

Rapid temporal processing in the olfactory bulb underlies concentration-invariant odor identification and signal decorrelation

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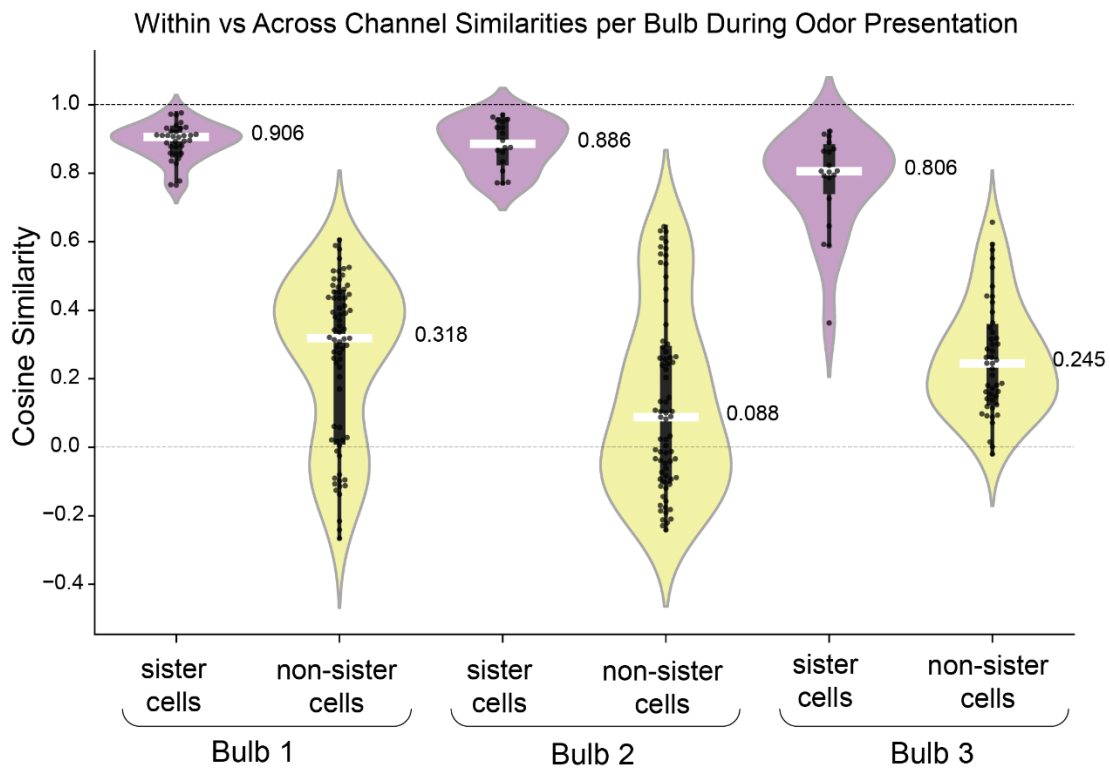
Supplementary Information

For the manuscript

Rapid temporal processing in the olfactory bulb underlies concentration invariant odor identification and signal decorrelation

by

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Supplementary Figure 1: Stereotype of responses in intra-glomerular channels for each bulb. Violin plots summarizing the distribution of cosine similarity values for intra-glomerular (purple) and inter-glomerular (yellow) MTC pairs during the odor phases. ($n = 71$ intra-glomerular and 221 inter-glomerular pairs in 2 animals). Mean cosine similarities were as follows intra-glomerular: 0.906, 0.886, 0.806; inter-glomerular: 0.318, 0.088, 0.245.

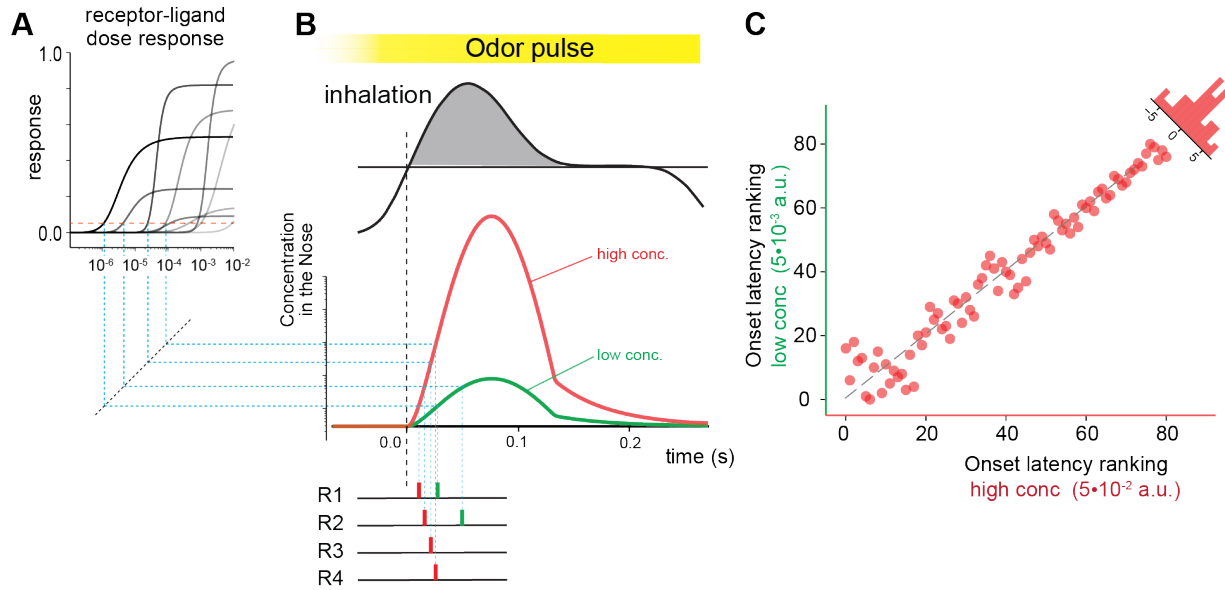
Modeling of concentration related changes of onset latency ranking

Odor inhalation was modeled as a 3 Hz positively rectified sinusoidal signal. The odor concentration developing in the nose (C) over time (t) was described by the differential equation $dC/dt = (C_{target} - C)/\tau$, where τ was set to 100 ms. We simulated (Supplementary Figure S2) 1000 olfactory sensory neuron (OSN) response curves using a Hill function for a monomolecular odorant presented at concentration C ¹:

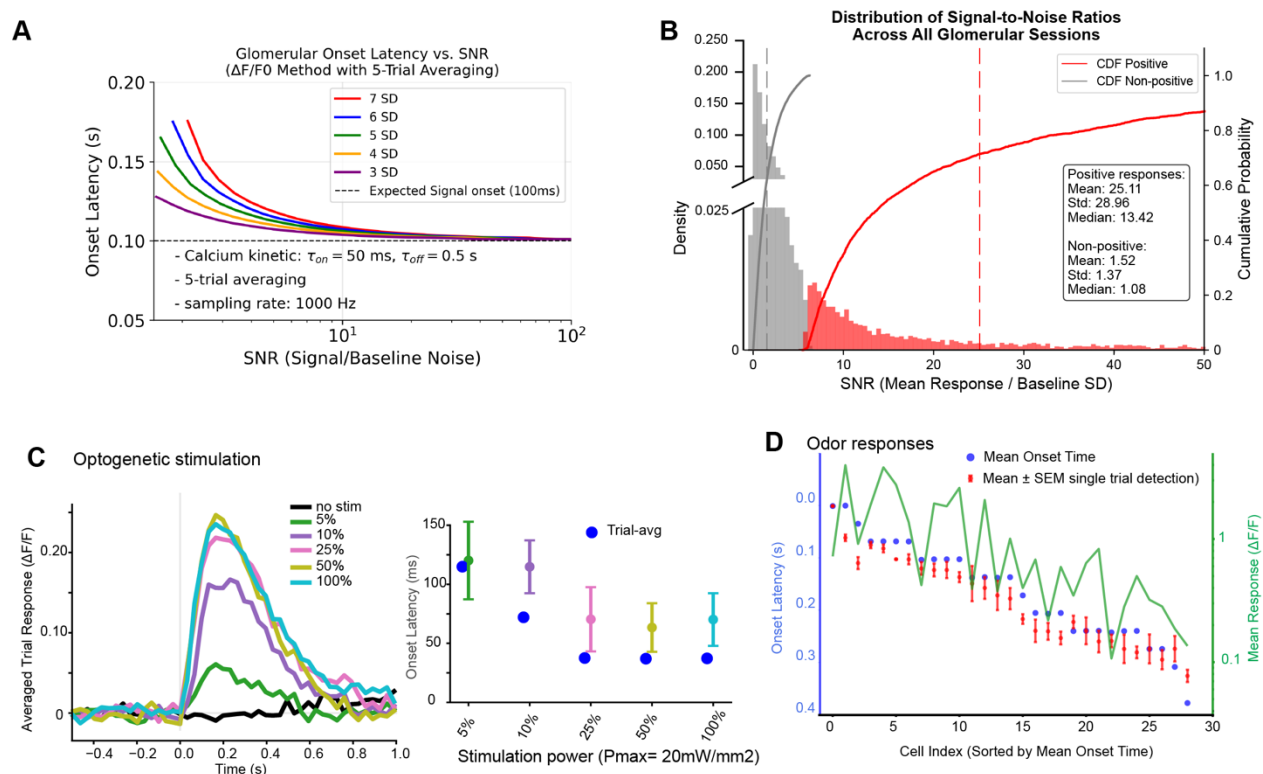
$$F_{i,c} = \frac{F_{i,max}}{1 + \left(\frac{1 + C/\kappa_i}{\eta_i C/\kappa_i} \right)^{n_i}}$$

Here, $F_{i,c}$ represent OSN firing rate, $F_{i,max}$ is the maximum physiologically possible firing rate and n_i the Hill coefficient, κ_i is control the affinity of odor to the receptor. The maximal response at saturating concentrations, $F_{\infty} = F_{max}/(1 + \eta^{-n})$ truncated below F_{max} by η , which controls the equilibrium level of activated receptors. For each OSN receptor, the F_{max} is sampled from a gamma distribution $\Gamma(\alpha, \beta)$, where $\alpha = 1.5, \beta = 2$. The Hill coefficient n is sampled uniformly from the range 2 to 4². All other parameters were used as described in¹. The threshold level for activation is set to 0.1.

The change of an onset latency rank may occur due to an interplay between slopes of receptor-ligand dose response curve and a rate of the concentration increase in the nose. Receptors with a relatively shallow dose response slopes are much stronger affected by the rate of concentration increase than those with a steep slope, which may lead to a swap of activation onset ranking between such receptors.



Supplementary Figure S2. Modeling of odor concentration dynamics and activation onset ranking. B. Examples of receptor-ligand dose response curves (following¹). **A.** Schematics of a respiration cycle (*top panel*) and the temporal profiles of odor concentration in the nose for low (green) and high (red) concentrations (*middle panel*). Schematics of the temporal sequences of receptor activation for low and high odor concentrations (*bottom panel*). Individual receptors become activated when the concentration in the nose crosses a specific threshold (red dashed line at panel A). **B.** Receptors-ligand dose response curve for a specific odor (see text below for details). **C.** Scatter plot of activation onset ranking with fixed threshold level at concentration $5 \cdot 10^{-2}$ a.u. versus rank at concentration $5 \cdot 10^{-3}$ a.u., demonstrating rank swapping across concentrations using a simple thresholding (threshold level = 0.1) method.



Supplementary Figure S3. Glomerular Onset Latency detection. **A.** Glomerular Onset Latency vs. SNR. Latency detection bias decreases with increasing SNR, approaching the expected latency of 0.1 seconds (dashed line) at high SNR values. Latency was determined from trial averaged signal amplitude in the 0.5-second response window exceeding different 3 - 7 standard deviations with respect to the baseline. **B.** Distribution of signal-to-noise ratios (SNR) for glomerular calcium responses across all experimental sessions. Gray histogram shows non-responsive glomeruli (mean SNR = 0.74), while red histogram shows positively responding glomeruli (mean SNR = 25.11). SNR is defined as mean odor response in 0.5 second window divided by baseline standard deviation. Positive responses: 2,547 odor-glomerulus pairs; non-responses: 9,919 odor-glomerulus pairs (6 standard deviation was used for threshold criteria). **C.** Onset latency detection for optogenetic and odor responses. *Left:* Averaged neural response traces ($\Delta F/F$) to optogenetic stimulation at increasing power levels (5% to 100%). *Right:* The onset latency decreases with higher stimulation power. The results from the trial-averaged detection method are compared to the mean ($\pm$ SEM) latency detected from individual trials. **D.** Onset latencies and mean response amplitudes for odor-evoked responses across a population of cells. Cells are sorted by onset time (determined from averaged response of 5 trials). The mean latency from single-trial detection (mean $\pm$ SEM) is shown alongside its mean response amplitude ($\Delta F/F$, calculated over a 0.5-second window).

The following animals were used in specific experiments:

Supplementary Table 1.

Animal model	# mice	Figure #
M72S50 X GP5.11 (Thy1-GCaMP6f)	4	Fig. 5, 6, Ext.Fig.7,8
OMP-ChR2 X GP5.11(Thy1-GCaMP6f)	4	Fig. 1,2,3E, F, 3, 4,5 Ext.Fig 2,3,5,6,10
M72S50 X Ai148 X Tbet-Cre	3	Fig. 1, 3A, B, E, F, Ext.Fig. 2,7,8
OMP-ChR2 X Ai148 X Tbet-Cre	2	Fig. 3E, F
OMP-ChR2 X Tbet-Cre (AAV5 GCaMP8f injection)	1	Fig. 3C, D
Ai93 X OMP-Cre	2	Ext.Fig. 4

All odors are obtained from Sigma-Aldrich and 0.5-1 mL of each odor was placed in a 45 mL vial, except 2HA, which was prepared as a liquid dilution (2uL in 5 mL mineral oil) to reach lower concentration. The following odors were used in specified experiments:

Supplementary Table 2.

Odor name	Abbreviation	Figure #	Air dilution range
2 HydroxyAcetopenone	2HA	5 ,6	0.1 -0.01
Benzaldehyde	BENZ	2,3,4,5,6 Ext. Fig. 3,4,5	0.05 – 0.0002
Methyl Valerate	MTV	2,3,4, Ext. Fig. 3,4,5	-
Ethyl Valerate	EVT	2,3,4, Ext. Fig. 3,4,5	-
2 MethylValerAldehyde	2MVA	2,3,4, Ext. Fig. 3,4,5	-
2 Methyl 2 Propionate	2MP2P	2,3,4, Ext. Fig. 3,4,5	-
Hexanal		2,3,4, Ext. Fig. 3,4,5	-
3- Heptanone	3-HEPN	2,3,4, Ext. Fig. 3,4,5	-
PhenylPropionate	PhPr	2,3,4, Ext. Fig. 3,4,5	-
Ethyl Tiglate	ETG	2,3,4, Ext. Fig. 3,4,5	-
Pinene		2,3,4, Ext. Fig. 3,4,5,	-
Heptanoic Acid		2,3,4, Ext. Fig. 3,4,5	-
IsovalerAldehyde		2,3,4, Ext. Fig. 3,4,5	-
2-Heptanone	2-HEPN	2,3,4, Ext. Fig. 3,4,5	-
2 Methyl Butyric Acid	2MBA	2,3,4, Ext. Fig. 3,4,5,	-
Butyric Acid	BA	2,3,4, Ext. Fig. 3,4,5	-
Ethyl Butyrate	EB	2,3,4, Ext. Fig. 3,4,5	-
Propionic Acid	PA	2,3,4, Ext. Fig. 3,4,5	-
Trans-CinnamAldehyde	CINALD	2,3,4, Ext. Fig. 3,4,5	-

- 1 Reddy, G., Zak, J. D., Vergassola, M. & Murthy, V. N. Antagonism in olfactory receptor neurons and its implications for the perception of odor mixtures. *Elife* **7** (2018). <https://doi.org/10.7554/eLife.34958>
- 2 Zak, J. D., Reddy, G., Vergassola, M. & Murthy, V. N. Antagonistic odor interactions in olfactory sensory neurons are widespread in freely breathing mice. *Nat. Commun.* **11**, 1-12 (2020). <https://doi.org/10.1038/s41467-020-17124-5>