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

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A “typical” overview of the insect olfactory system.
Outlines

• Synaptic inhibition in the AL and MB for odor coding

• ORN adaptation for background-invariant odor recognition
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- Synaptic inhibition in the AL and MB for odor coding
- ORN adaptation for background-invariant odor recognition
Odor triggers oscillatory responses in the AL

**Locust**
- LFP
- PN

**Moth**
- MB LFP (5-30 Hz)
- PN (DM1)
- 10% Hexanol

**Fly**

Ito et al., 2008
Tanaka and Stopfer 2009

Bazhenov, et al., Neuron, 2000
Odor triggered AL oscillations depend on inhibition
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 mechanism of synchronization in neural circuits.

For example, in the neocortex, feedback inhibition by interneurons synchronizes principal neurons.
Sleep spindle oscillations

Inhibitory cells

RE

TC

50 mV

0.5 sec

Timofeev and Bazhenov, 2005
Spindle sequences in RE-TC network

A

B

TIME (sec)

50mV

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

PY
PY
PY
IN
GABA
AMPA
Inhibitory cells

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

4 PNs from the network

- PN1
- PN2
- PN3
- PN4

Synchronized
Non synchronized

Time (in LFP cycles)

MB (LFP)

AL (PNs)

20 odor trials
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.

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.

For a given PN different number of presynaptic LNs is active at different times of odor stimulation.
Simple network with 2 inhibitory neurons

Spike adaptation is responsible for active states alternation

Assisi, Stopfer, Bazhenov Neuron, 2010
Dimensionality reduction

\[
\frac{dA_i}{dt} = c \times f_i \quad A_i, \\
f_i = F_0 \left( I_{i}^{\text{ext}} \quad A_i \right), \\
\frac{dA_j}{dt} = A_j, \\
f_j = 0, \quad j = 1, \ldots, N, \quad j \neq i
\]

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

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

Komarov and Bazhenov, in preparation
Phase space of 2 neuron model

Weak adaptation

Strong adaptation

\[ V_1 \]

\[ V_2 \]

\[ \text{time} \]

\[ 80 \text{ mV} \]

\[ 100 \text{ mS} \]

\[ 200 \text{ mS} \]
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

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

\[ I_0 + \Delta_1 \rightarrow 1 \rightarrow 2 \rightarrow \Delta_2 \rightarrow 3 \rightarrow I_0 + \Delta_2 \]
For a given odor concentration different ORNs would show different response intensity.

**ORN activation curve**

**Input to PNs**

- High concentration
- Low concentration

**Order of PN spiking for intermittent concentration**
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.
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
LH neurons receive PN input and their activity depends on odor concentration.

**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.

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.

**Coincidence detection**

![Diagram](image)
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 et al, PLoS Comp Bio, submitted
FB and FF inhibition create different phase relationships between spiking in populations of PNs, KCs, LHNs and GGN.

Kee et 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
• 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 et 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

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

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 receptor independently.

\[
\begin{align*}
\frac{dC}{dt} &= -\alpha R(t)C + \beta O + \delta I \\
\frac{dO}{dt} &= \alpha R(t)C - \beta O - \gamma O \\
\frac{dI}{dt} &= \gamma O - \delta I
\end{align*}
\]
Inactivation model replicates experimentally measured ORN activity

**Mean ORN Activity**

- **Firing Rate (Hz)**
  - Baseline
  - Onset
  - Steady
  - Offset

**Hexanal**

- Time (s)
  - 0, 2, 4, 6, 8

**ORN Summed Act. (Arb. Units)**

- **Time**
  - 1, 3, 5

**Mint**

- Time
  - 0, 2, 4, 6, 8
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 misoriented 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
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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