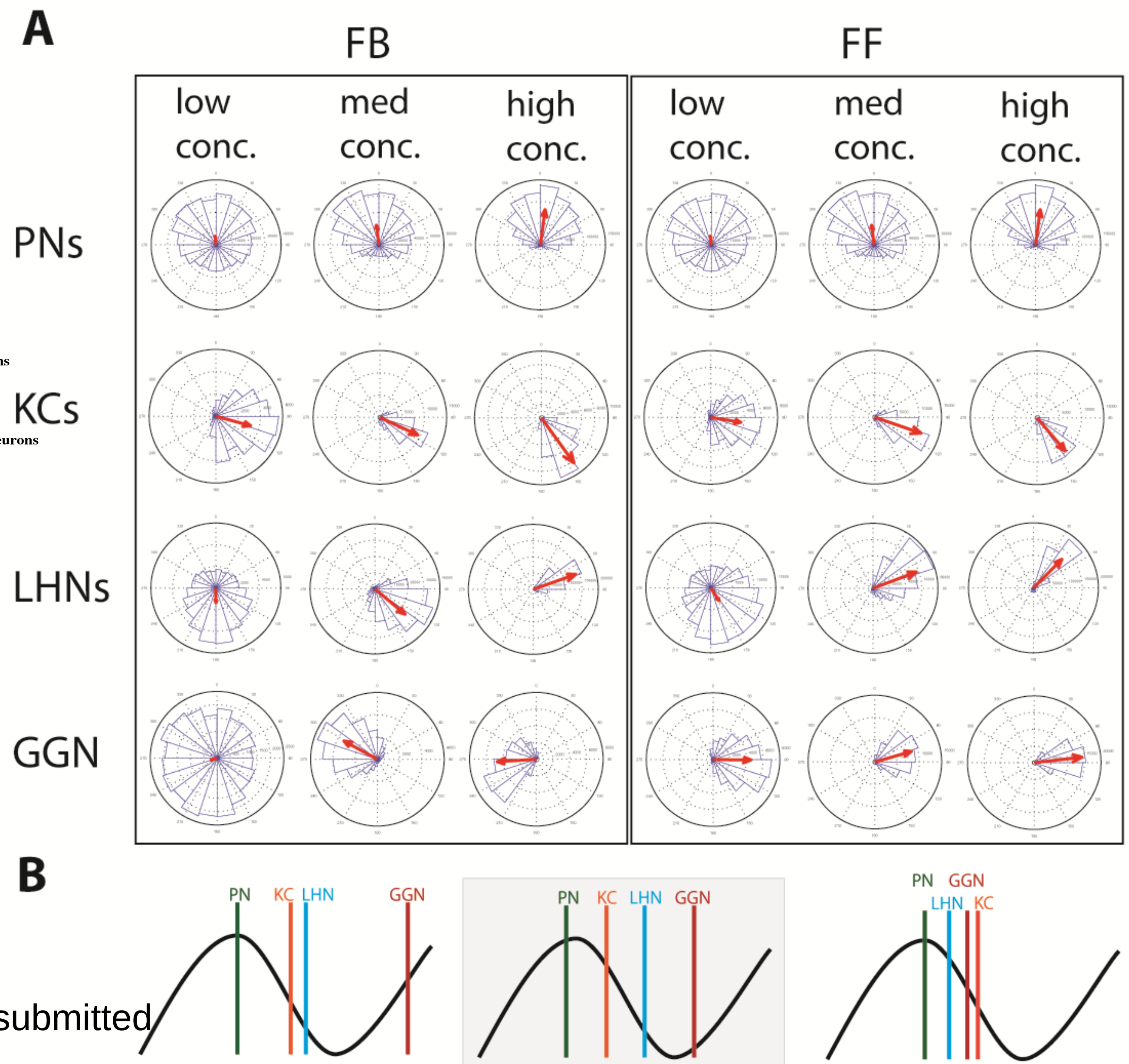
FB inhibition can maintain low KC spike count across concentrations



Kee at al, PLoS Comp Bio, submitted

FB and FF inhibition create different phase relationships between spiking in populations of PNs, KCs, LHNs and GGN





Kee at al, PLoS Comp Bio, submitted

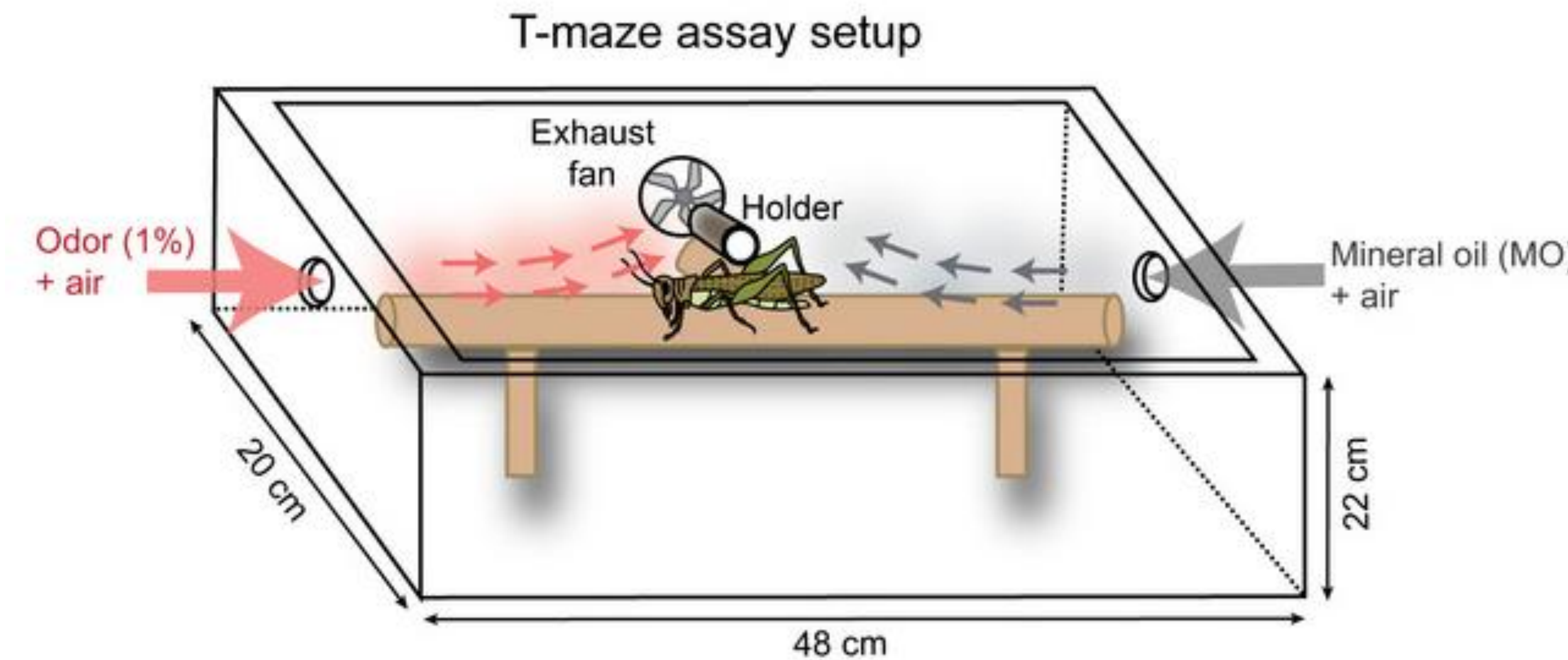
Conclusions

- Inhibition in the MB plays important role in maintaining sparseness of KCs responses
- While data suggest FB nature of MB inhibition, both FB and FF can preserve the sparseness of KCs responses
- Only FB model provides experimentally observed phase relationship between spiking in different cell populations

Outlines

- Synaptic inhibition in the AL for odor coding
- ORN adaptation for background-invariant odor recognition

Natural occurrence of odors commonly involves overlap



The natural occurrence of odors may include simultaneous presentation of many odors.
Novel (foreground) odors may need to be identified even in the presence of a persistent background odor.

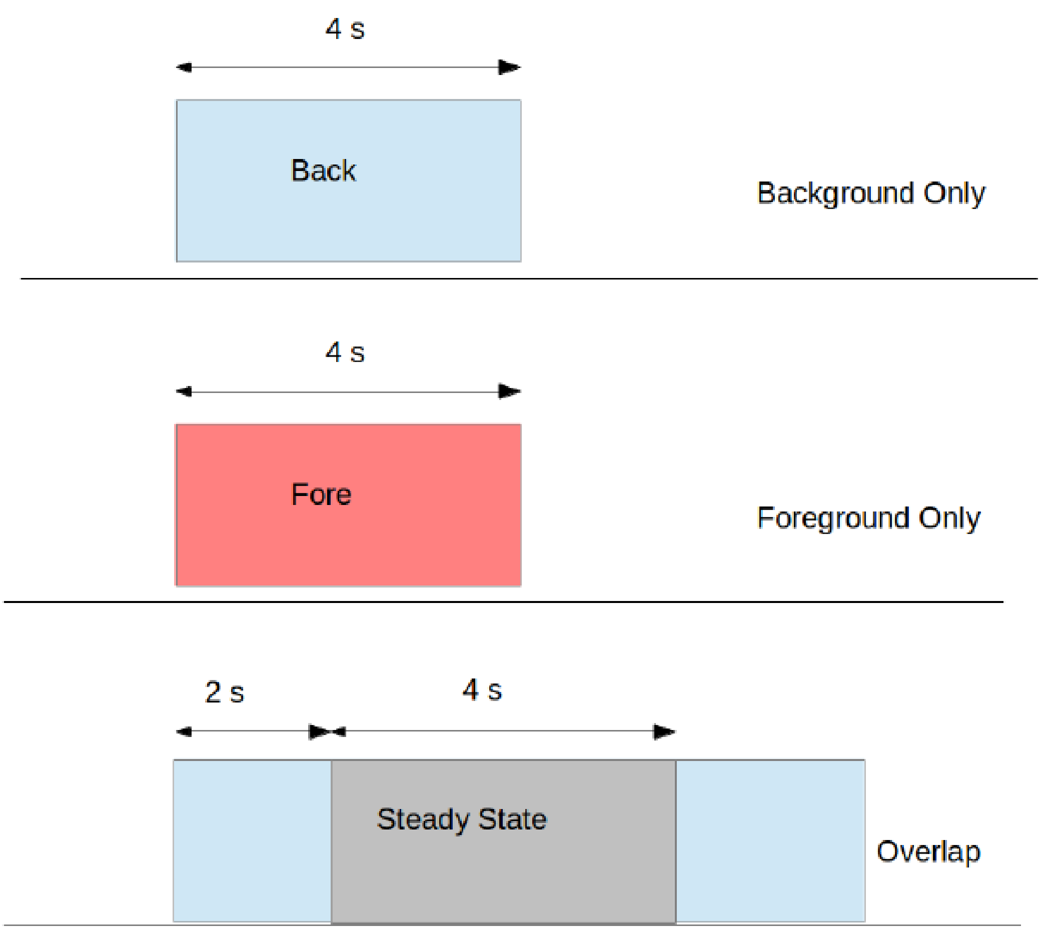
Saha at al, NN 2013

Experimental set up

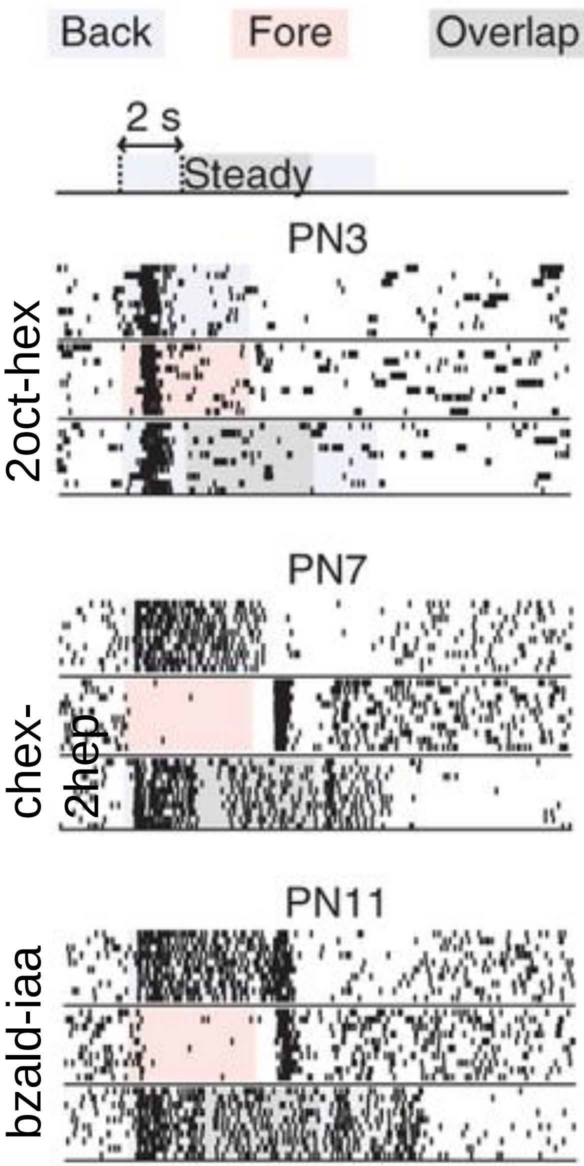
Background Only (Back; BG)

Foreground Only (Fore; FG)

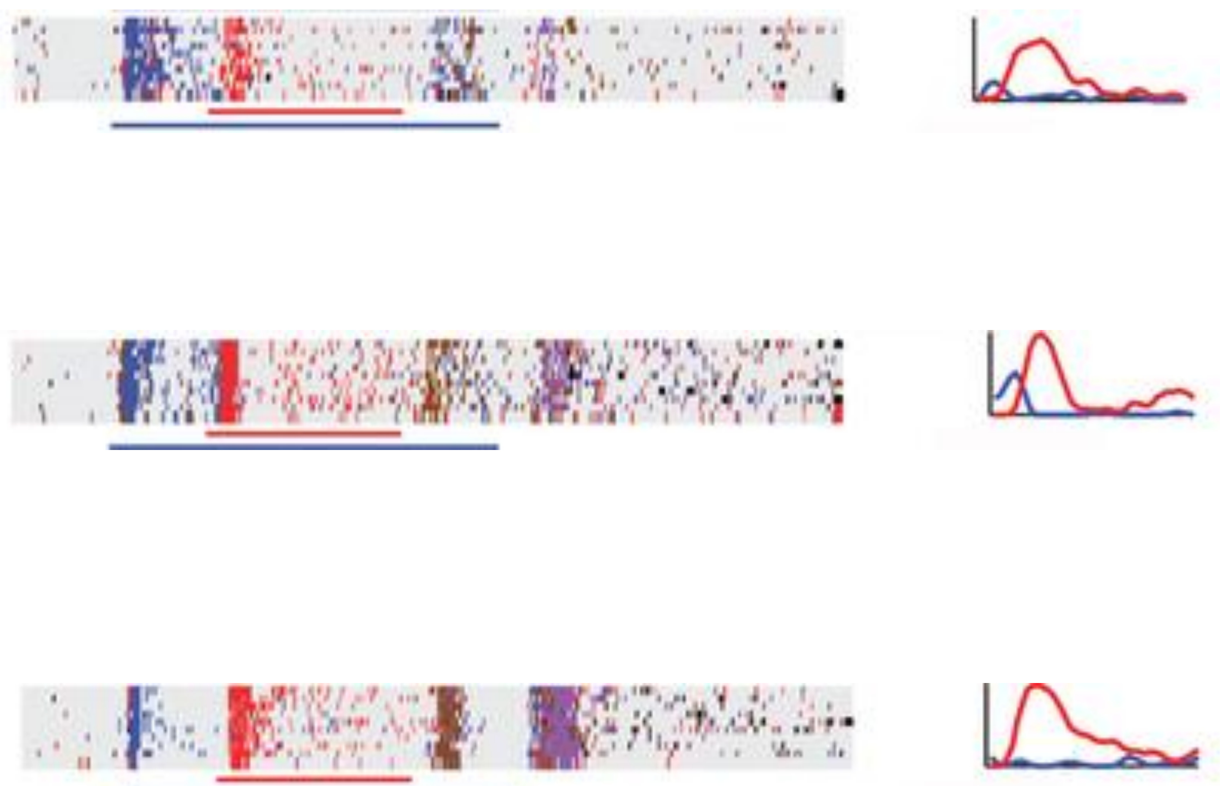
FG over BG (Overlap): Here the foreground odor presentation happens 2 sec after background odor presentation.



Locust olfactory system successfully detects FG odor in presence of BG odor



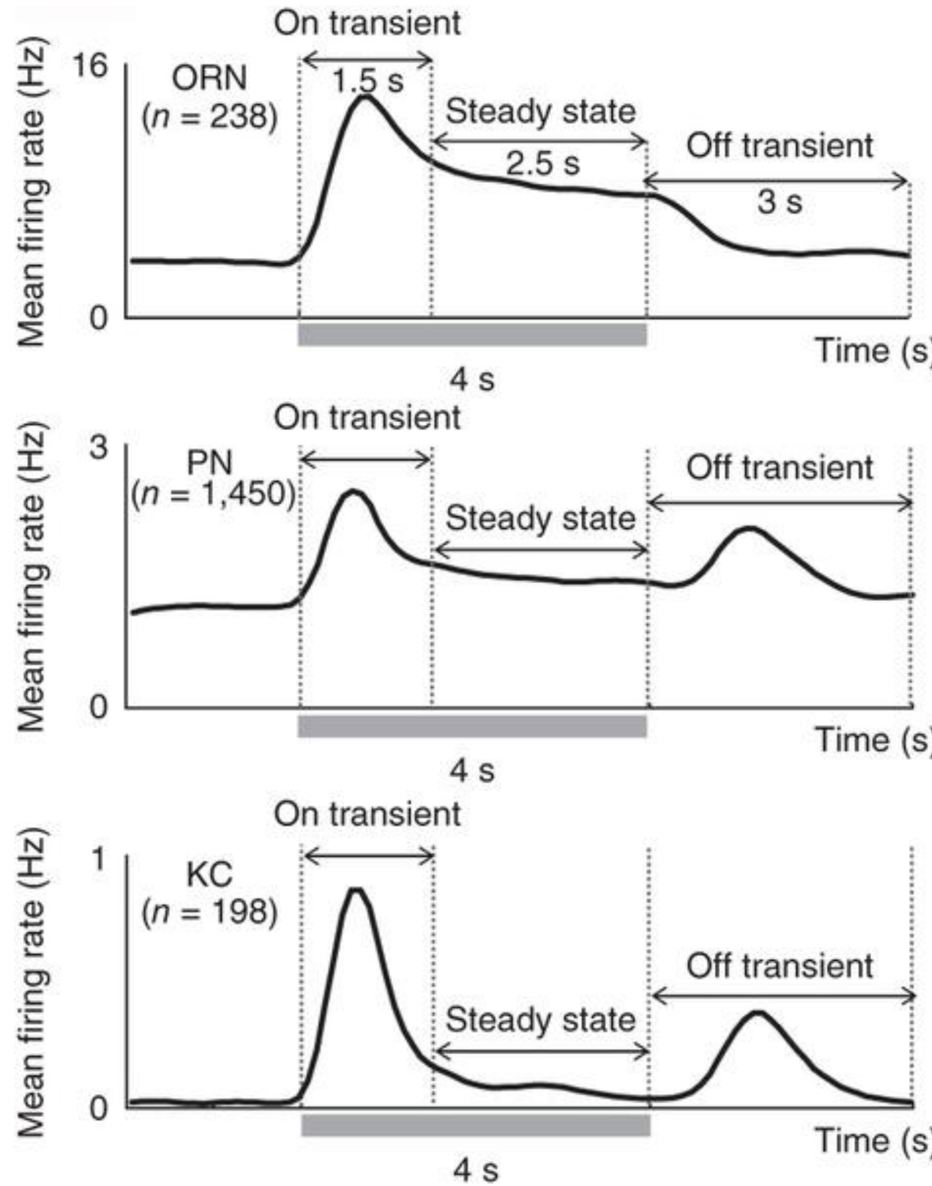
Classification



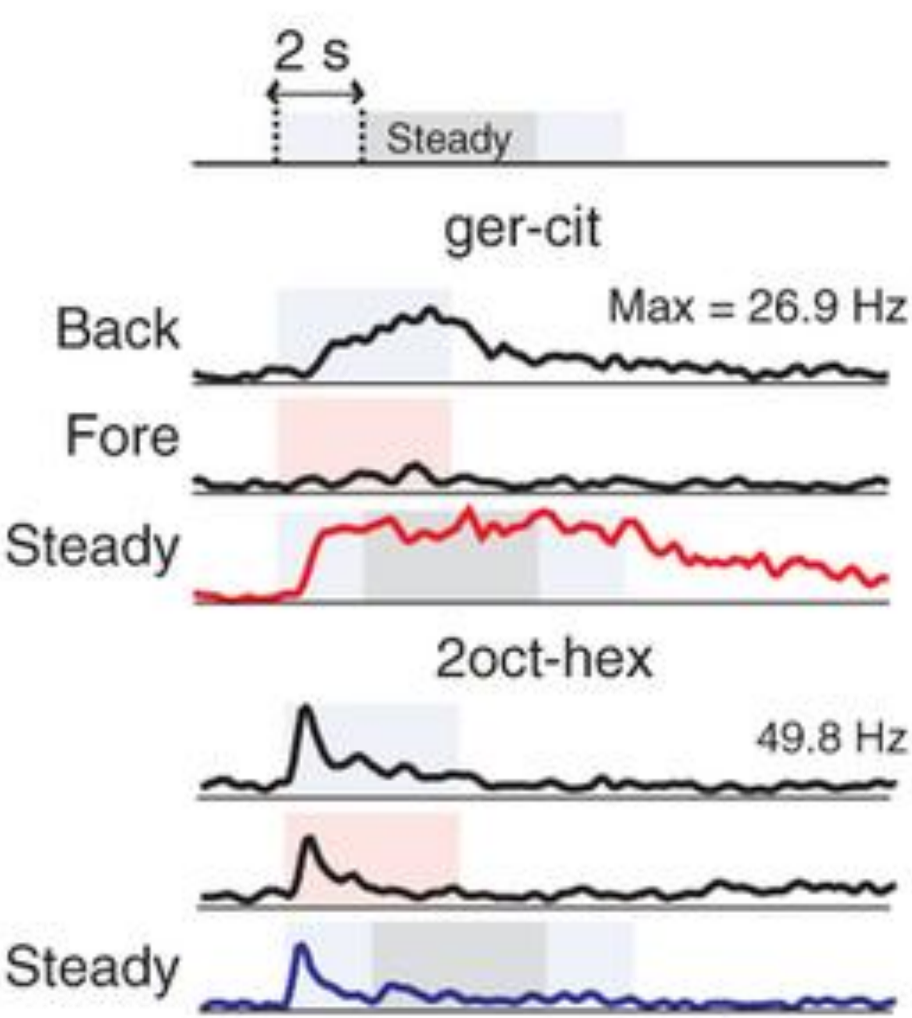
Saha at al, NN 2013

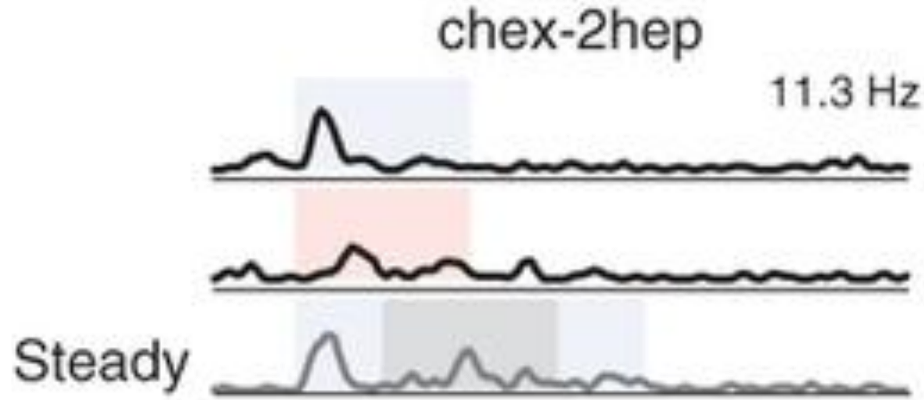
ORNs, PNs and KCs responses show distinct phases: (a) On transient, (b) Steady state, (c) Off transient

Topically during steady state ORNs adapt below peak of response

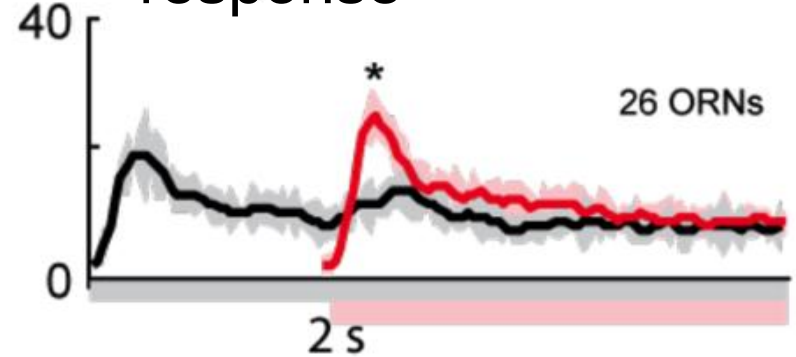


ORN responses during FG over BG odor presentation

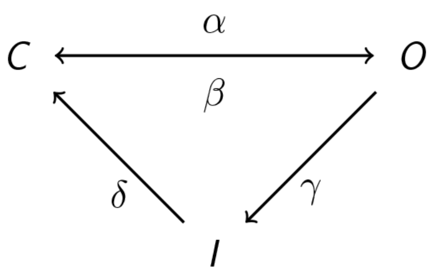


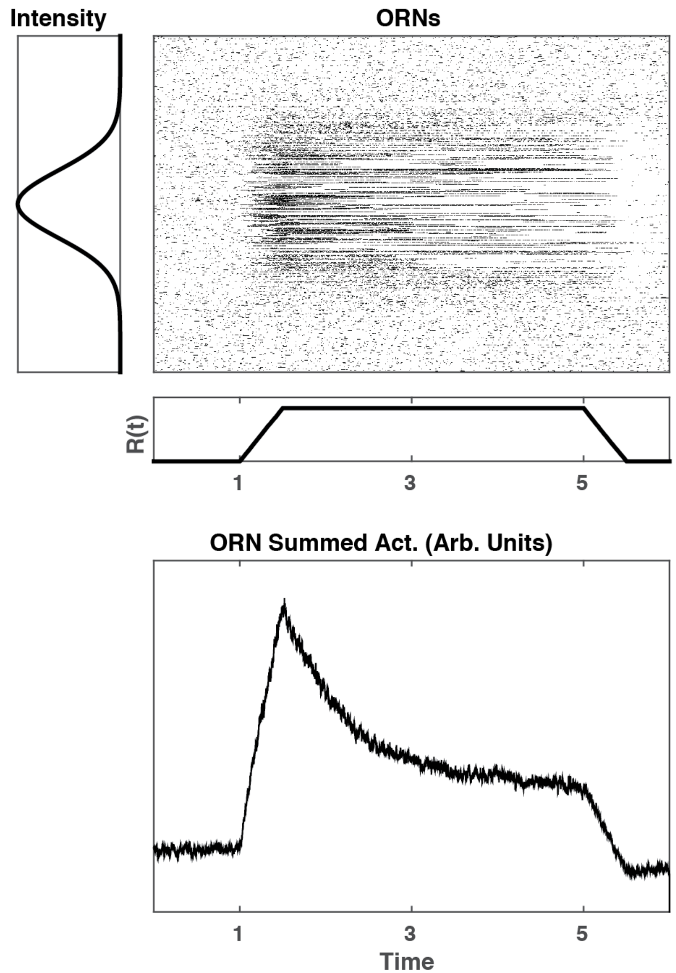


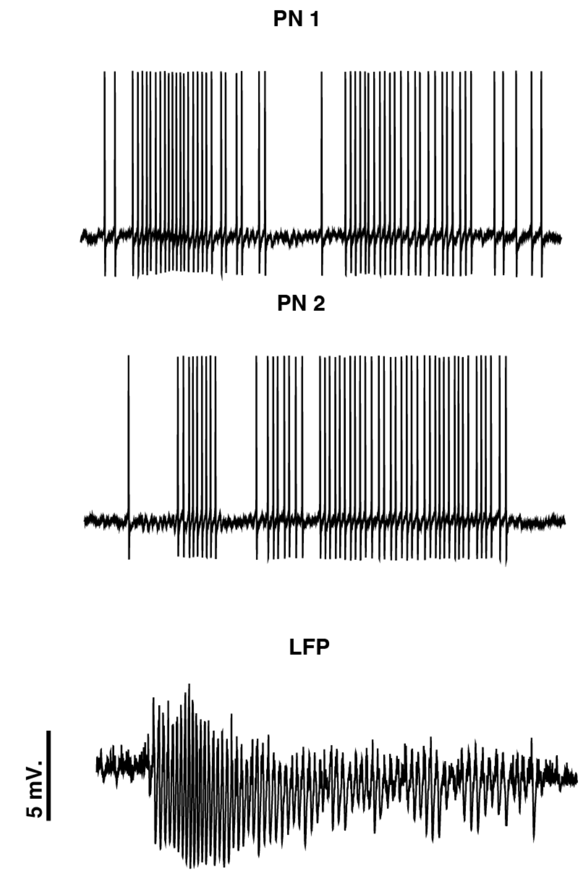
Second presentation of the same odor leads to largely silent ORN response



We designed kinetic model of the ORNs



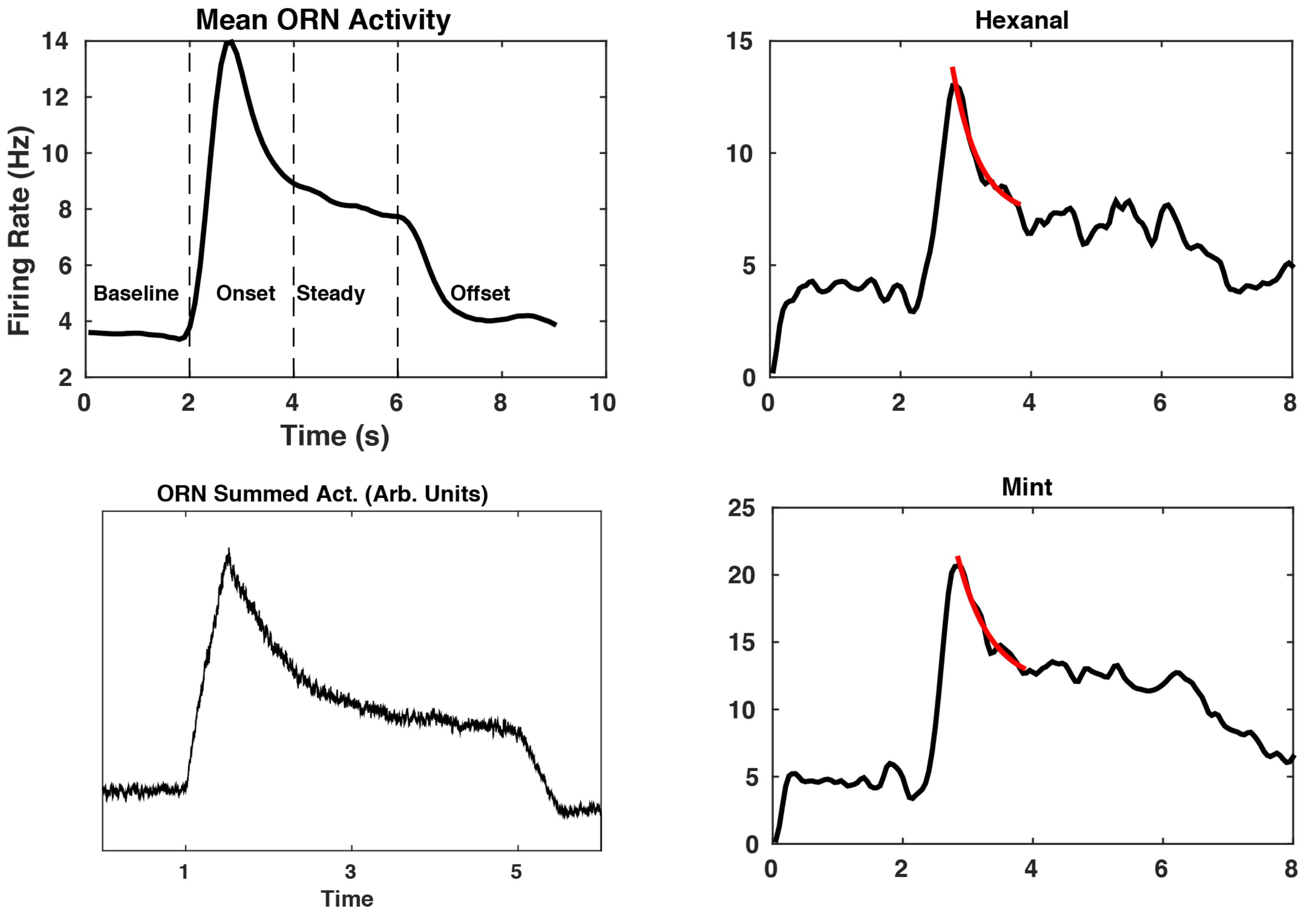




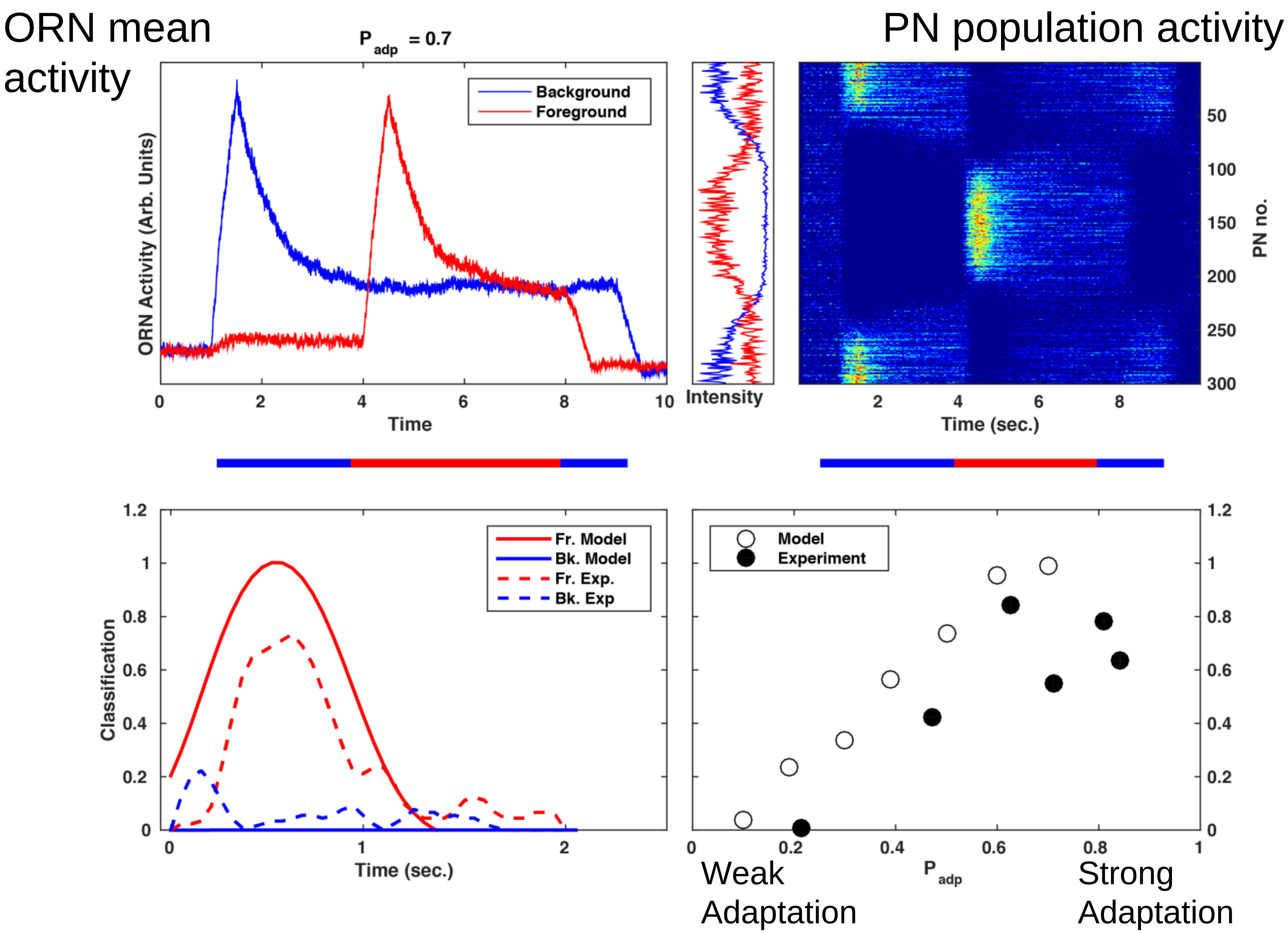
$$\frac{dC}{dt} = -\alpha R(t)C + \beta O + \delta I$$
$$\frac{dO}{dt} = \alpha R(t)C - \beta O - \gamma O$$
$$\frac{dI}{dt} = \gamma O - \delta I$$

I is the inactive state, O is the open state, C is the closed state. We use mass action kinetics and an individual-based stochastic model to simulate these transitions for each

Inactivation model replicates experimentally measured ORN activity

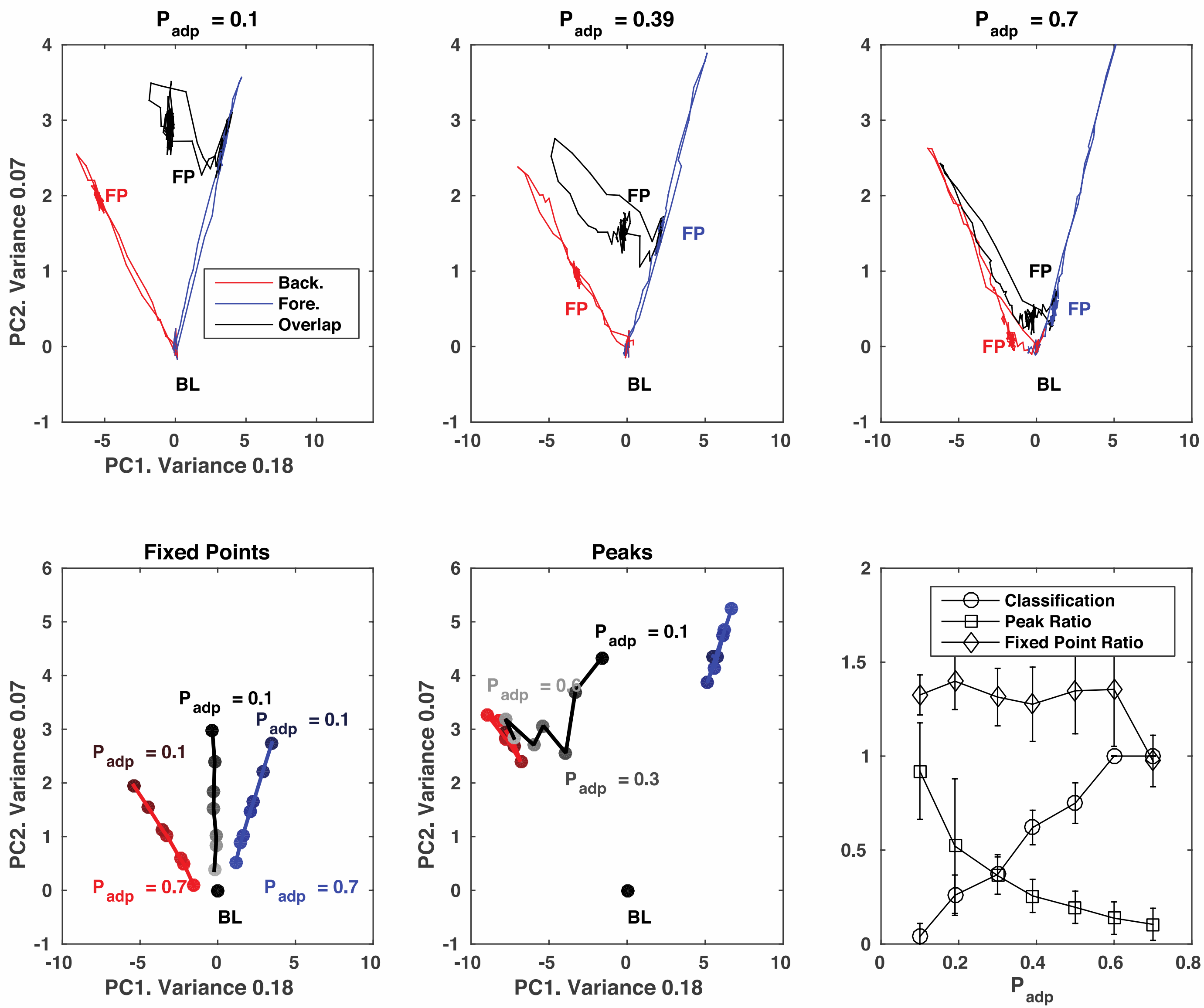


Averaging classification over time for two odors are presented simultaneously

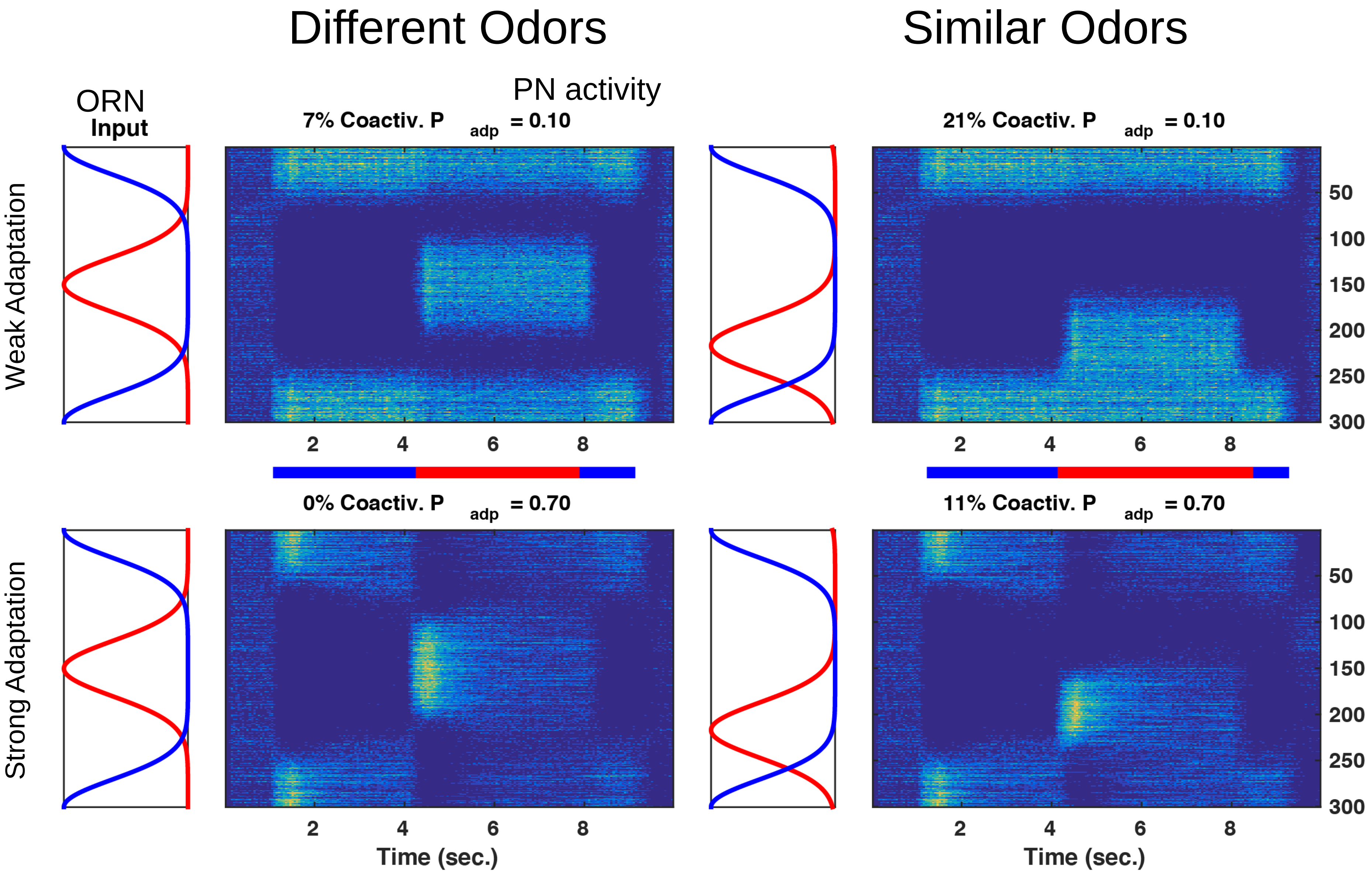


The model was exposed to two different odors with 3s delay between BG and FG odor presentations

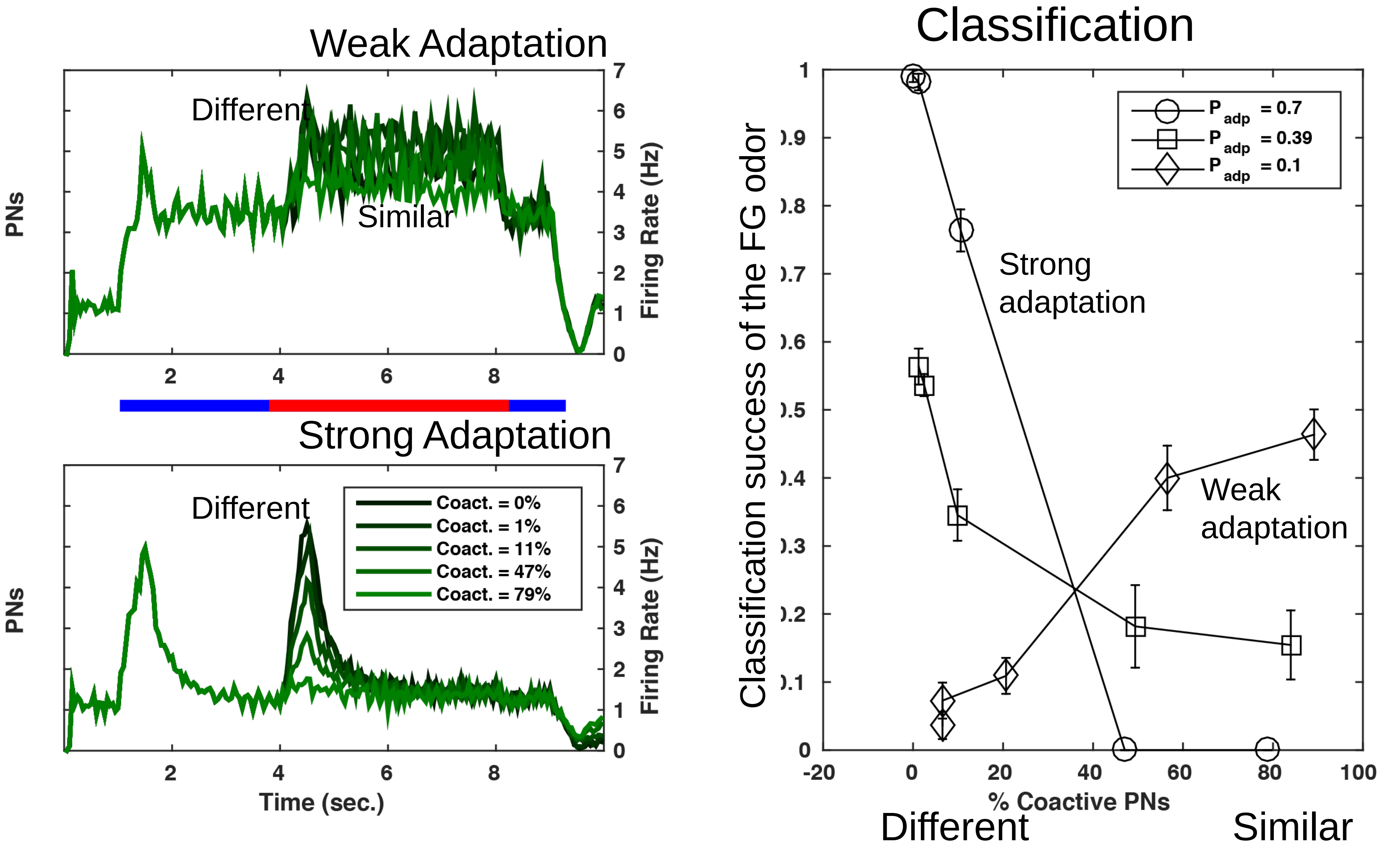
ORN adaptation allows FG odor to start with initial conditions close to Baseline point



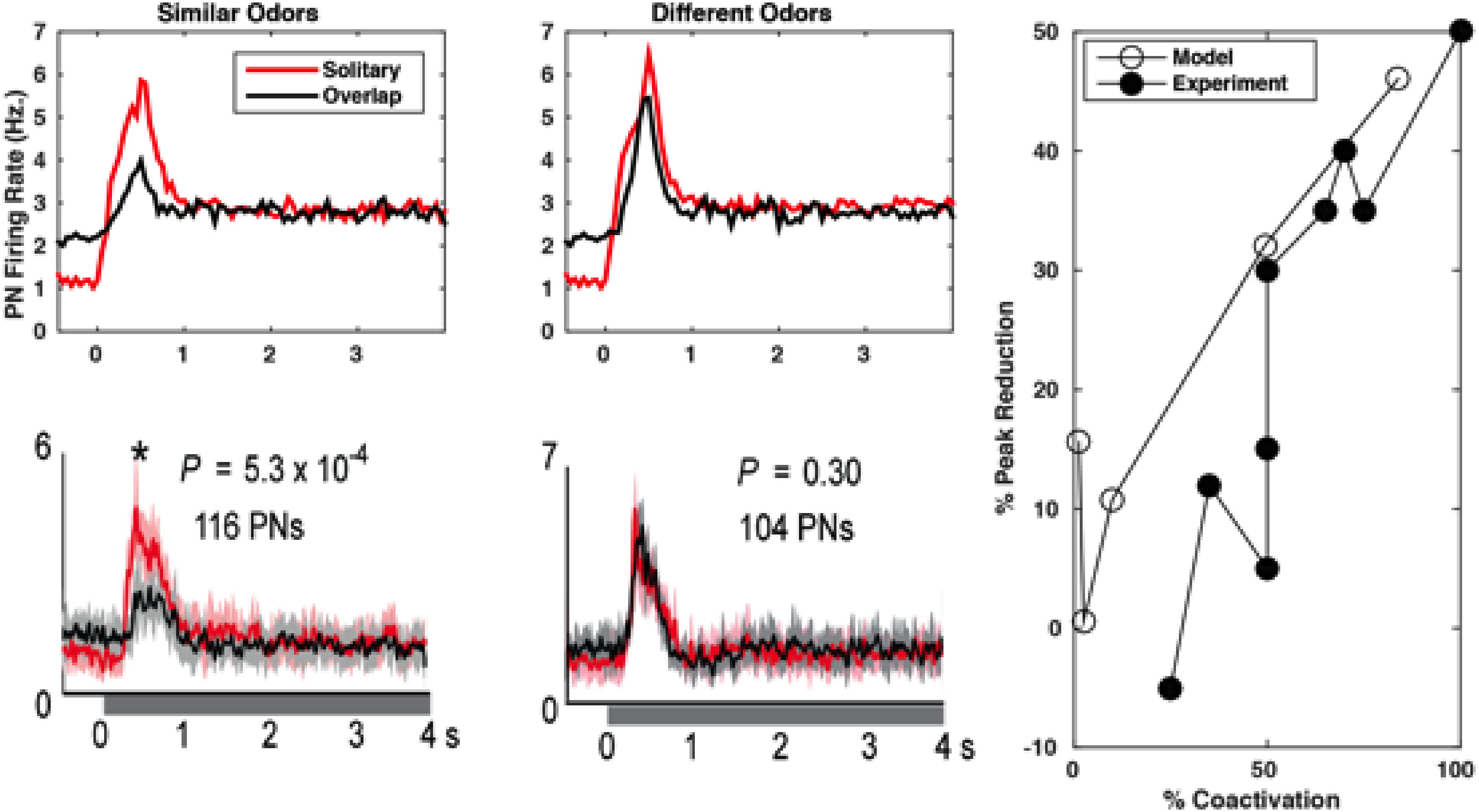
Strong adaptation leads to silencing of PN responses in the overlap between similar BG and FG odors



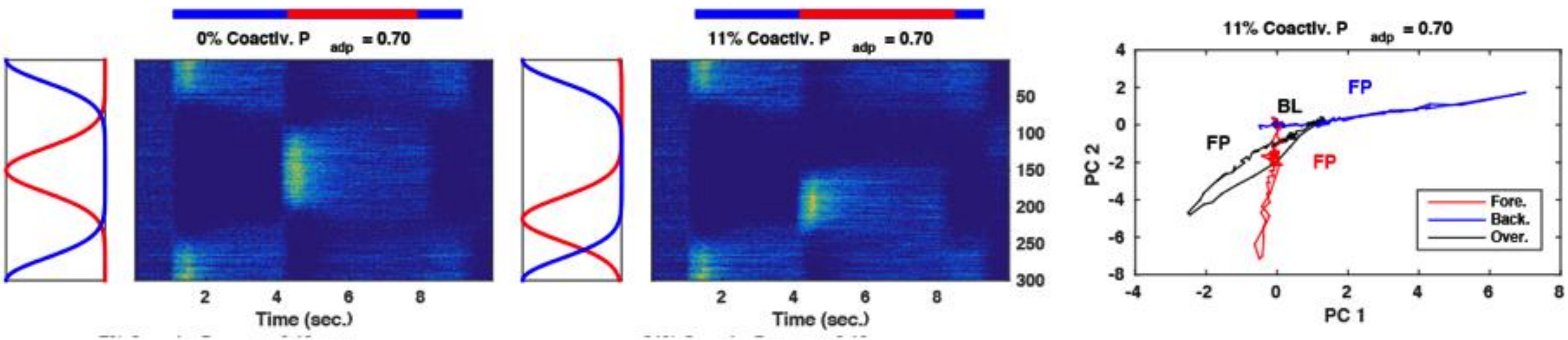
ORN adaptation causes differential effects on classification of FG odor presented on top of BG odor depending on the odors similarity.



Presentation of a 2d odor (FG) similar to the 1st one (BG) leads to reduced response both in vivo and in the model



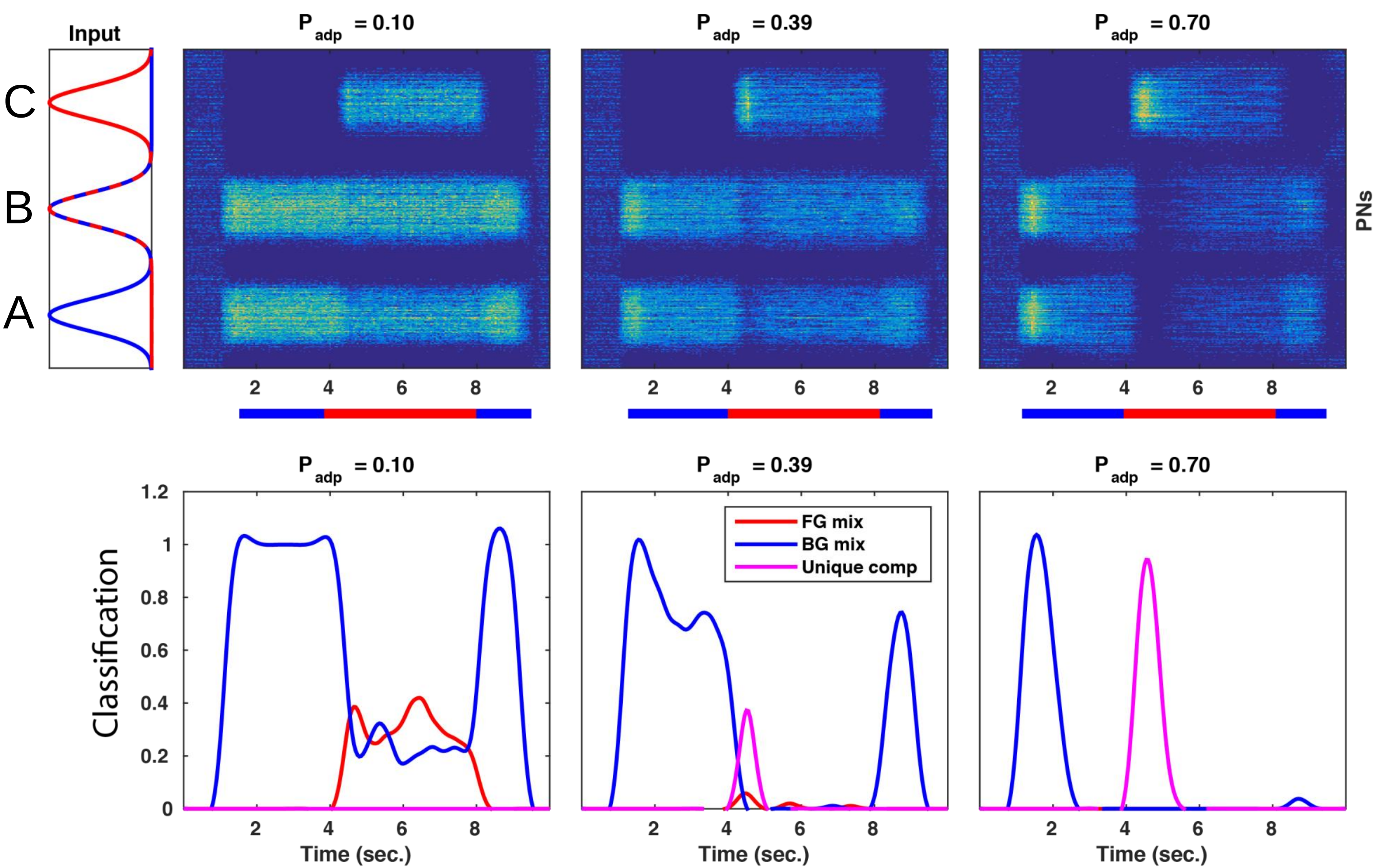
Why odor overlap leads to decrease of classification success?

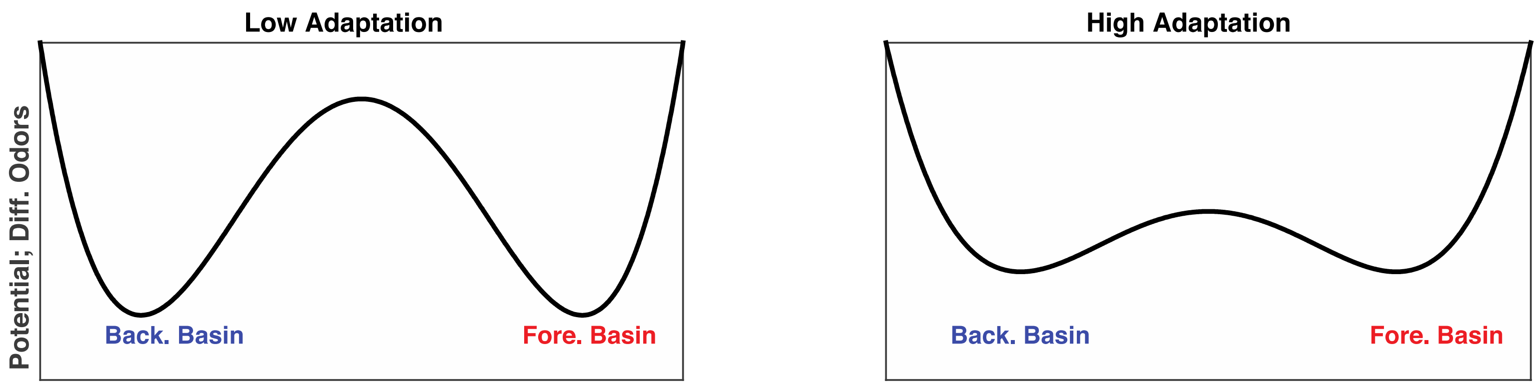


PNs responding to both odors in the overlap of two similar odors get silenced and thus the PN trajectory gets miss oriented from foreground odor.

This effect is initiated in the ORNs by (a) adaptation mechanism and (b) is then amplified in the AL by local inhibition.

“Illusion” - Presentation of A+B mixture (BG) followed by B+C mixture (FG) may perceived as presentation of C alone




Low Adaptation
High Adaptation
Potential; Diff. Odors
Back. Basin
Fore. Basin
Back. Basin
Fore. Basin

Conclusions

ORN adaptation can significantly increase classification of different odorants, by aligning overlap with foreground trajectories.

In the case of similar odorants adaptation has a negative effect on classification and may lead to “illusions”

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