Selectivity improvement of olfactory projection neurons at low concentration of odors

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Outline

dog

bird

limax

moth

Quality of olfaction

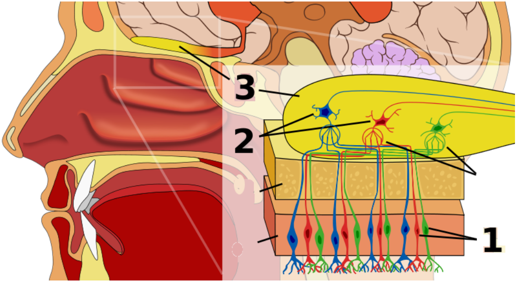
- Sensitivity
- Selectivity
- Speed of odor perception

High selectivity

Burger, B.V. et al., 2011. Olfactory Cue Mediated Neonatal Recognition in Sheep, Ovis aries. *Journal of Chemical Ecology*, 37(10), p.1150-63.

Outline

Primary olfactory pathways



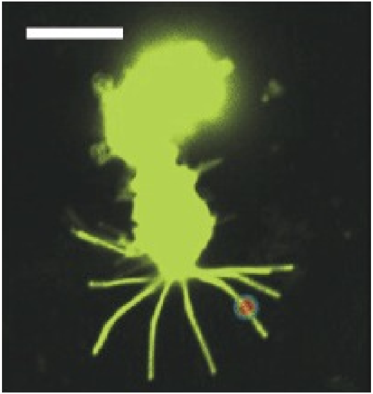
To the primary olfactory cortex →

1 — Receptor neurons (ORN)

2 — Projection neurons (PN)

3 — Olfactory bulb

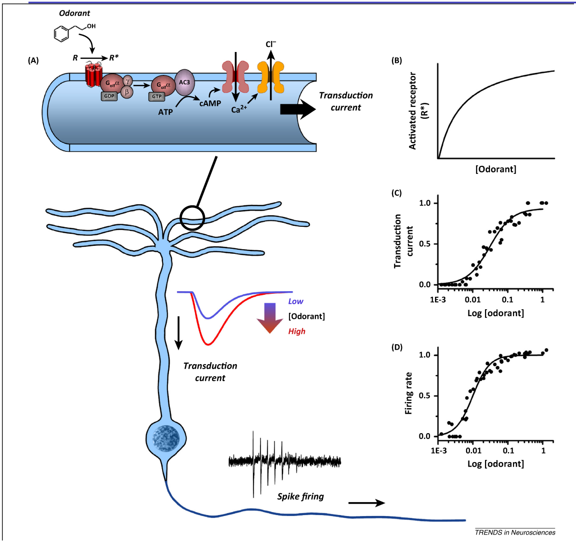
Real olfactory receptor neuron (human)



ORN, bar = $10\mu m$

From: Pifferi S, Menini A, Kurahashi T. Signal Transduction in Vertebrate Olfactory Cilia. In: Menini A, editor. The Neurobiology of Olfaction. Boca Raton (FL): CRC Press/Taylor & Francis; 2010. Chapter 8.

Receptor neuron and its receptor proteins



From: Mainland,J.D., Lundström,J.N., Reisert,J., Lowe,G. "From molecule to mind: an integrative perspective on odor intensity." Trends in Neurosciences **37**(8):443-454 (2014)

Stages of odor selectivity buildup

constructive element	type of response
receptor proteins	fraction of bound receptors
↓	
receptor neurons	firing rate
↓	
projection neurons	firing rate
↓	
primary olfactory cortex	activity in local cortical circuits (combinatorial code)

Stages of odor selectivity buildup

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constructive element	type of response
receptor proteins ↓	fraction of bound receptors
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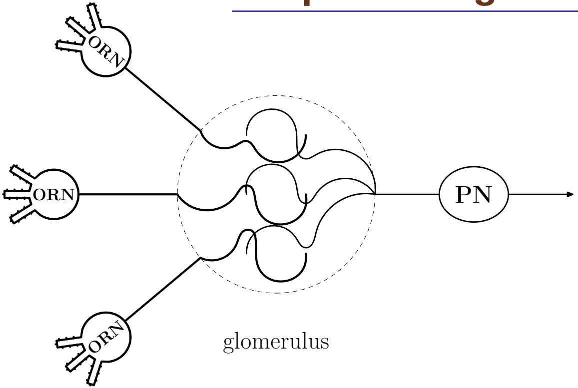
Simplified fragment



Schematic example of communication between ORNs and PN. Here up to several thousands ORNs, (concrete number, $N = 5000$, for mouse) can converge through a single glomerulus onto a single PN. All those ORNs express the same receptor protein.

Outline

Selectivity, perhaps, high c

From:

Duchamp-Viret,P., Duchamp,A., Sicard,G.

Olfactory discrimination over a wide concentration range. Comparison of receptor cell and bulb neuron abilities.

Brain Research **517**:256-262 (1990)

"...In both receptor cells and bulb neurons, qualitative discrimination abilities were found to increase with stimulus concentration."

Selectivity, perhaps, intermediate c

From:

Duchamp,A., Sicard,G.

Influence of stimulus intensity on odour discrimination by olfactory bulb neurons as compared with receptor cells.

Chemical Senses **8**(4):355-366 (1984)

“It can be provisionally concluded that, within the range of concentrations explored in this study, the discrimination of odour quality by bulbar neurons is relatively <u>independent</u> from variations affecting stimulus intensity”

Selectivity, perhaps, low c

From:

Tan,J., Savigner,A., Ma,M., Luo,M.

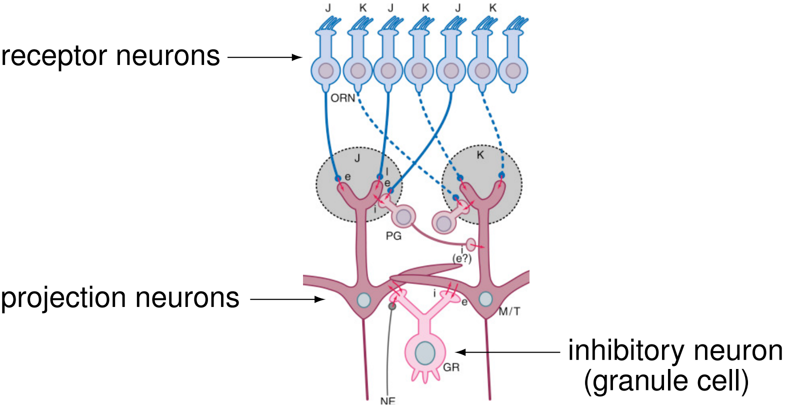
Odor Information Processing by the Olfactory Bulb Analyzed in Gene-Targeted Mice.

Neuron **65**(6):912-926 (2010)

“Increasing the concentration significantly reduces response selectivity for both OSNs and M/T cells,...”

Outline

Lateral inhibition



From: Scott,K. Chapter 23 - Chemical Senses: Taste and Olfaction in: Squire,L.R., Berg,D., Bloom,F.E., du Lac,S., Ghosh,A., Spitzer,N.C.(ed.) Fundamental Neuroscience (Fourth Edition) pp.

Outline

No lateral inhibition at low c

From:

Duchamp,A.

Electrophysiological responses of olfactory bulb neurons to odour stimuli in the frog. A comparison with receptor cells.

Chemical Senses **7**(2):191-210 (1982)

“The suppressive responses were therefore much more affected (about twice as much) than the excitatory ones by the decrease in stimulus concentration.”

Improper sniffing

Correct sniffing

Professional sniffing

Original Paper in *Neurophysiology* journal

DOI 10.1007/s11062-019-09808-6
Neurophysiology, Vol. 51, No. 3, May, 2019

Possible Stochastic Mechanism for Improving the Selectivity of Olfactory Projection Neurons

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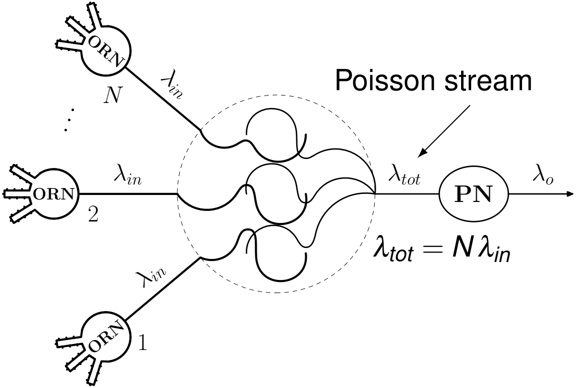
Received December 18, 2018

A possible mechanism that provides increased selectivity of olfactory bulb projection neurons, as compared to that of the primary olfactory receptor neurons, has been proposed. The mechanism operates at low concentrations of the odor molecules, when the lateral inhibition mechanism becomes inefficient. The mechanism proposed is based on a threshold-type reaction to the stimuli received by a projection neuron from a few receptor neurons, the stochastic nature of these stimuli, and the existence of electrical leakage in the projection neurons. The mechanism operates at the level of the single individual projection neuron and does not require the involvement of other bulbar neurons.

Keywords: odors, olfactory bulb, olfactory receptor neurons, projection neurons, spike activity, selectivity, stochastic process.

Outline

Selectivity gain definition for odors O and O′



$\lambda_{tot} = N\,\lambda_{in}$

$\lambda'_{in} > \lambda_{in}, \quad \lambda'_{in} = \lambda_{in} + \Delta\lambda_{in}$

$s = \frac{\Delta\lambda_{in}}{\lambda_{in}}$ – ORN's selectivity

$\lambda'_{o} > \lambda_{o}, \quad \lambda'_{o} = \lambda_{o} + \Delta\lambda_{o}$

$S = \frac{\Delta\lambda_{o}}{\lambda_{o}}$ – PN's selectivity

$$\lambda_o = \frac{1}{T_o}$$

selectivity gain: $g = \frac{S}{s}$, or $g = \frac{\lambda_{in}}{\lambda_o}\frac{d\lambda_o}{d\lambda_{in}}$, or $\boxed{g = -\frac{\lambda_{in}}{T_o}\frac{d\,T_o}{d\,\lambda_{in}}}$

Outline

Projection neuron model, 1

perfect integrator

height of input impulse:	h
states of depolarization:	$0, h, 2h, 3h, \ldots$
numbers of states:	$0, 1, 2, \quad 3, \ldots, N_0 - 1$
threshold depolarization:	V_0
threshold depolarization:	$N_0 \approx \frac{V_0}{h}$

leakage

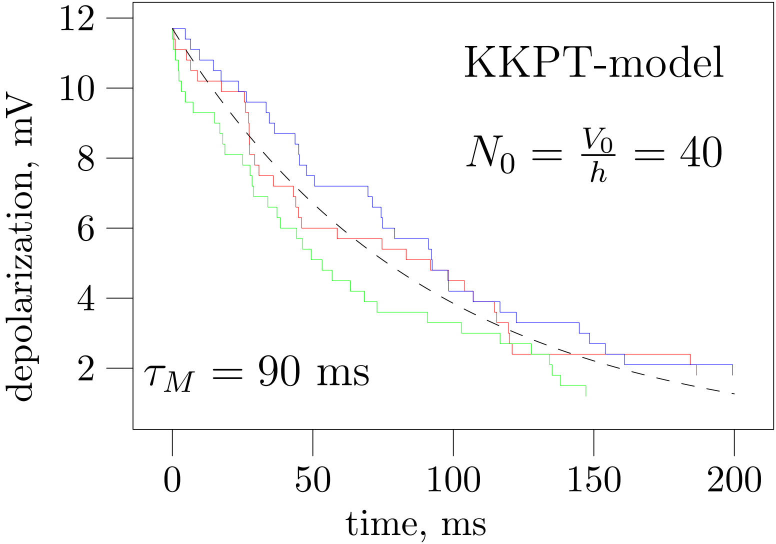
random decay of obtained impulses: $p = \mu\, dt$

on the average: $V(t + \Delta t) = V(t) e^{-\mu \Delta t}, \quad \mu = 1/\tau_M$

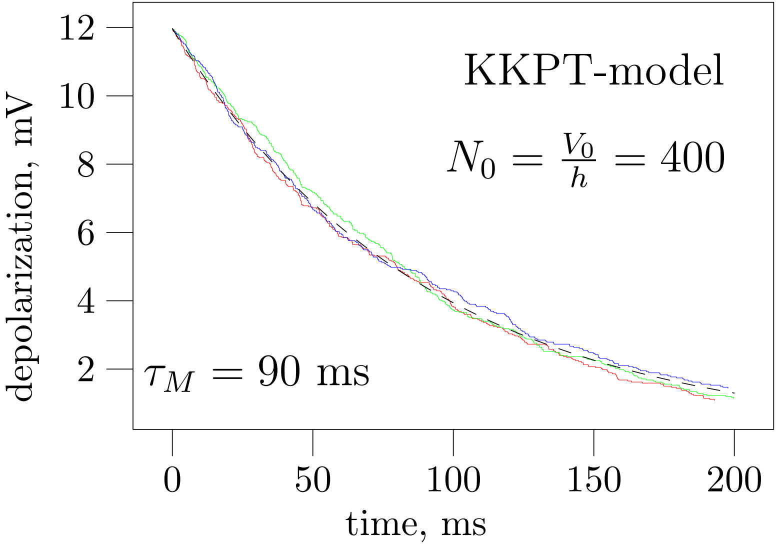
Korolyuk,V.S., Kostyuk,P.G., Pjatigorskii,B.Ya., Tkachenko,E.P. Mathematical model of spontaneous activity of some neurons in the CNS. *Biofizika* **12**(5):895-899 (1967)

“KKPT-model”

Projection neuron model, 2

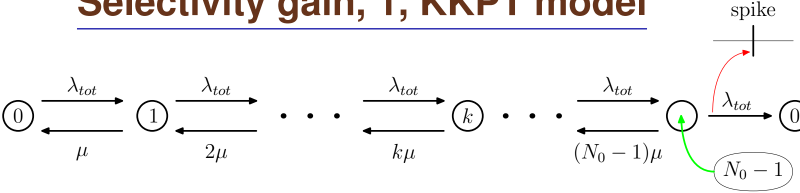


Projection neuron model, 3



Outline

Selectivity gain, 1, KKPT model



$$T_o = \sum_{0 \le l \le N_0 - 1} \Lambda_l \sum_{0 \le k \le l} \frac{1}{r_k^+ \Lambda_k},$$

$$\Lambda_0 = 1, \qquad \Lambda_n = \prod_{1 \le k \le n} \frac{r_k^-}{r_k^+}, \qquad n \in \{1, \dots, N_0 - 2\},$$

$$\Lambda_{N_0-1} = \Lambda_{N_0-2} \frac{r_{N_0-1}^-}{r_{N_0-1}^+}. \qquad \boxed{r_k^+ = \lambda_{tot} = N \lambda_{in}, \quad r_k^- = k\mu}$$

A.K.Vidybida. *Stochastic models*. NAS of Ukraine, BITP, Kyiv; 2006.

Selectivity gain, 2, T_o

$$T_o = \frac{1}{\lambda_{tot}} \sum_{0 \le j \le N_0 - 1} \frac{1}{j+1} \left(\frac{\mu}{\lambda_{tot}} \right)^j \frac{N_0!}{(N_0 - 1 - j)!}, \quad \lambda_{tot} = N \lambda_{in}$$

$$\boxed{g = -\frac{\lambda_{in}}{T_o} \frac{d\, T_o}{d\, \lambda_{in}}}$$

Selectivity gain, 3, final expression

$$g = 1 + \frac{\sum_{j=0}^{N_0-1} \frac{j}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}}{\sum_{j=0}^{N_0-1} \frac{1}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}}.$$

$$\mu = \frac{1}{\tau_M}$$

Selectivity gain, 4, no leakage

$$g = 1 + \frac{\displaystyle\sum_{j=1}^{N_0-1} \frac{j}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}}{\displaystyle\frac{1}{N_0-1} + \sum_{j=1}^{N_0-1} \frac{1}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}}.$$

no leakage $\Rightarrow$ $\tau = \infty$ $\Rightarrow$ $\mu = 0$ $\Rightarrow$ $g = 1$ $\Rightarrow$ no gain

Selectivity gain, 5, high c

$$g = 1 + \frac{\sum_{j=1}^{N_0-1} \frac{j}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}}{\frac{1}{N_0-1} + \sum_{j=1}^{N_0-1} \frac{1}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}}.$$

high odor concentration:

high λ_{in} $\Rightarrow$ $\frac{\mu}{N\lambda_{in}} \approx 0$ $\Rightarrow$ $g \approx 1$ $\Rightarrow$ no gain

Selectivity gain, 6, low concentration

$$g = 1 + \frac{\displaystyle\sum_{j=1}^{N_0-1} \frac{j}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}}{\displaystyle\sum_{j=0}^{N_0-1} \frac{1}{j+1} \left(\frac{\mu}{N\lambda_{in}}\right)^j \frac{1}{(N_0-j-1)!}} \quad \xrightarrow[\lambda_{in}\to 0]{} \quad N_0\,.$$

low odor concentration:

$$\lambda_{in} \to 0 \quad \Rightarrow \quad g \approx N_0$$

HIGH SELECTIVITY GAIN

Outline

Numerical examples, 1

threshold depolarization, V_0, mV	height of EPSP, h, μV	ORN spikes frequency, λ_{in}, 1/ms	PN membrane relaxation time, τ_M, ms
5 - 12, [1, 2]	30 - 665, the mean is 131, [5]	10^{-3}, [3]	90, [4]

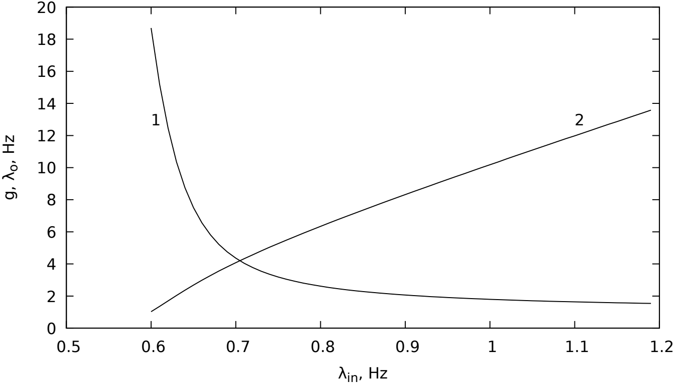
Experimental values for parameters, sources are indicated in brackets.

Numerical examples, 2

threshold N_0	output frequency λ_o, 1/s	g
300	10.3	1.78
400	5.3	3.15
500	0.67	30.3

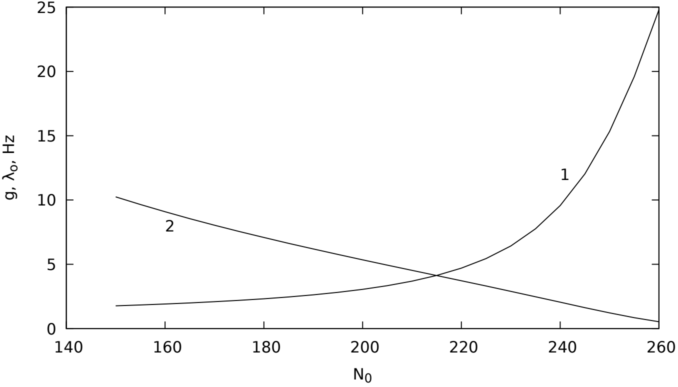
Results of numerical calculation.

Numerical examples, 3



Dependencies of g, 1 and λ_o, 2 on λ_{in} for threshold $N_0 = 300$, $N = 5000$, $\tau = 90$ ms. g is dimensionless.

Numerical examples, 4

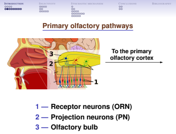


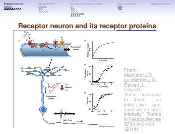
Dependencies of g, 1 and λ_o, 2 on threshold N_0 for $\lambda_{in} = 0.5$ Hz.

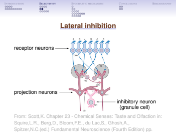
Outline

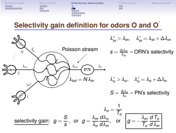
Prerequisites

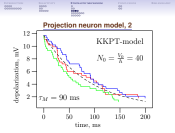
- Leakage in the secondary neuron
- Stochastic nature of input to the PN
- Threshold-type response in the PN ($N_0 > 1$)

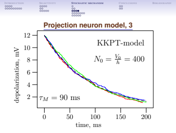

Primary olfactory pathways
To the primary olfactory cortex
1 — Receptor neurons (ORN)
2 — Projection neurons (PN)
3 — Olfactory bulb

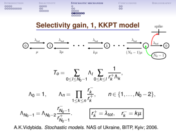

Receptor neuron and its receptor proteins
From: Mainland,J.D., Lundström,J.N., Reisert,J., Lowe,G. "From molecule to mind: an integrative perspective on odor intensity." Trends in Neurosciences 37(8):443-454 (2014)

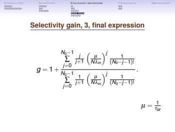

Lateral inhibition
receptor neurons
projection neurons
inhibitory neuron (granule cell)
From: Scott,K. Chapter 23 - Chemical Senses: Taste and Olfaction in: Squire,L.R., Berg,D., Bloom,F.E., du Lac,S., Ghosh,A., Spitzer,N.C.(ed.) Fundamental Neuroscience (Fourth Edition) pp.

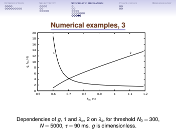

Selectivity gain definition for odors O and O′
Poisson stream
– ORN's selectivity
– PN's selectivity
selectivity gain:


Projection neuron model, 2
KKPT-model
$N_0 = \frac{V_0}{h} = 40$
$\tau_M = 90$ ms
depolarization, mV
time, ms


Projection neuron model, 3
KKPT-model
$N_0 = \frac{V_0}{h} = 400$
$\tau_M = 90$ ms
depolarization, mV
time, ms


Selectivity gain, 1, KKPT model
spike
A.K.Vidybida. Stochastic models. NAS of Ukraine, BITP, Kyiv; 2006.


Selectivity gain, 3, final expression


Numerical examples, 3
Dependencies of g, 1 and λ_o, 2 on λ_{in} for threshold $N_0 = 300$, $N = 5000$, $\tau = 90$ ms. g is dimensionless.

Outline

Missed reality

- The ORNs are not identical
- ORN's input is presynaptically inhibited
- ORN's axon arborizes: several inputs from a single ORN
- Dendritic preprocessing in the projection neuron
- Spontaneous activity in the ORNs

N.N. Urban, B. Sakmann.
Reciprocal intraglomerular excitation and intra- and interglomerular lateral inhibition between mouse olfactory bulb mitral cells.
The Journal of Physiology. 2002;542(2):355–367.

S.D. Burton, N.N. Urban.
Greater excitability and firing irregularity of tufted cells underlies distinct afferent-evoked activity of olfactory bulb mitral and tufted cells.
The Journal of Physiology. 2014;592(10):2097–2118.

J. Tan, A. Savigner, M. Ma, M. Luo.
Odor Information Processing by the Olfactory Bulb Analyzed in Gene-Targeted Mice.
Neuron. 2010;65(6):912–926.

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Electrophysiological analysis of mitral cells in the isolated turtle olfactory bulb.

The Journal of Physiology. 1981;314(1):281–294.

R.J. Sayer, M.J. Friedlander, S.J. Redman.
The time course and amplitude of EPSPs evoked at synapses between pairs of CA3/CA1 neurons in the hippocampal slice.
The Journal of Neuroscience. 1990;10(3):826.