Lecture I

Introduction to Olfaction

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NYU NEUROSCIENCE

Chemical senses:

olfaction
gustation
nociception

stimulus
↓
receptors
↓
neural networks
↓
behavior

Levels of understanding:

computational theory
algorithms and representation
hardware implementation

how it works
how it is built
how it evolved

bacteria
c-elegans
fly, larvae
mouse
human

Chemical senses:
olfaction

One of human senses

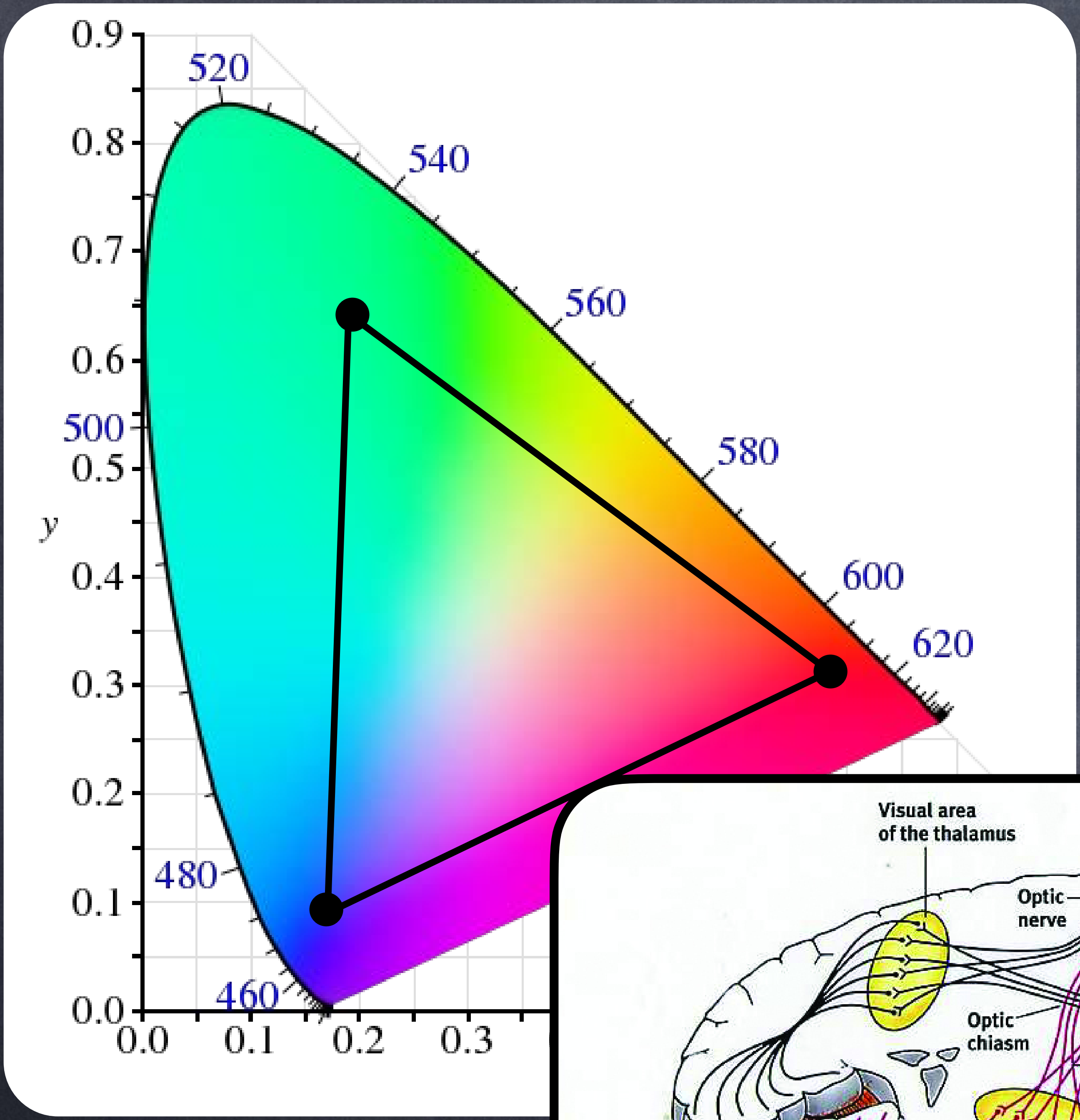
A window to the brain

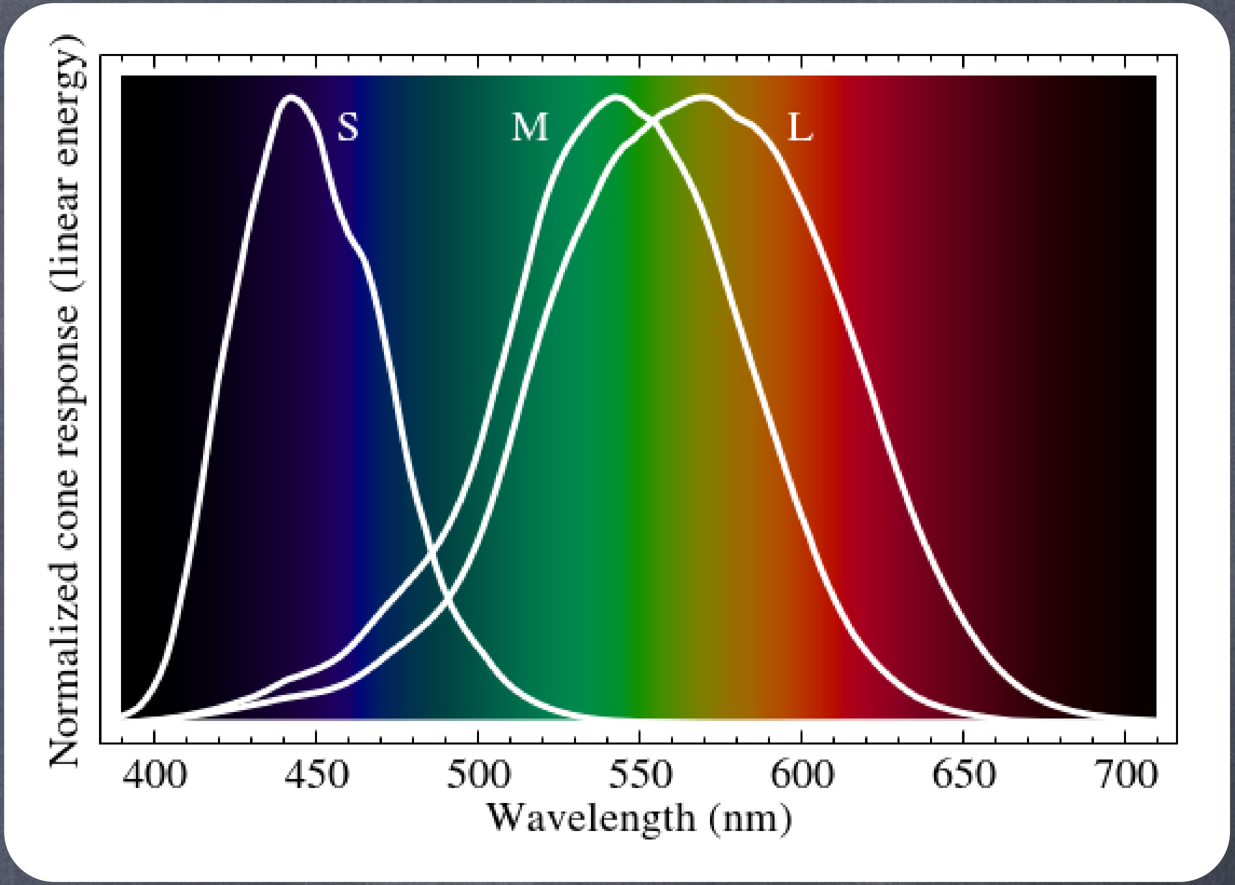
An interface with a poorly understood world of chemicals

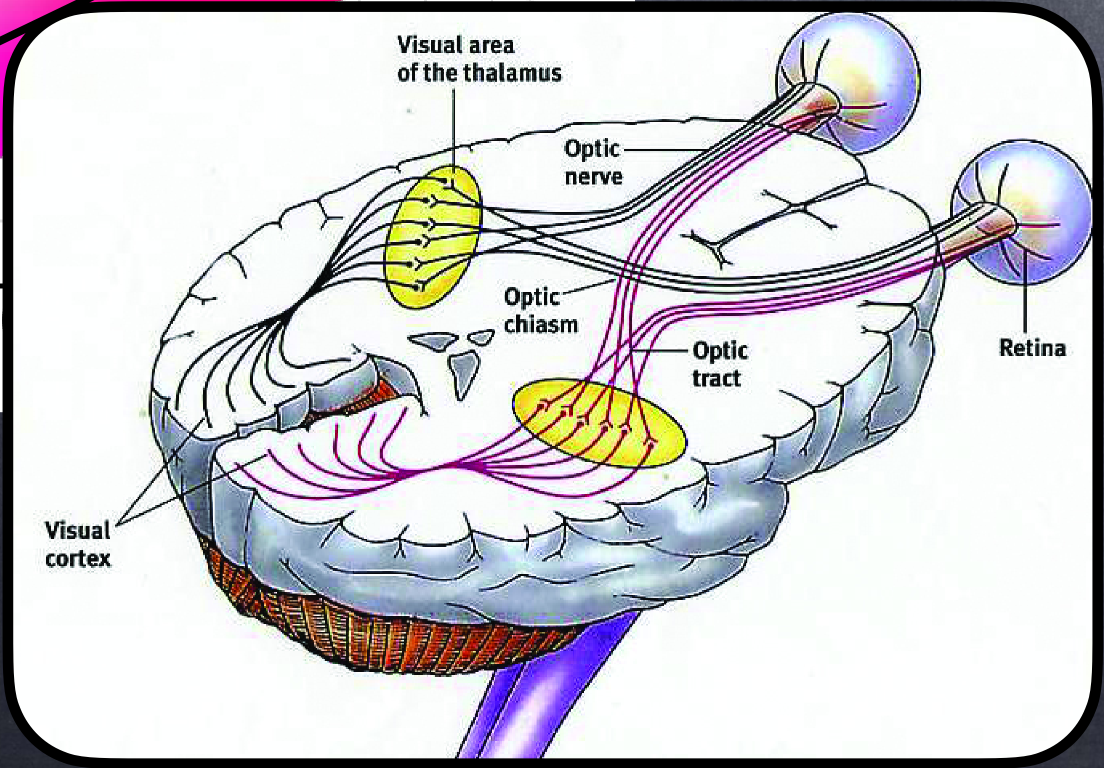
“Did you ever try to measure a smell? Can you tell whether one smell is just twice as strong as another. Can you measure the difference between one kind of smell and another. It is very obvious that we have very many different kinds of smells, all the way from the odor of violets and roses up to asafetida. But until you can measure their likenesses and differences you can have no science of odor. If you are ambitious to found a new science, measure a smell.”If you are ambitious to found a new science, measure a smell.”

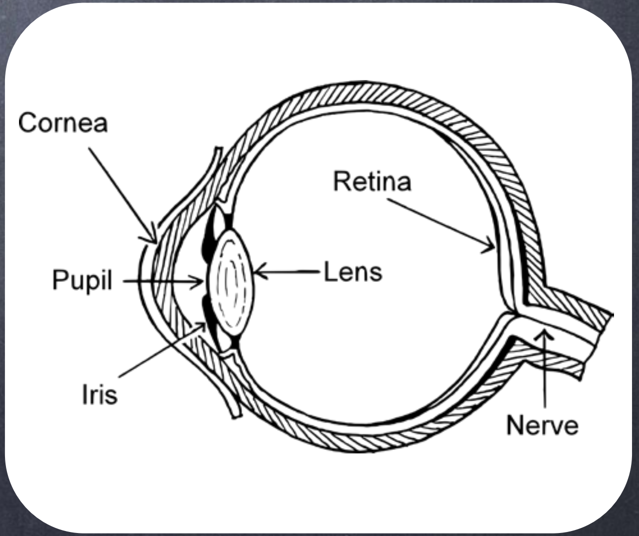
- Alexander Graham Bell (1914)

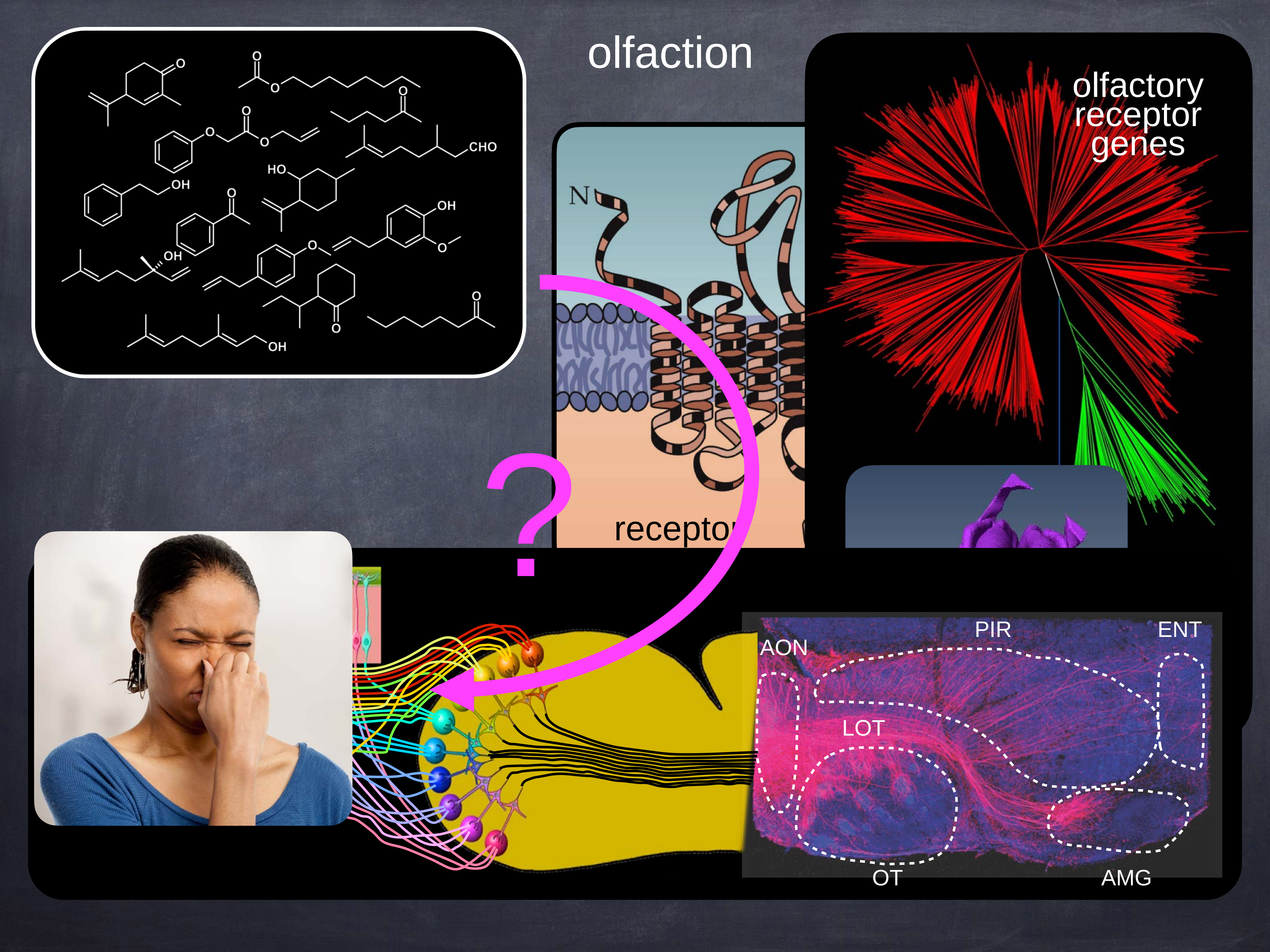
Human color vision

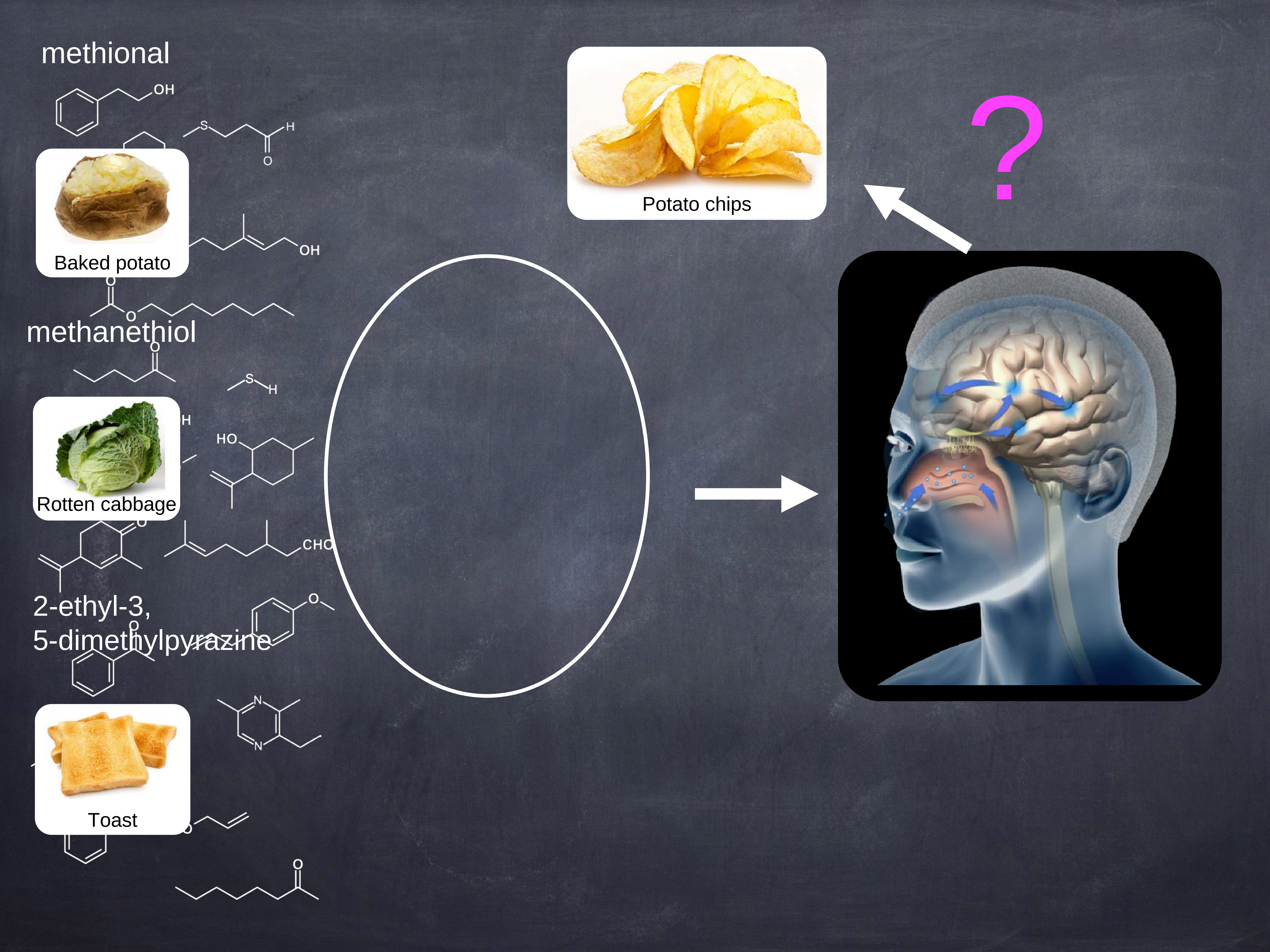




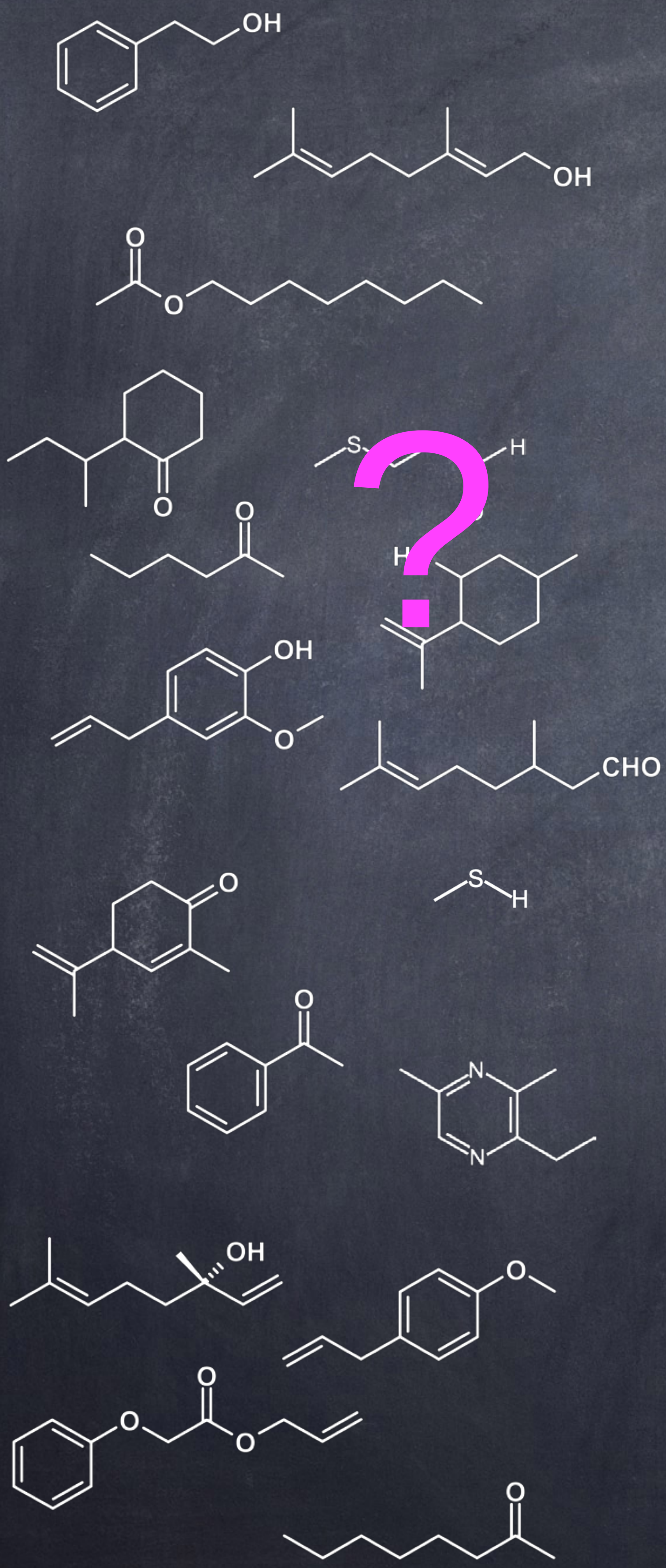


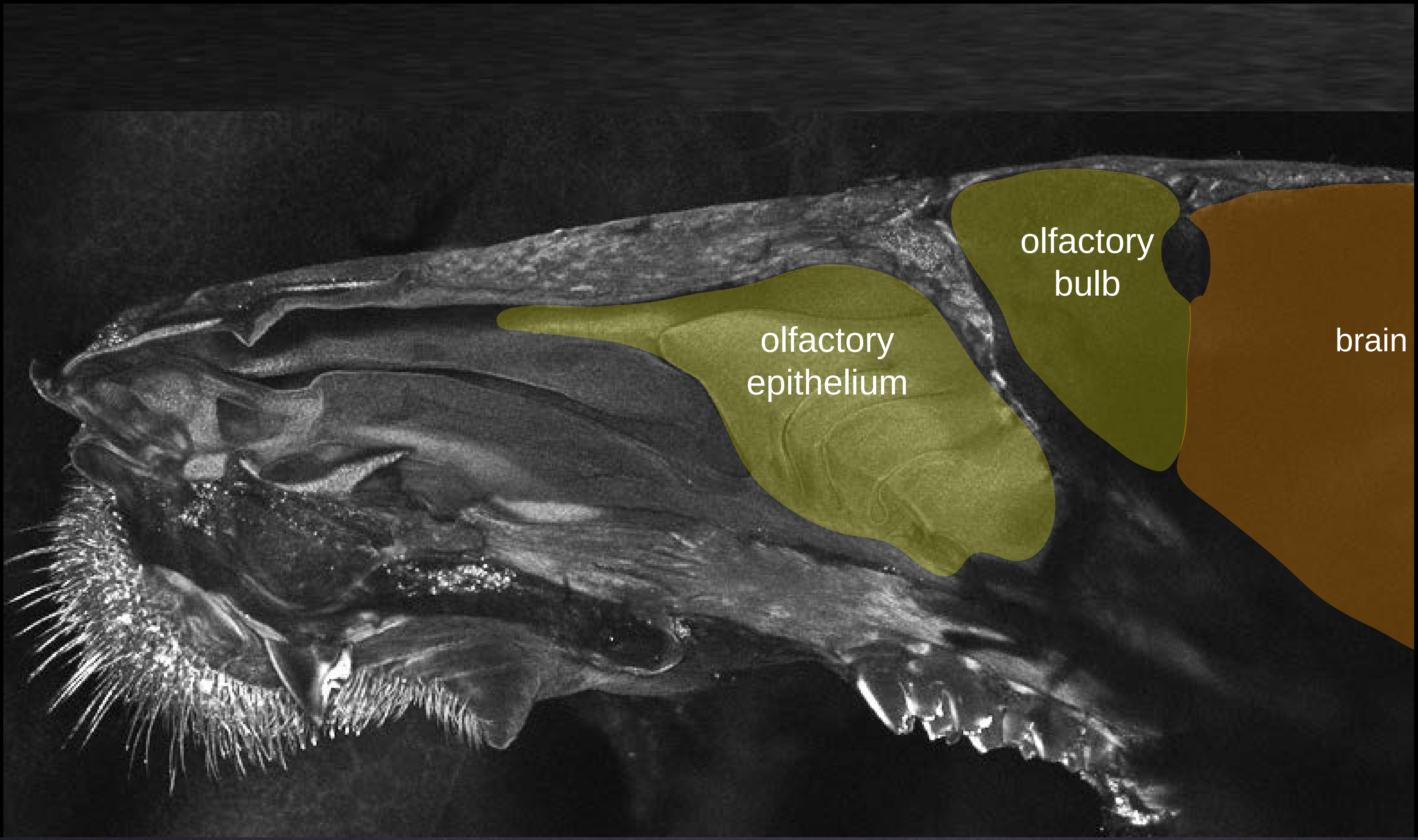


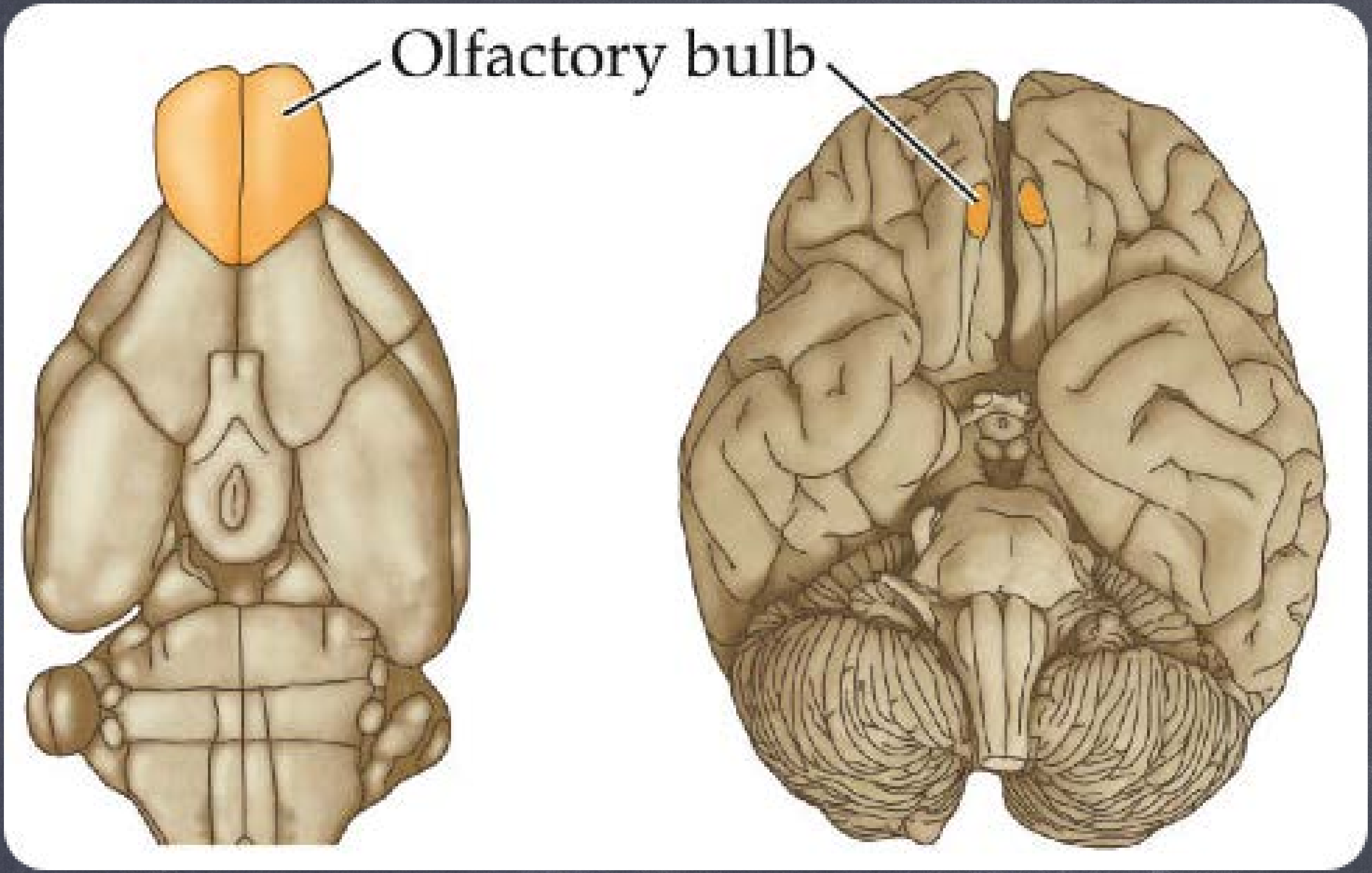

olfaction
olfactory receptor genes
N
recepto
?
AON
PIR
ENT
LOT
OT
AMG


methional
Baked potato
methanethiol
Rotten cabbage
2-ethyl-3,
5-dimethylpyrazine
Toast
Potato chips
?

Chemical detection



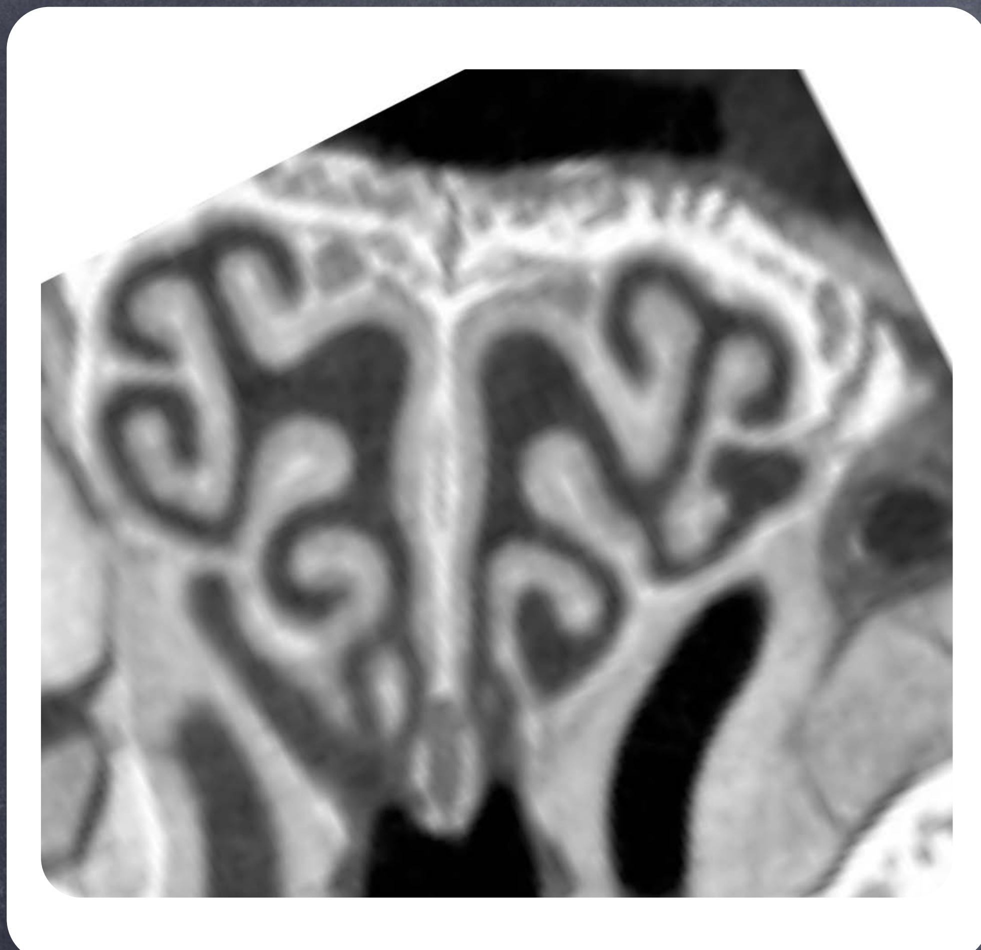

olfactory
bulb
olfactory
epithelium
brain

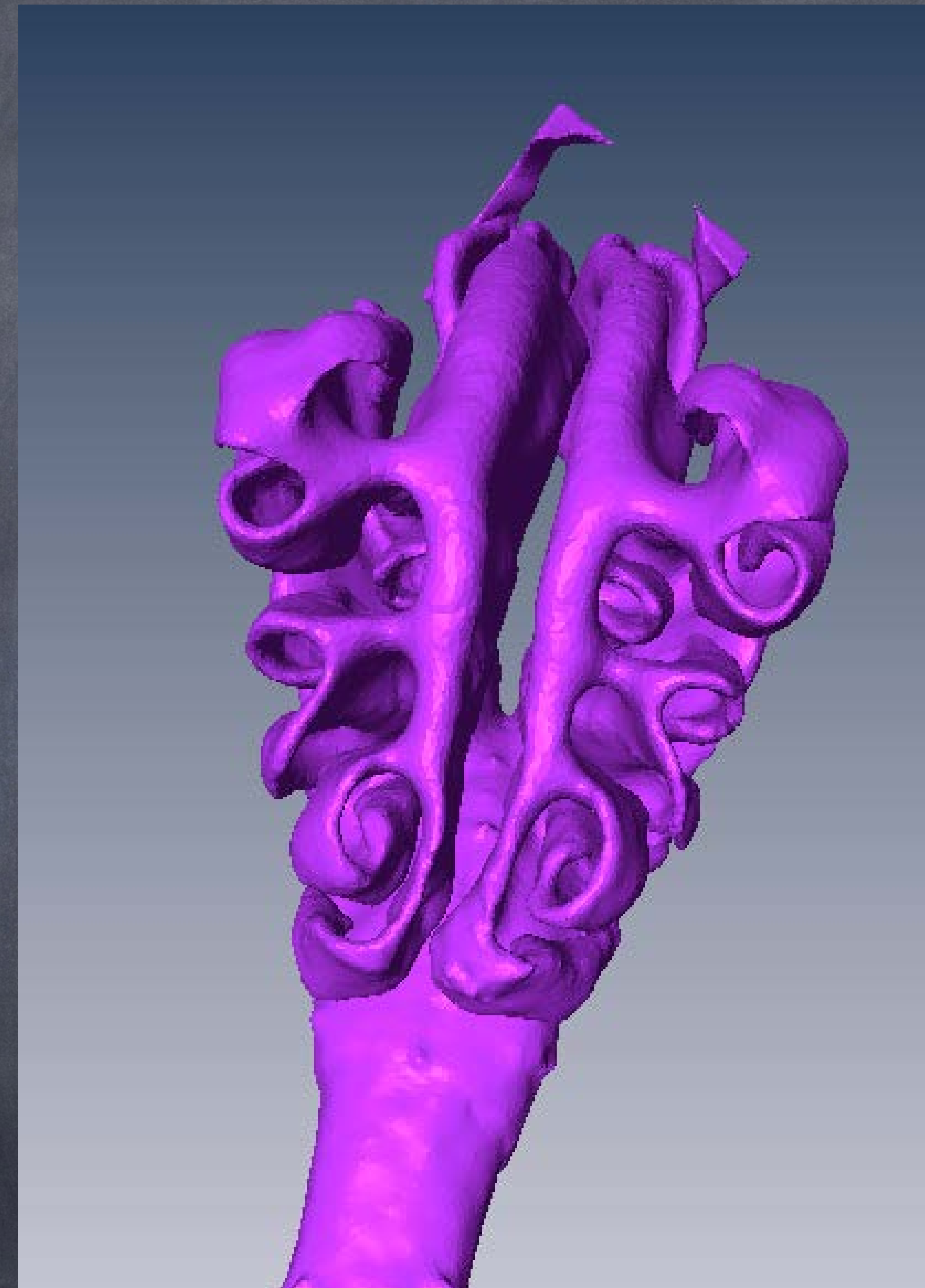


rat/mouse human

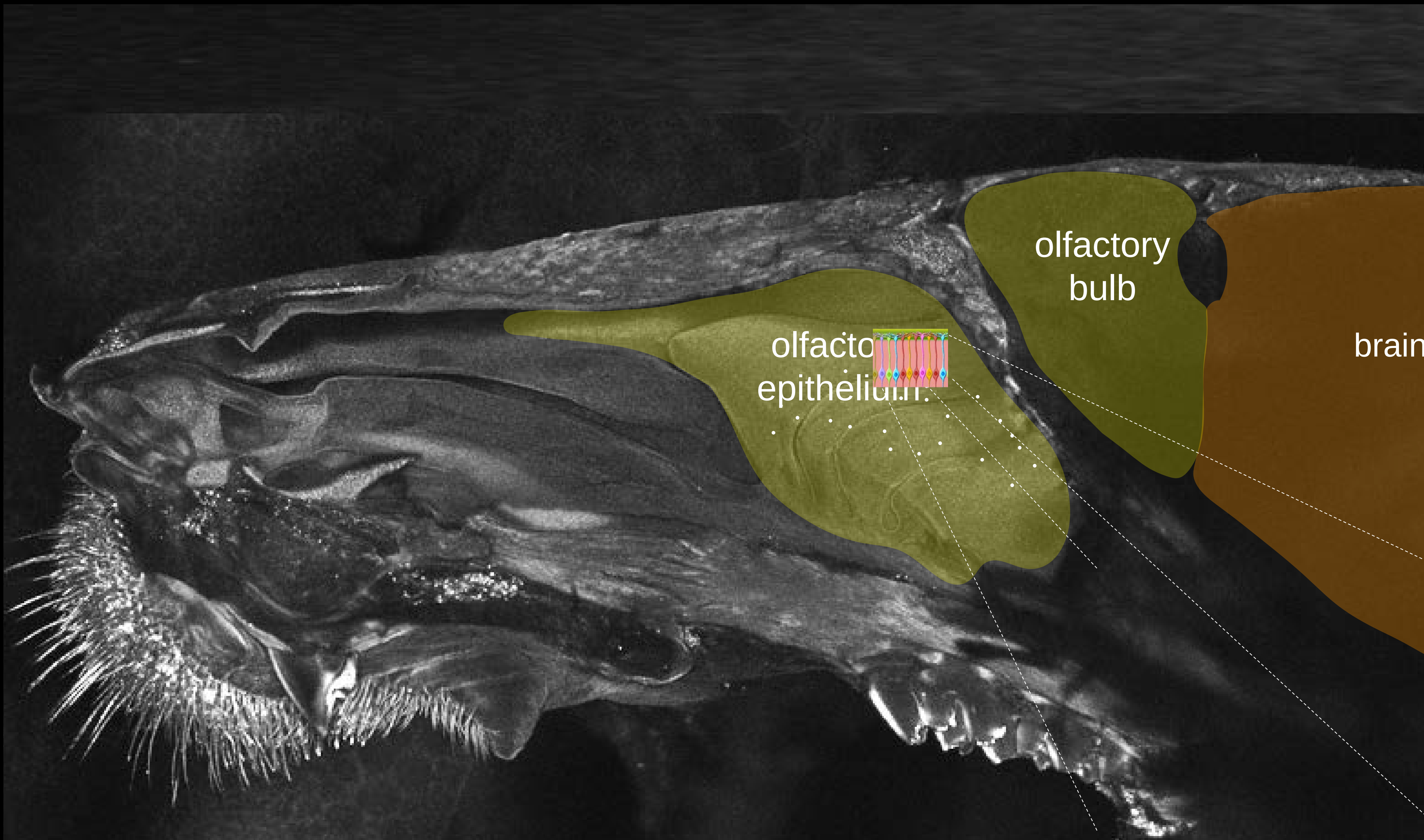
5% 0.2%

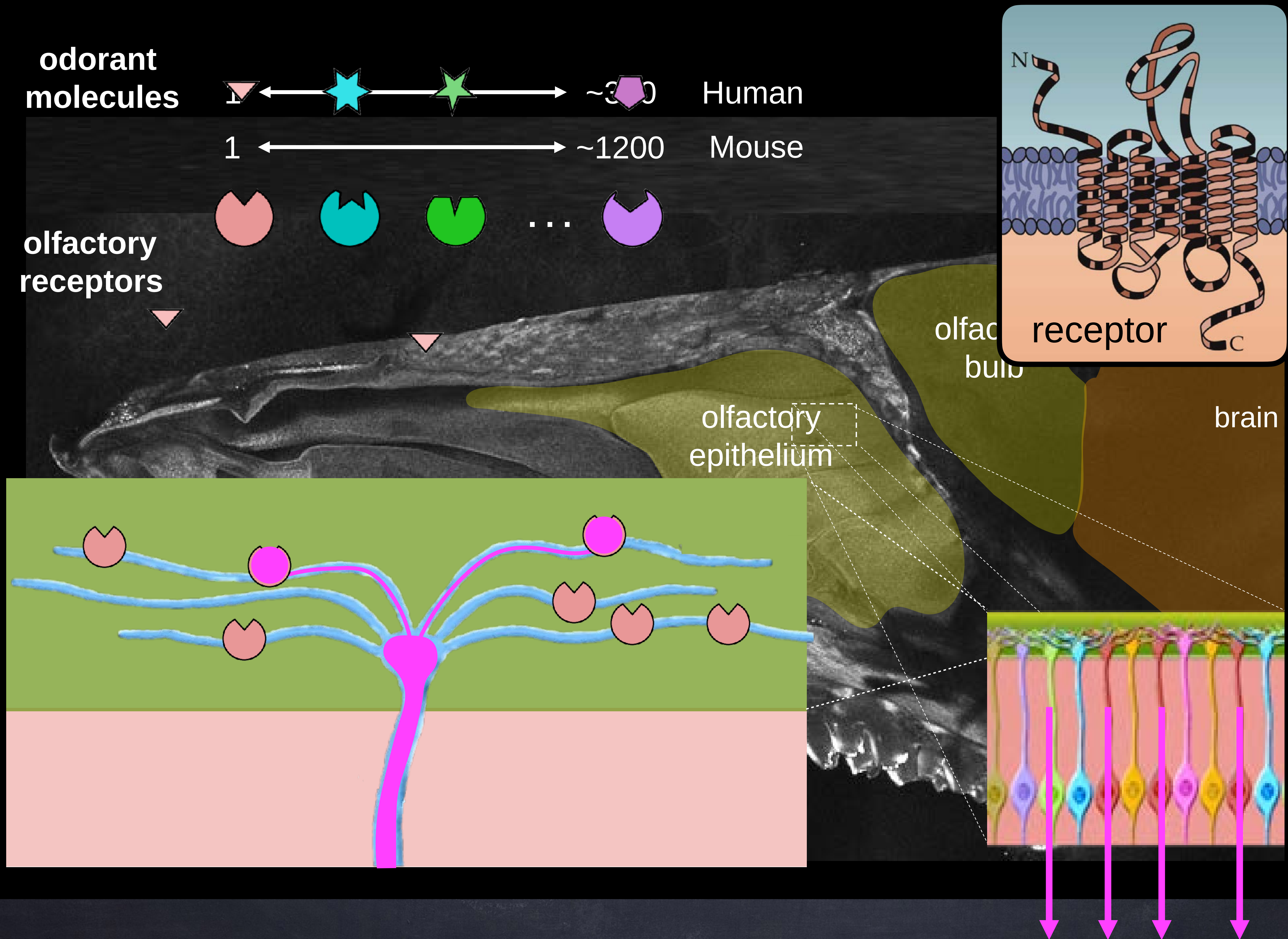
mouse nose



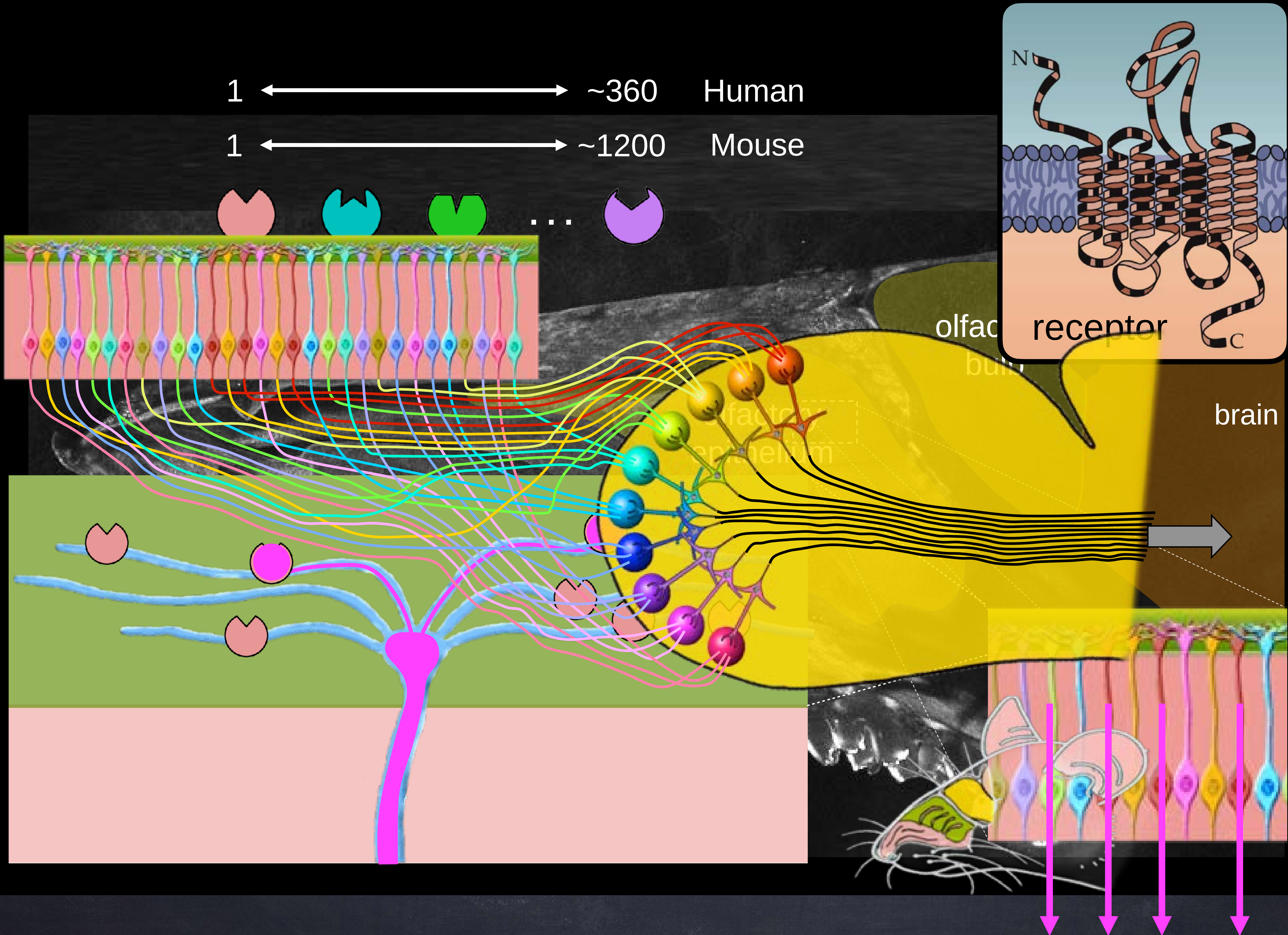


courtesy of Kay Zhao,
Monell Chemical Senses Center

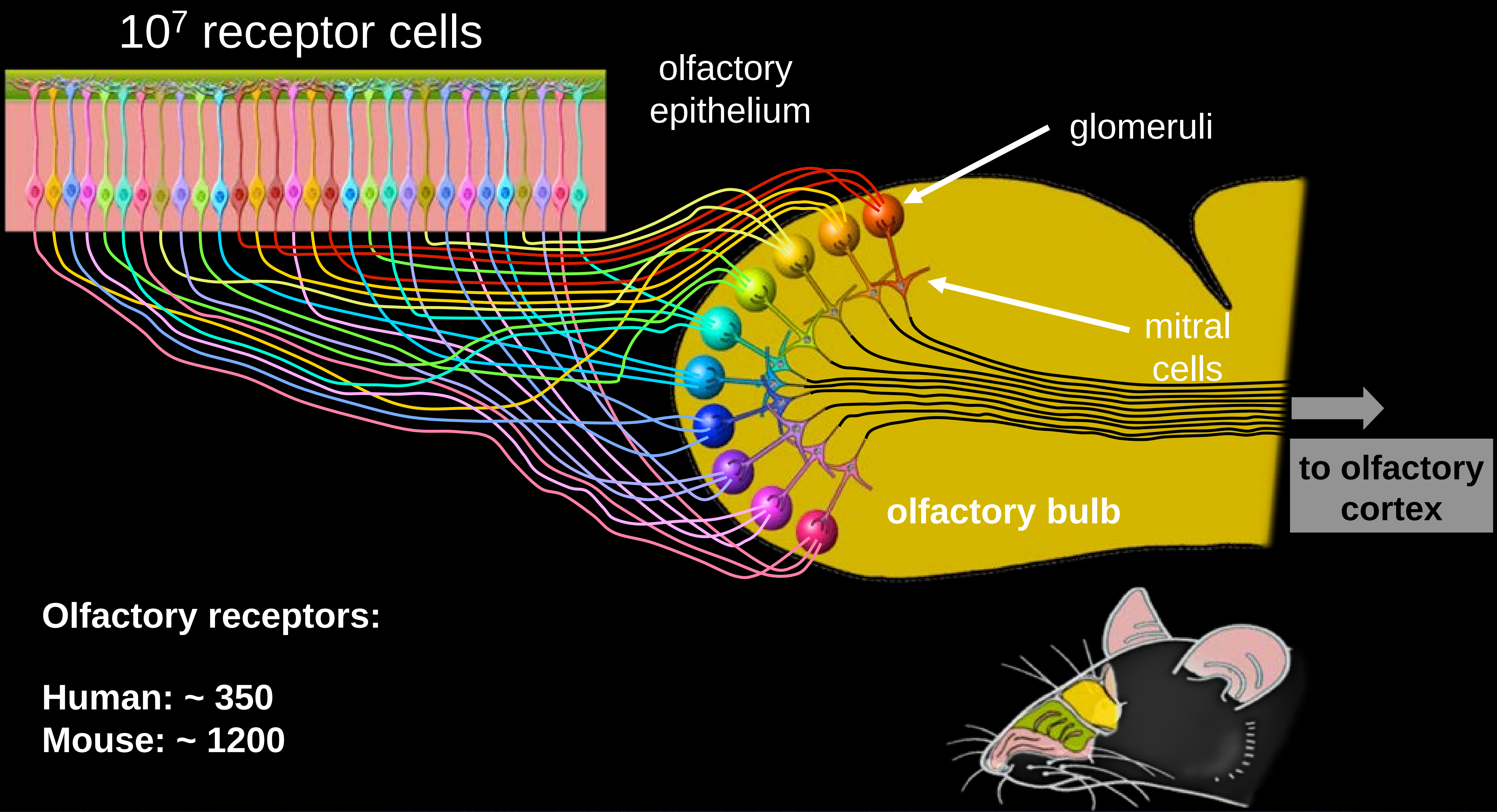

olfactory
bulb
brain
olfacto
epitheli



odorant molecules
1
~350
Human
1
~1200
Mouse
olfactory receptors
N
C
receptor
olfac
bulb
brain
olfactory epithelium



Modified from the artwork of Graeme Lowe



Olfactory receptors:

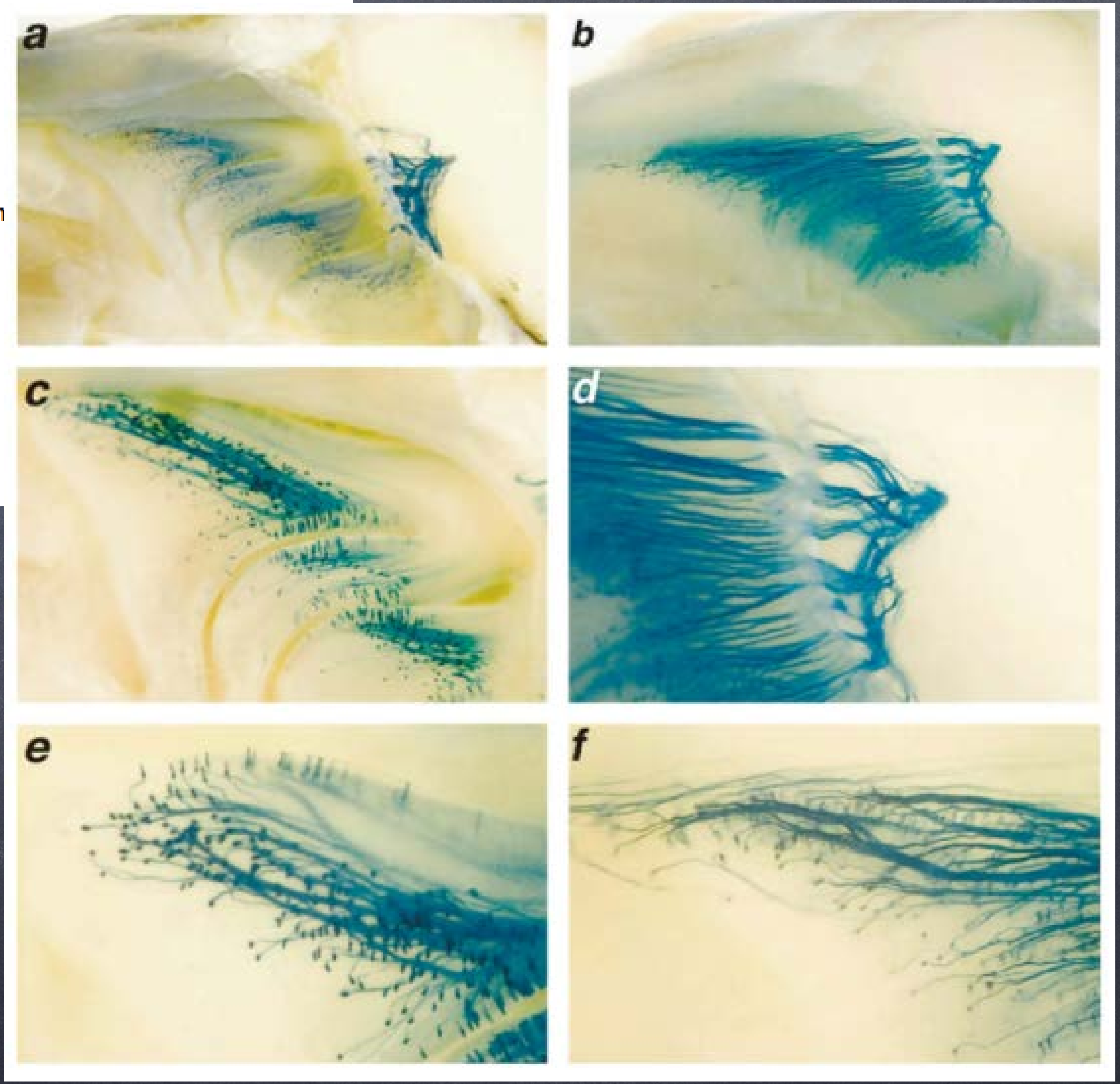
Human: ~ 350
Mouse: ~ 1200

Modified from the artwork of Graeme Lowe

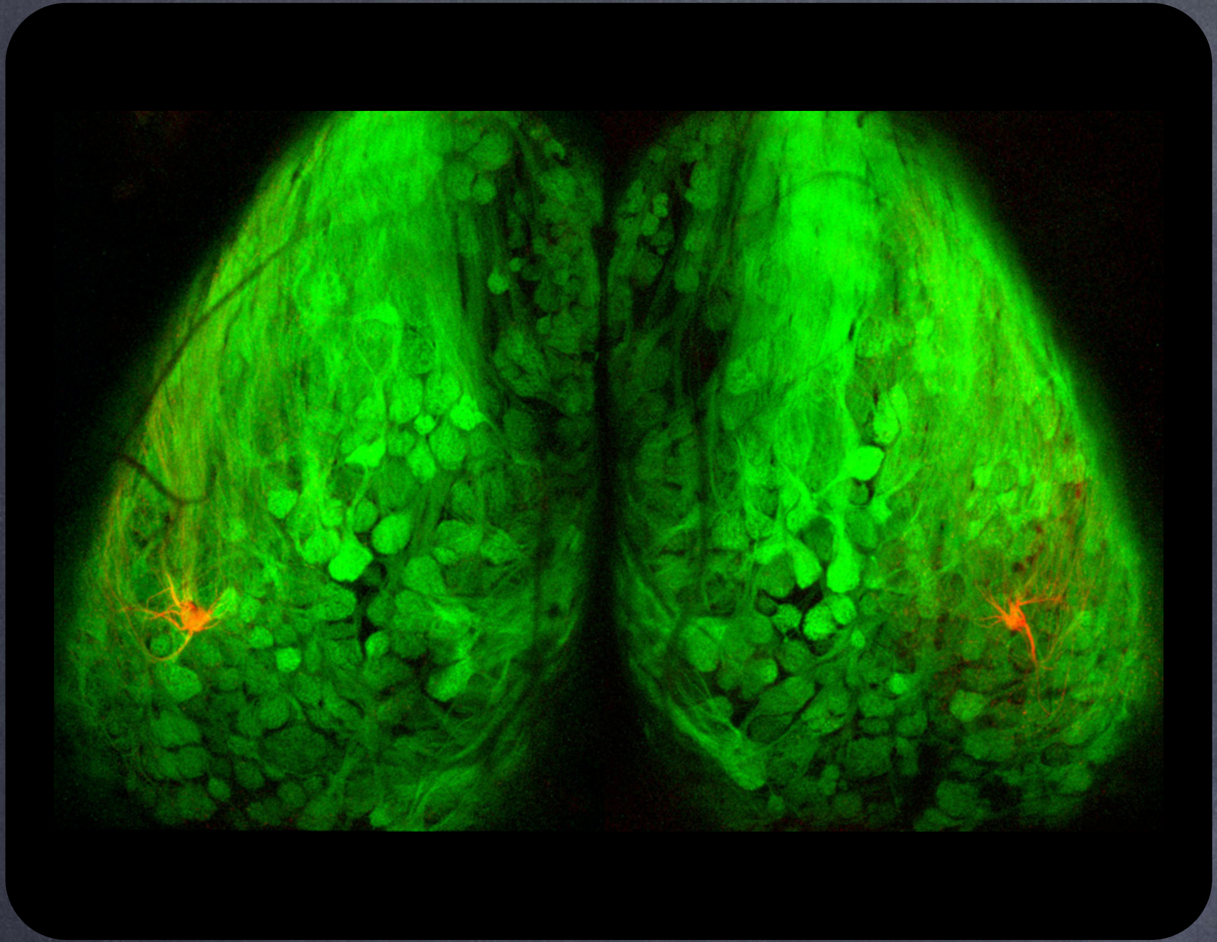
Cell, Vol. 87, 675–686, November 15, 1996, Copyright ©1996 by Cell Press

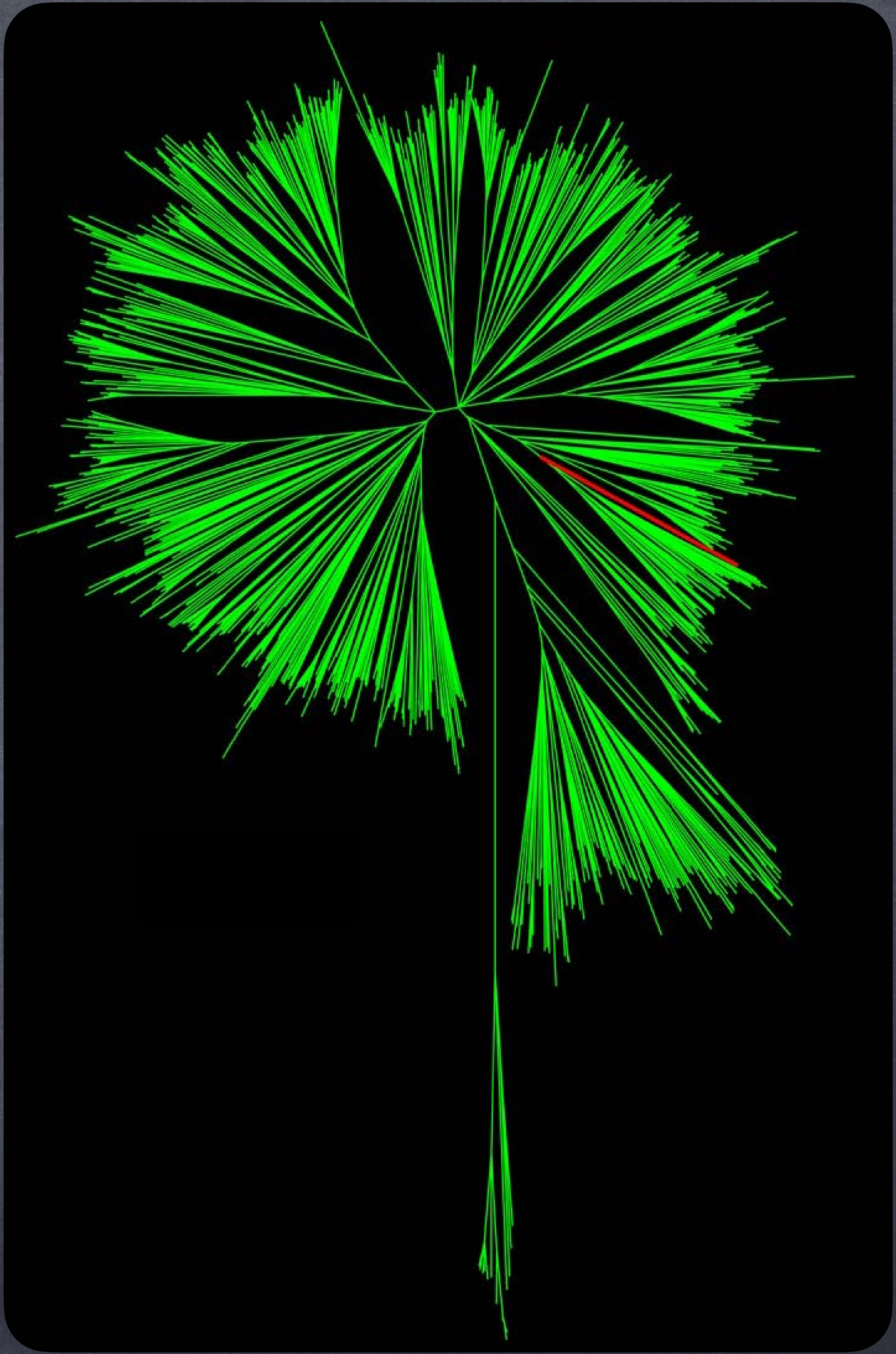
Visualizing an Olfactory Sensory Map

Peter Mombaerts,* Fan Wang, Catherine Dulac,
Steve K. Chao, Adriana Nemes, Monica Mendelsohn
James Edmondson, and Richard Axel
Department of Biochemistry
and Molecular Biophysics
Howard Hughes Medical Institute
and Center for Neurobiology and Behavior
College of Physicians and Surgeons
Columbia University
New York, New York 10032



The OR repertoire is mapped onto the olfactory bulb





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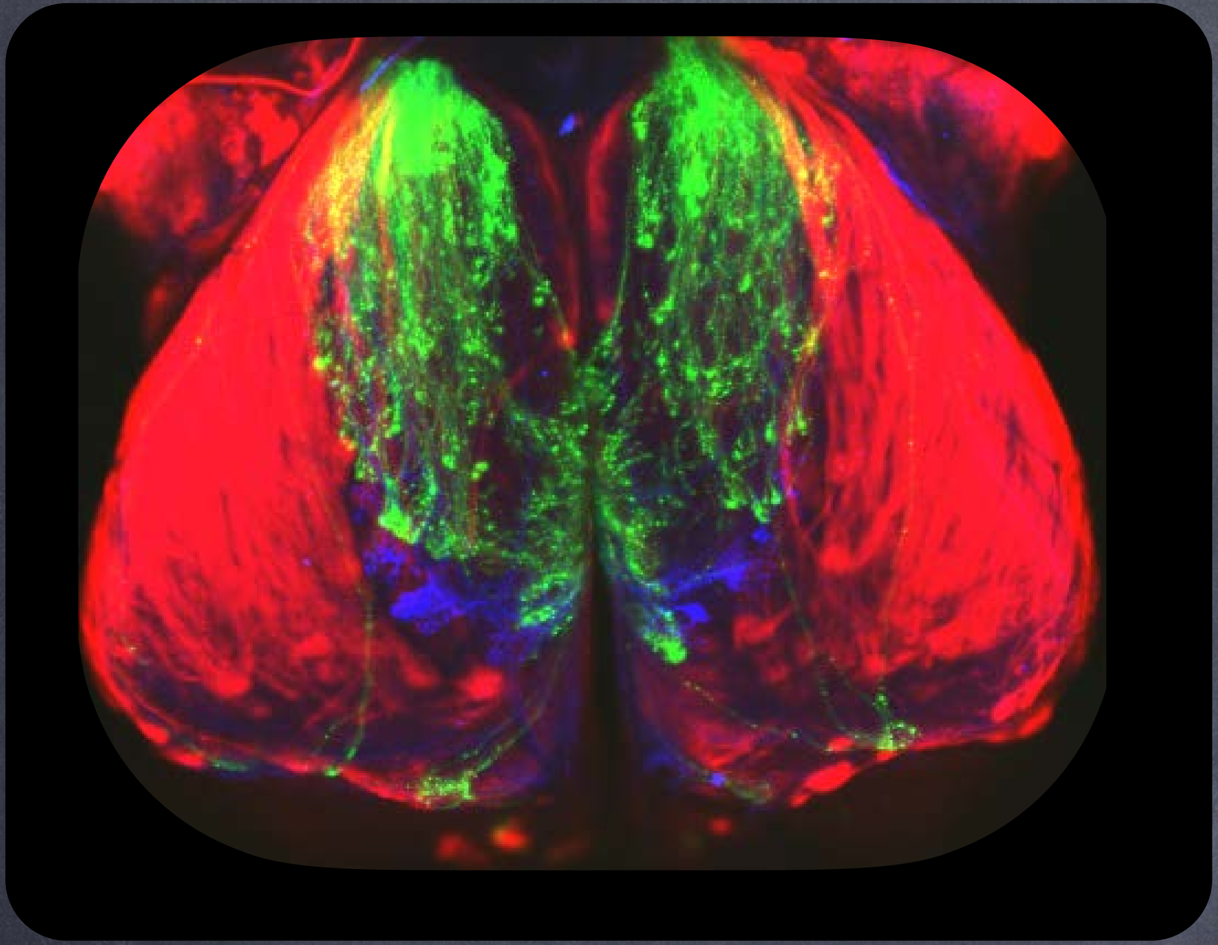
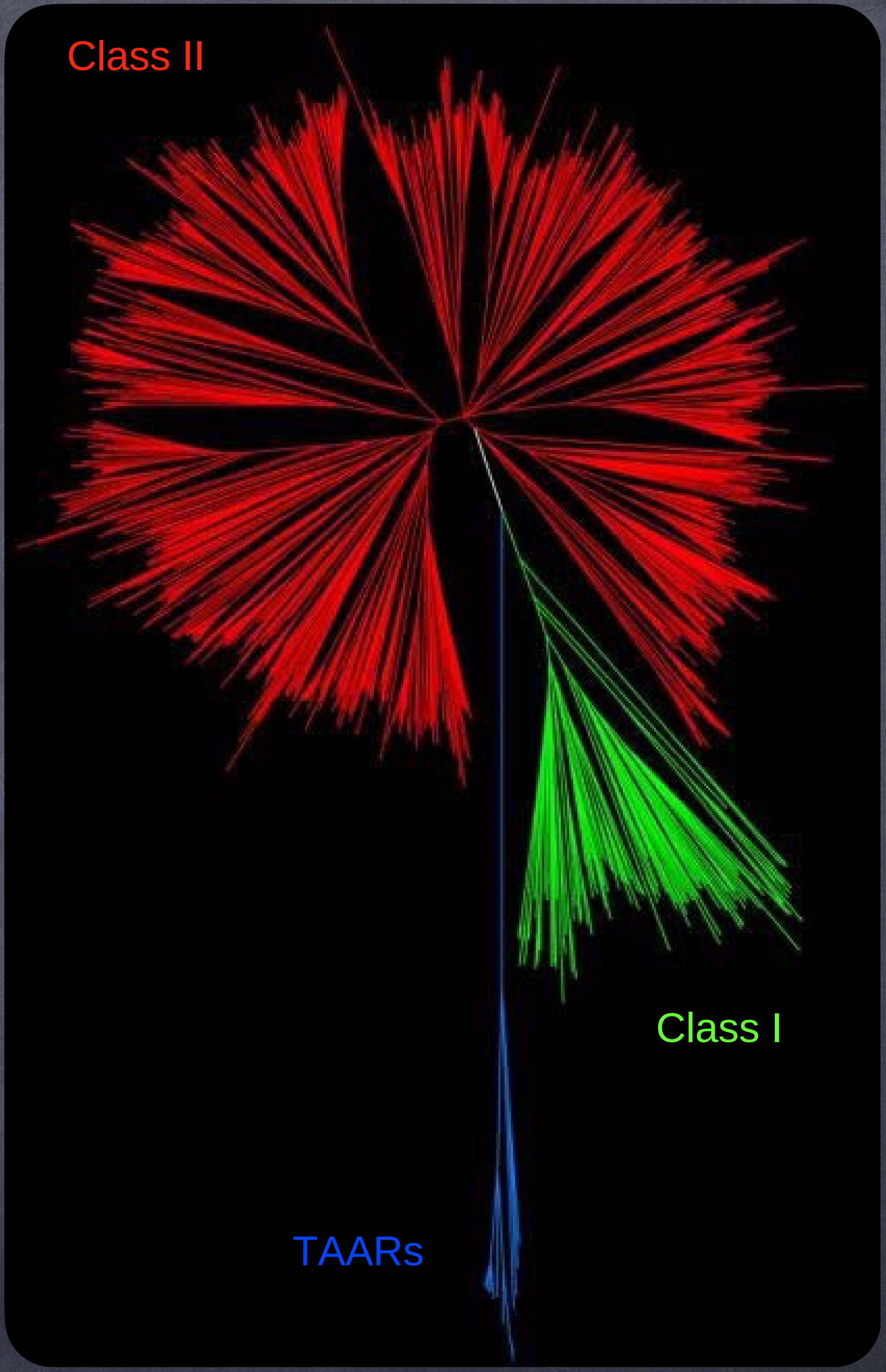
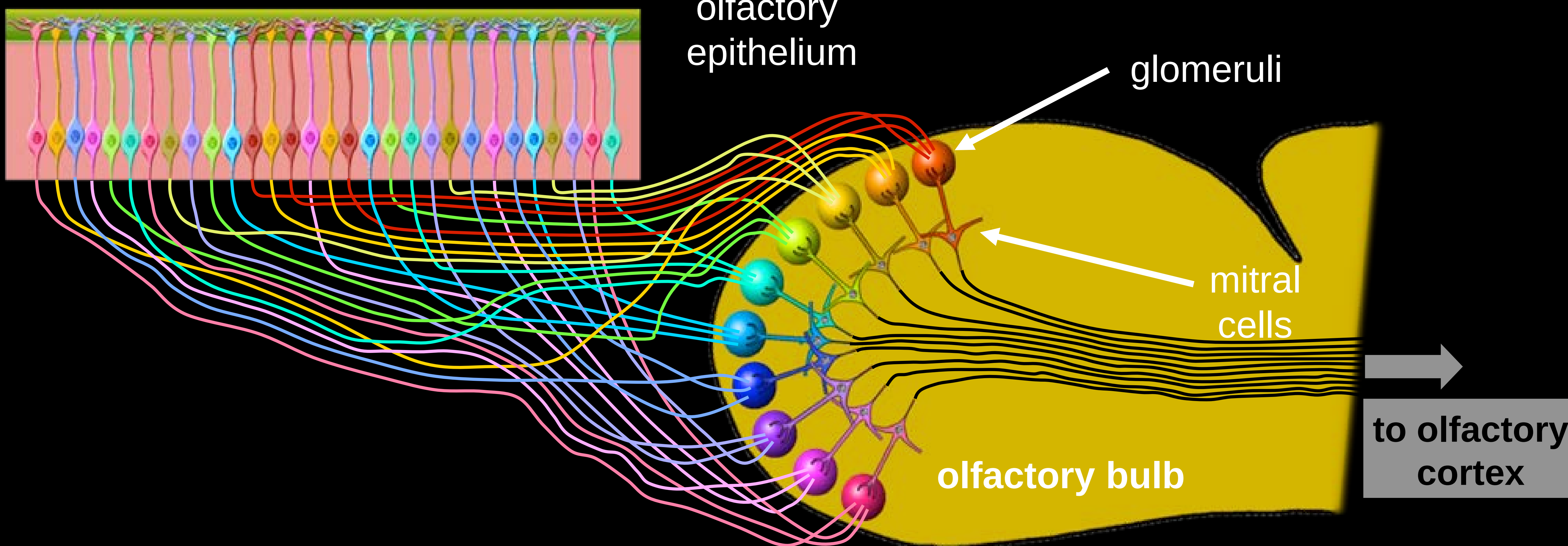




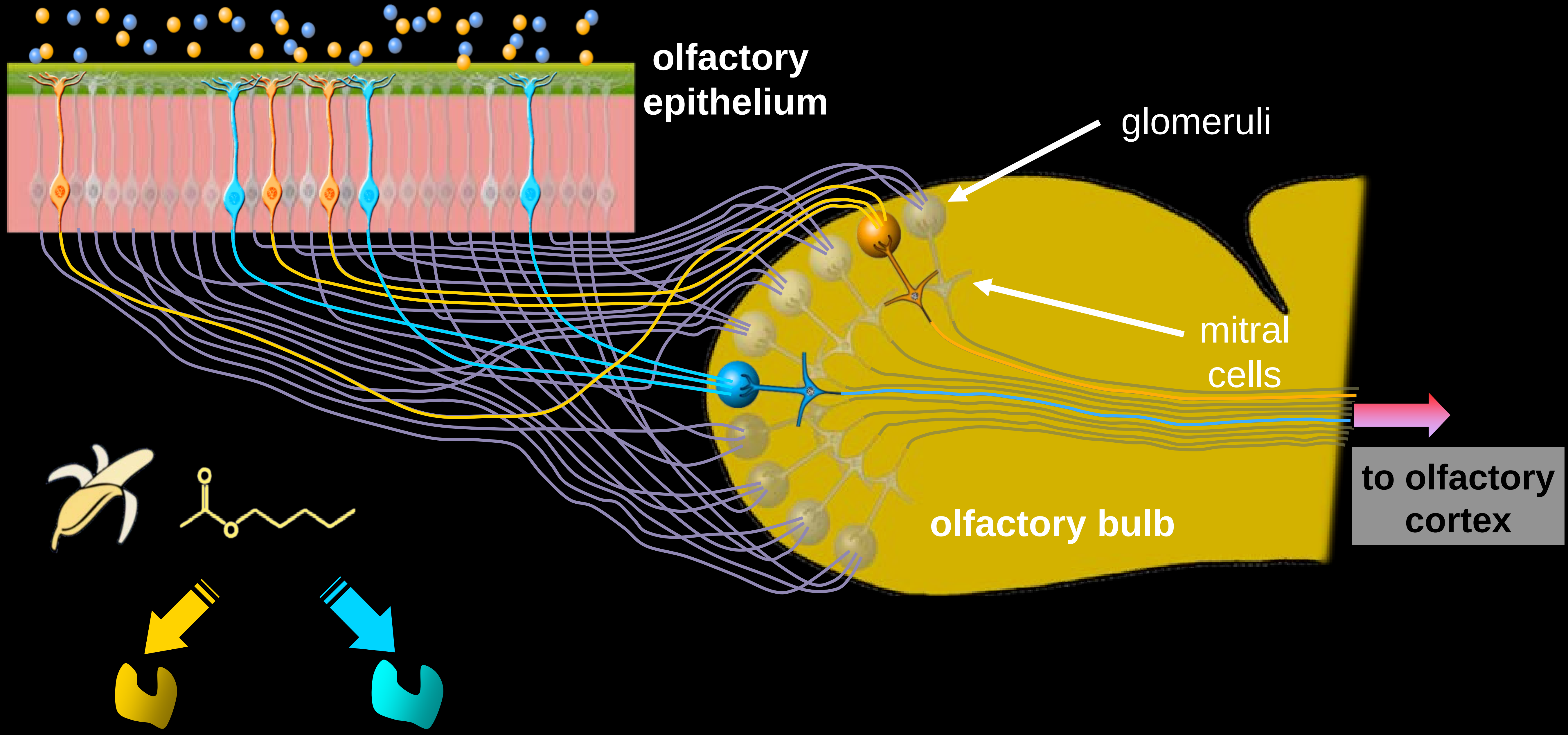
10^7 receptor cells



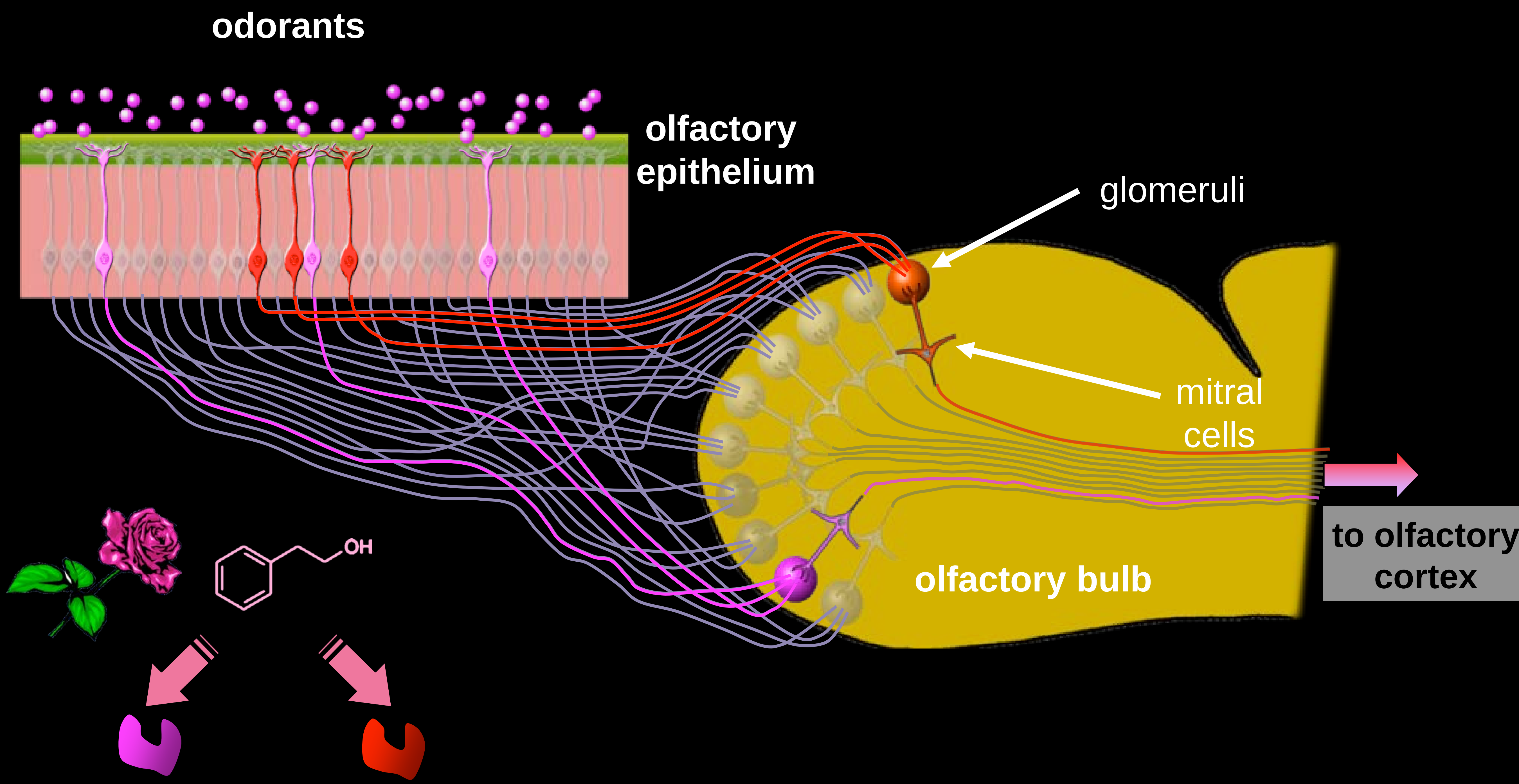
Olfactory receptors:

Human: ~ 350
Mouse: ~ 1200

Modified from the artwork of Graeme Lowe



Modified from the artwork of Graeme Lowe



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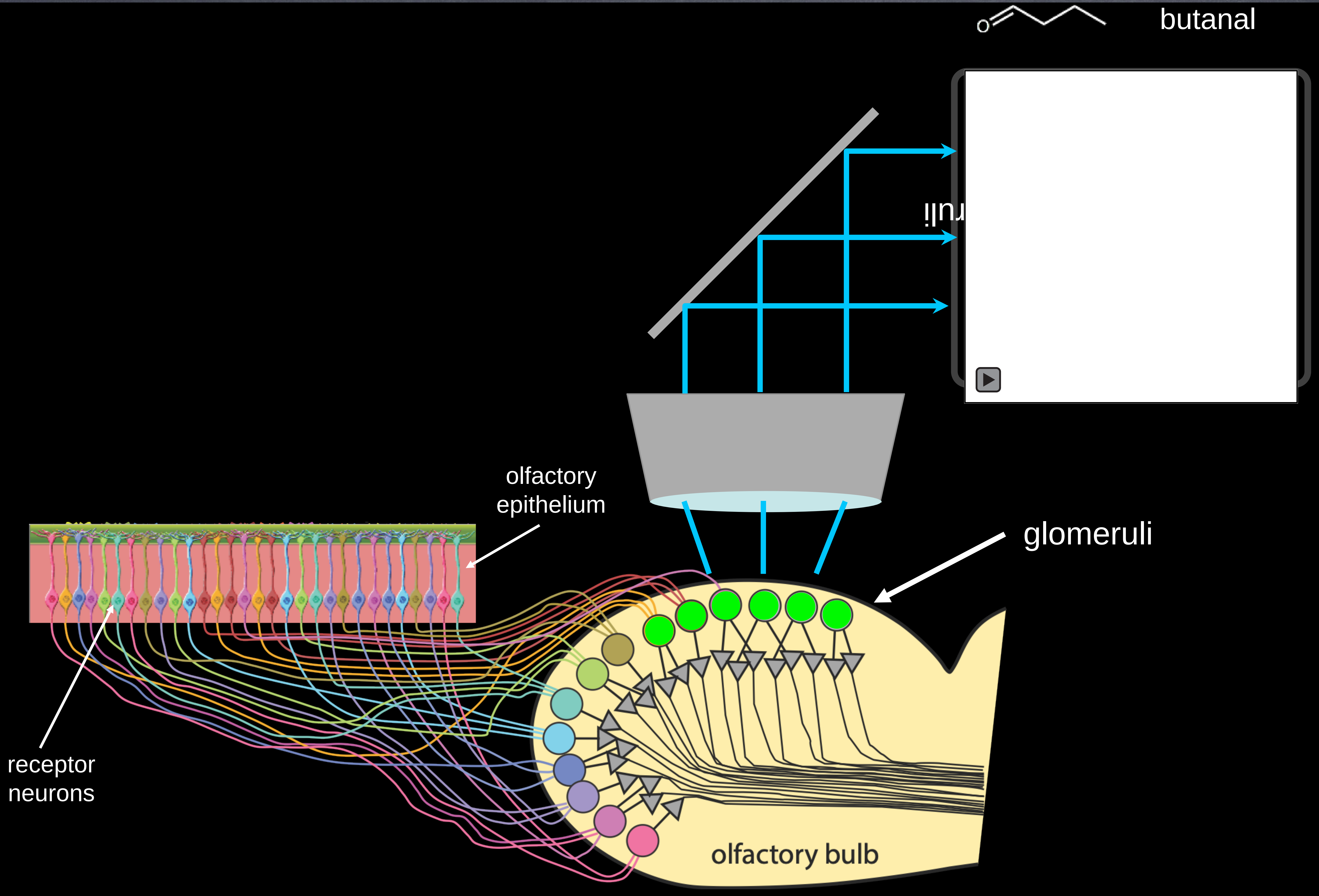
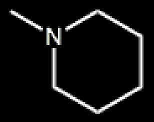
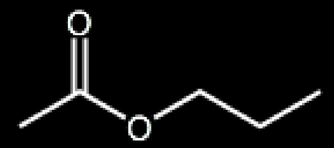


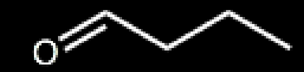
butanal
glomeruli
olfactory epithelium
receptor neurons
olfactory bulb



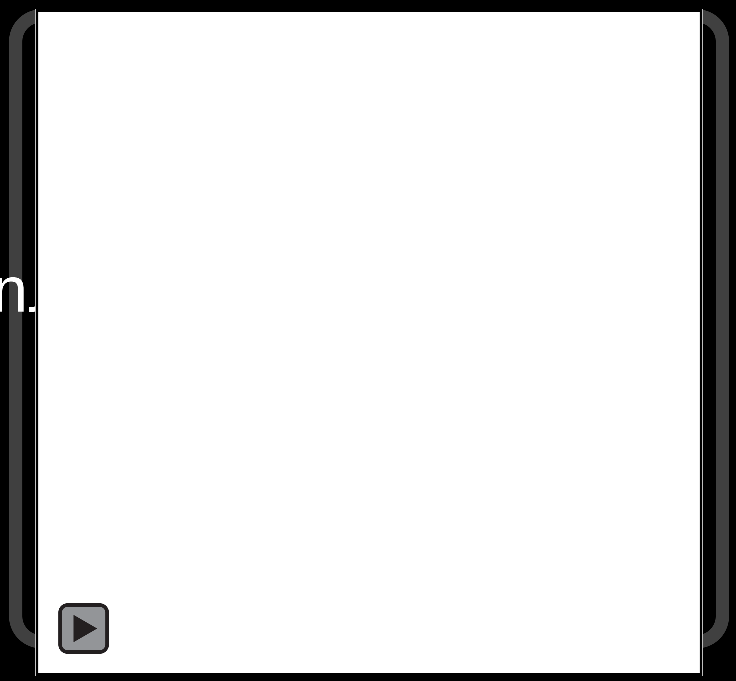
N-methylpiperidine

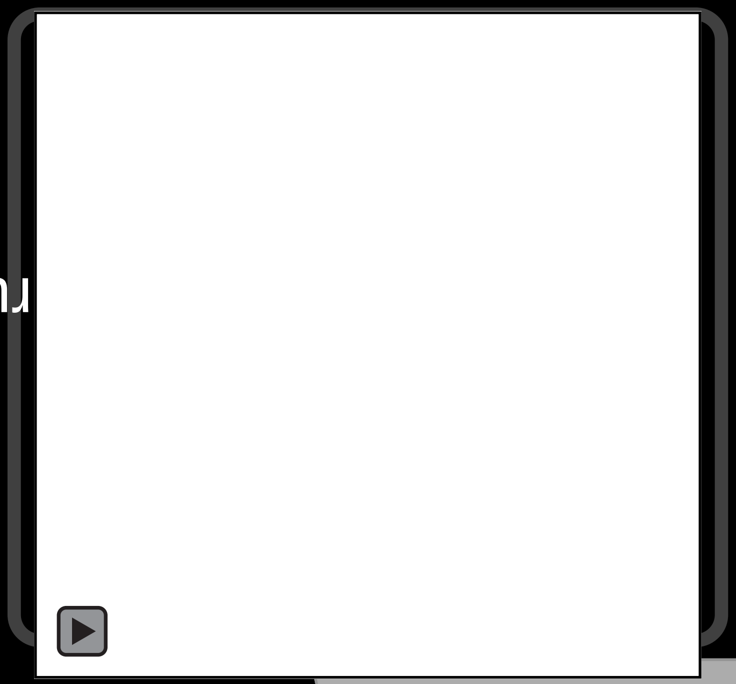


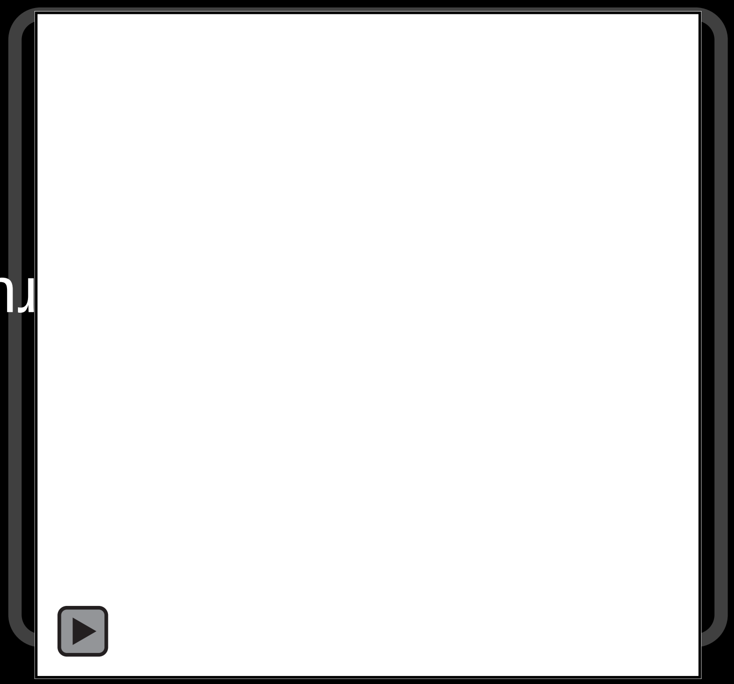
propylacetate

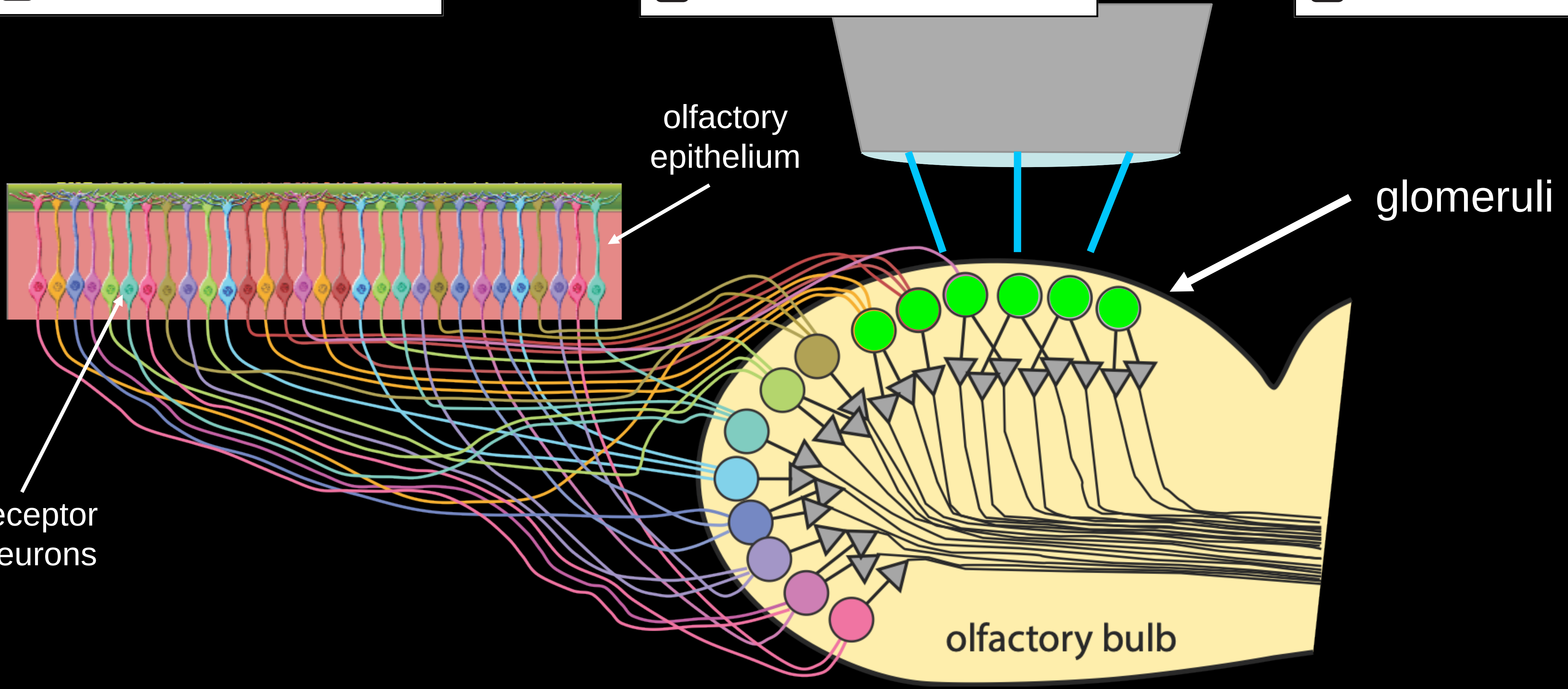


butanal



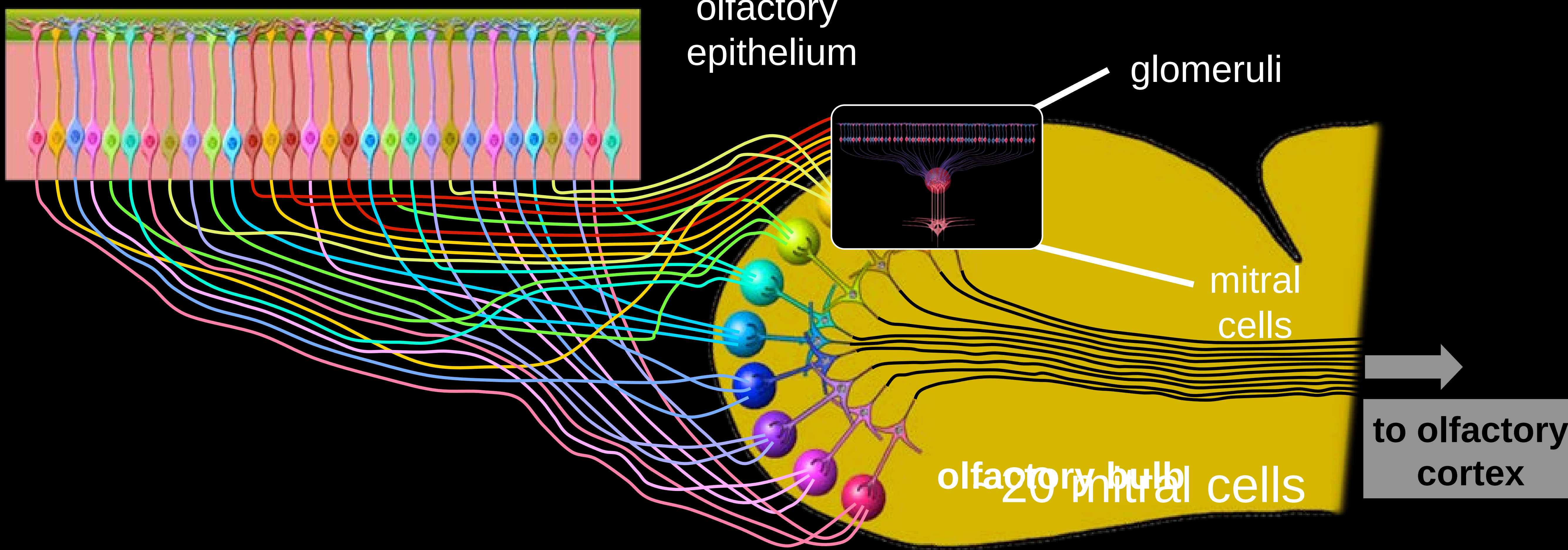






~5000 receptor cells

10^7 receptor cells



Olfactory receptors:

Human: ~ 350
Mouse: ~ 1200

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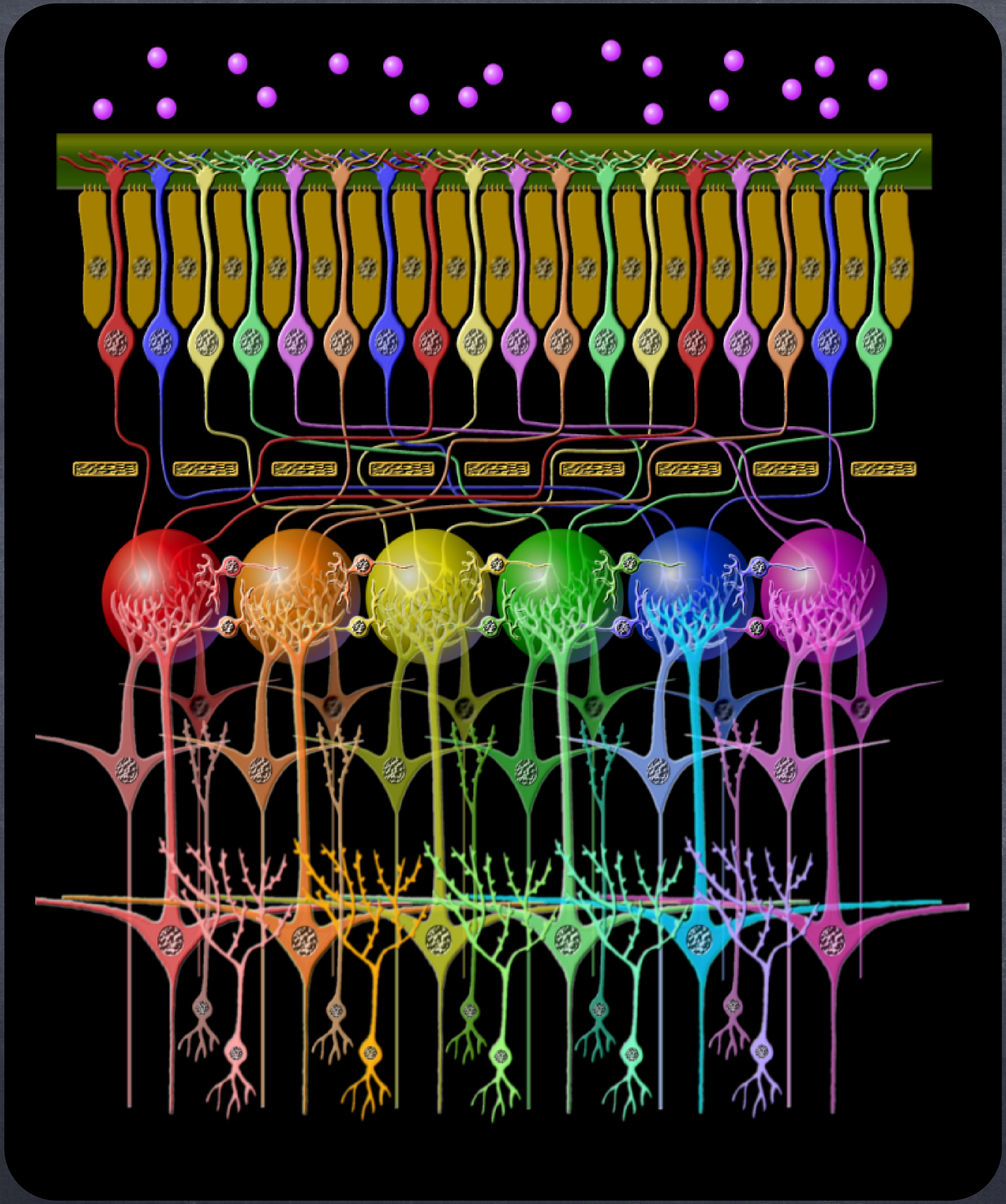
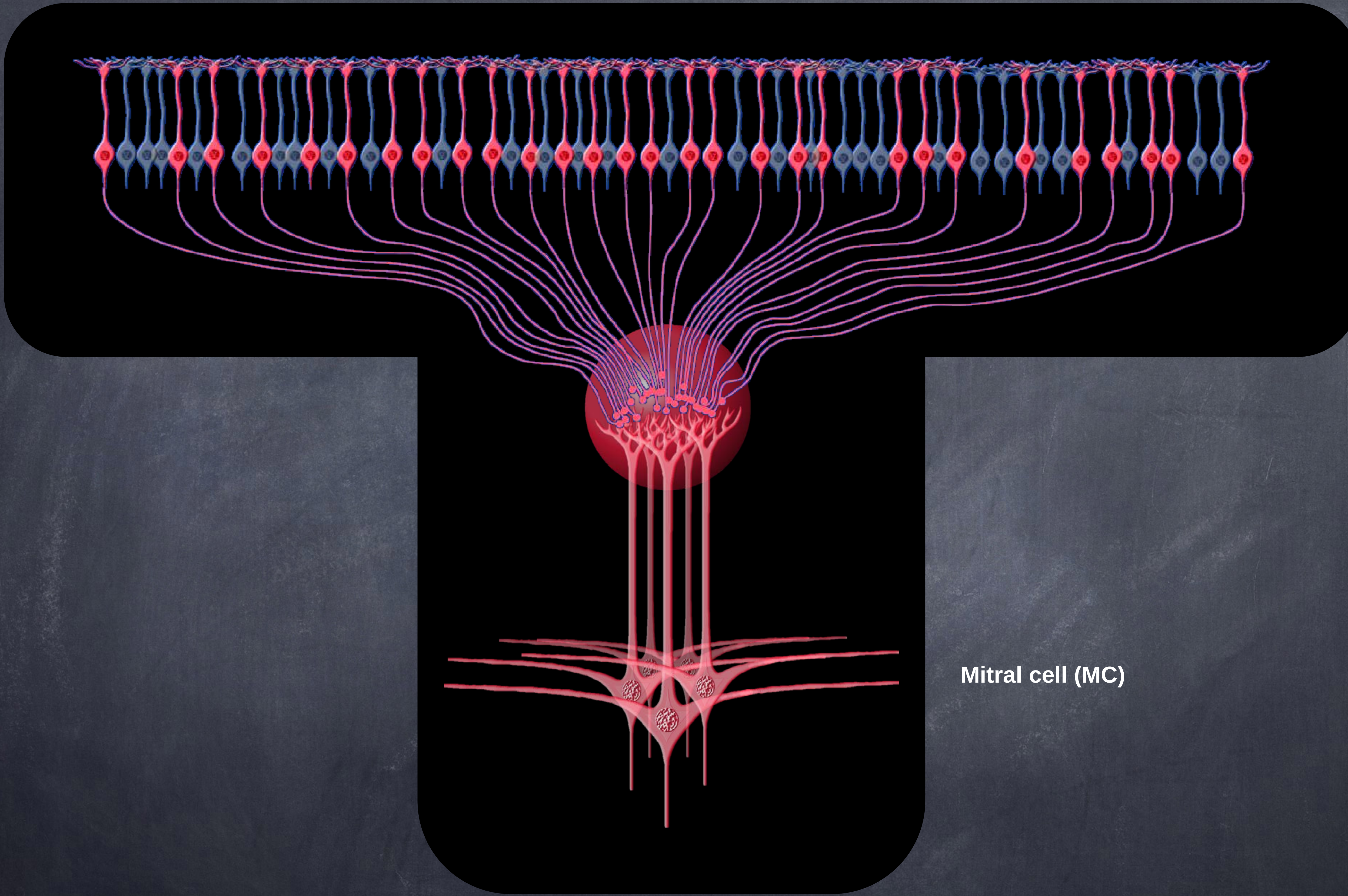
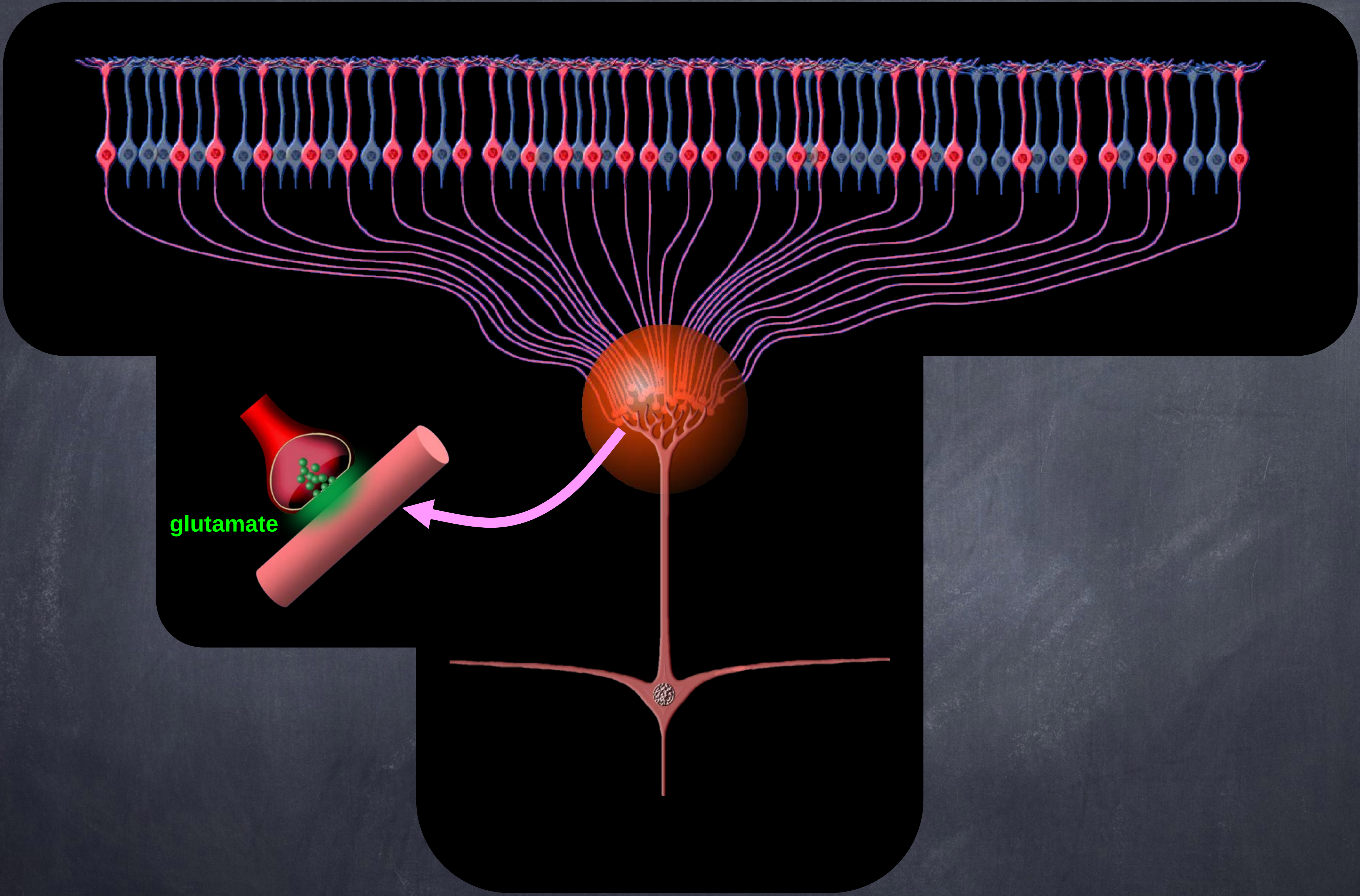


Odorants
Mucus
Olfactory epithelium
Cribrifor
m
plate
Olfactory Bulb
Supporting cell
Receptor cell (RC)
Periglomerular cell (PG)
Tufted cell (TC)
Mitral cell (MC)
Granule cell (GC)



Mitral cell (MC)



glutamate

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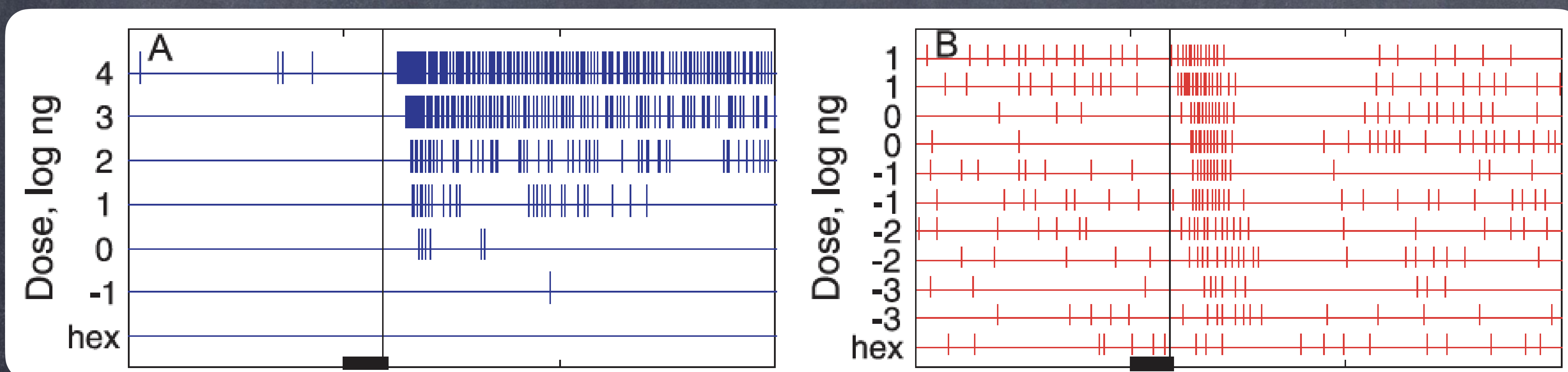
PLOS | COMPUTATIONAL BIOLOGY

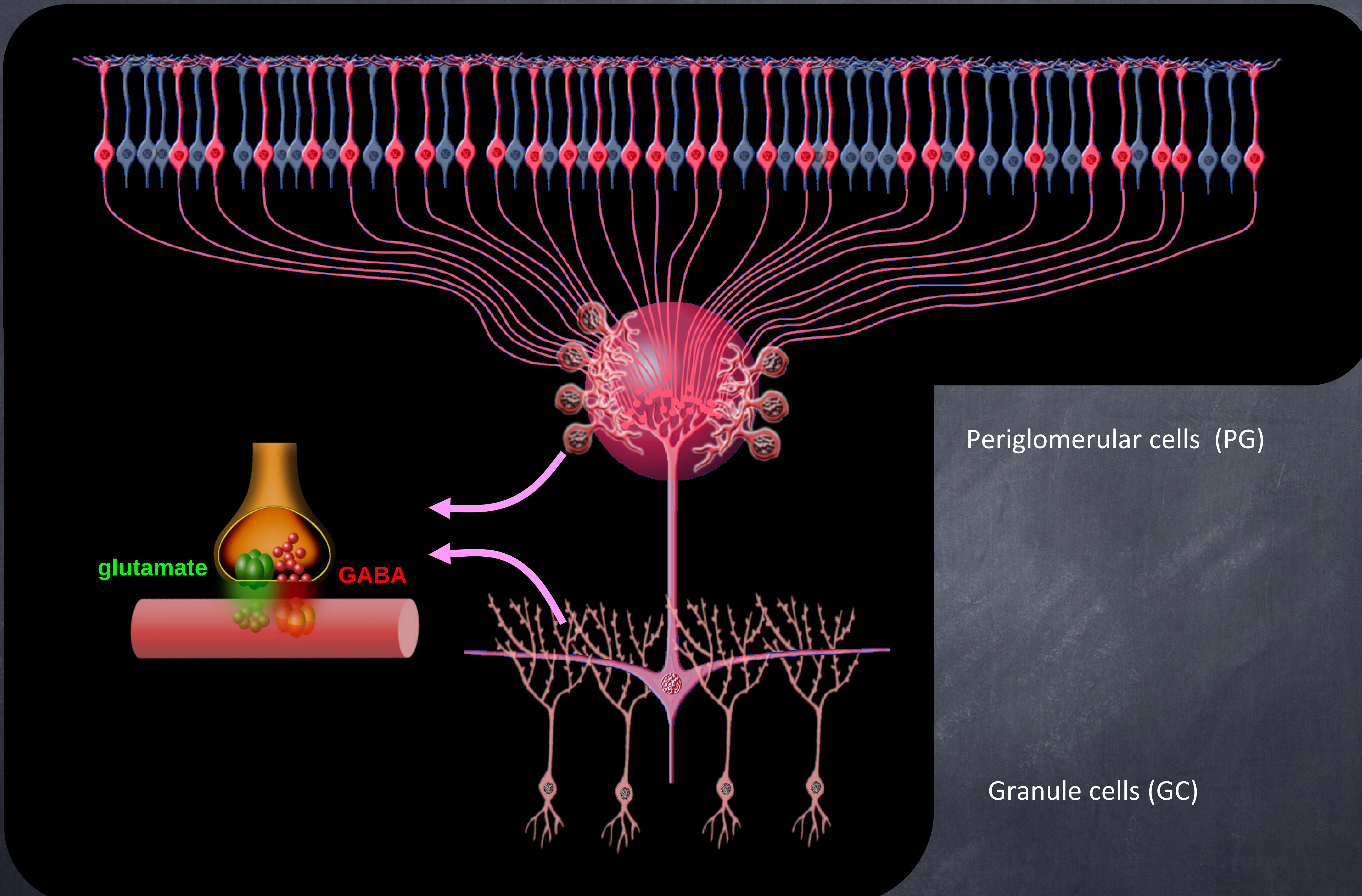
Heterogeneity and Convergence of Olfactory First-Order Neurons Account for the High Speed and Sensitivity of Second-Order Neurons

Jean-Pierre Rospars[1]*, Alexandre Grémiaux[1¤a], David Jarriault[1¤b], Antoine Chaffiol[1¤c], Christelle Monsempes[1], Nina Deisig[1], Sylvia Anton[1¤d], Philippe Lucas[1], Dominique Martinez[1,2]

1 Institut National de la Recherche Agronomique (INRA), Unité Mixte de Recherche 1392 Institut d'Ecologie et des Sciences de l'Environnement de Paris, Versailles, France,
2 Laboratoire Lorrain de Recherche en Informatique et ses Applications (LORIA), Unité Mixte de Recherche 7503, Centre National de la Recherche Scientifique (CNRS), Vandœuvre-lès-Nancy, France

OSNs PNs

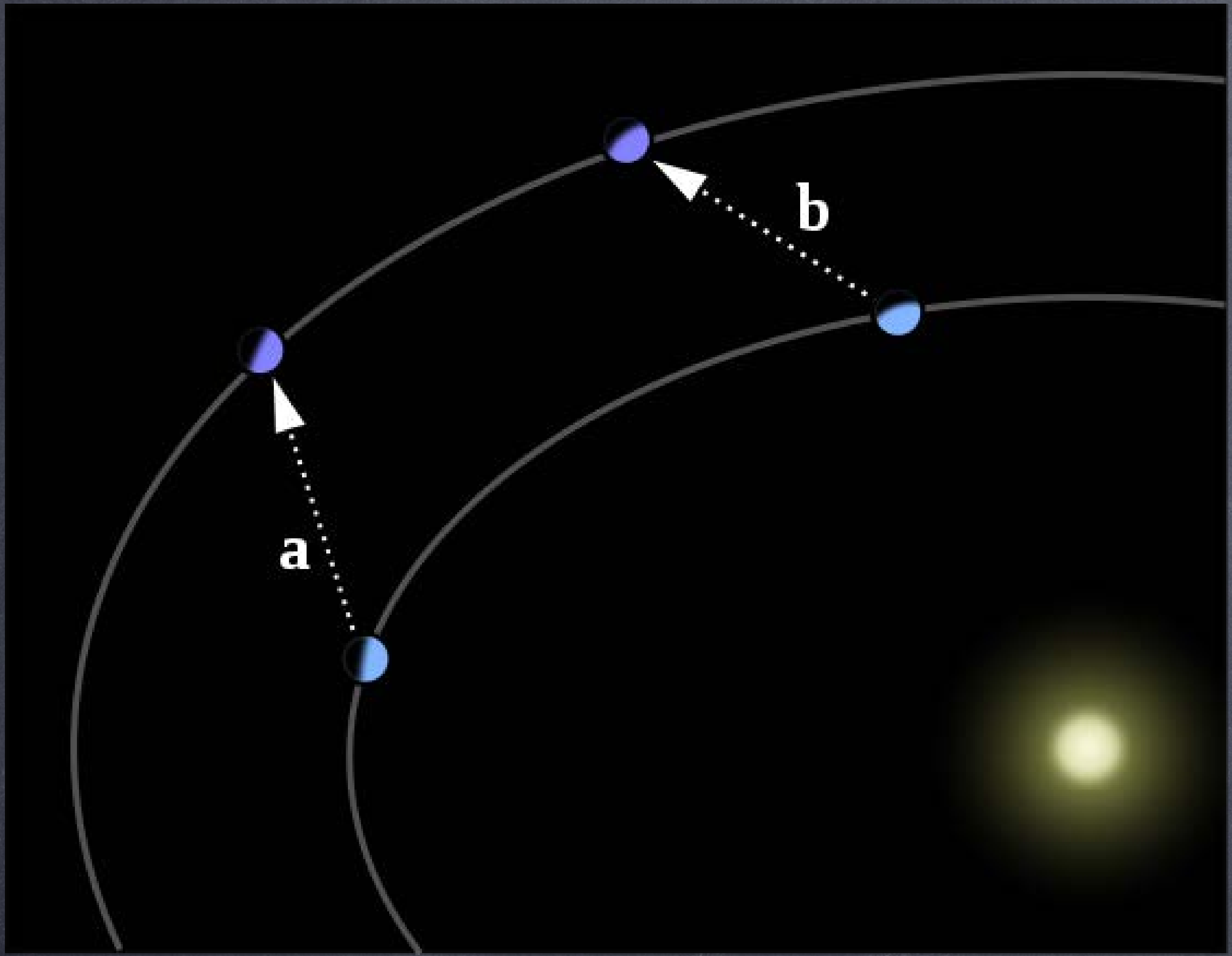




Periglomerular cells (PG)

Granule cells (GC)

Discovery of Neptune (September 24, 1846)



Urbain Le Verrier (1811-1877)
Johann Gottfried Galle (1812-1910)
Heinrich Louis d'Arrest (1822-1975)

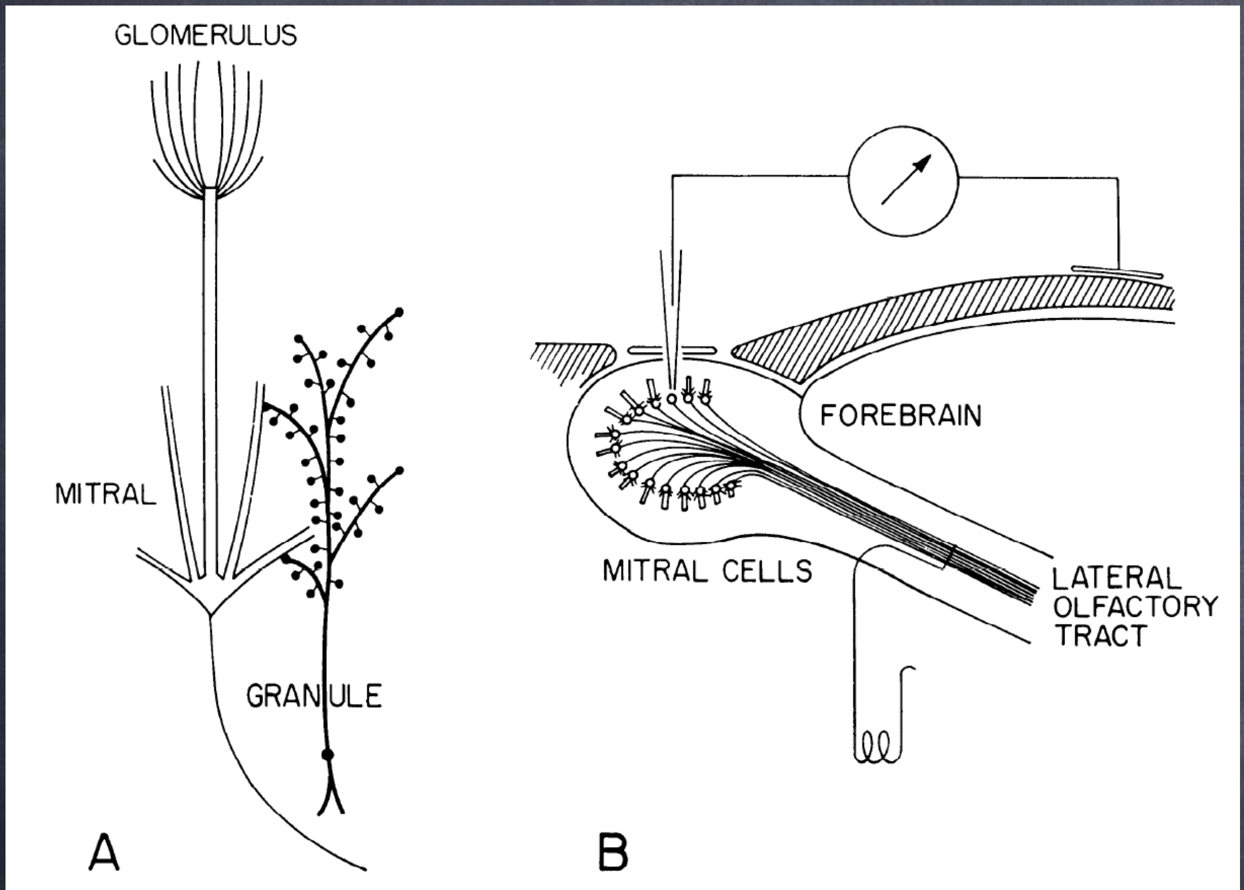
EXPERIMENTAL NEUROLOGY 14, 44-56 (1966)

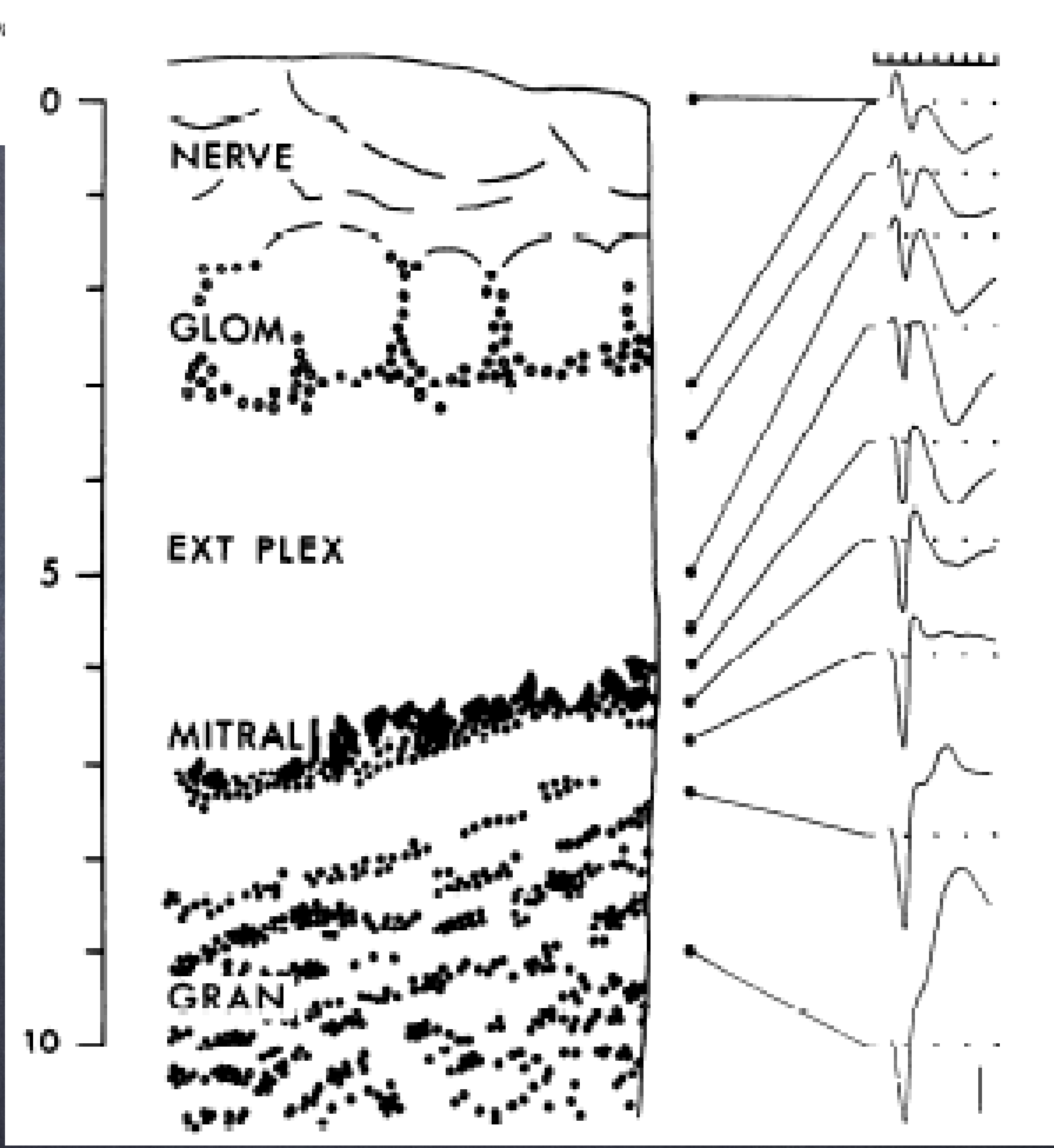
Dendrodendritic Synaptic Pathway for Inhibition in the Olfactory Bulb

WILFRID RALL, G. M. SHEPHERD, T. S. REESE, AND M. W. BRIGHTMAN[1]

Office of Mathematical Research, and the Laboratory of Neuroanatomical Scien
National Institutes of Health, Bethesda, Maryland

Received July 22, 1965





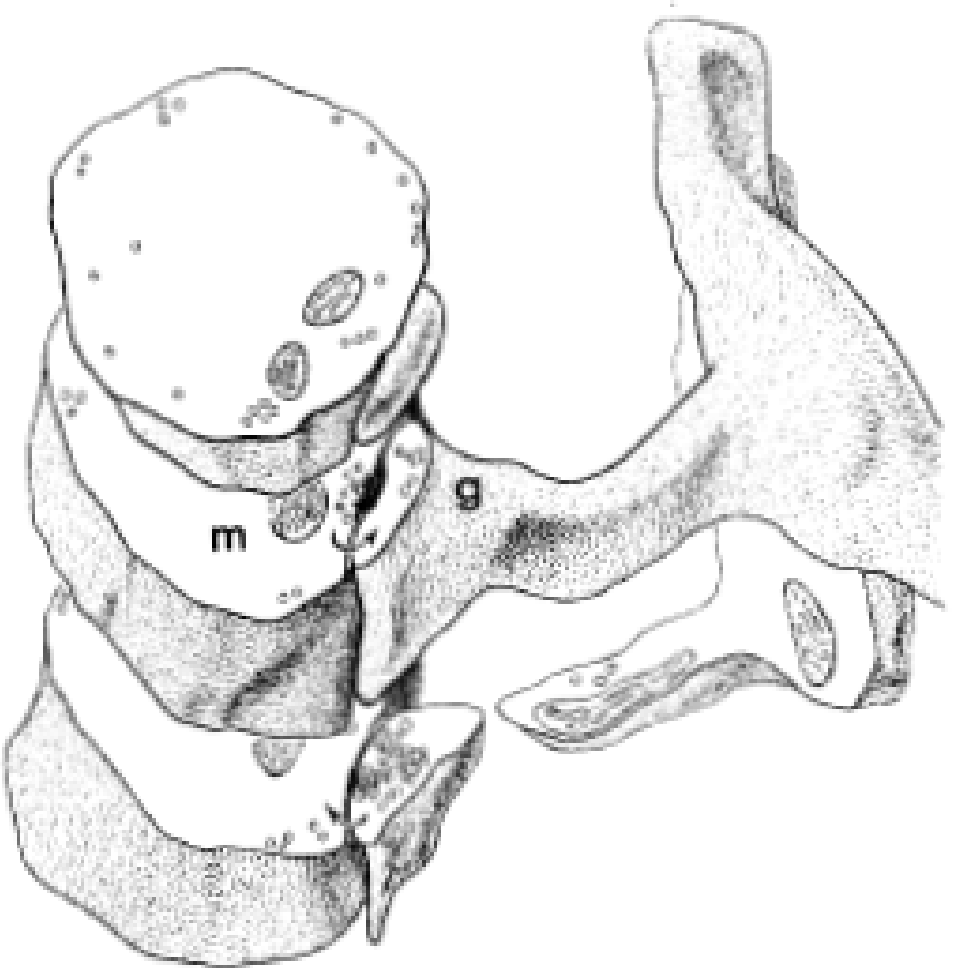


FIG. 3. Graphical reconstruction (12) of a granule synaptic ending (g) on a mitral secondary dendrite (m). The granule ending is shaped like a gemmule and arises from a granule dendrite lying approximately perpendicular to the mitral dendrite. Within a single ending are two synaptic contacts with opposite polarities (indicated by arrows). The reconstruction was made directly from a series of tracings of twenty-three consecutive electron micrographs; no sections are omitted in showing cut surfaces. Microtubules and endoplasmic reticulum are not shown. × 20 000.

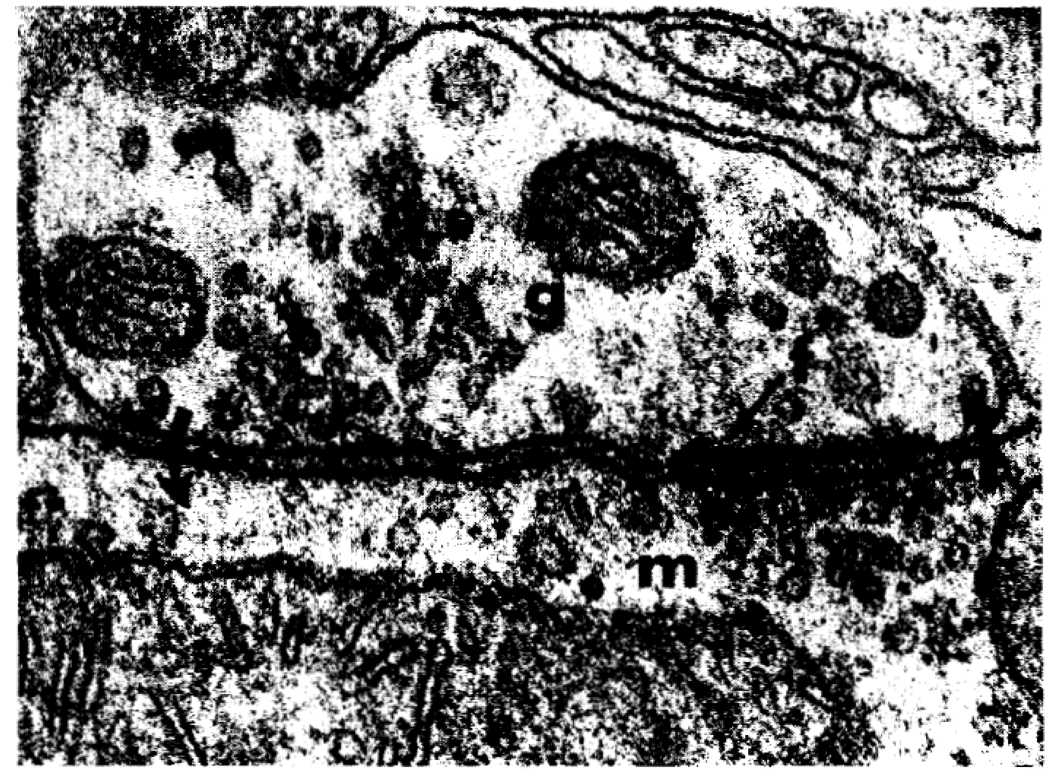
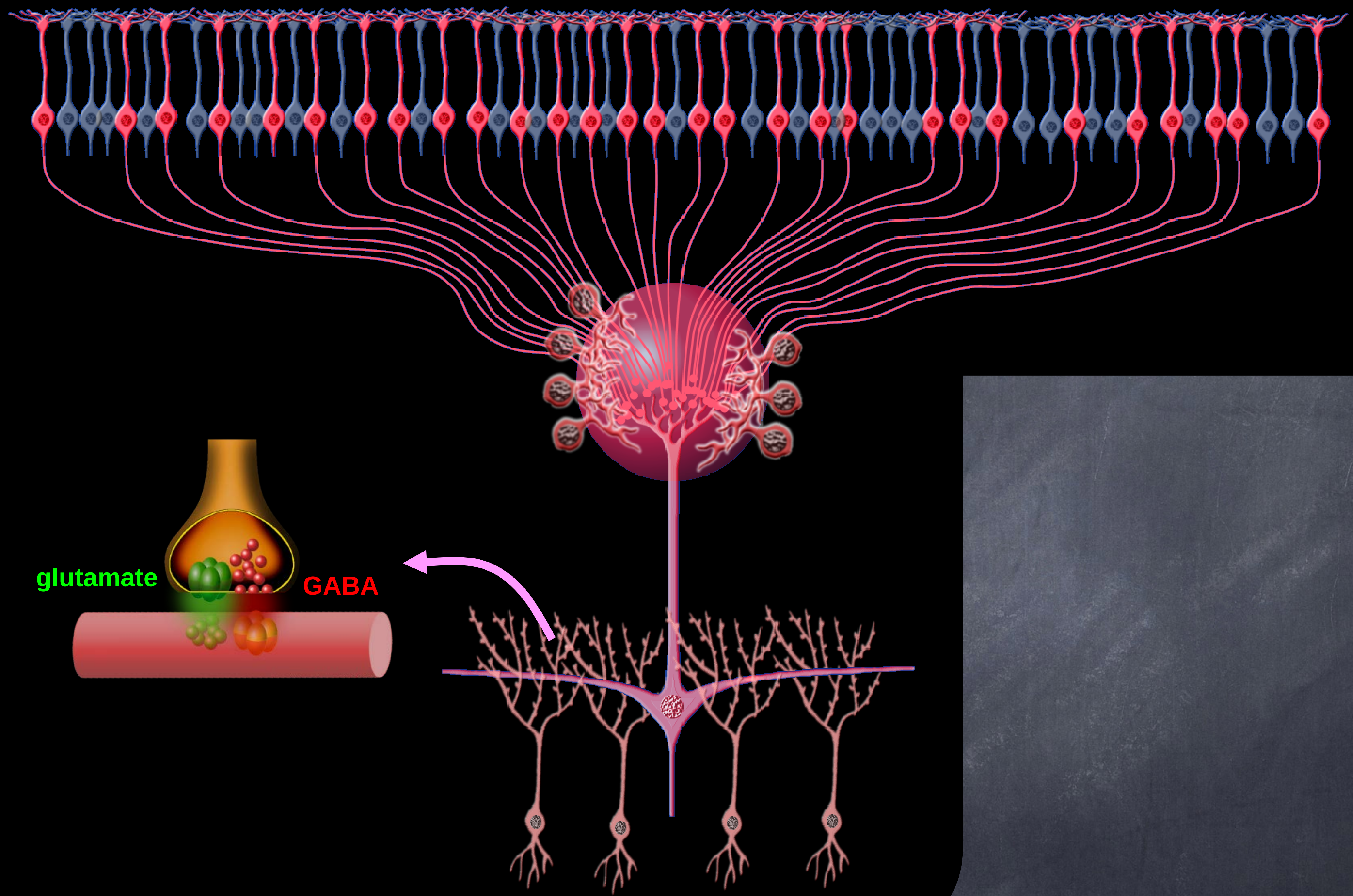
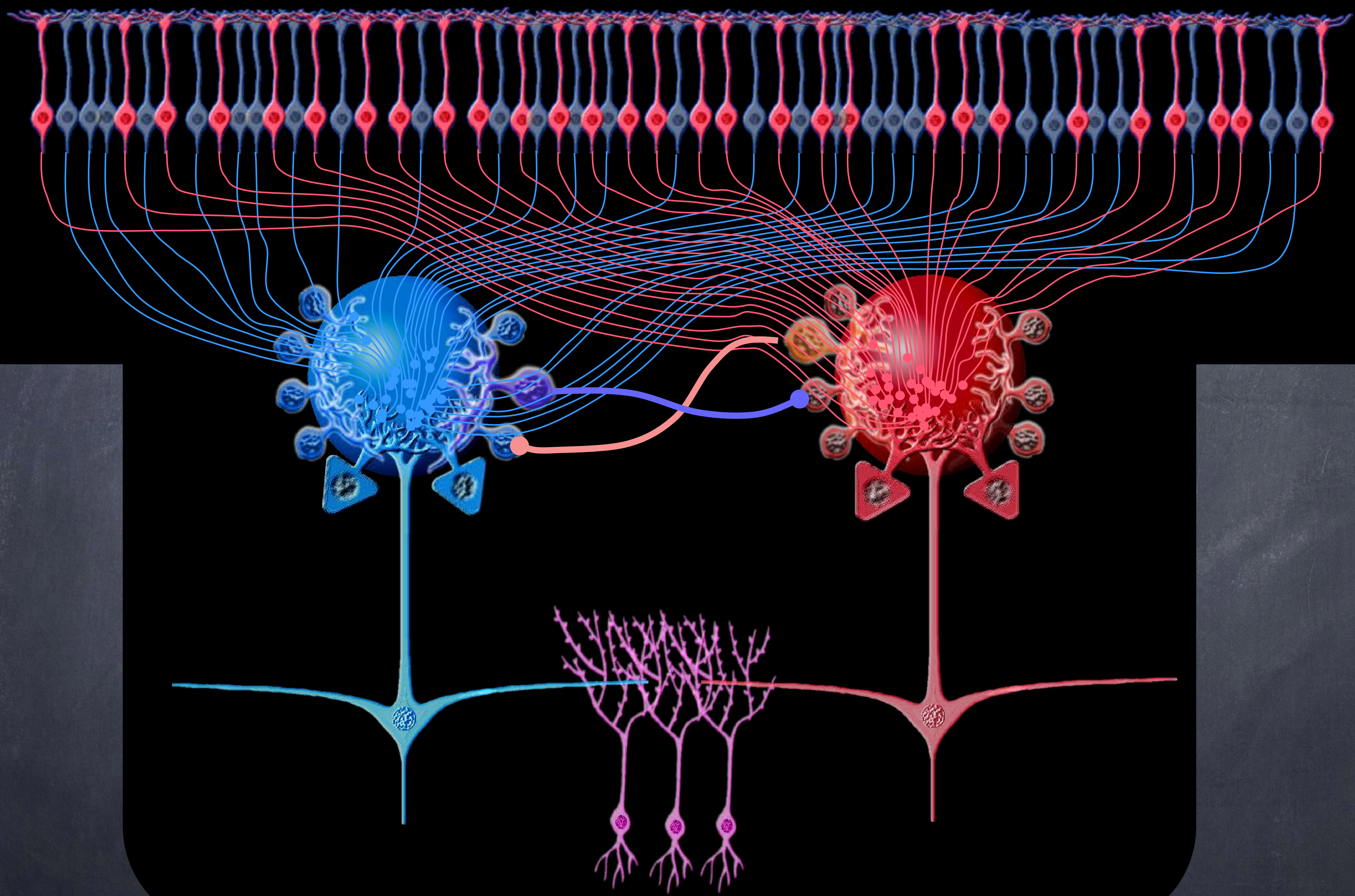
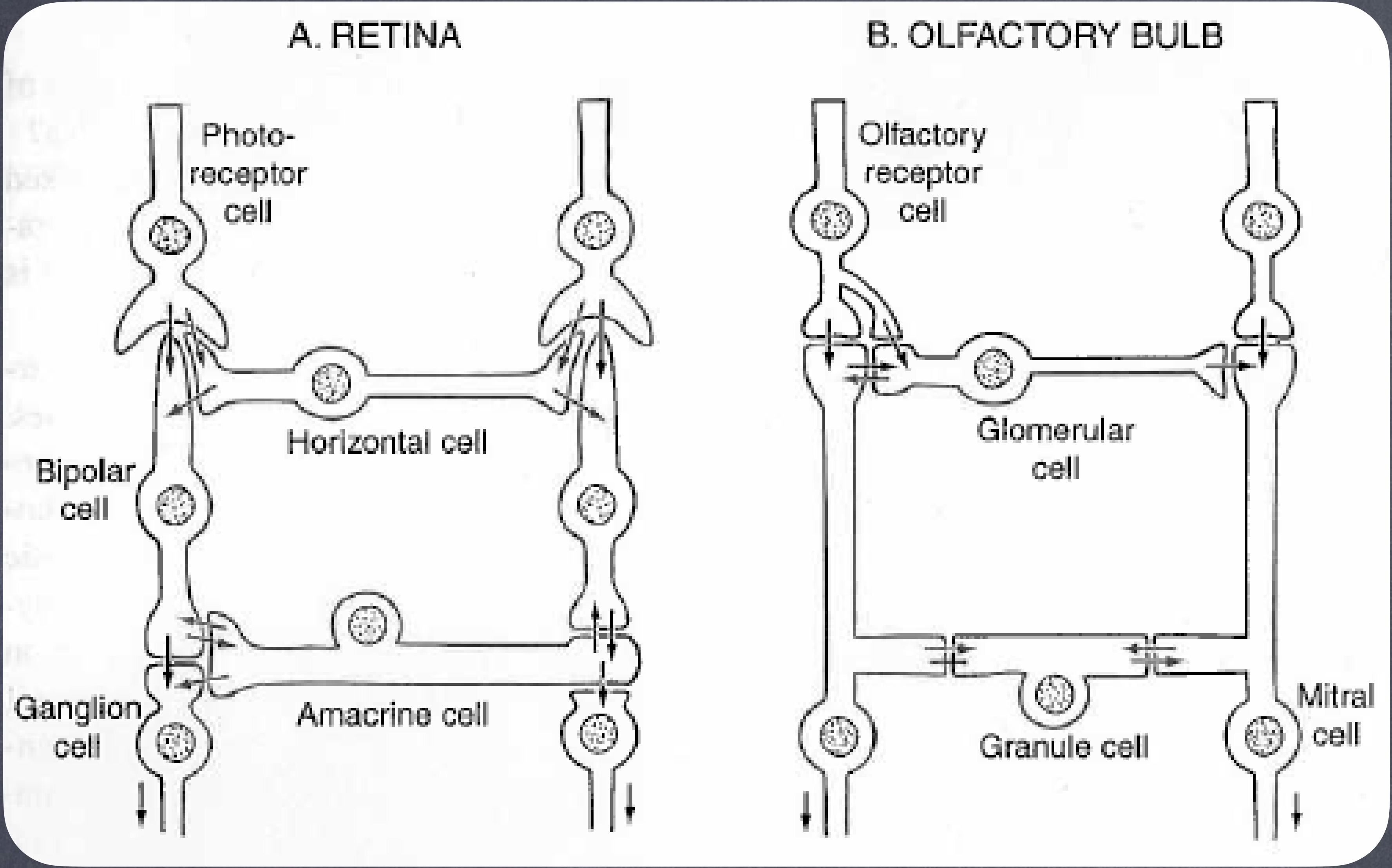
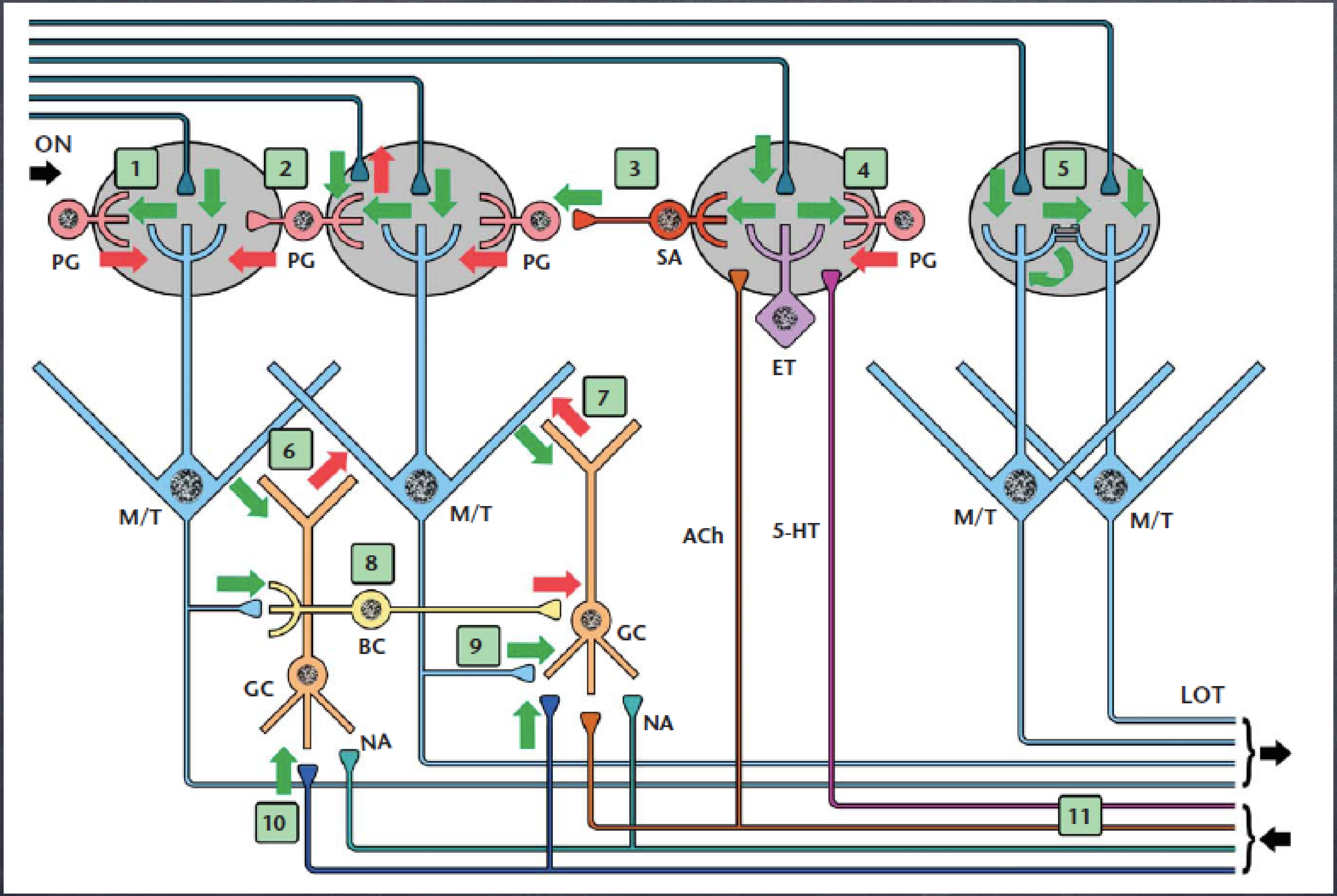


FIG. 4. A mitral secondary dendrite (m) and one of the many synaptic endings (g), presumed to be gemmules from granule cells. There are two synaptic contacts with opposite polarities (indicated by arrows). Where the polarity is from the mitral dendrite to the granule dendrite (as judged by the grouping of vesicles), a dense filamentous material (f) is attached to the postsynaptic cell membrane. Lead citrate; × 90 000.


glutamate
GABA




A. RETINA
Photo-receptor cell
Horizontal cell
Bipolar cell
Amacrine cell
Ganglion cell
B. OLFACTORY BULB
Olfactory receptor cell
Glomerular cell
Granule cell
Mitral cell

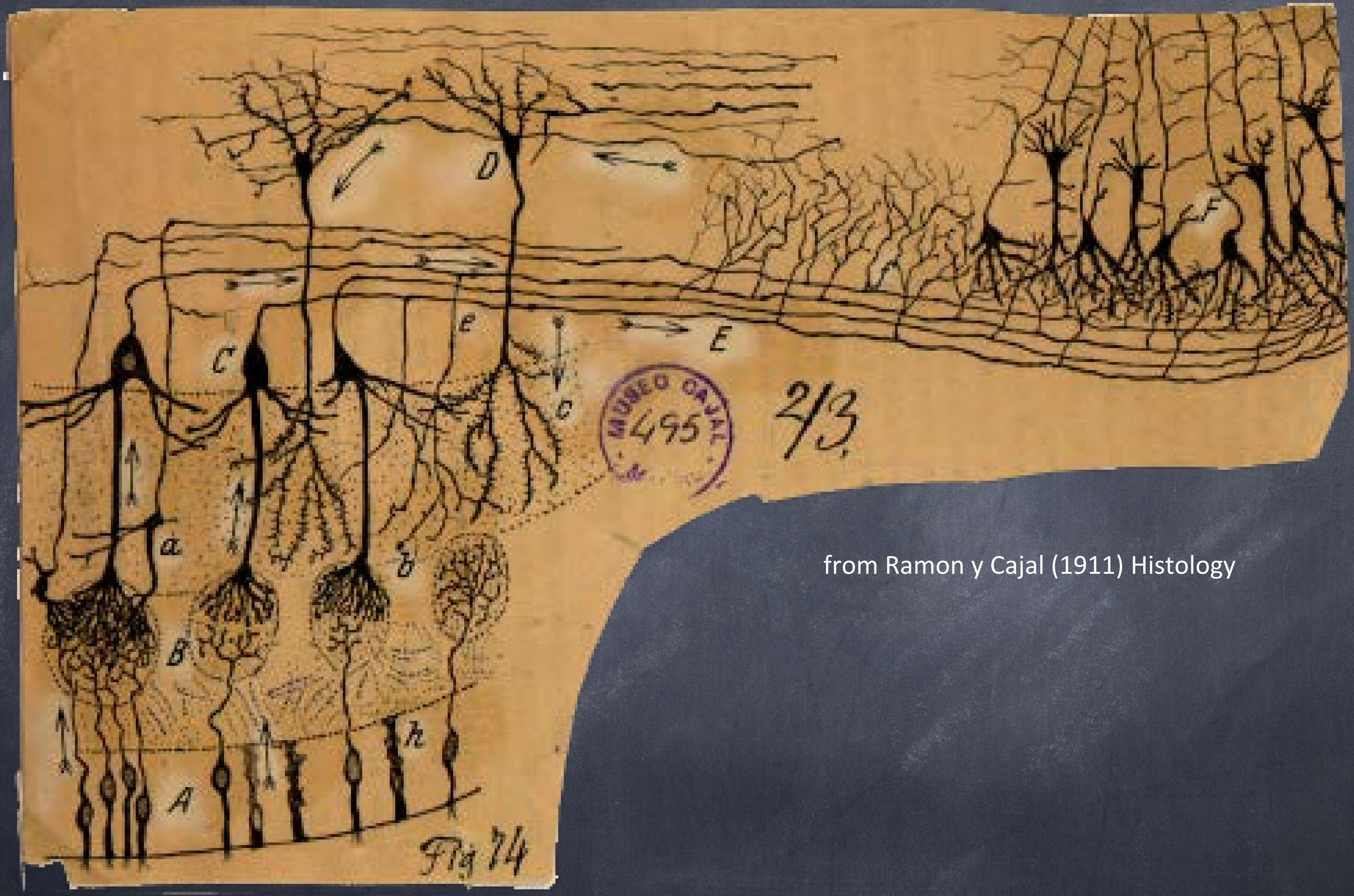


M/T - mitral tufted cells
PG - periglomerular cell

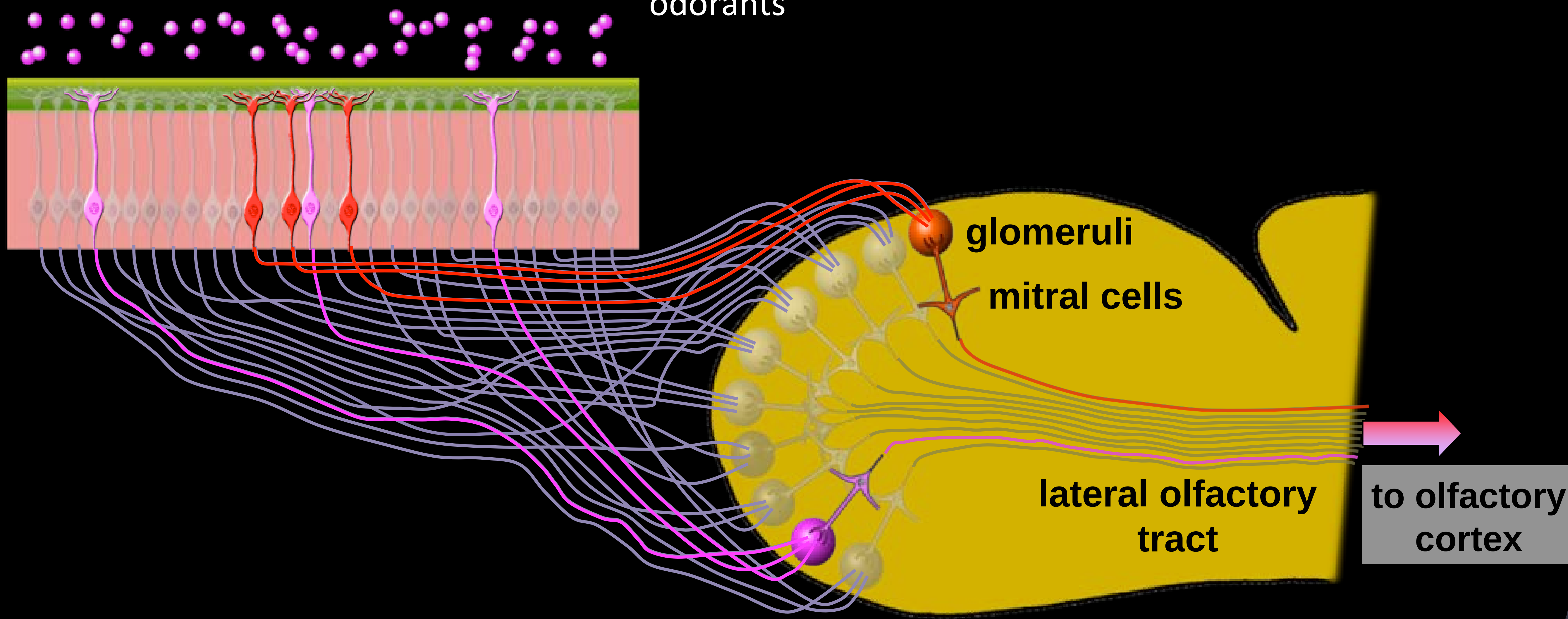
ET - external tufted cell
SA - short axon cell

GC - granule cell
BC - Blane cell

Graeme Lowe, **Olfactory Bulb: Synaptic Organization,** Encyclopedia of Life Sciences, 2007



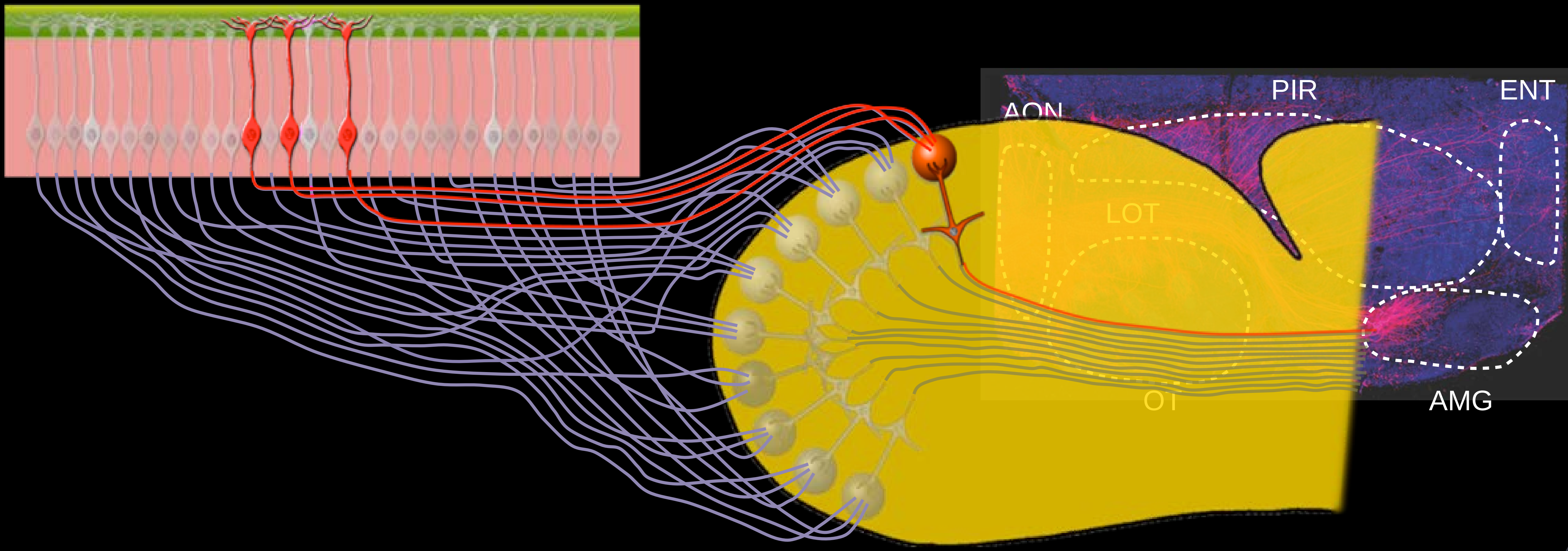
from Ramon y Cajal (1911) Histology


odorants
glomeruli
mitral cells
lateral olfactory tract
to olfactory cortex

Distinct representations of olfactory information in different cortical centres

Dara L. Sosulski[1], Maria Lissitsyna Bloom[1]†, Tyler Cutforth[1]†, Richard Axel[1] & Sandeep Robert Datta[1]†

Nature **472,** 213–216 (2011).



Distinct representations of olfactory information in different cortical centres

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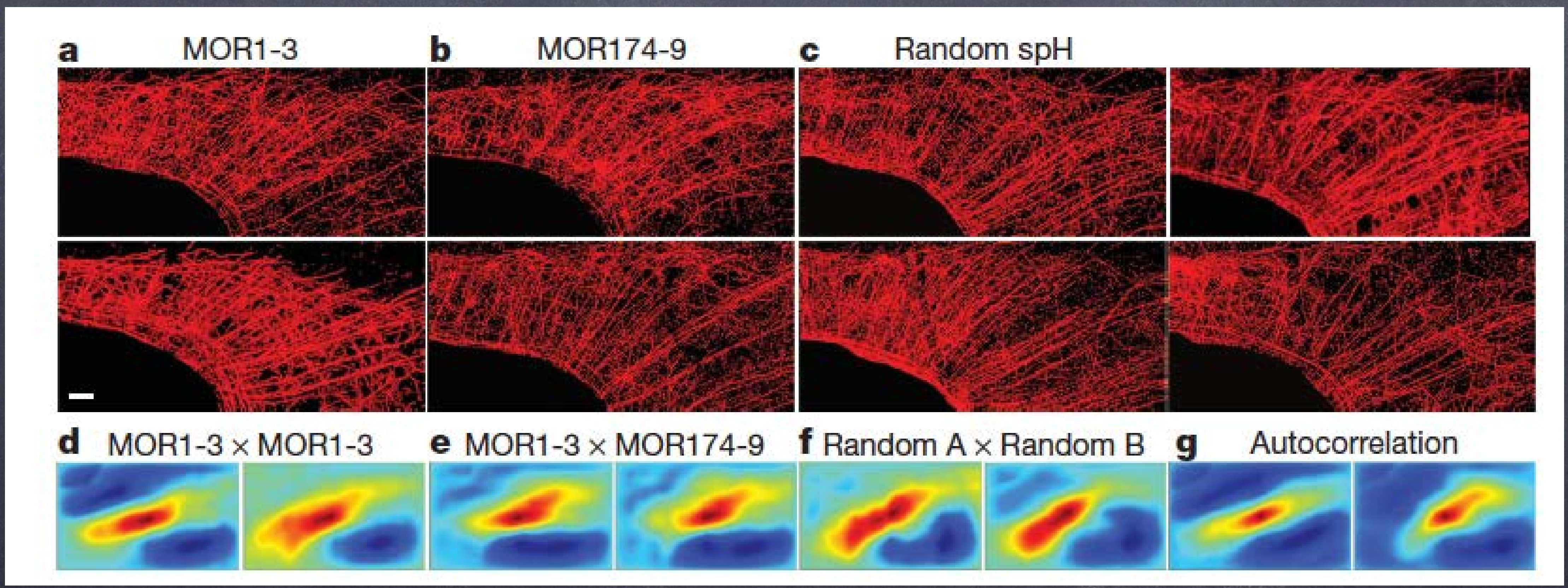

Distinct representations of olfactory information in different cortical centres

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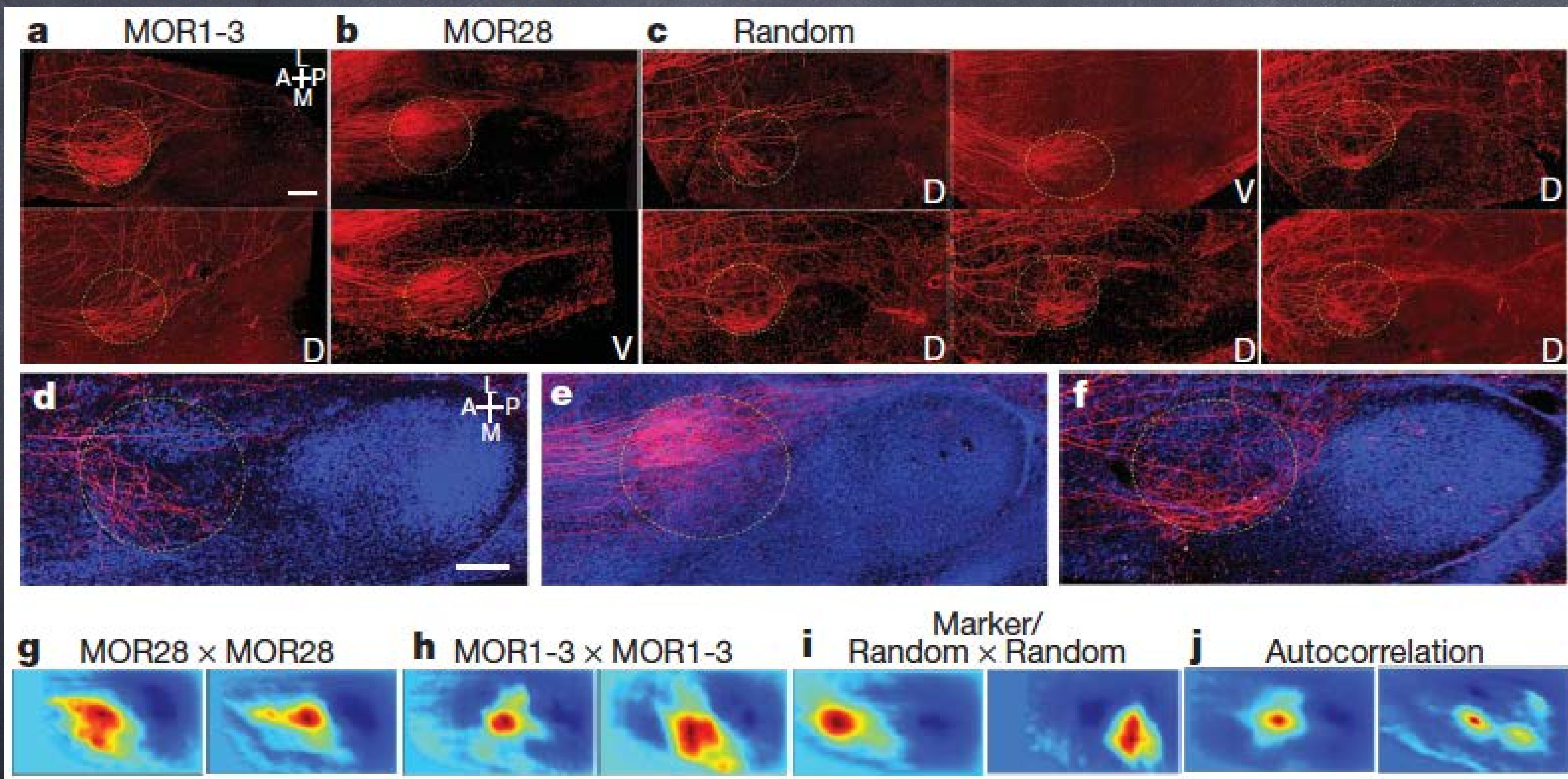
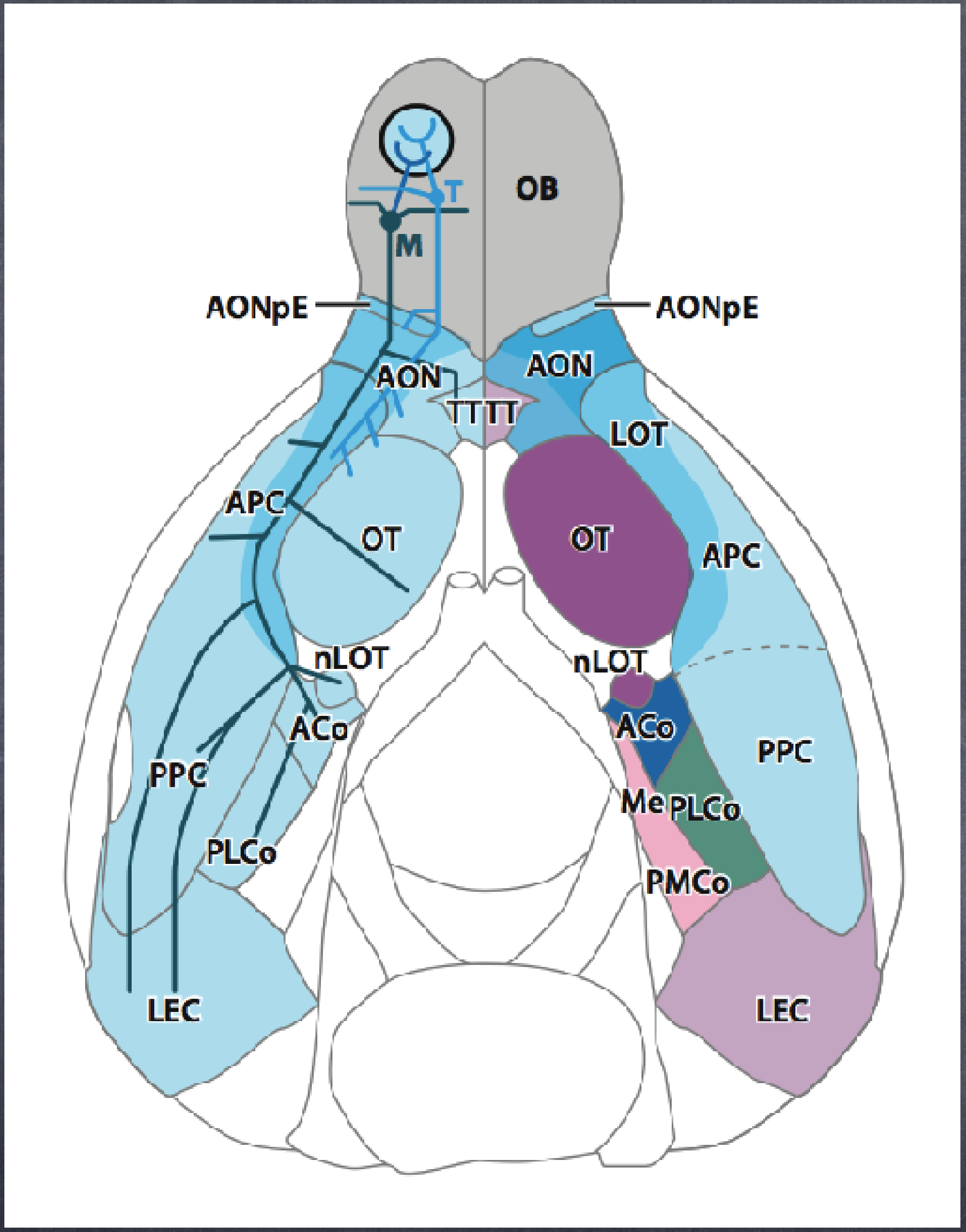
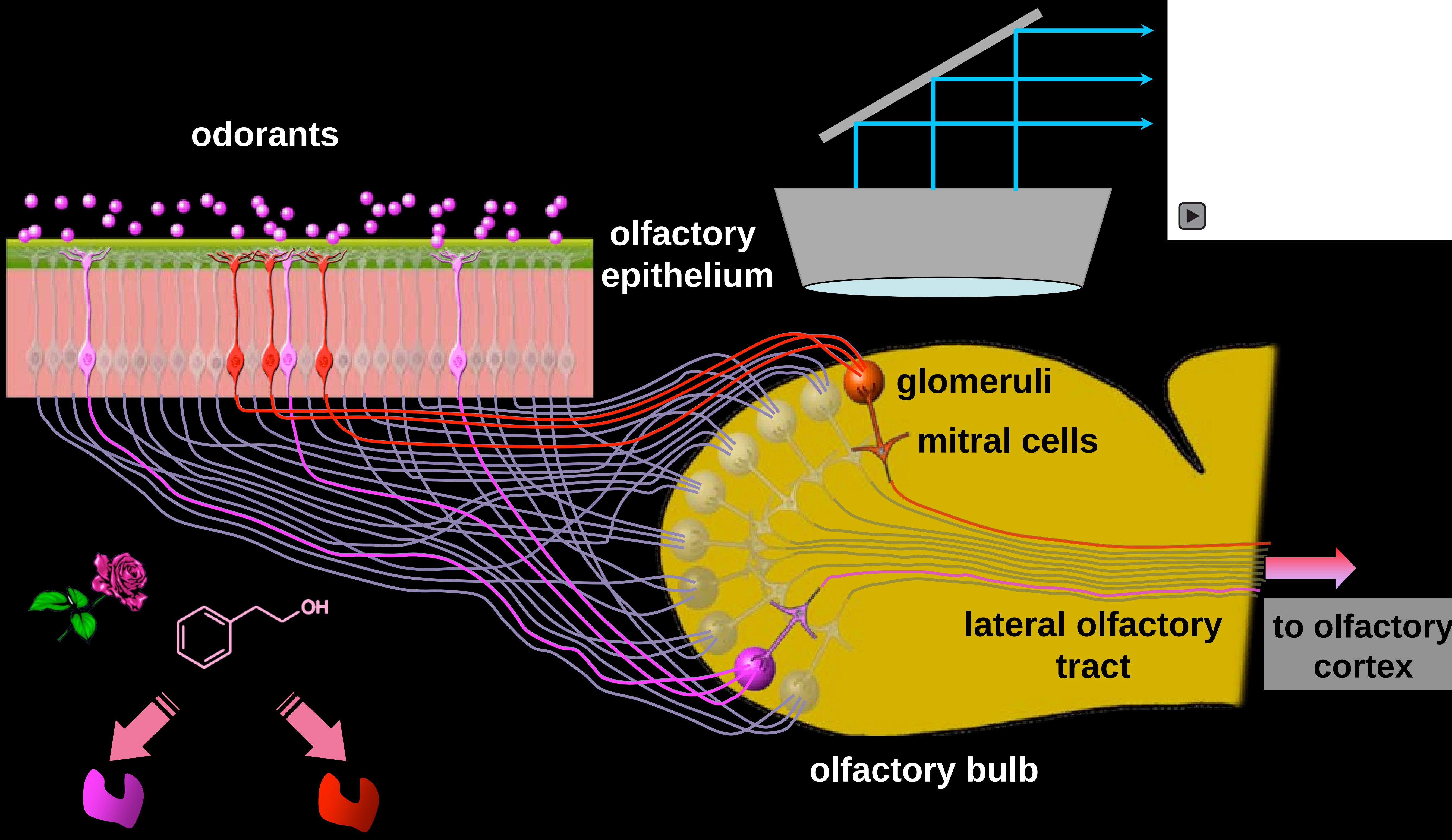
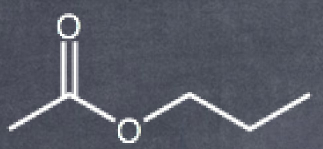




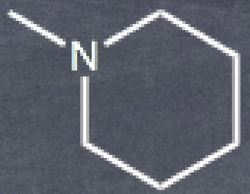
From Mori & Sakano, 2011; adapted from Luskin & Price, 1983


odorants
olfactory epithelium
glomeruli
mitral cells
OH
lateral olfactory tract
to olfactory cortex
olfactory bulb

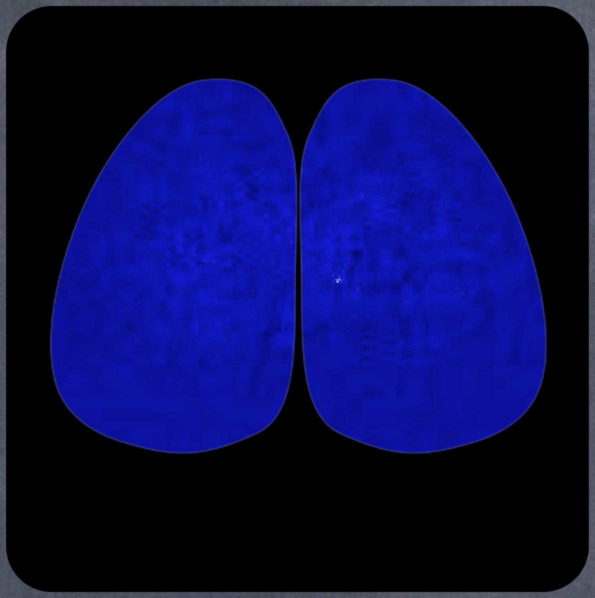
butanal

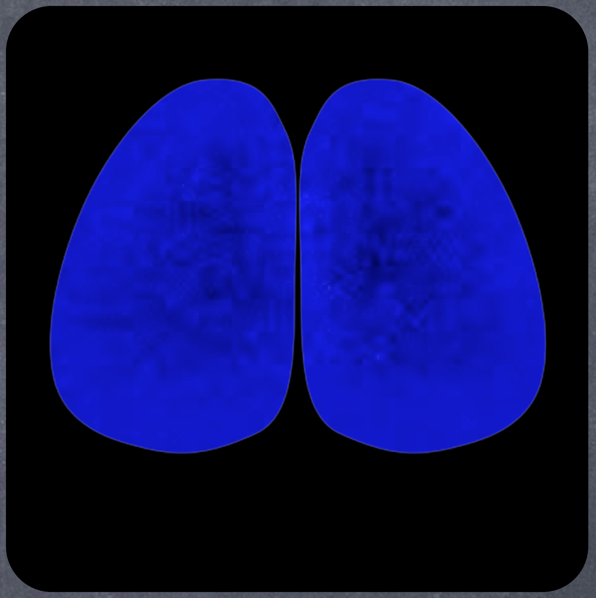


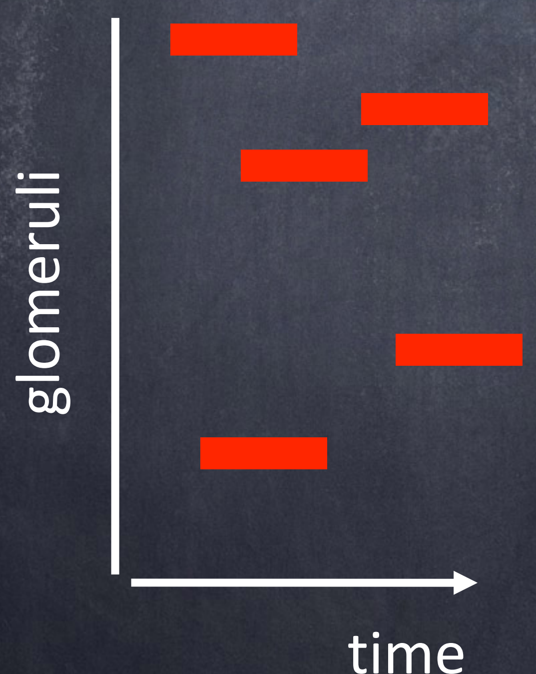
propylacetate

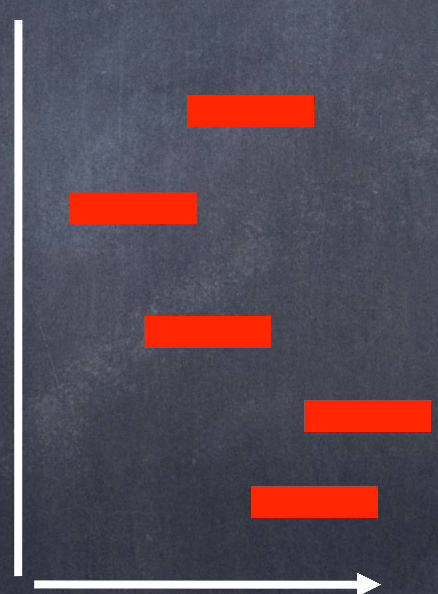


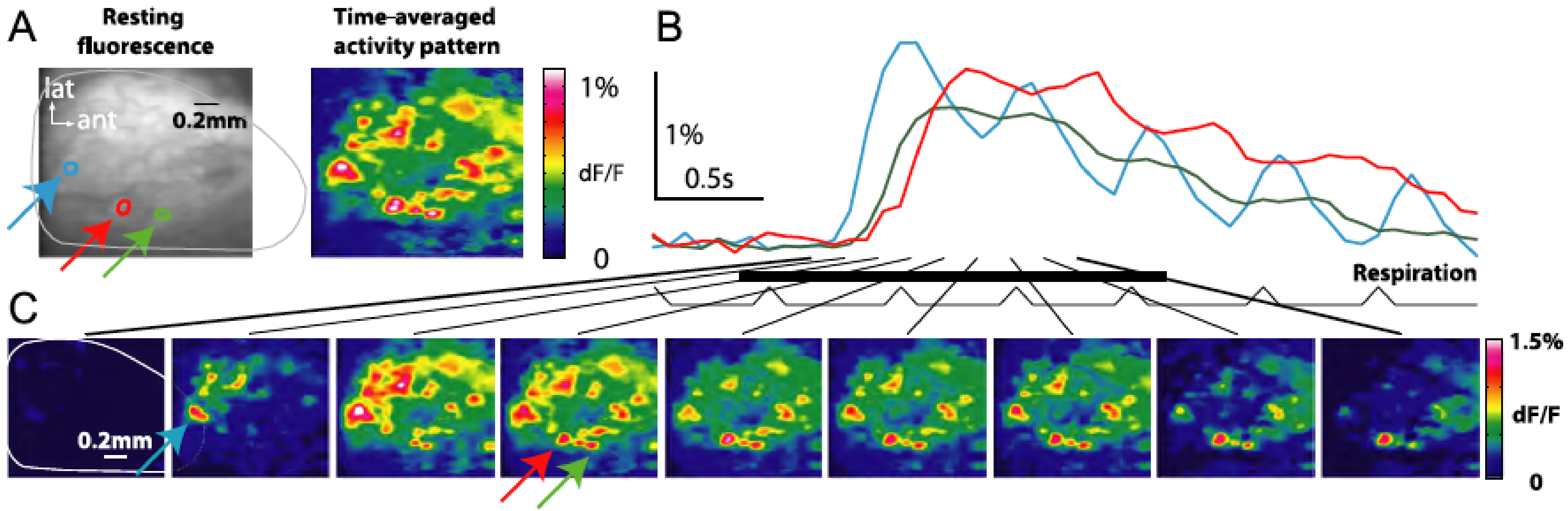
N-methylpiperidine



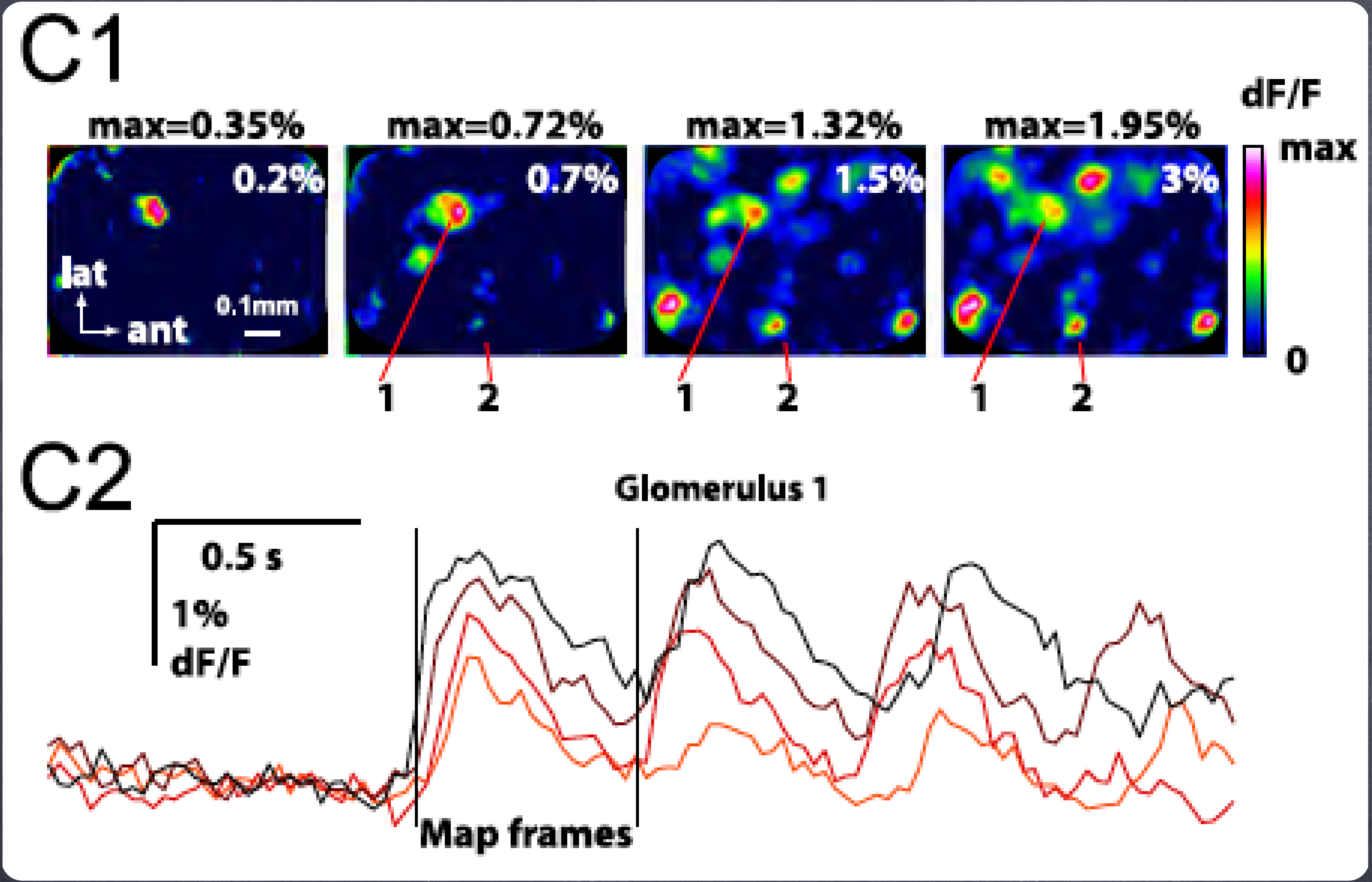






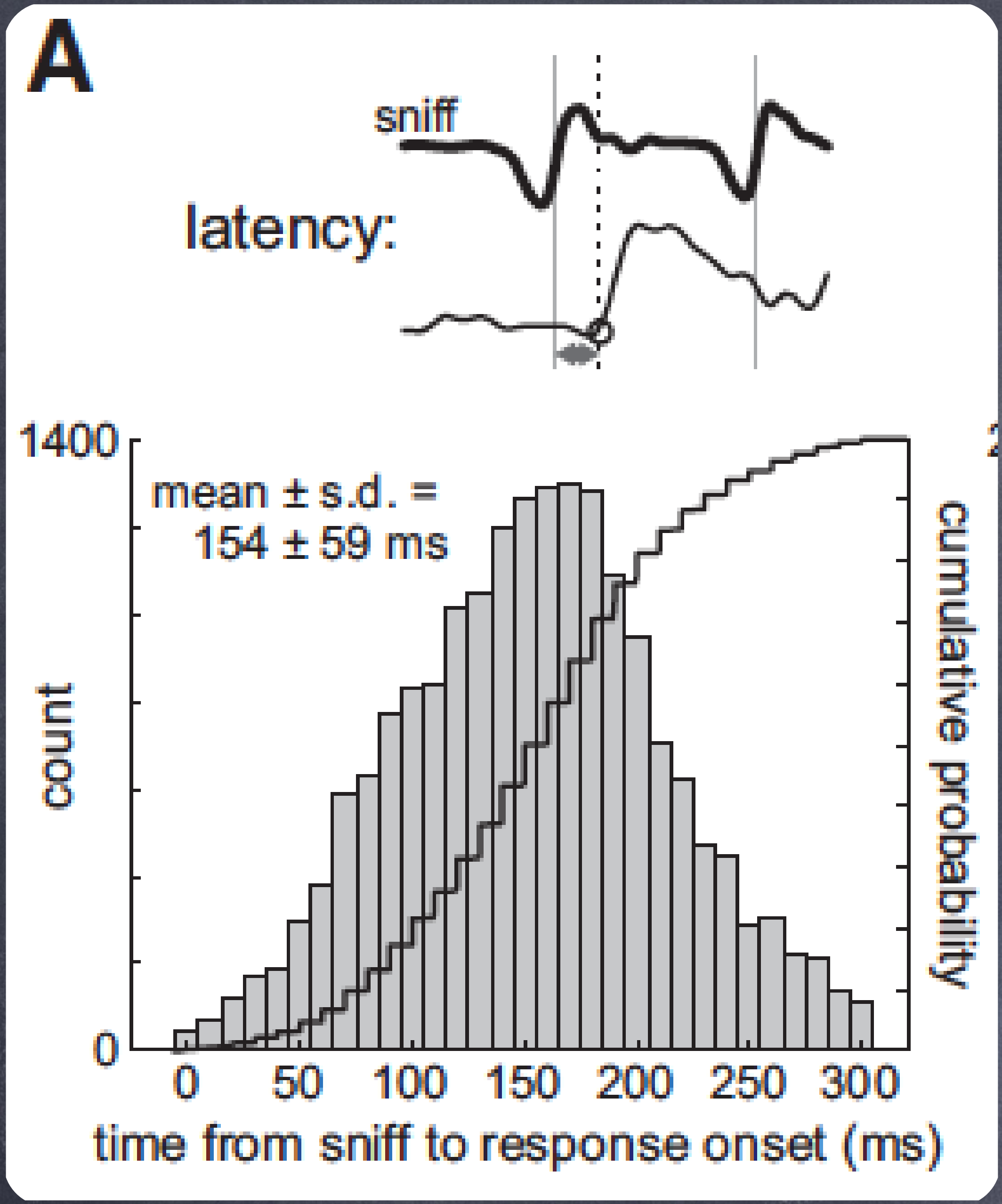


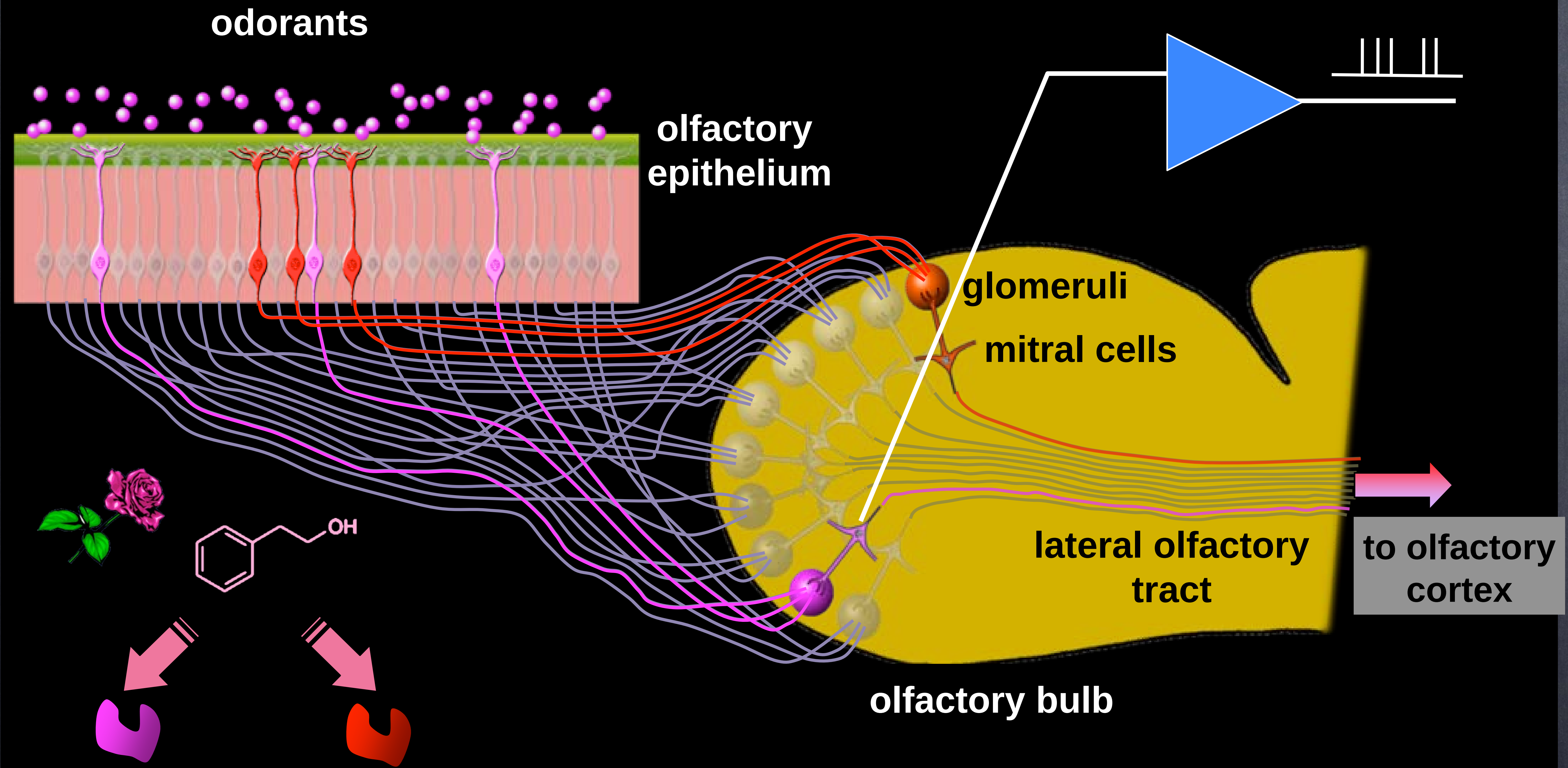
A
Resting fluorescence
lat
ant
0.2mm
Time-averaged activity pattern
1%
dF/F
0
B
1%
0.5s
Respiration
C
0.2mm
1.5%
dF/F
0


C1
max=0.35%
max=0.72%
max=1.32%
max=1.95%
0.2%
0.7%
1.5%
3%
lat
ant
0.1mm
1
2
1
2
1
2
dF/F
max
0
C2
Glomerulus 1
0.5 s
1%
dF/F
Map frames

R Carey, et. al., J. Neurophysiol. 2009

Temporal structure of receptor neuron input to the olfactory bulb imaged in behaving rats.




odorants
olfactory epithelium
glomeruli
mitral cells
OH
lateral olfactory tract
to olfactory cortex
olfactory bulb

EEG Clin Neurophysiol **2**: 377-388 **(1950).**

Edgar Adrian
1889-1977

THE ELECTRICAL ACTIVITY OF THE MAMMALIAN OLFACTORY BULB

E. D. ADRIAN, M.D.
Physiological Laboratory, Cambridge, England

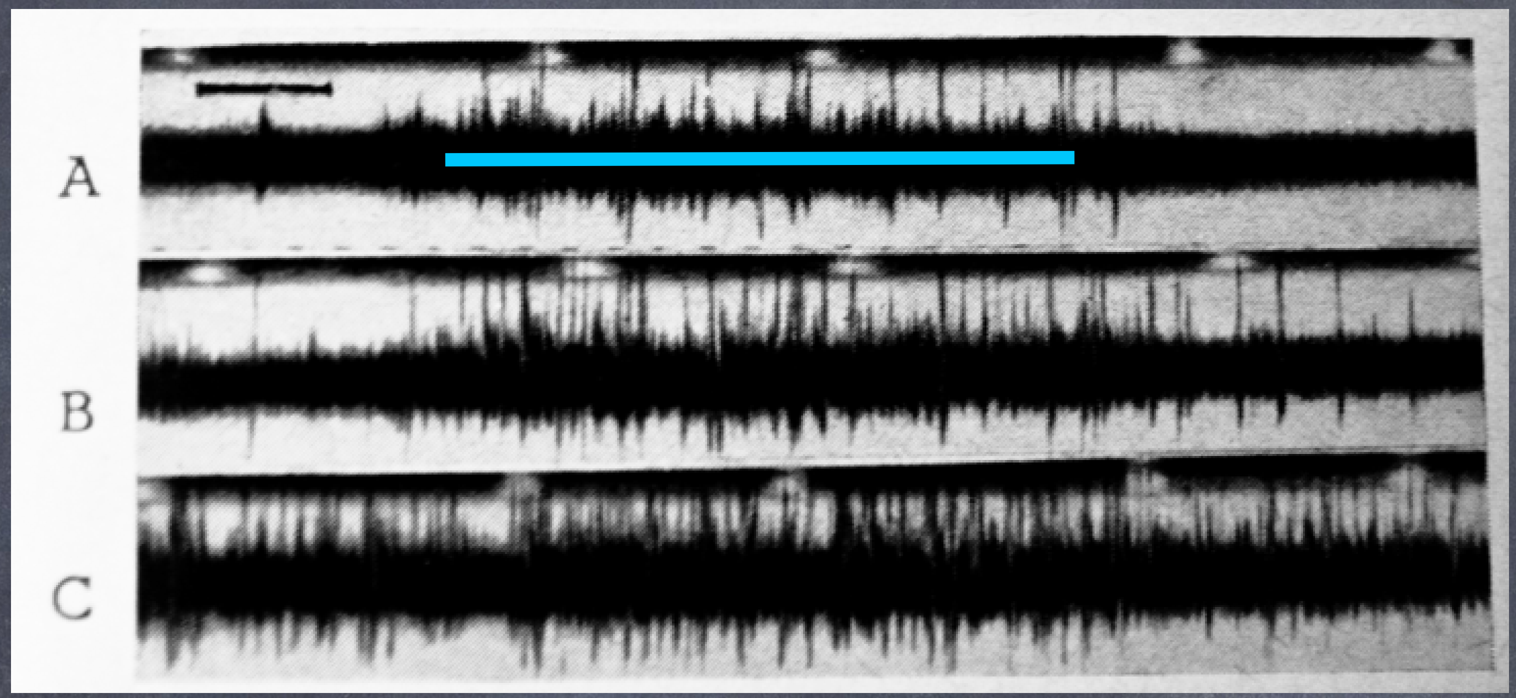
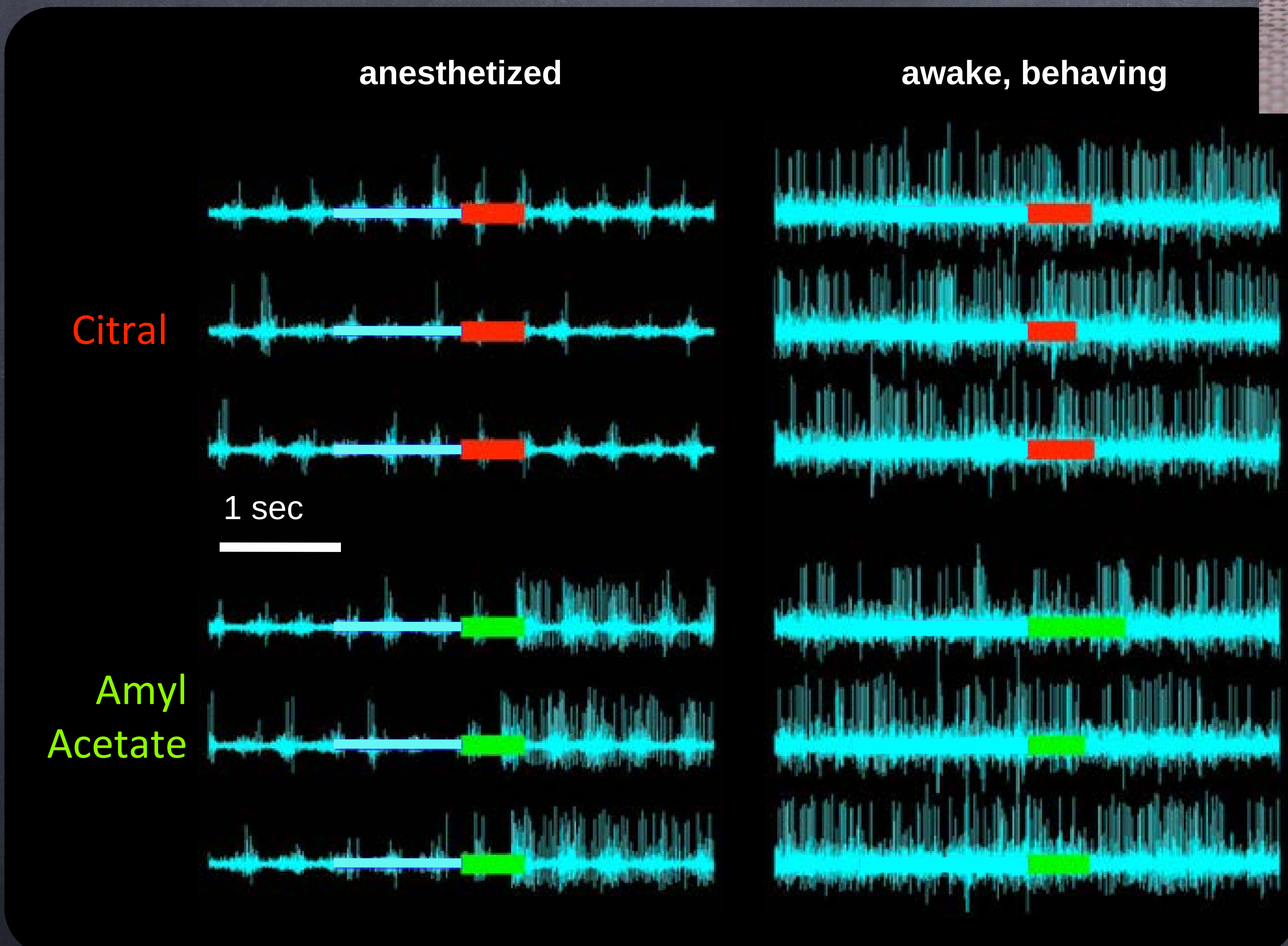


Fig.9

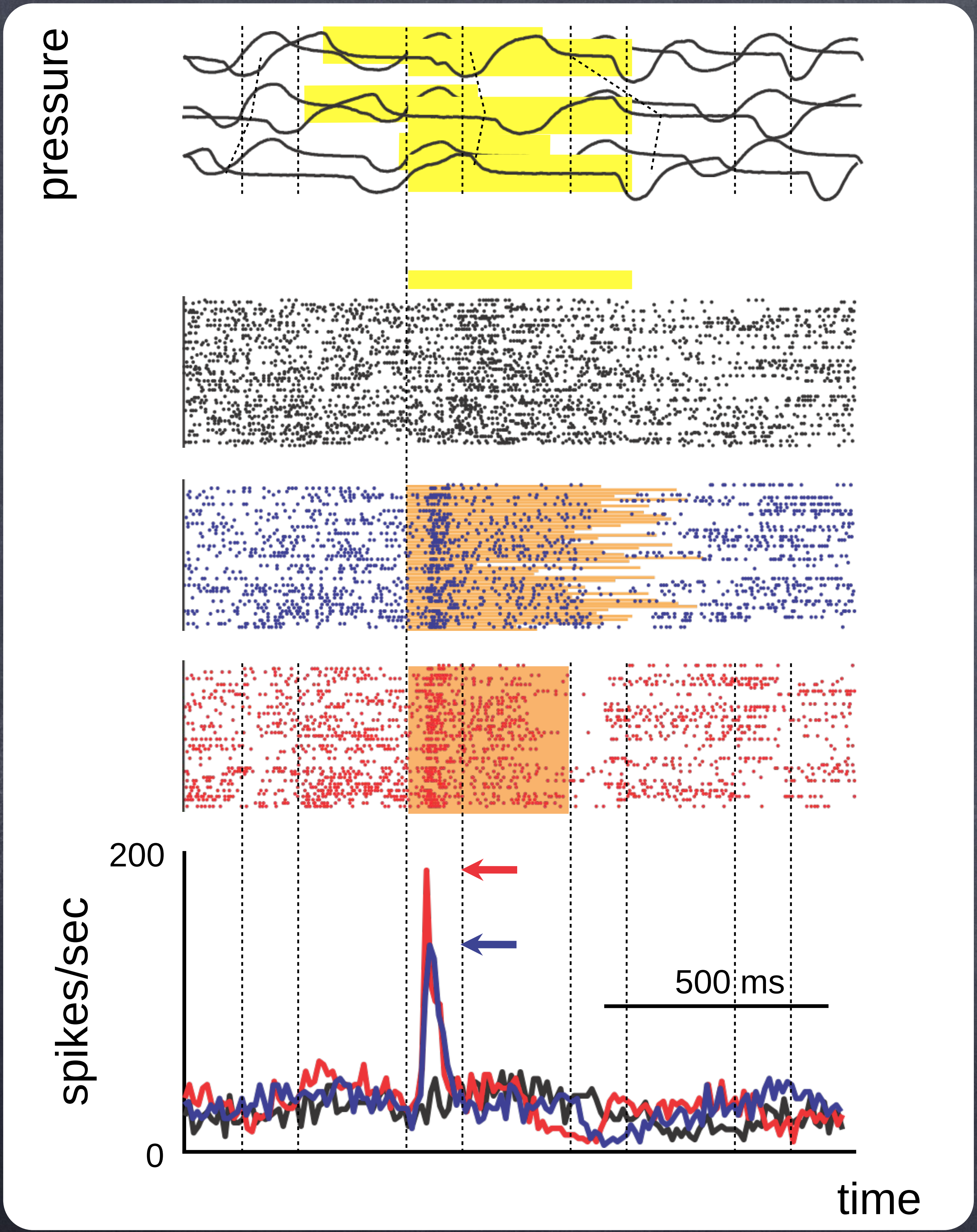
"In very deep anaesthesia when the bulb is quiet, a moderate olfactory stimulus sets up a discharge of impulses in the mitral axons at each inspiration and there are no impulses between (Fig. 9A). In less deep anaesthesia the olfactory discharges appear against a background of continuous irregular activity and as the anaesthesia lightens the continuous activity becomes more and more prominent until it may be no longer possible to detect any changes due to the stimulus (fig 9C)"

50+ years later...



D. Rinberg, A. Koulakov,
A. Gelperin. J. Neurosci., (2006)

R Shusterman, et.al., Nature Neuroscience, 2011

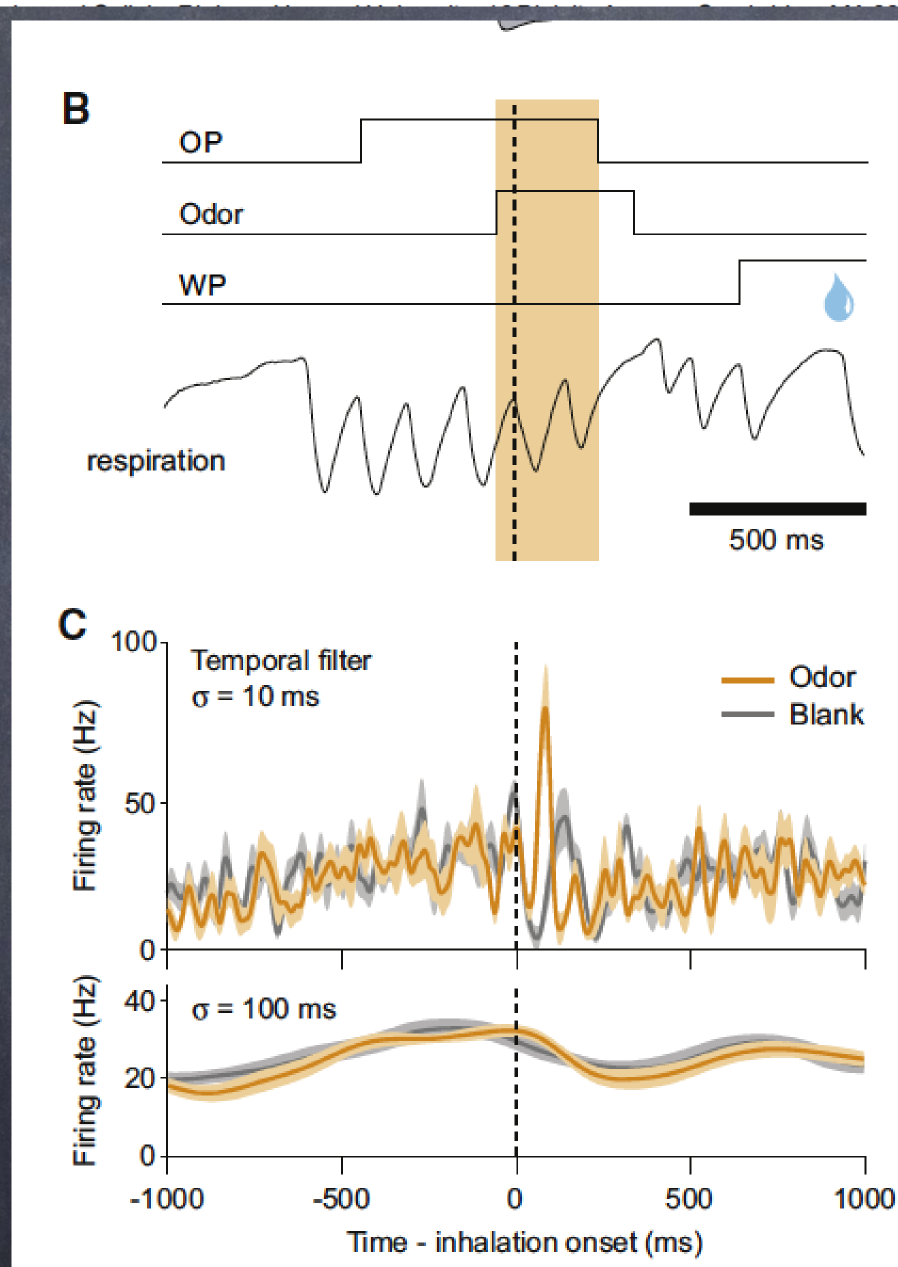


- locked to the phase of the sniffing cycle
- precise
- temporally diverse

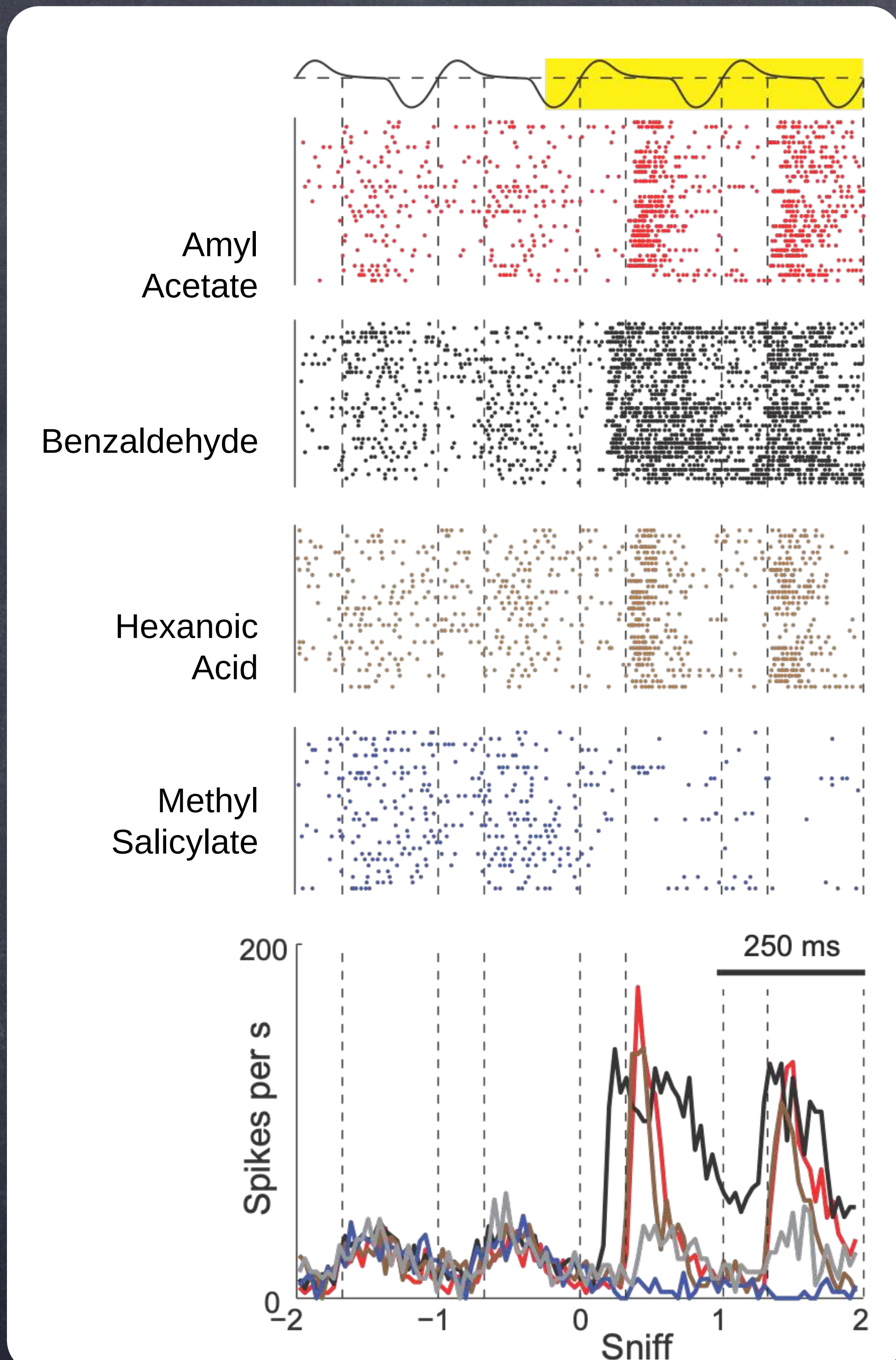
Neuron
Article

Robust Odor Coding via Inhalation-Coupled Transient Activity in the Mammalian Olfactory Bulb

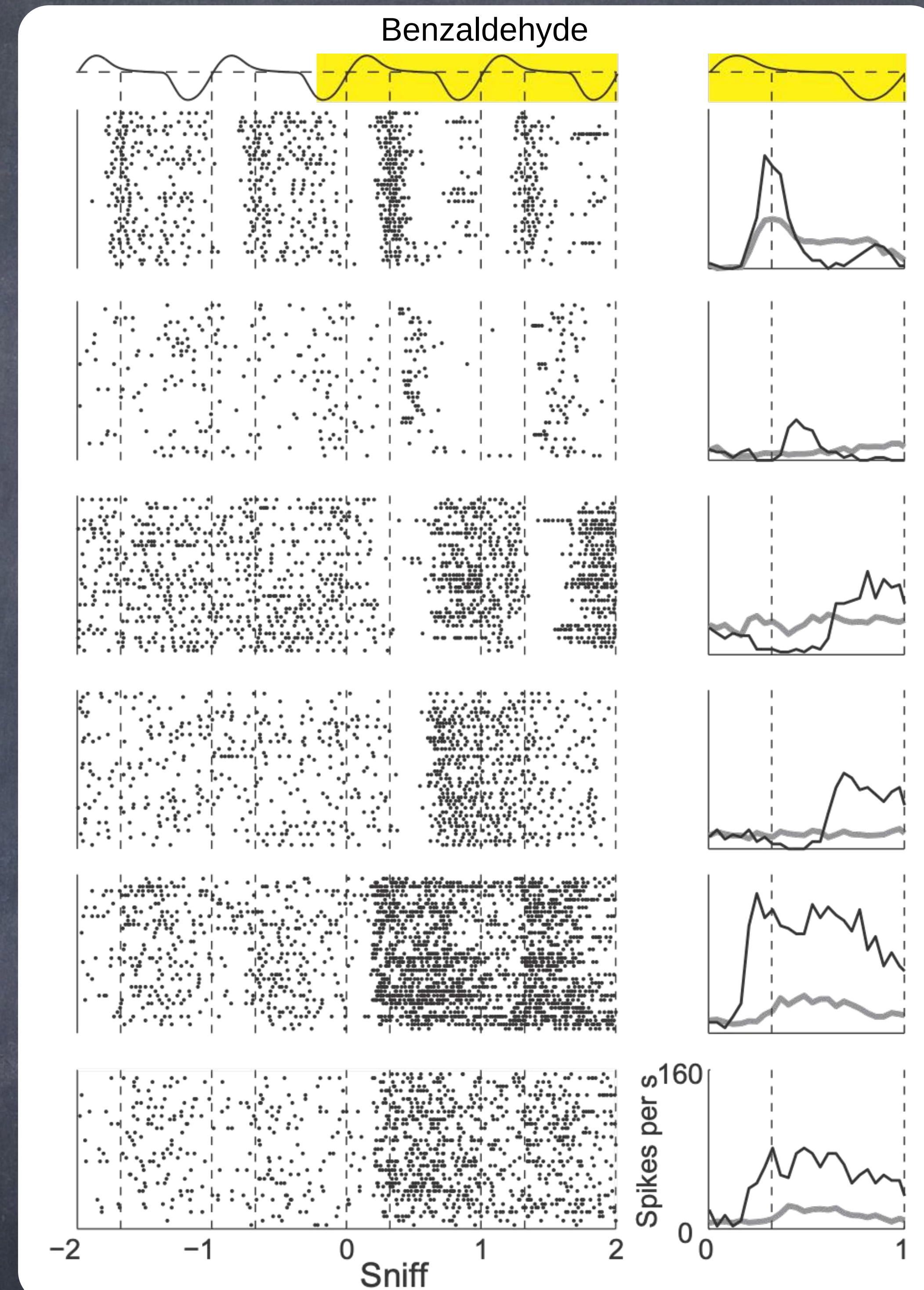
Kevin M. Cury[1] and Naoshige Uchida[1,*]



one cell - many odors



many cells - one odor

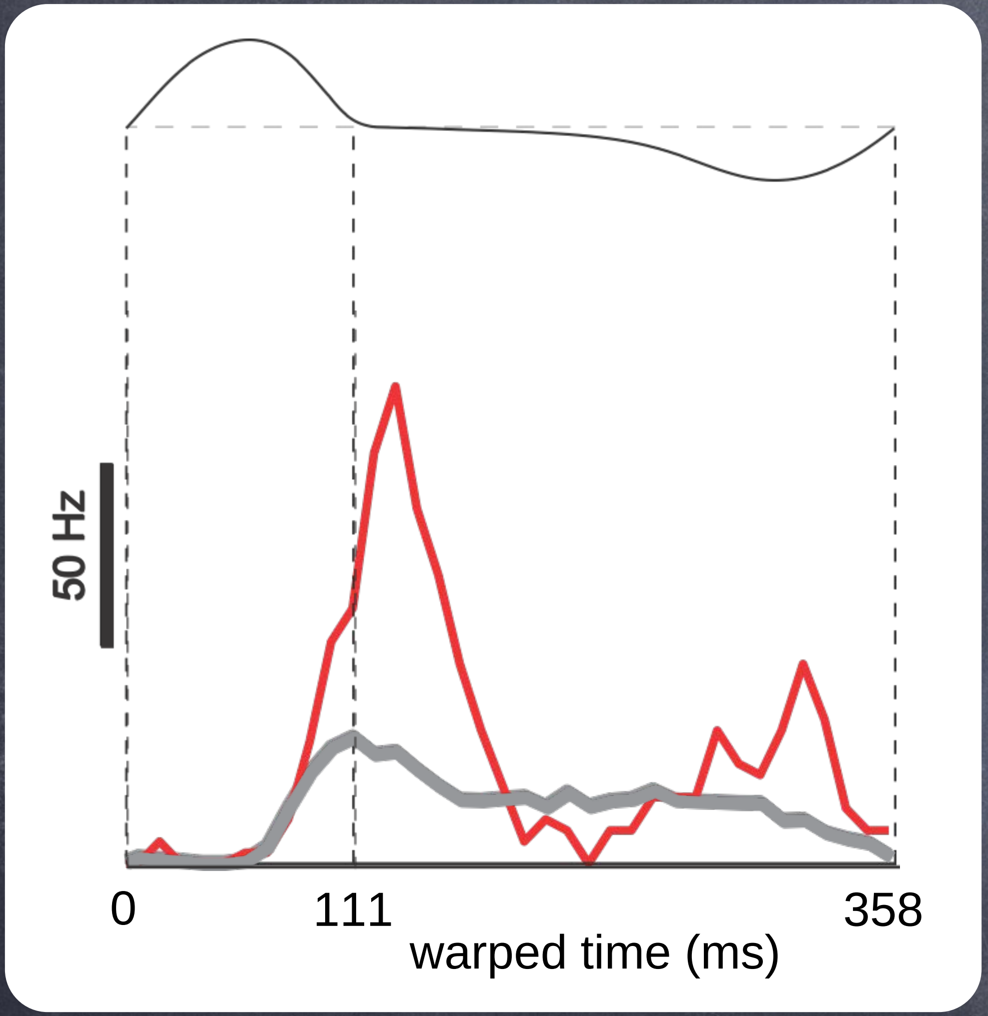


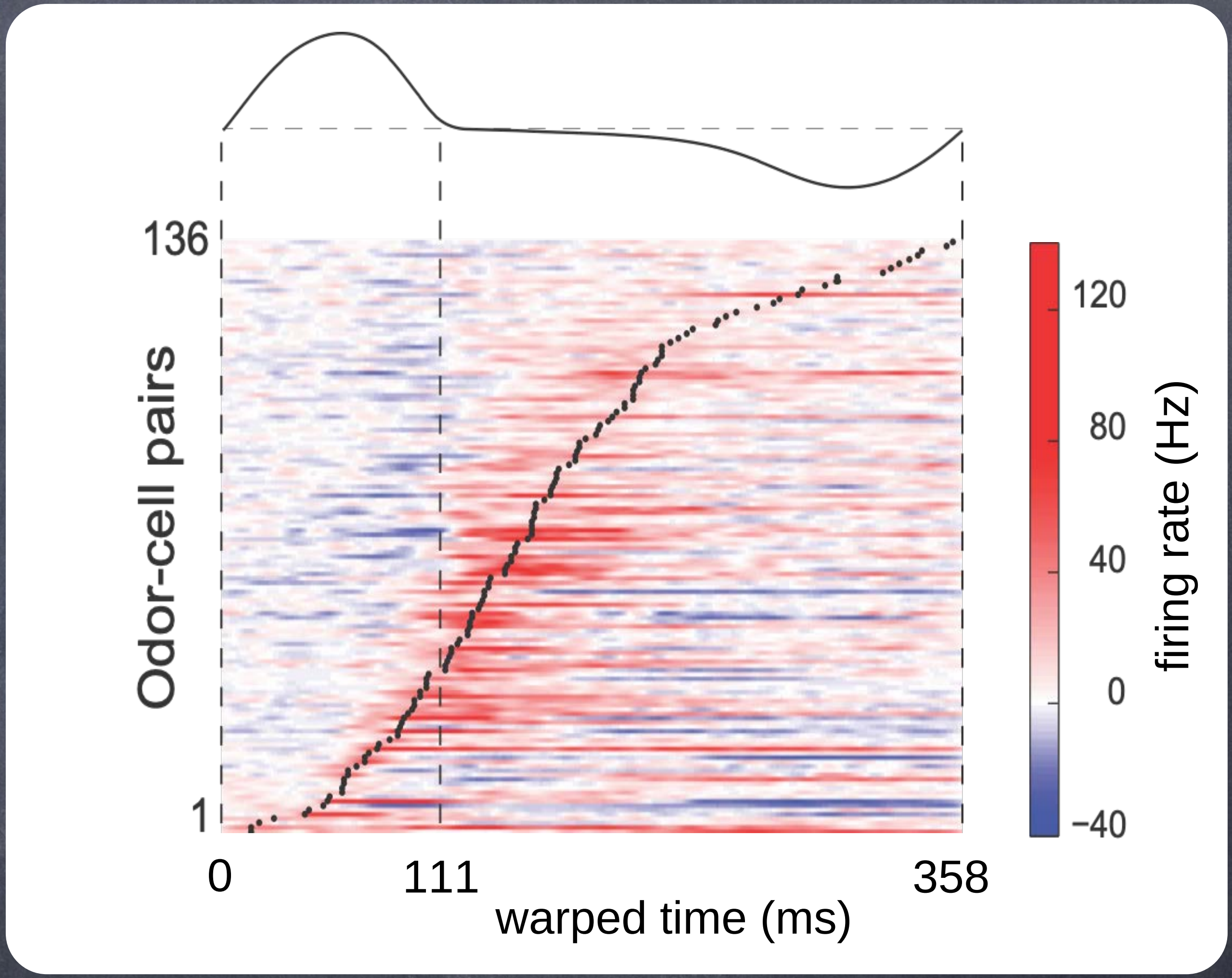
R Shusterman, et.al., Nature Neuroscience, 2011

odor responses are temporally diverse

460 cell-odor pairs: 136 excitatory responses
139 inhibitory responses

excitatory response

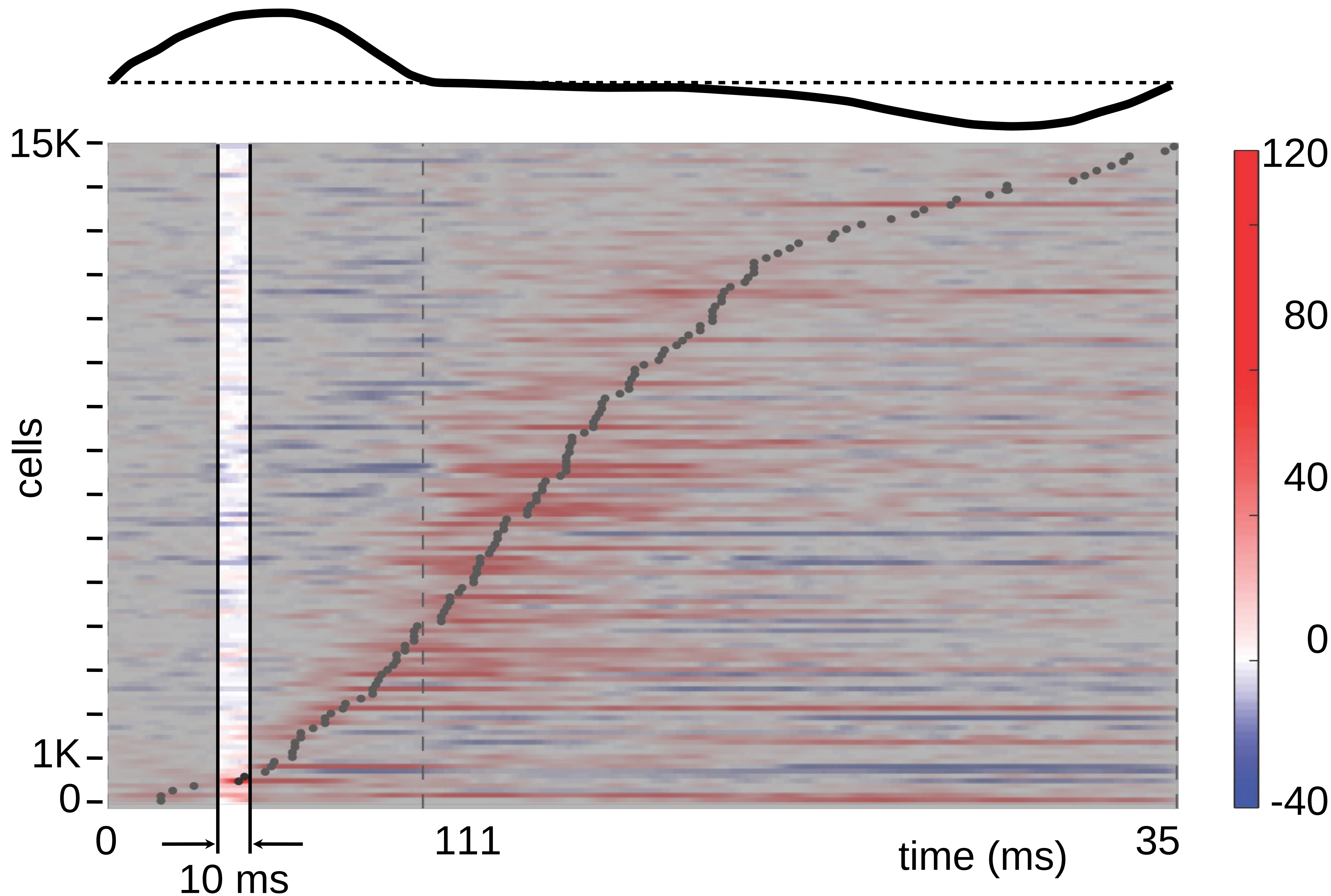




R Shusterman, et.al., Nature Neuroscience, 2011

460 cell-odor pairs:
136 excitatory responses

~50.000 M/T cells
~15.000 excitatory responses



Neuron
Article

Odor Representations in Olfactory Cortex: “Sparse” Coding, Global Inhibition, and Oscillations

Cindy Poo[1] and Jeffry S. Isaacson[1,*]
[1]Department of Neuroscience, School of Medicine, University of California, San Diego, La Jolla, CA 92093, USA
*Correspondence: jisaacson@ucsd.edu
DOI 10.1016/j.neuron.2009.05.022

Neuron 2009

pyramidal neuron integration time: ~10 ms

Oscillations and Sparsening of Odor Representations in the Mushroom Body

Javier Perez-Orive,* Ofer Mazor,* Glenn C. Turner,
Stijn Cassenaer, Rachel I. Wilson, Gilles Laurent†

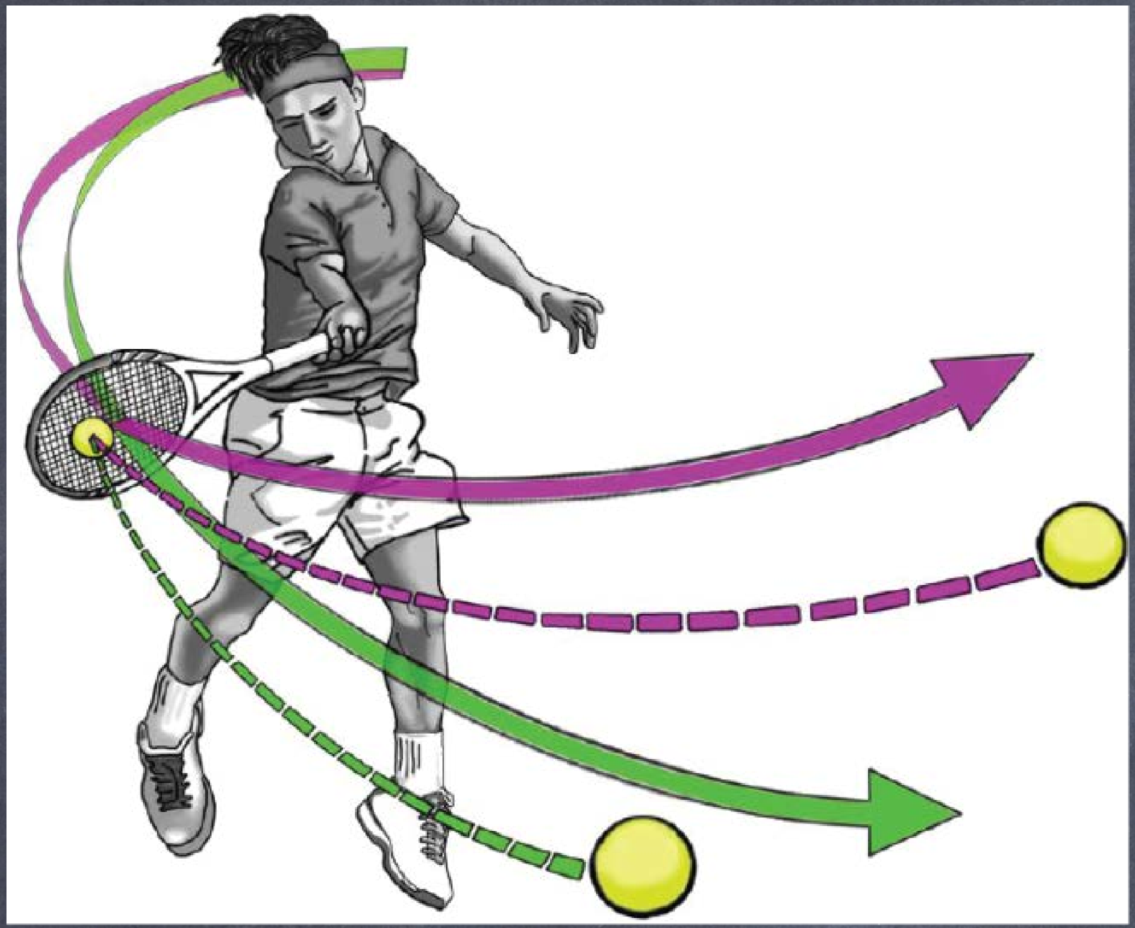
Science, 2002

Lecture II

Sensory (olfactory) coding from behavioral perspective

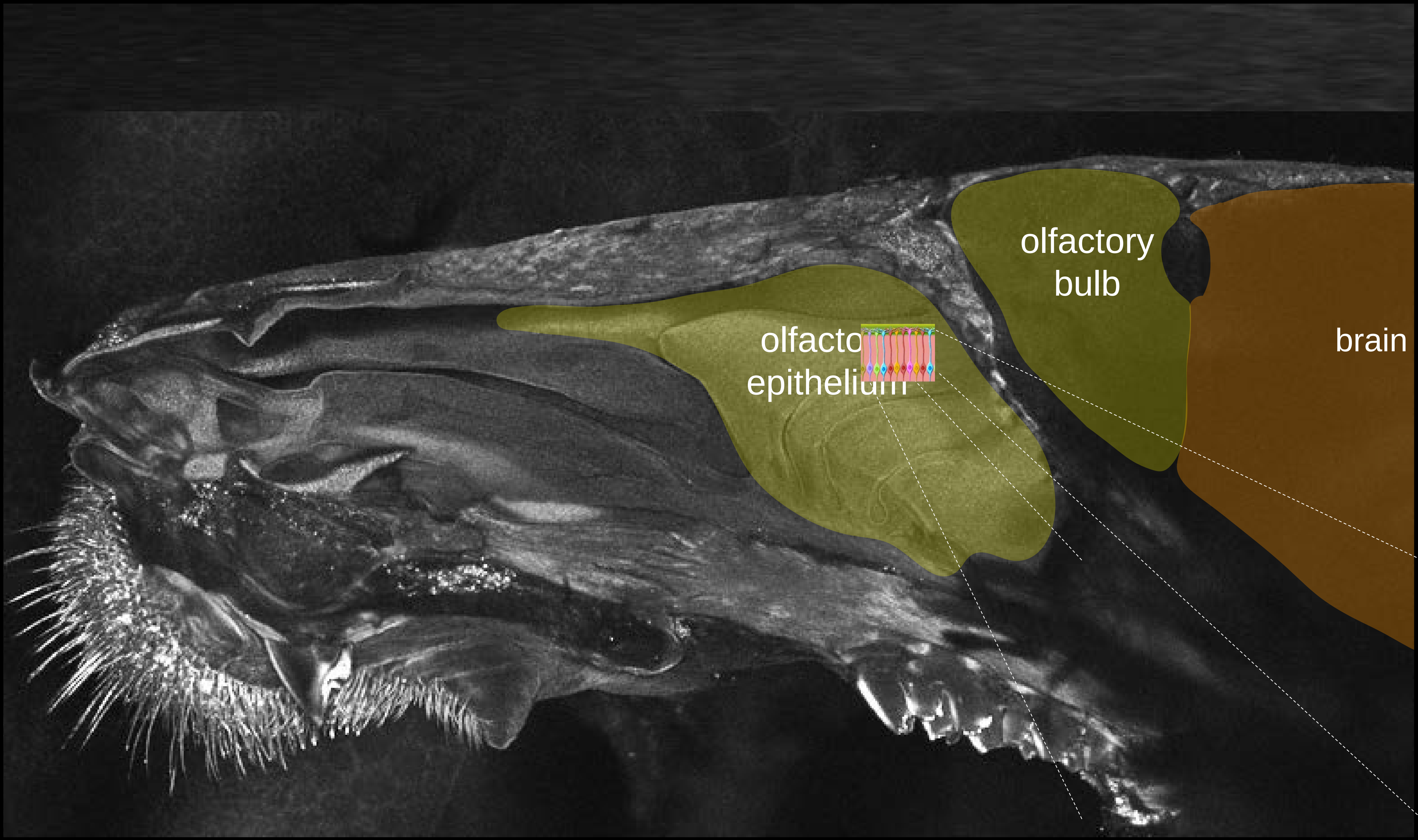
Dima Rinberg
rinberg@nyu.edu

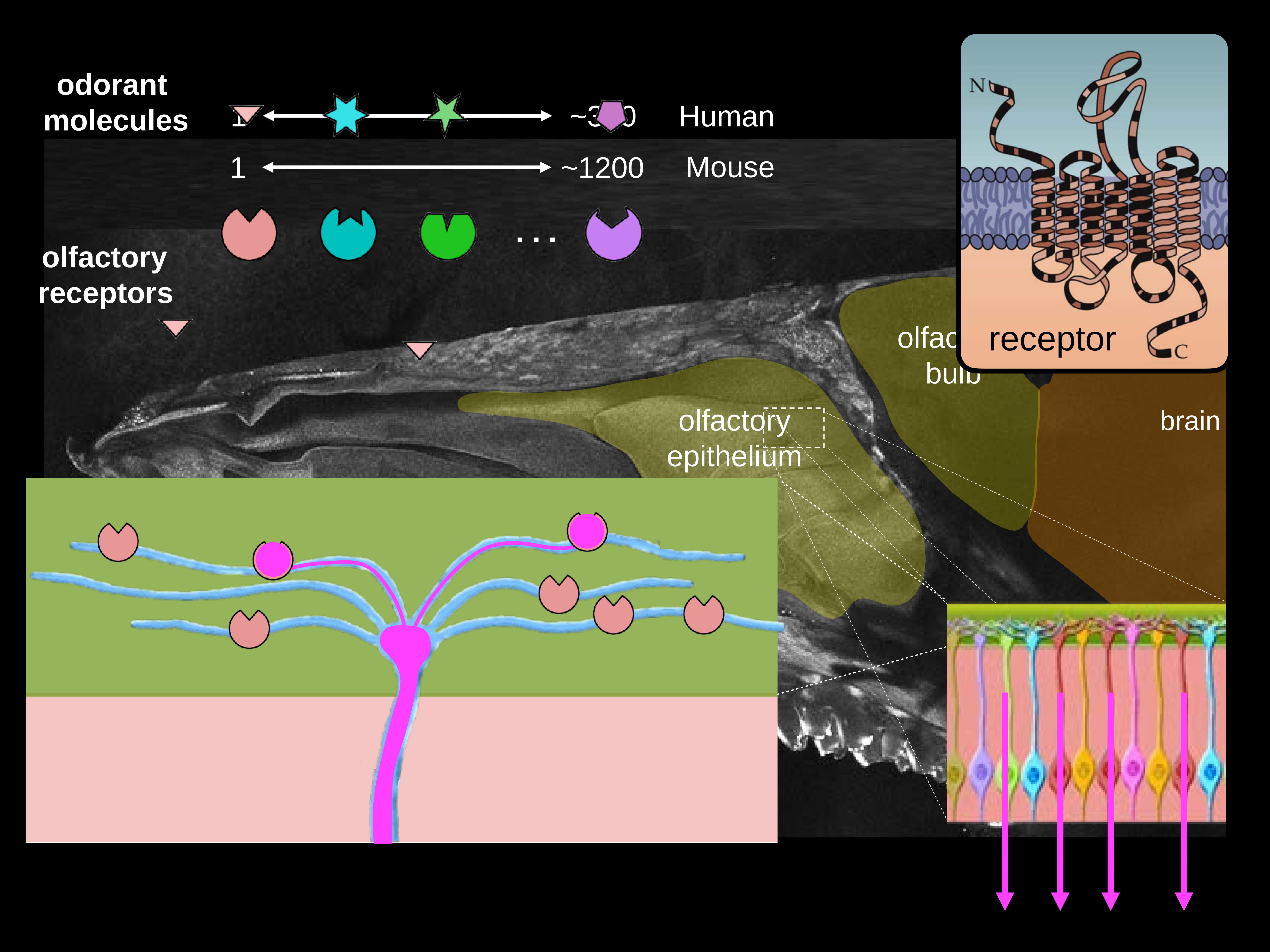
NYU NEUROSCIENCE



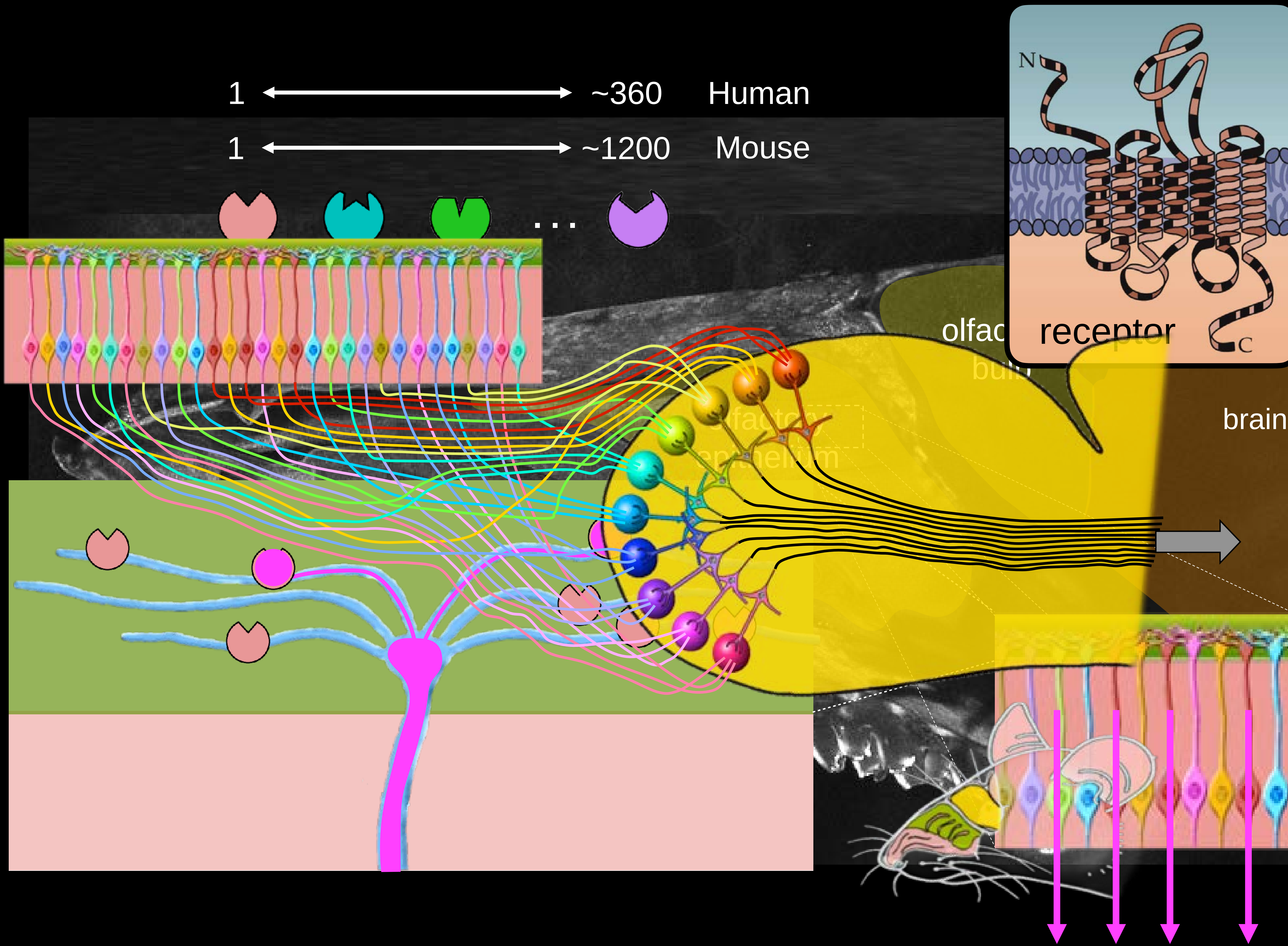
$$\vec{S} \xrightarrow{f} \vec{N} \xrightarrow{?} B$$

stimulus | *neural representation* | *behavior*

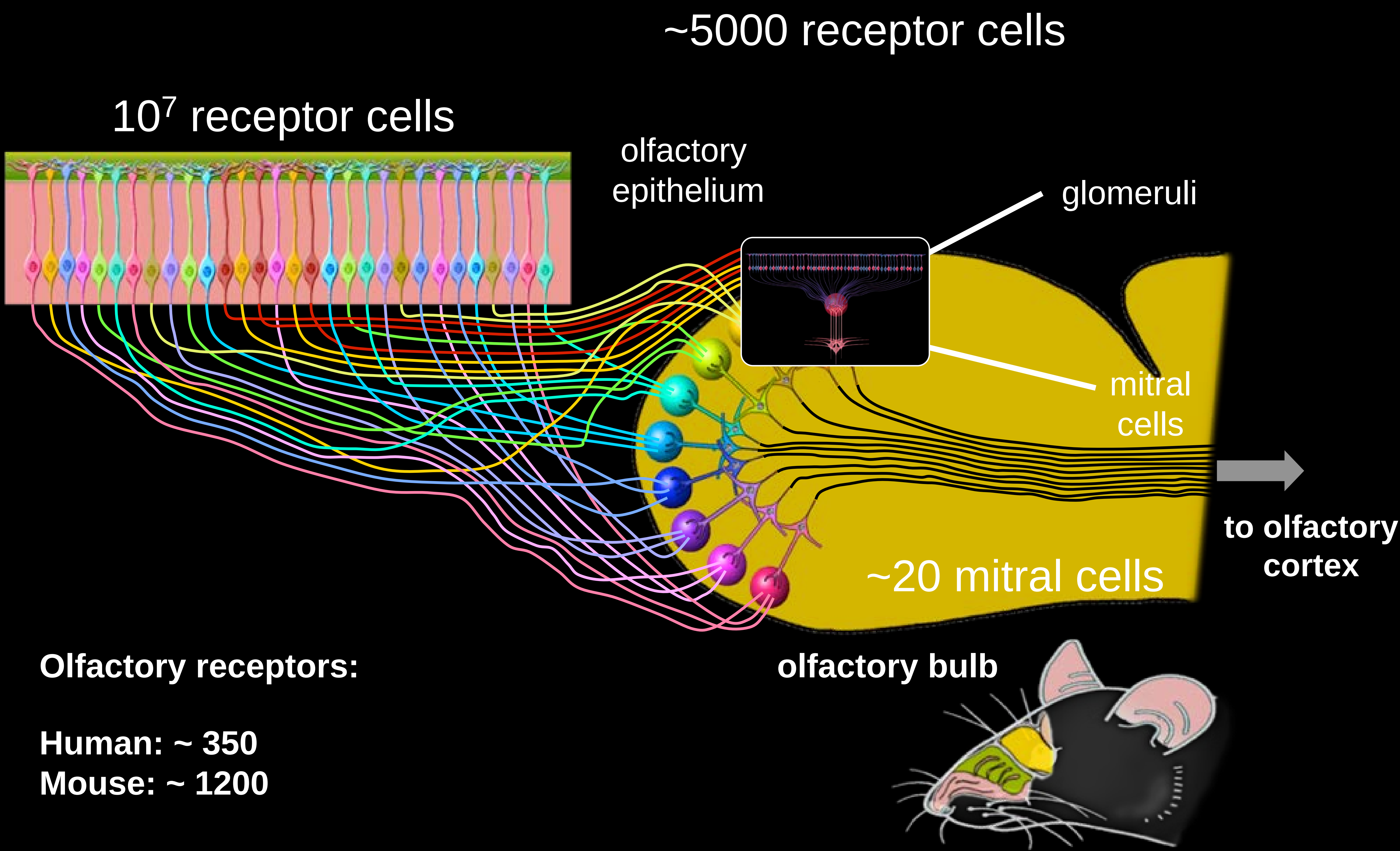

olfactory
bulb
olfacto
epithelium
brain



odorant molecules
Human
1
~1200
Mouse
olfactory receptors
olfactory epithelium
brain
receptor
N
C



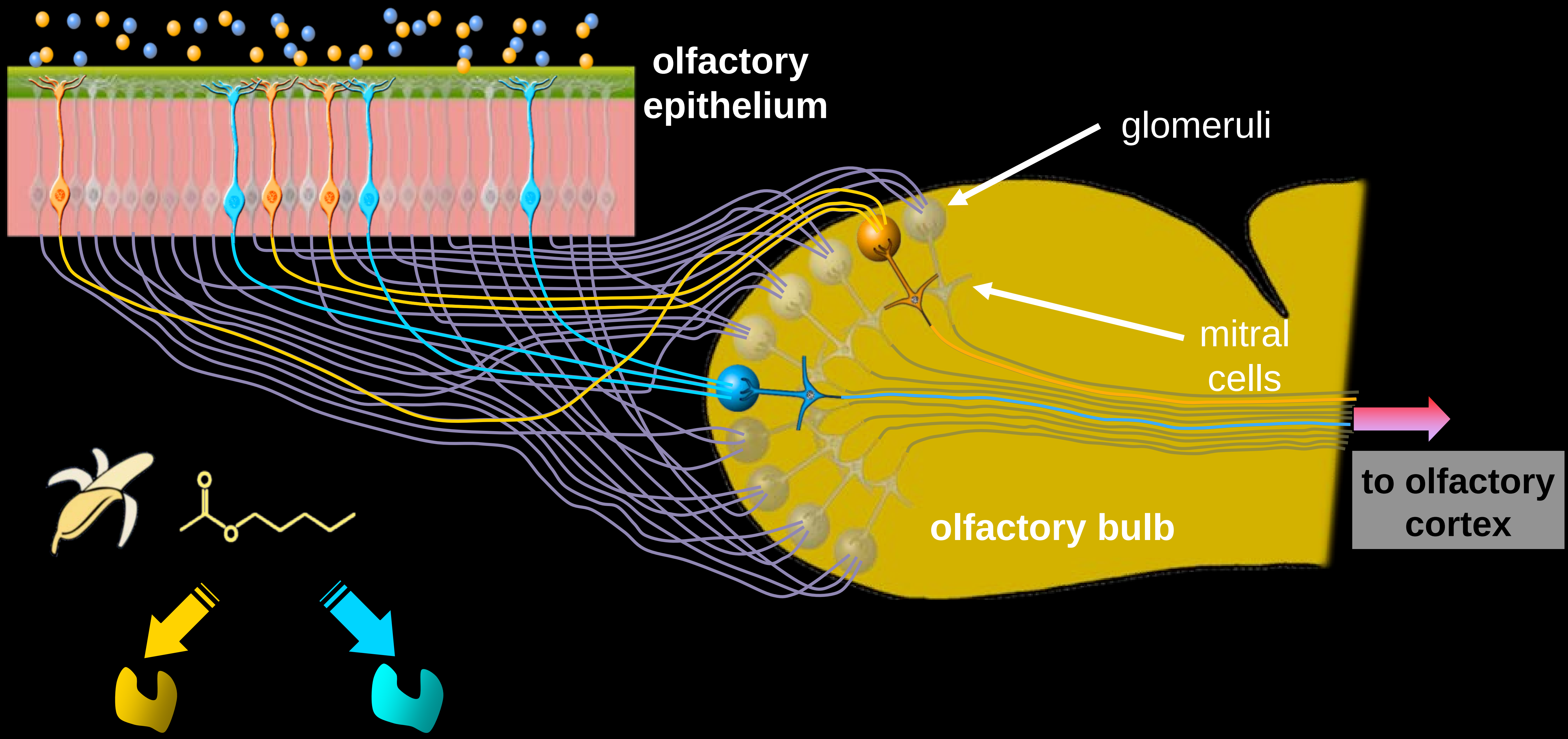
Modified from the artwork of Graeme Lowe



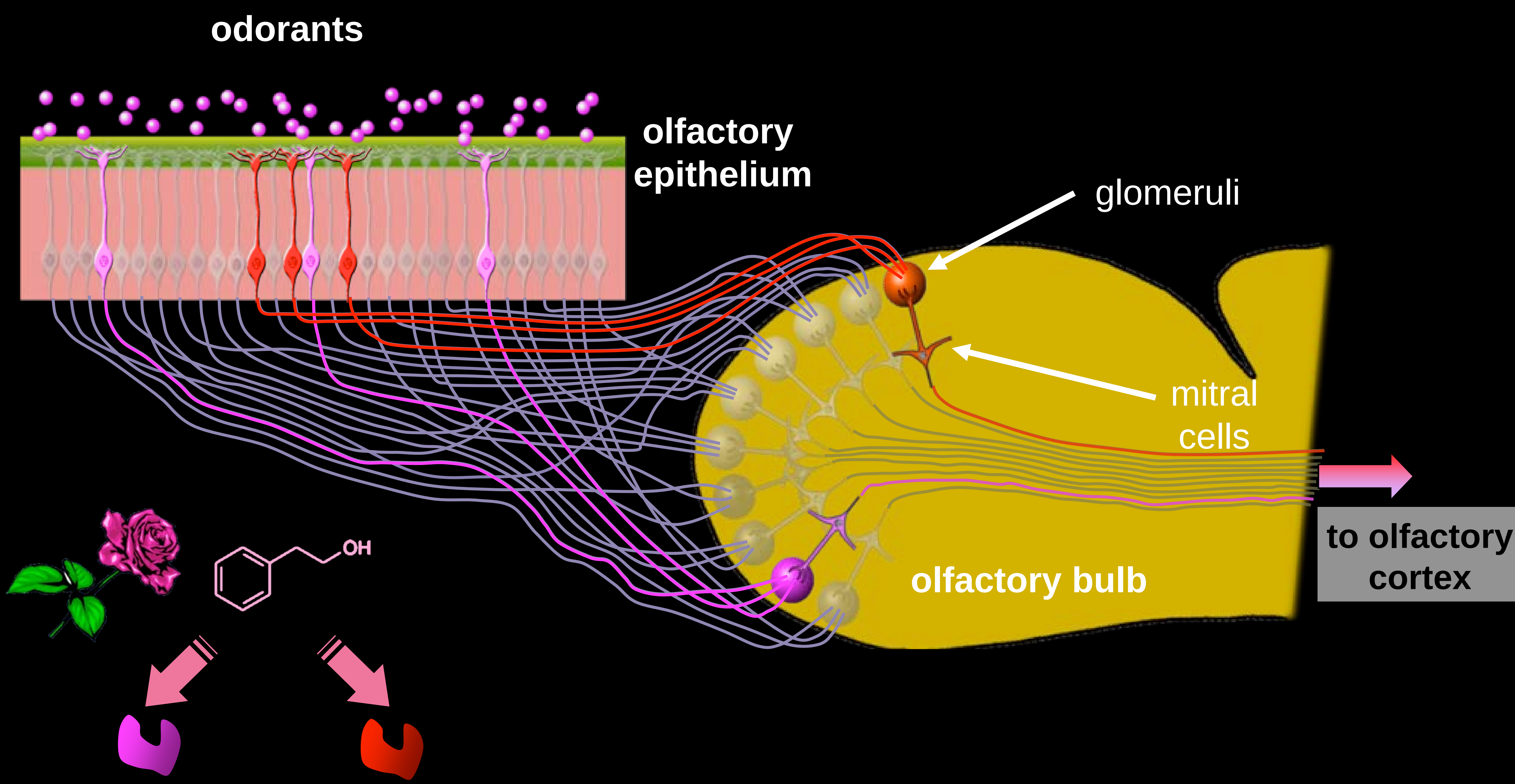
Olfactory receptors:

Human: ~ 350
Mouse: ~ 1200

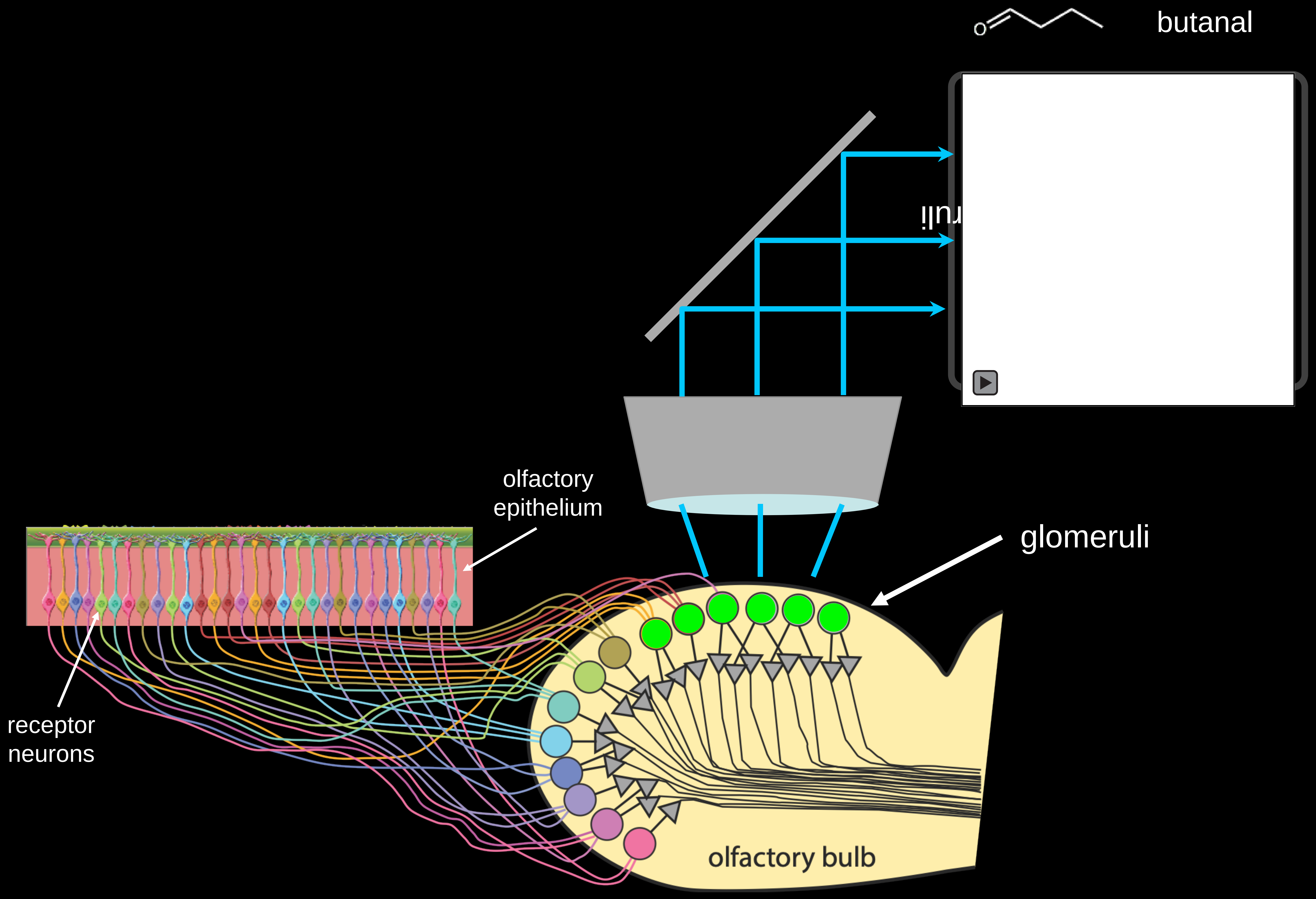
Modified from the artwork of Graeme Lowe

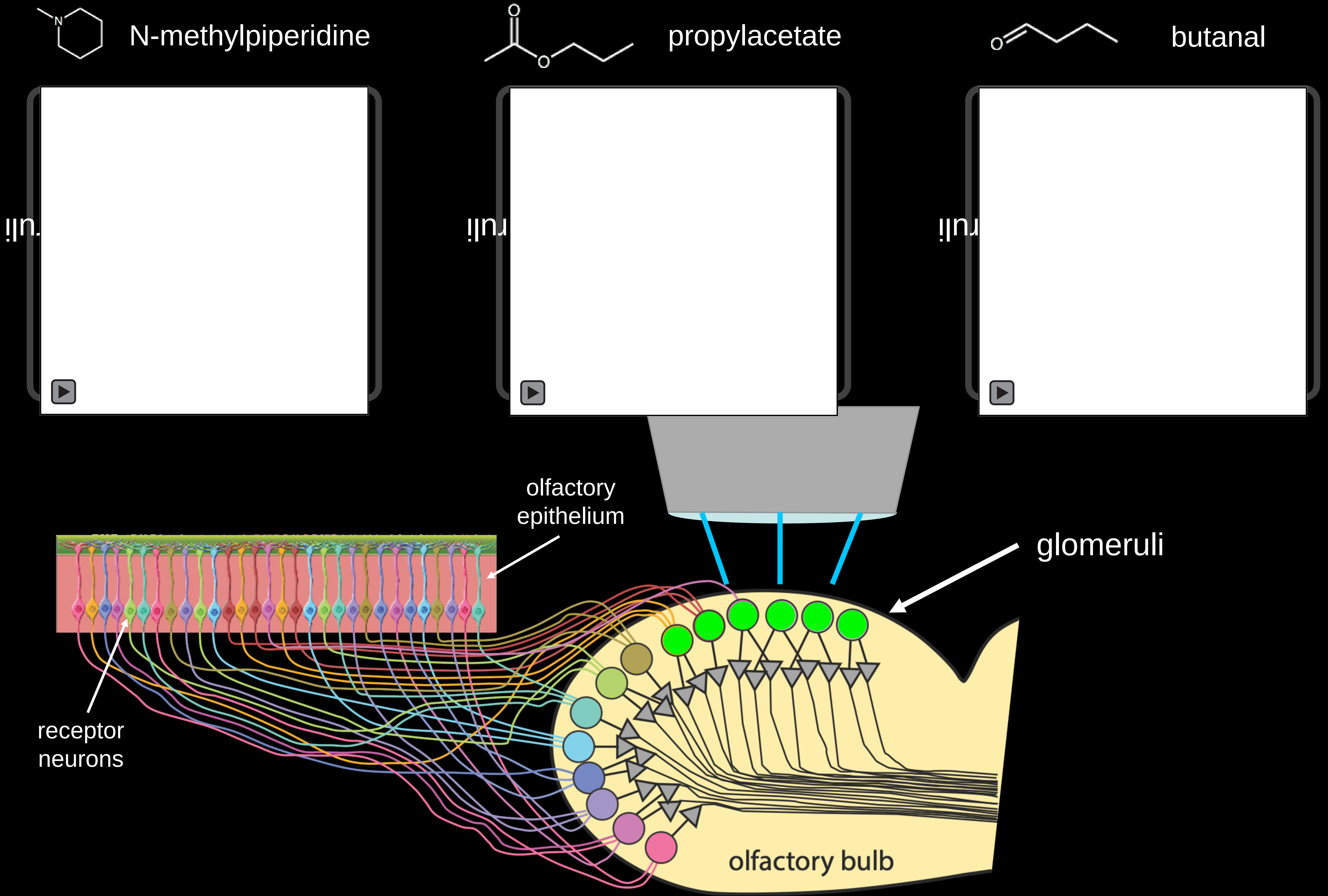


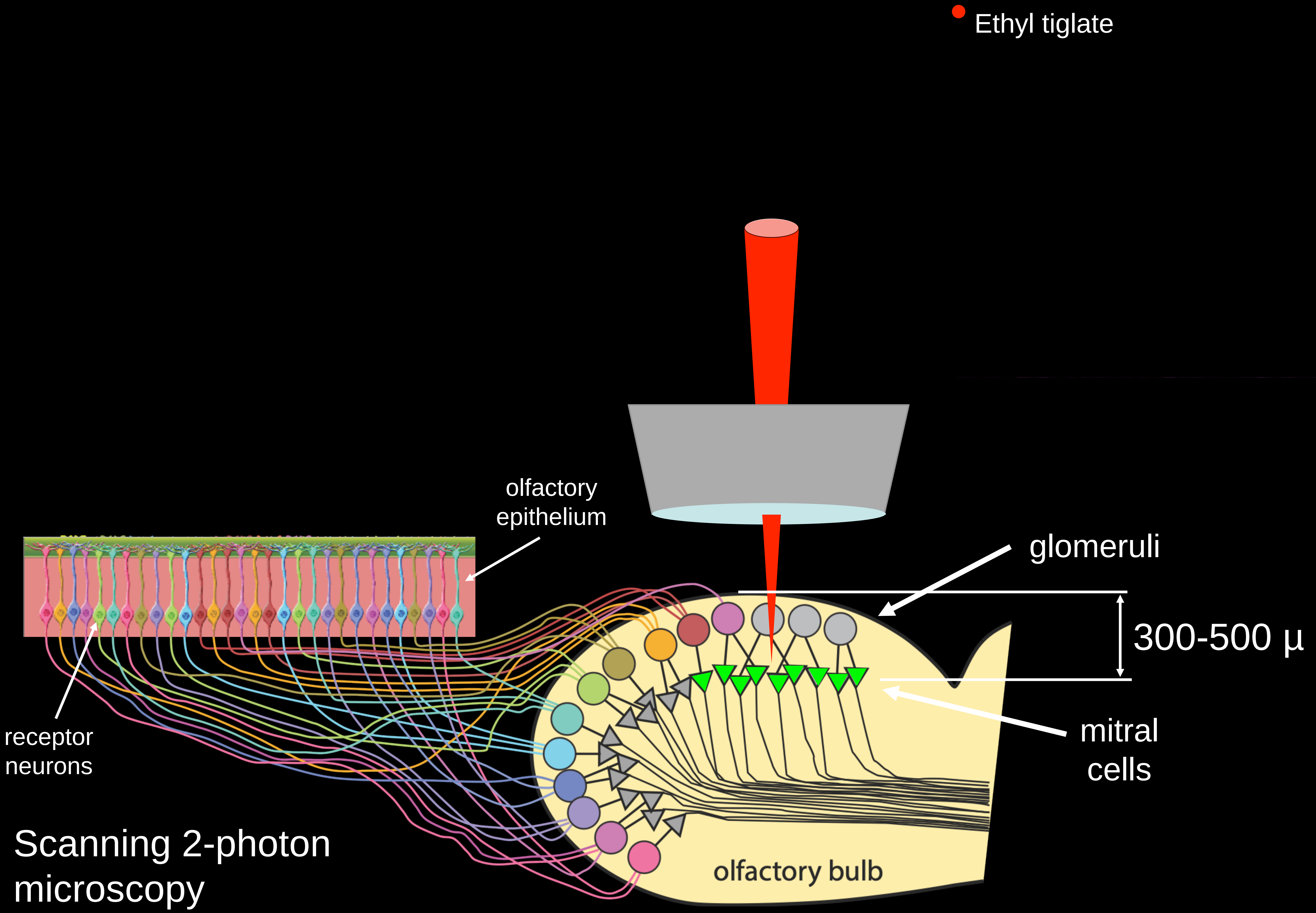
Modified from the artwork of Graeme Lowe

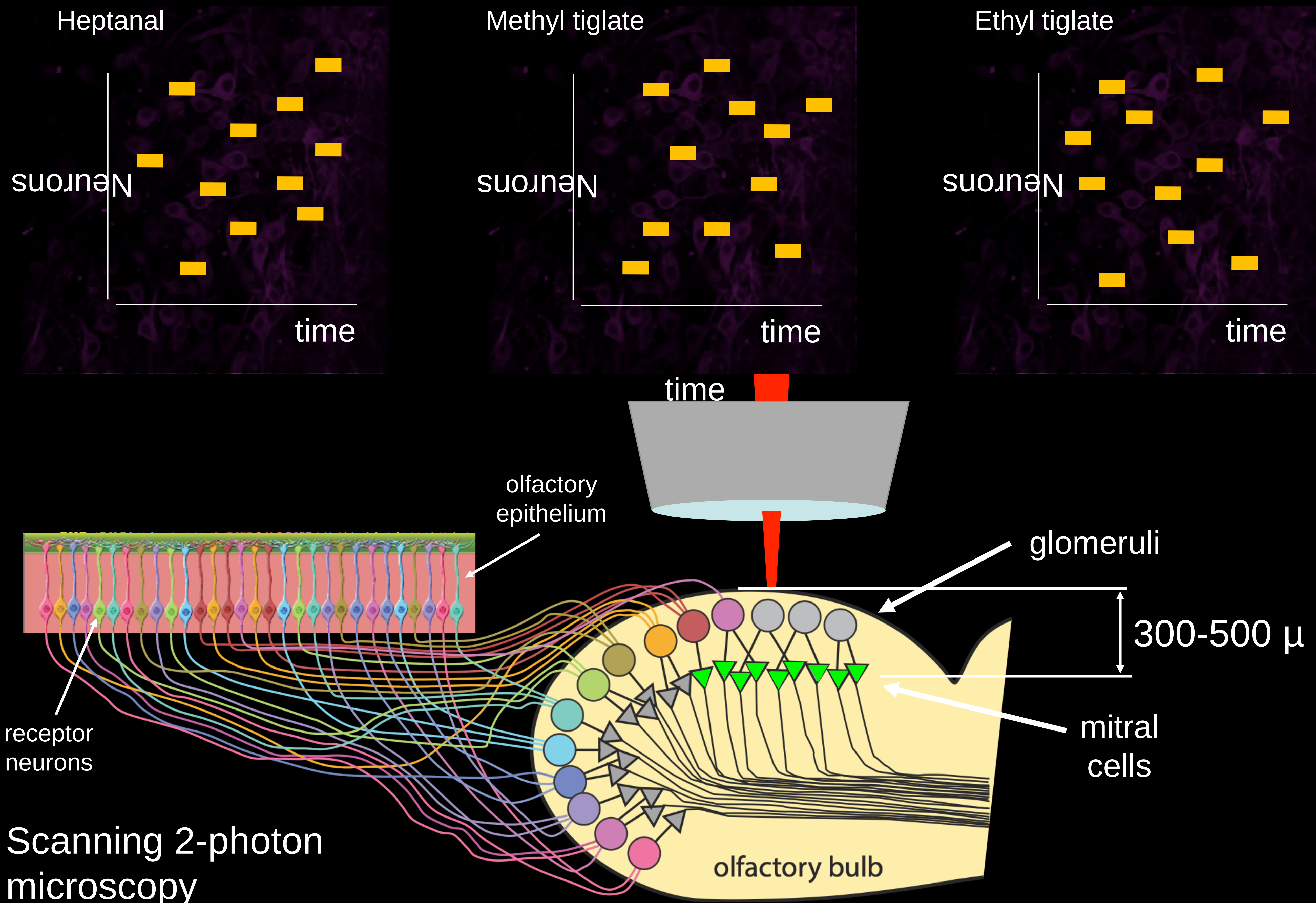


Modified from the artwork of Graeme Lowe

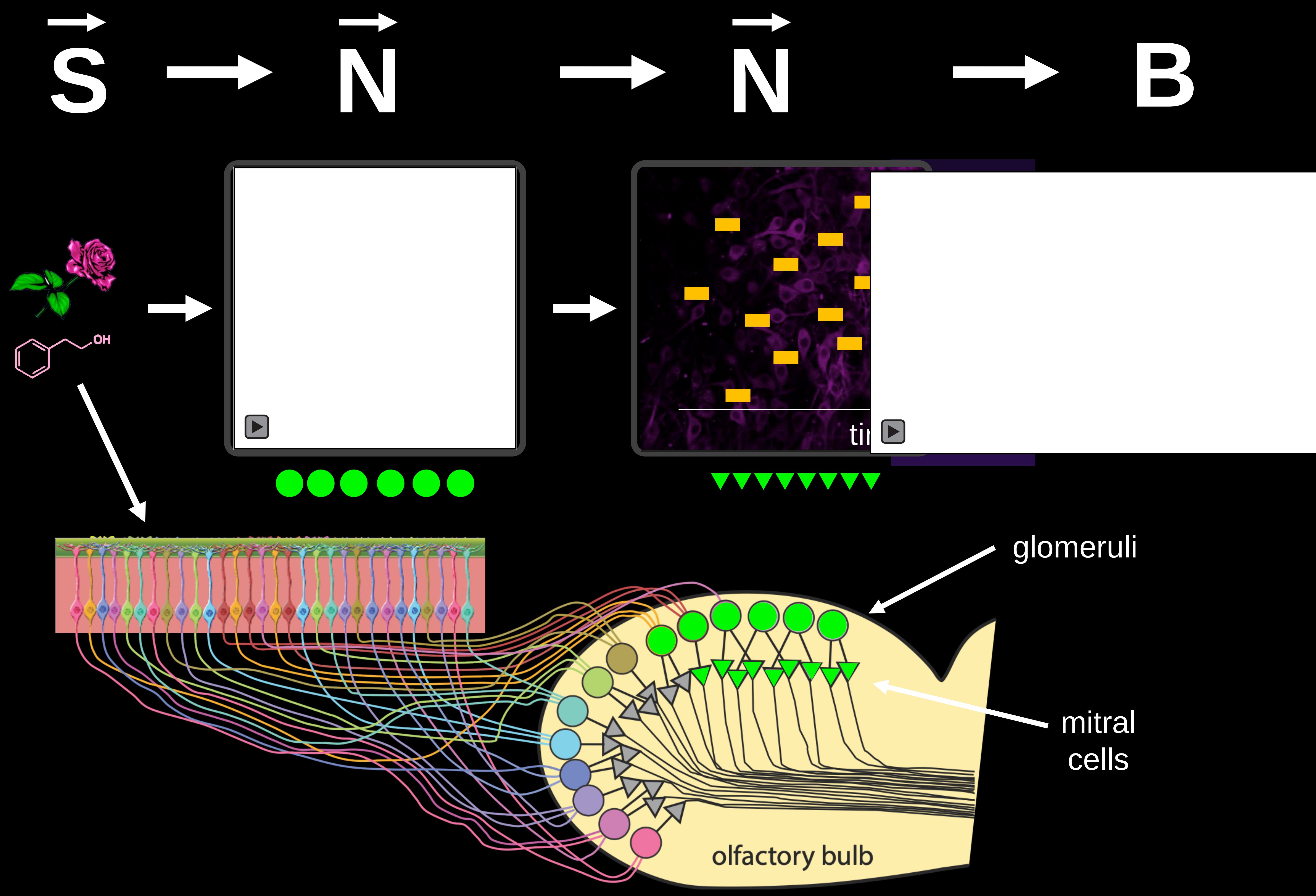

butanal
olfactory
epithelium
glomeruli
receptor
neurons
olfactory bulb


N-methylpiperidine
propylacetate
butanal
olfactory
epithelium
glomeruli
receptor
neurons
olfactory bulb

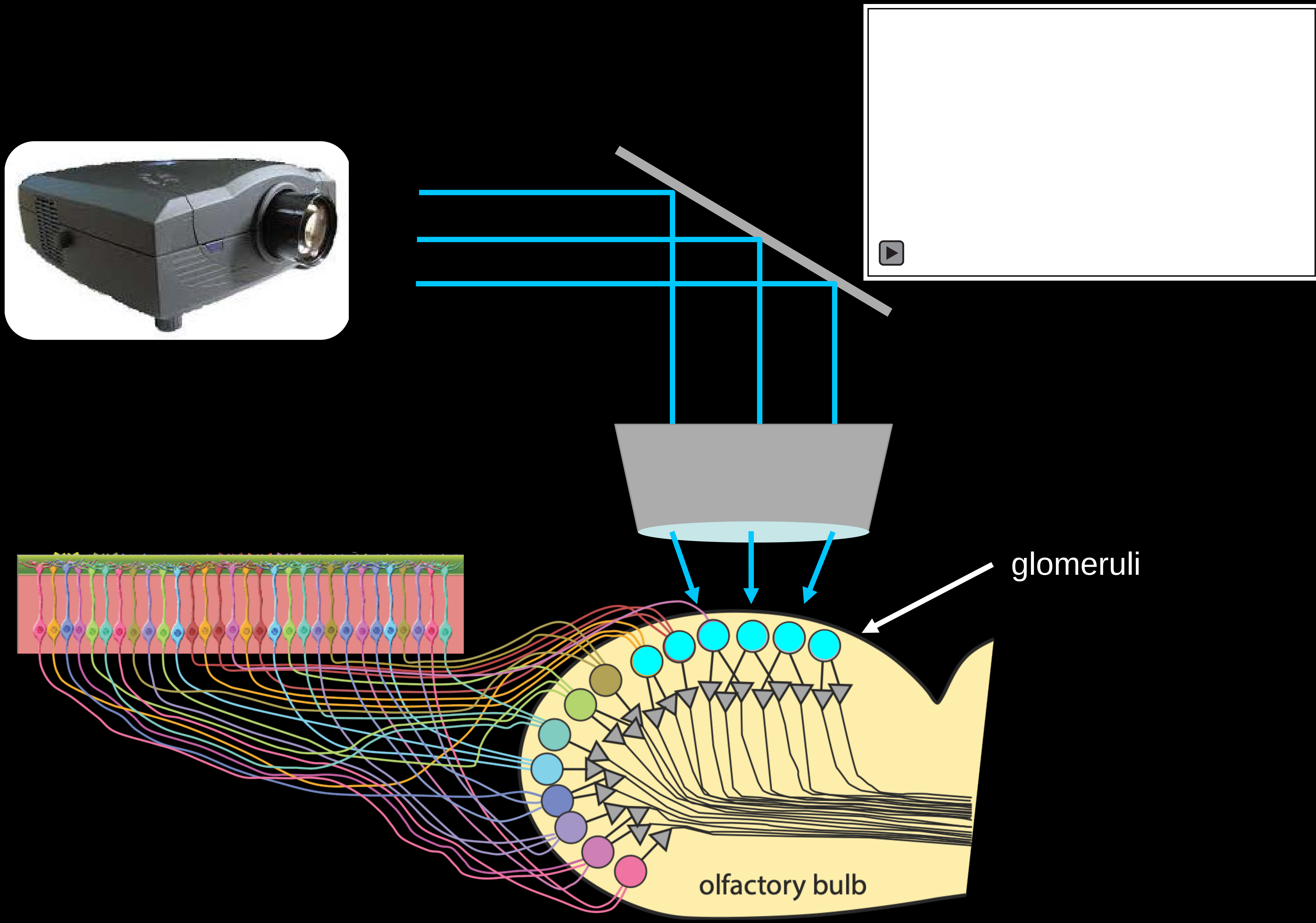

Ethyl tiglate
olfactory
epithelium
glomeruli
300-500 µ
mitral
cells
receptor
neurons
olfactory bulb
Scanning 2-photon
microscopy

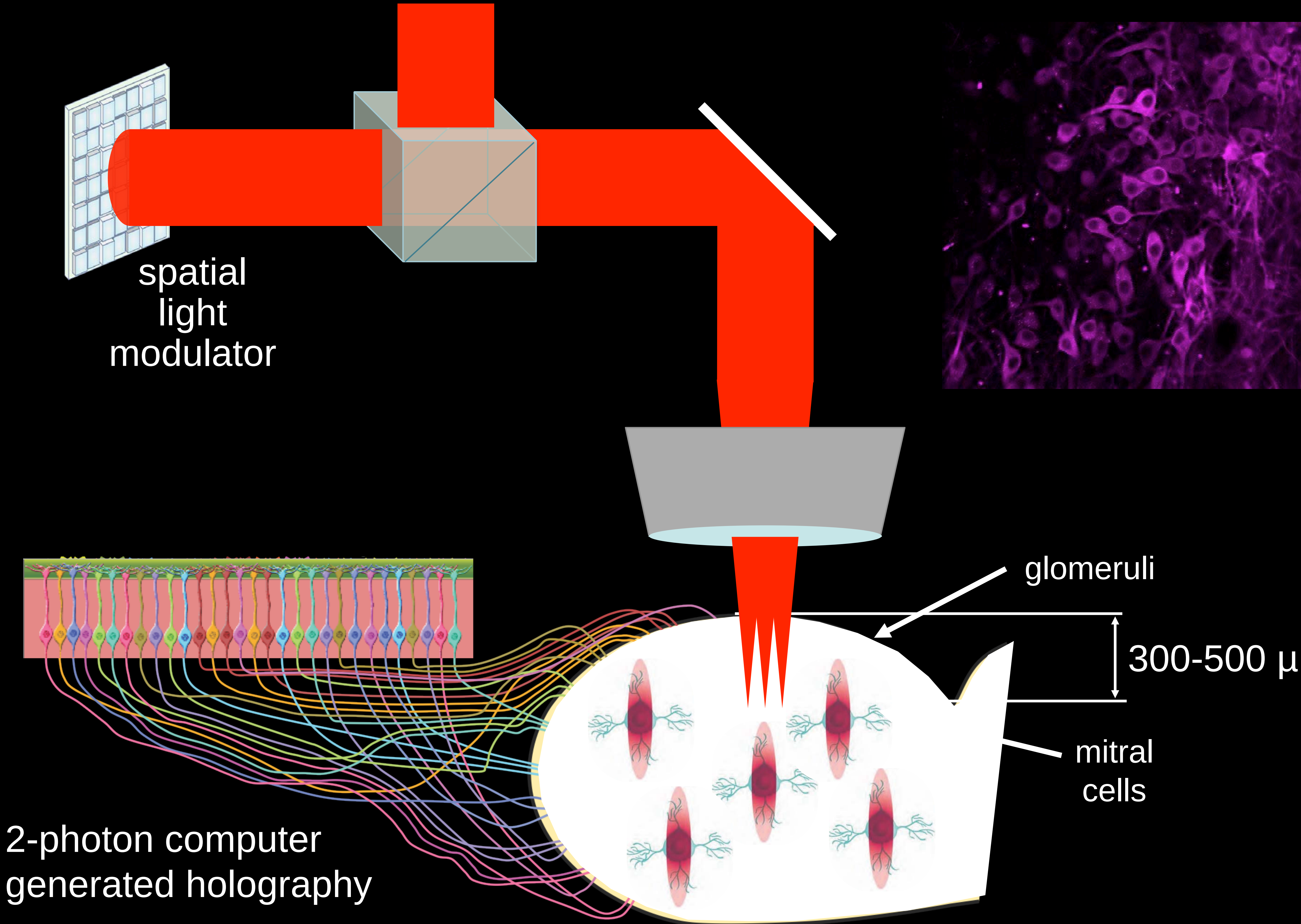


Scanning 2-photon microscopy

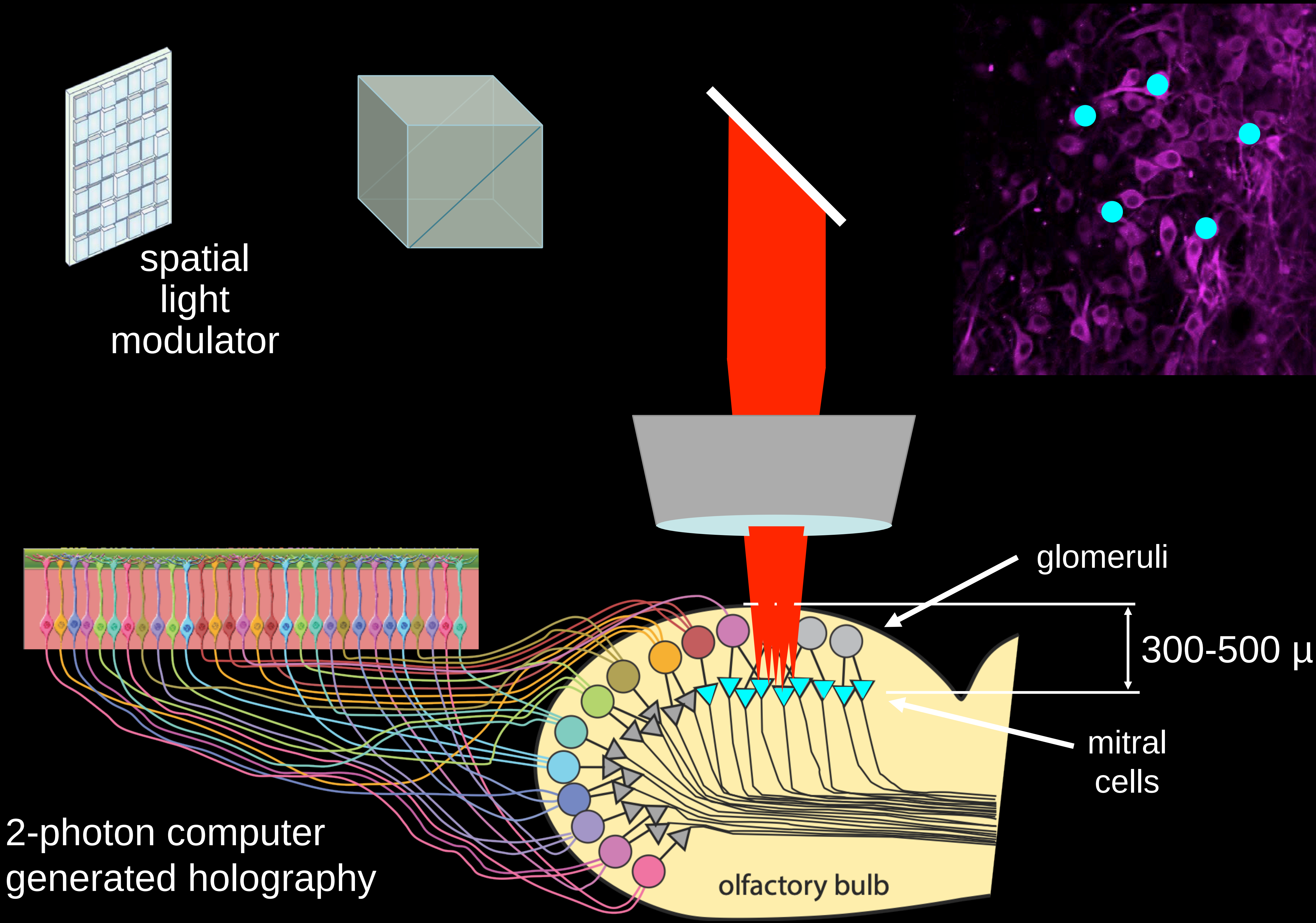


S → N → N → B
OH
glomeruli
mitral
cells
olfactory bulb


glomeruli
olfactory bulb



Gill, J. V., Lerman, G. M., Zhao, H., Stetler, B. J., Rinberg, D., & Shoham, S.
Precise Holographic Manipulation of Olfactory Circuits Reveals Coding Features Determining Perceptual Detection.
Neuron, 108(2), 382–393.e5. (2020).



Gill, J. V., Lerman, G. M., Zhao, H., Stetler, B. J., Rinberg, D., & Shoham, S.
Precise Holographic Manipulation of Olfactory Circuits Reveals Coding Features Determining Perceptual Detection.
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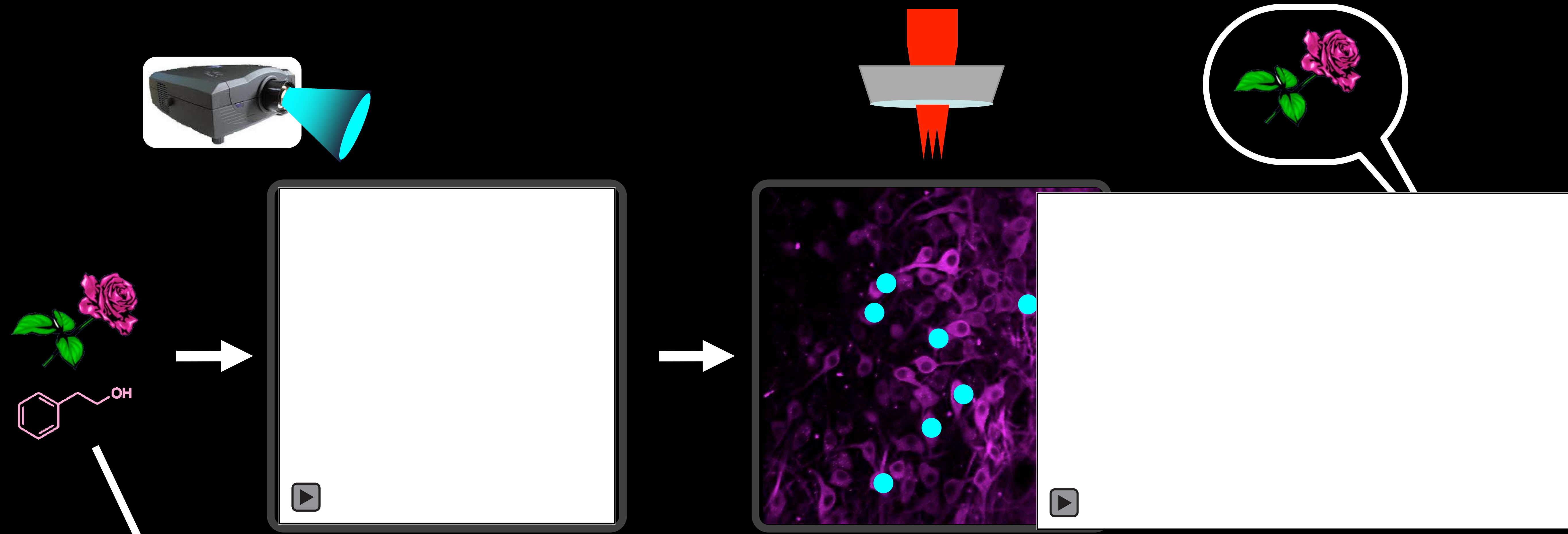
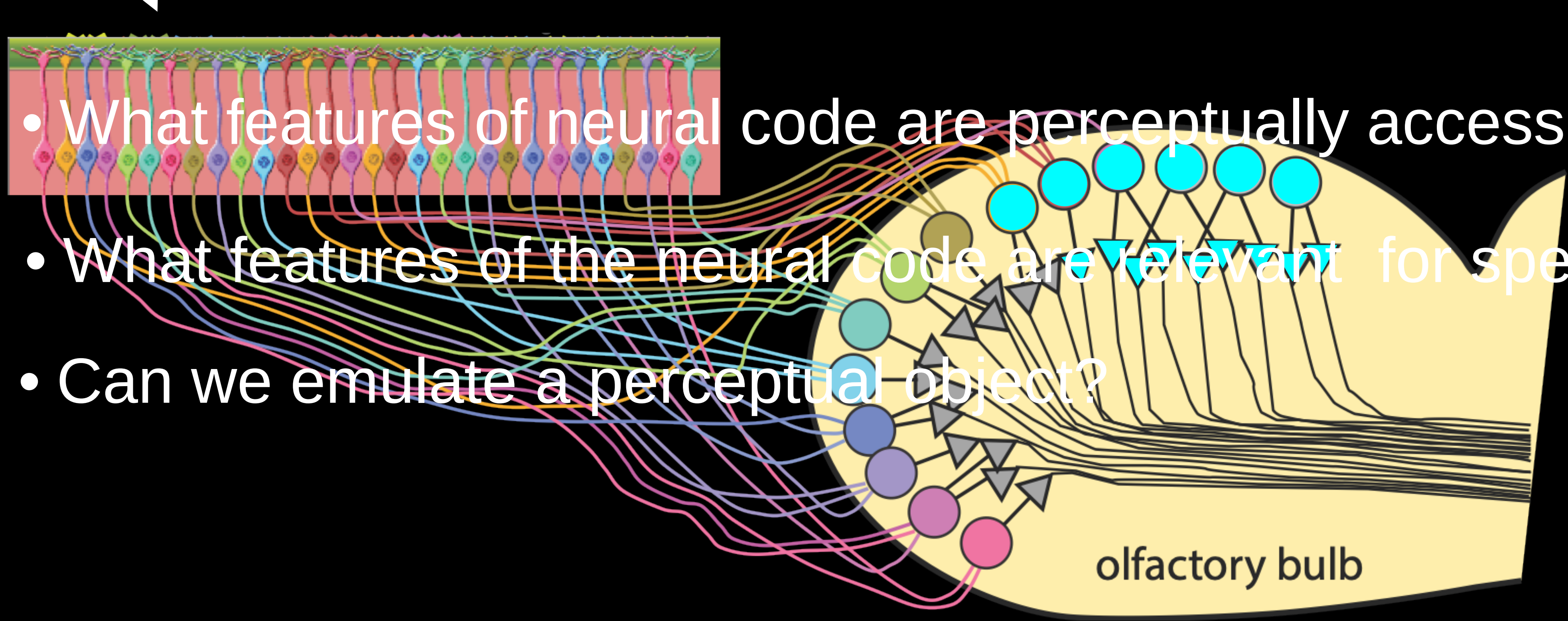
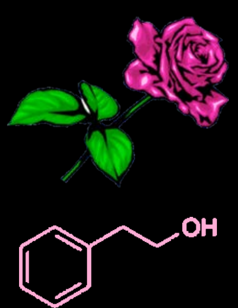
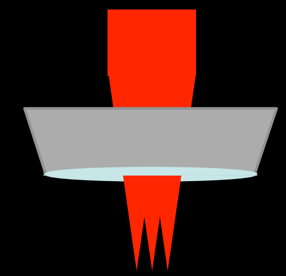
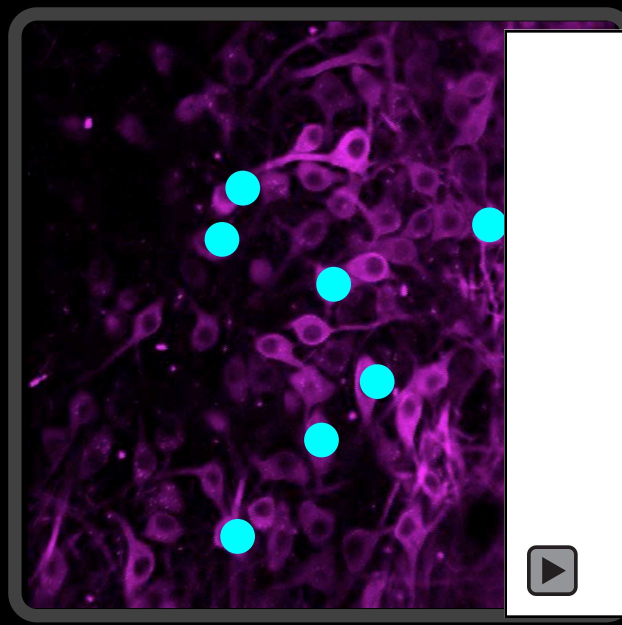


- What features of neural code are perceptually accessible?
- What features of the neural code are relevant for specific behaviors?
- Can we emulate a perceptual object?









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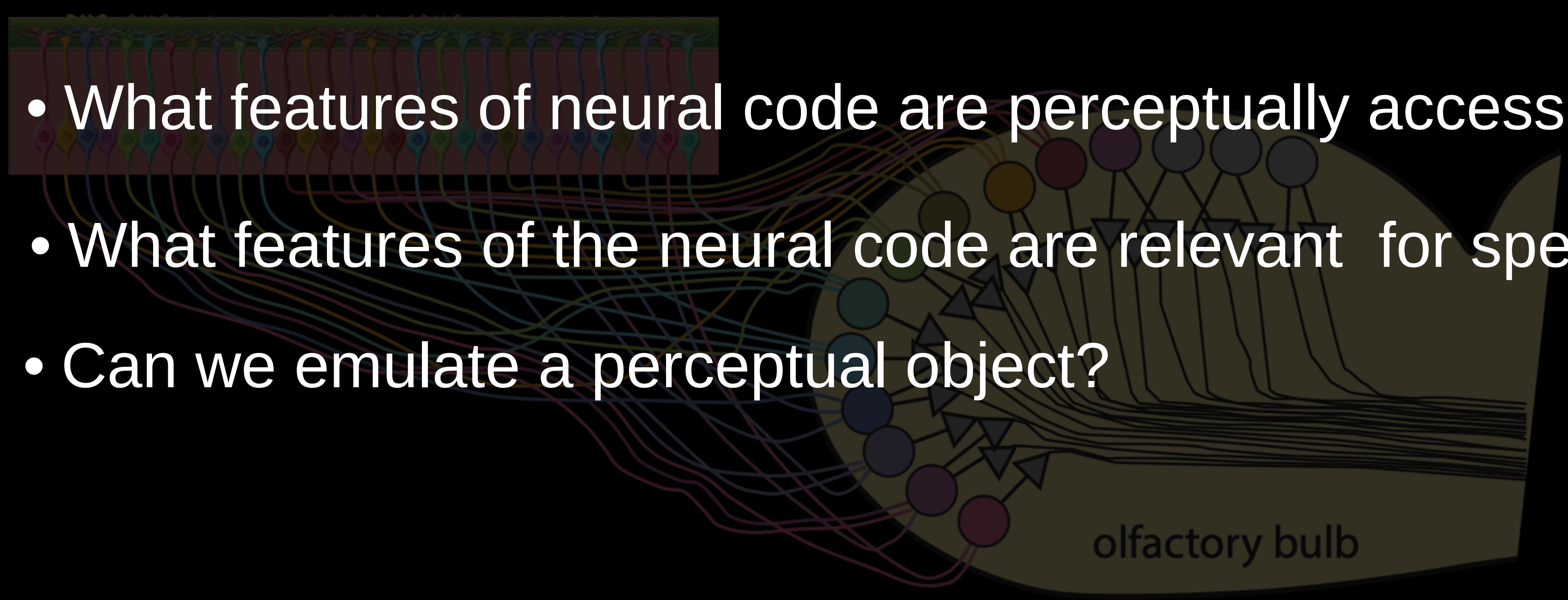
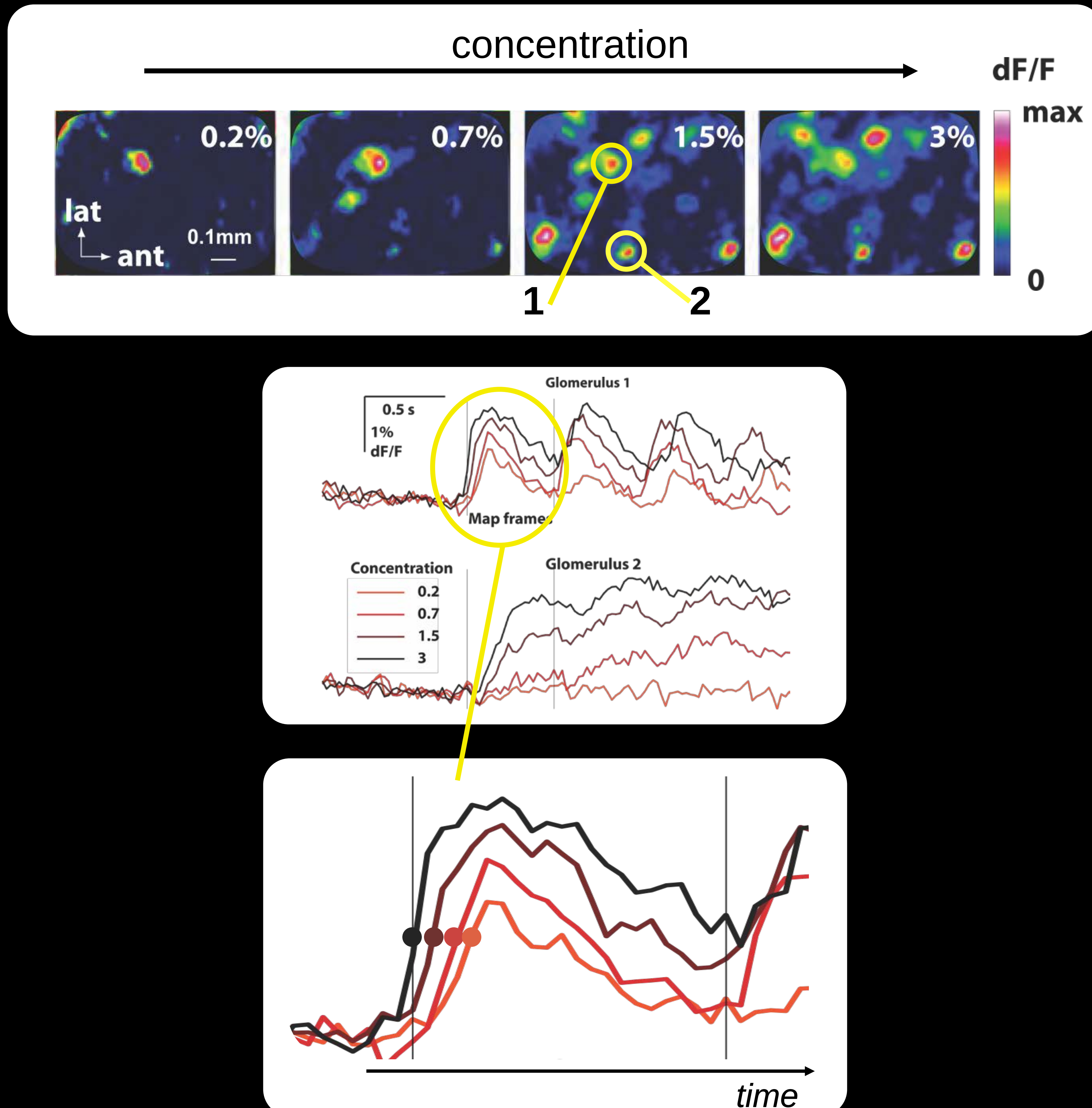
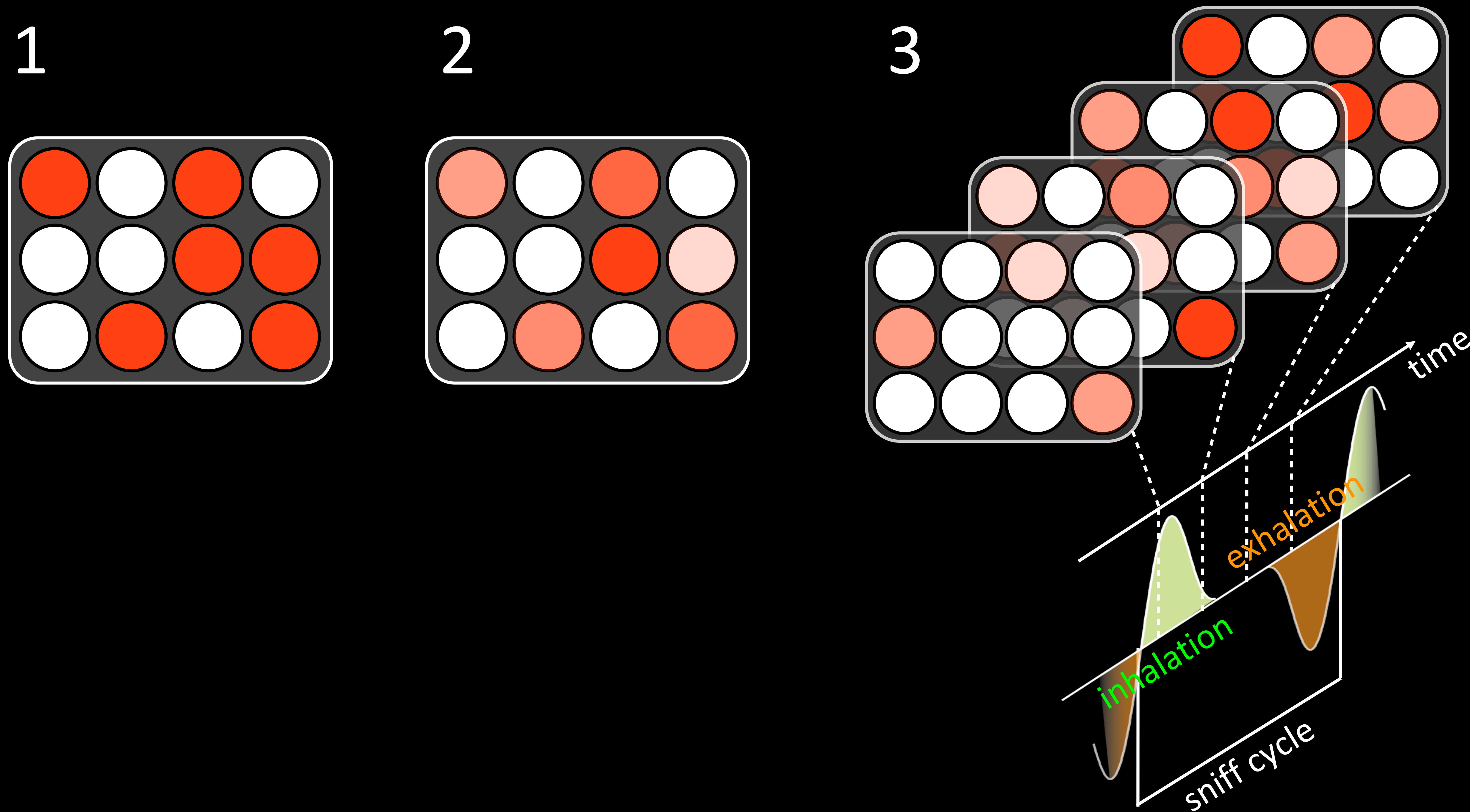


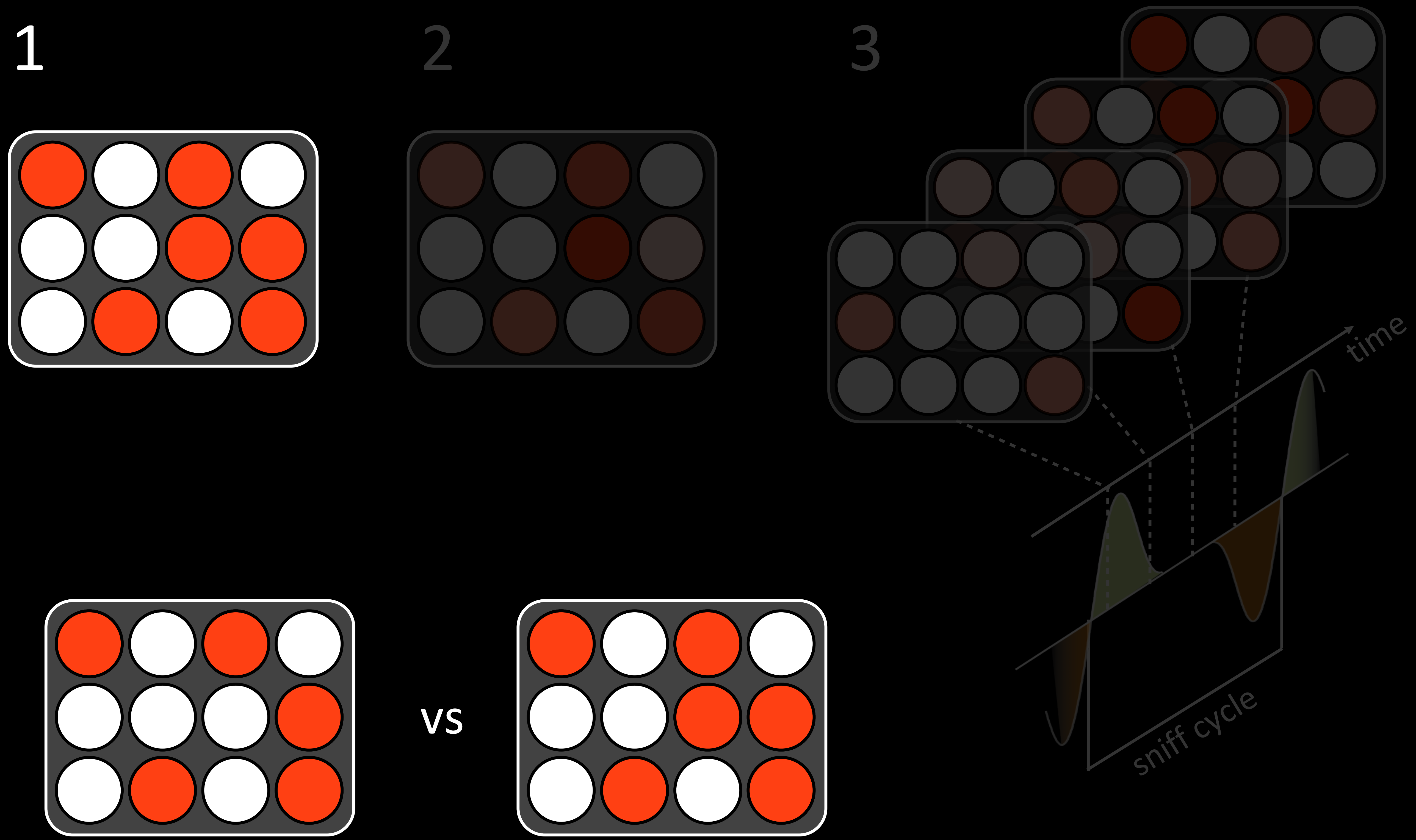


H. Spors, M. Wachowiak, L.B. Cohen, & R.W. Friedrich. **Temporal dynamics and latency patterns of receptor neuron input to the olfactory bulb**. *J Neurosci* **26,** 1247–1259 (2006).

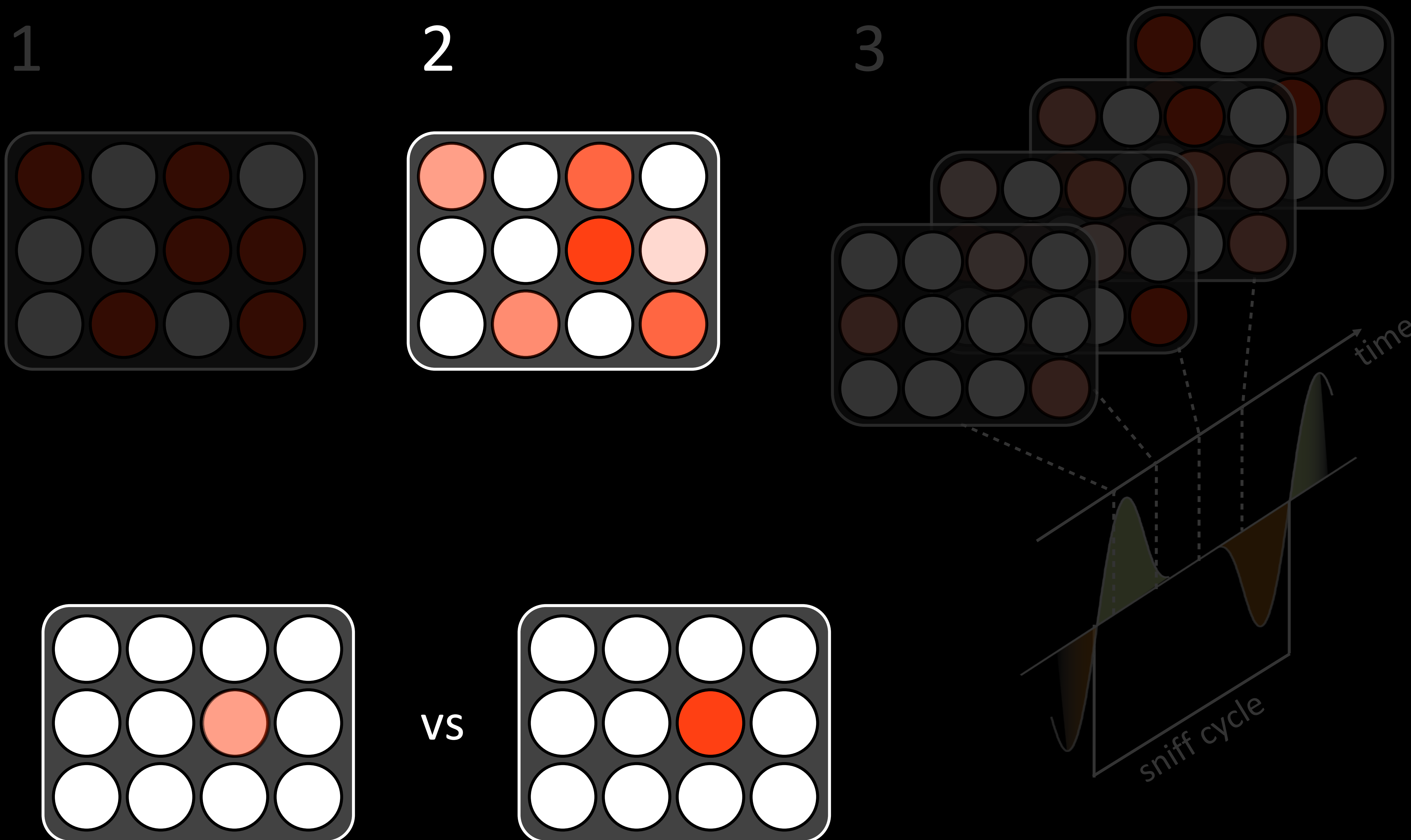
olfactory coding schemes



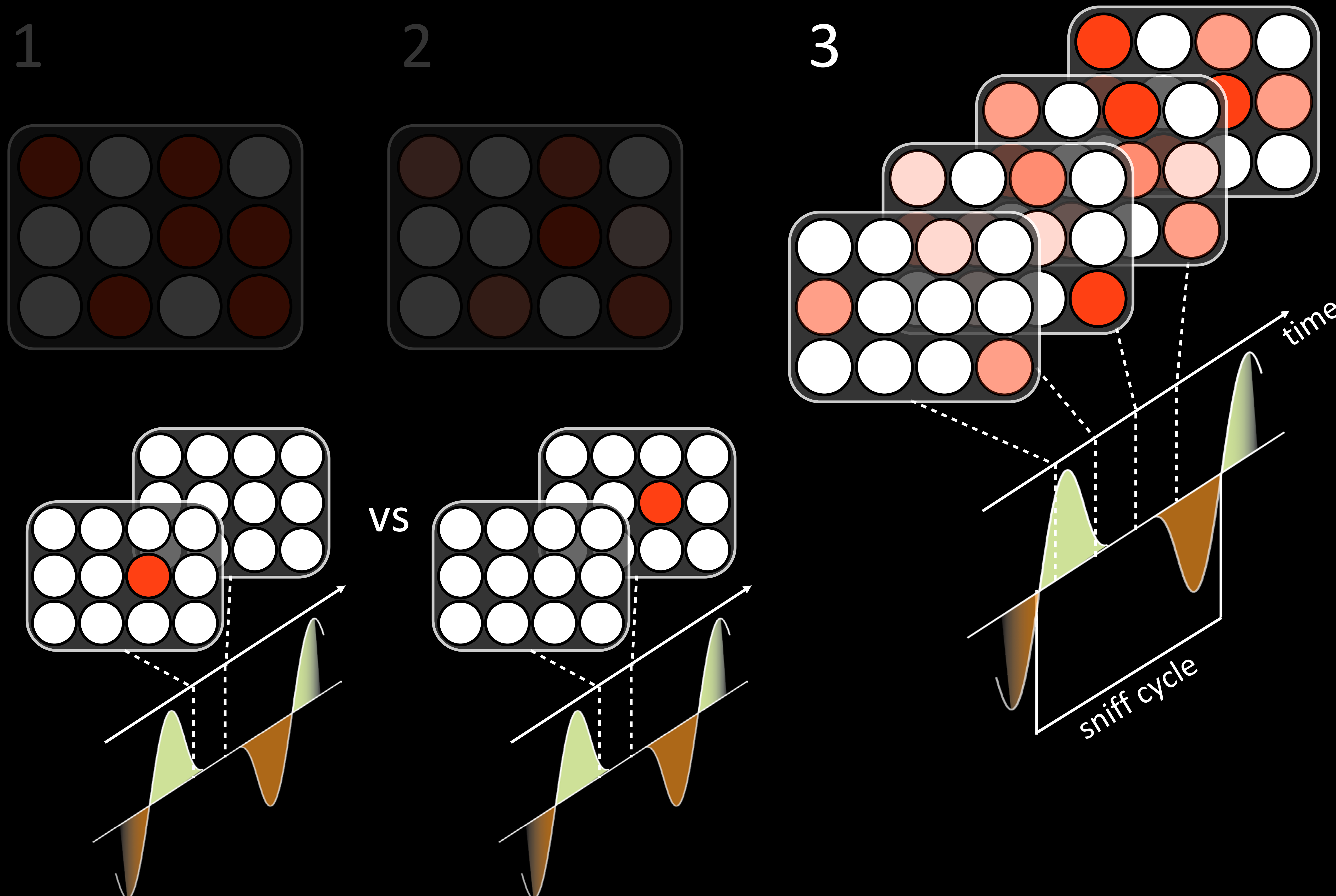
olfactory coding schemes

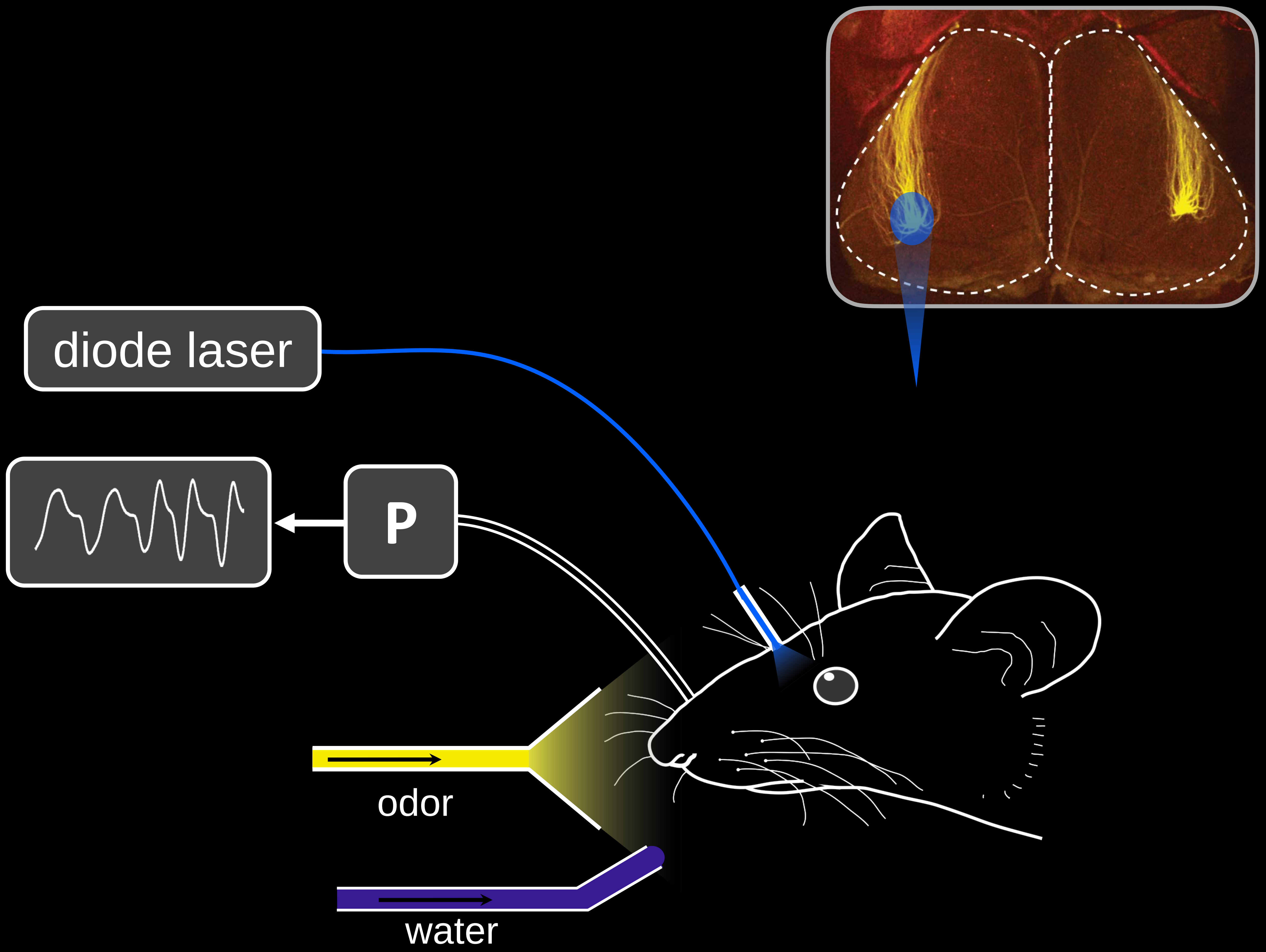


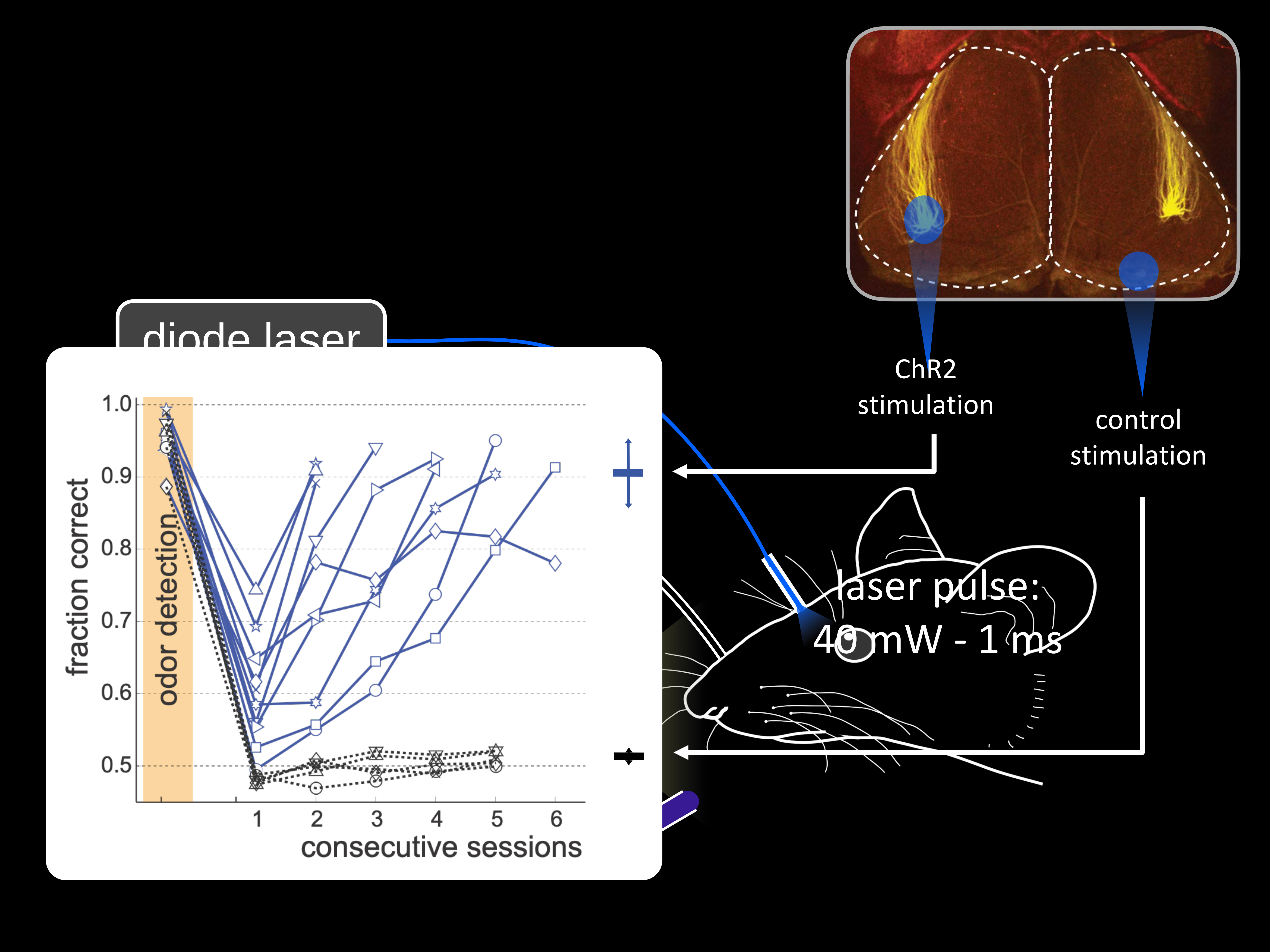
olfactory coding schemes



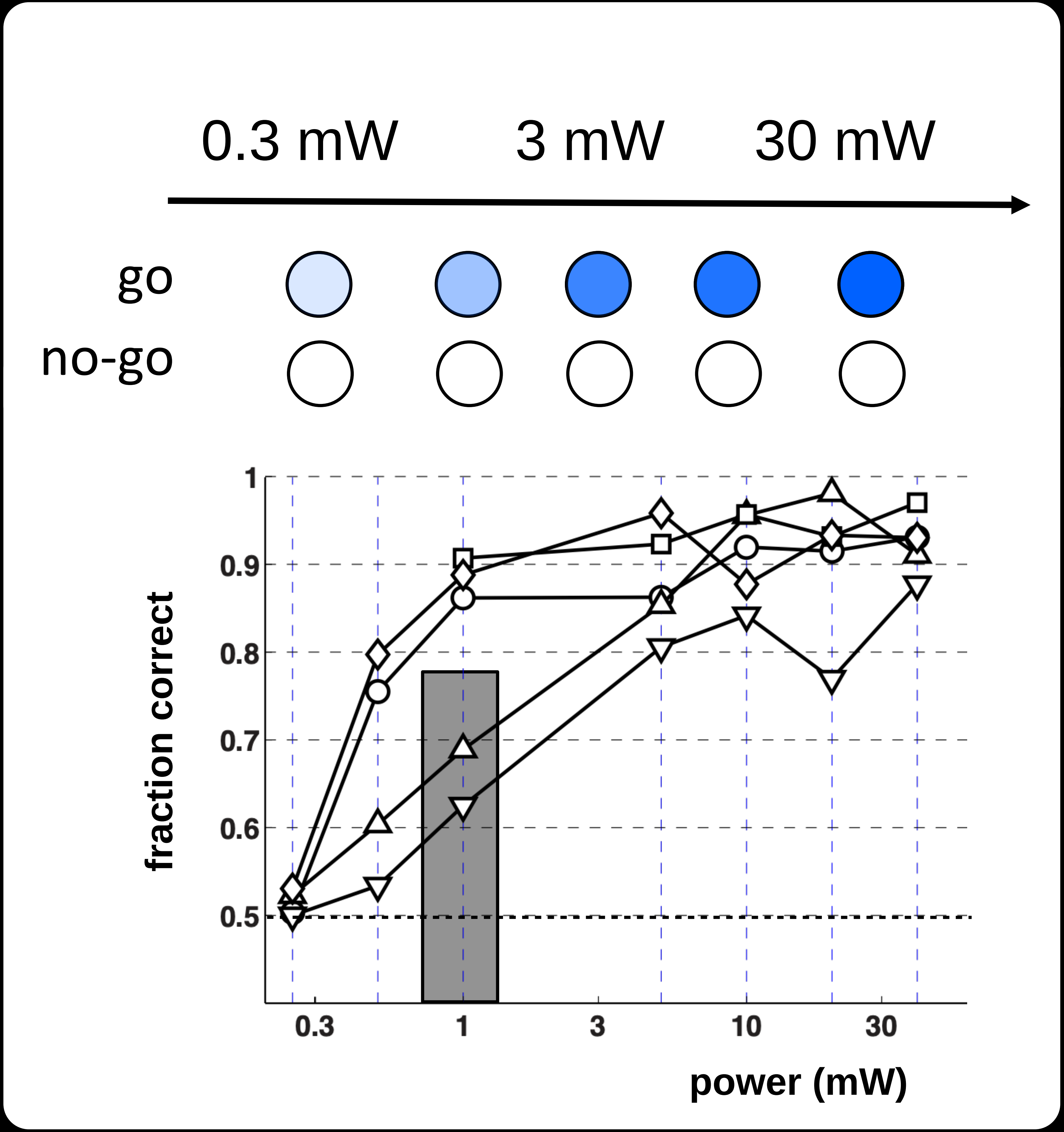
olfactory coding schemes

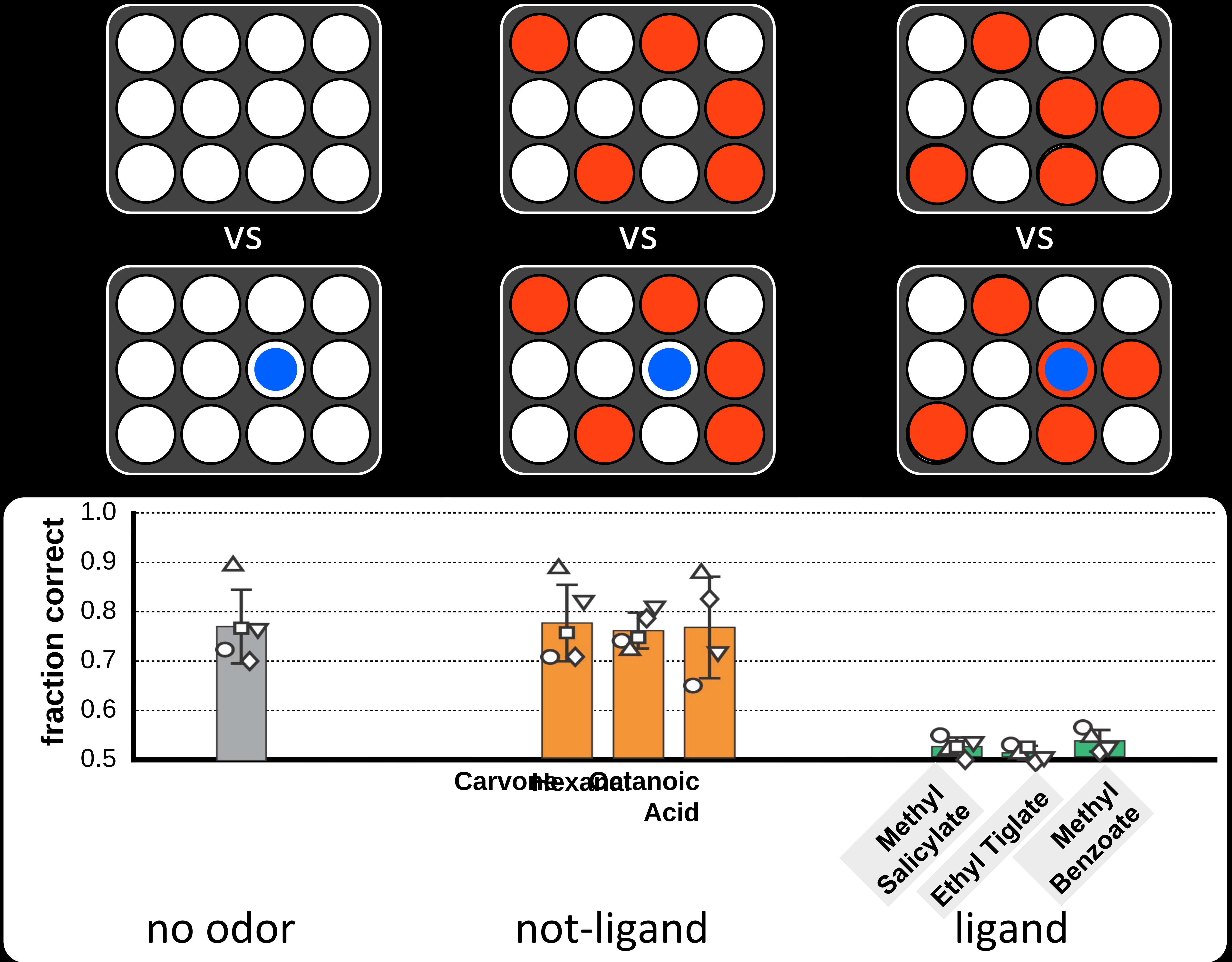


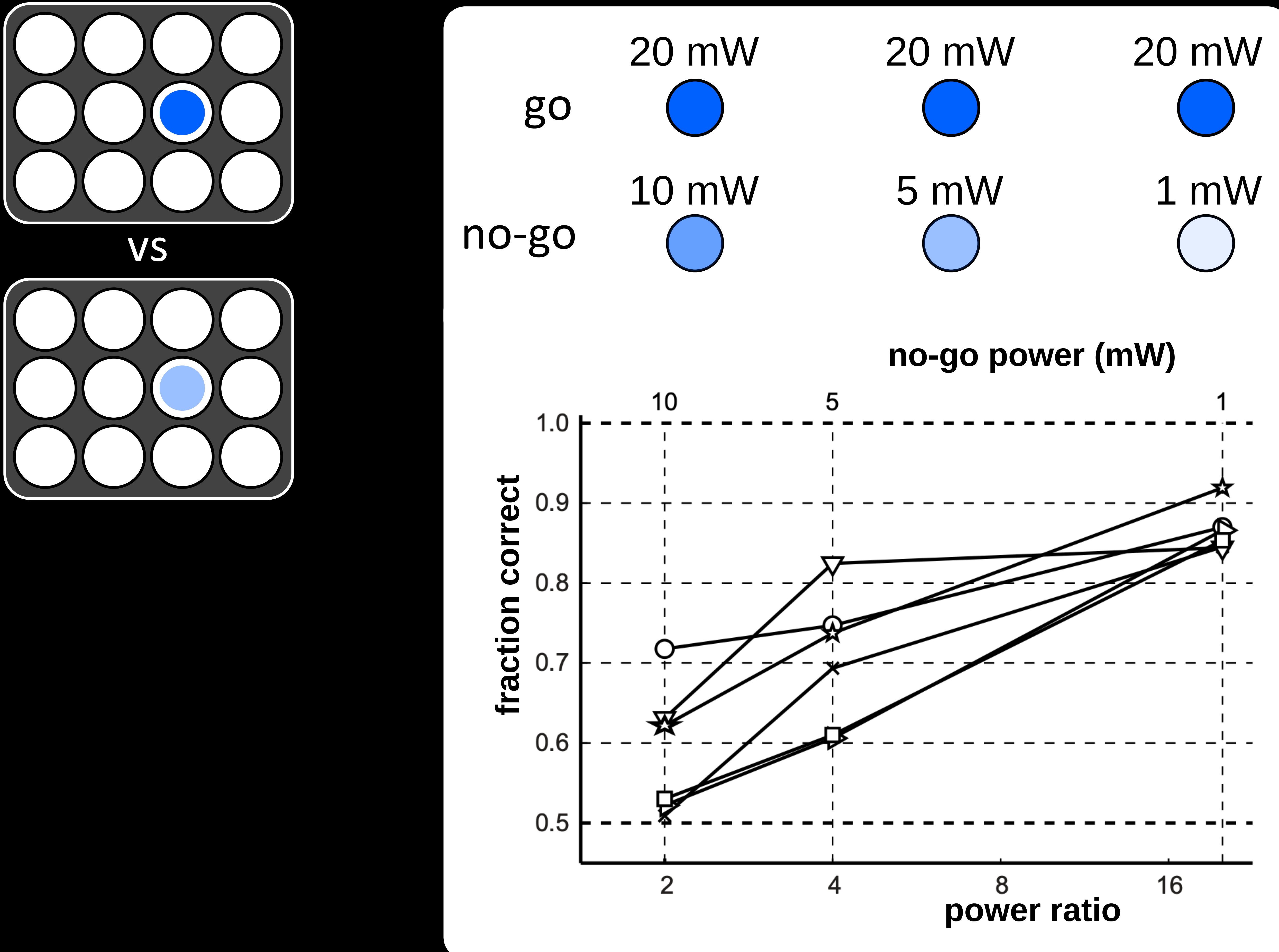

diode laser
P
odor
water

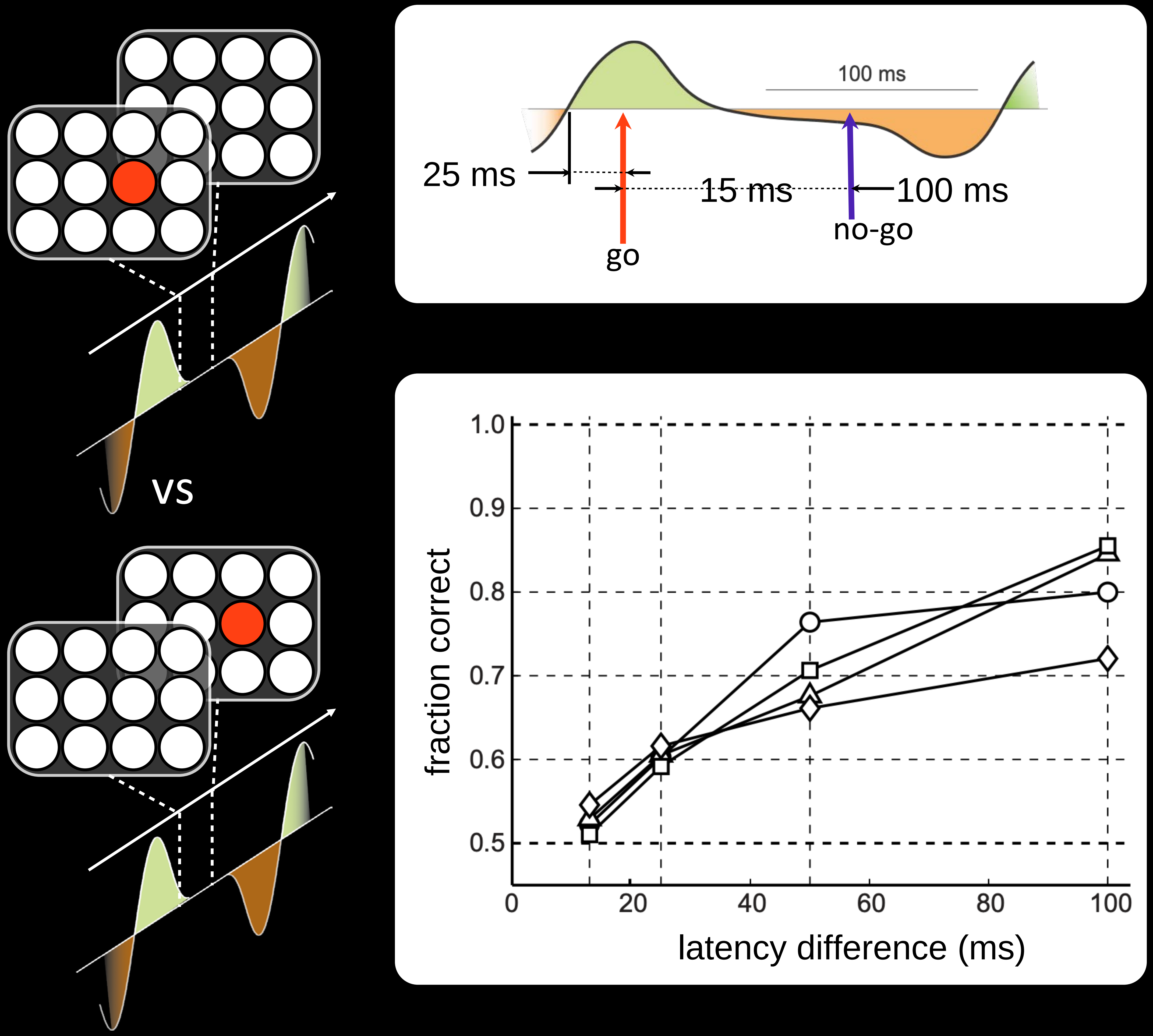

diode laser
1.0
0.9
0.8
0.7
0.6
0.5
fraction correct
odor detection
1
2
3
4
5
6
consecutive sessions
ChR2
stimulation
control
stimulation
laser pulse:
40 mW - 1 ms

light pulse:
1 ms

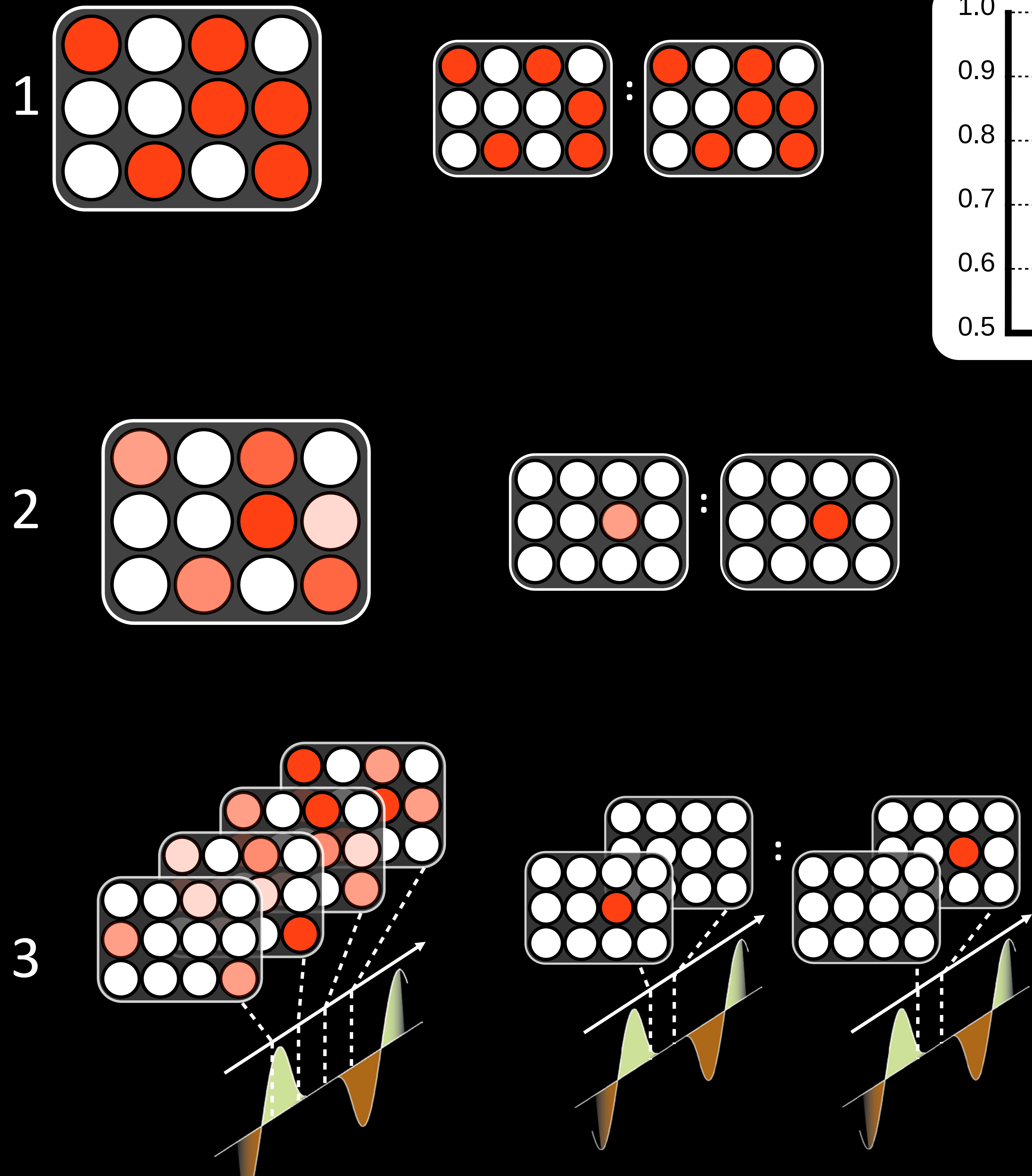


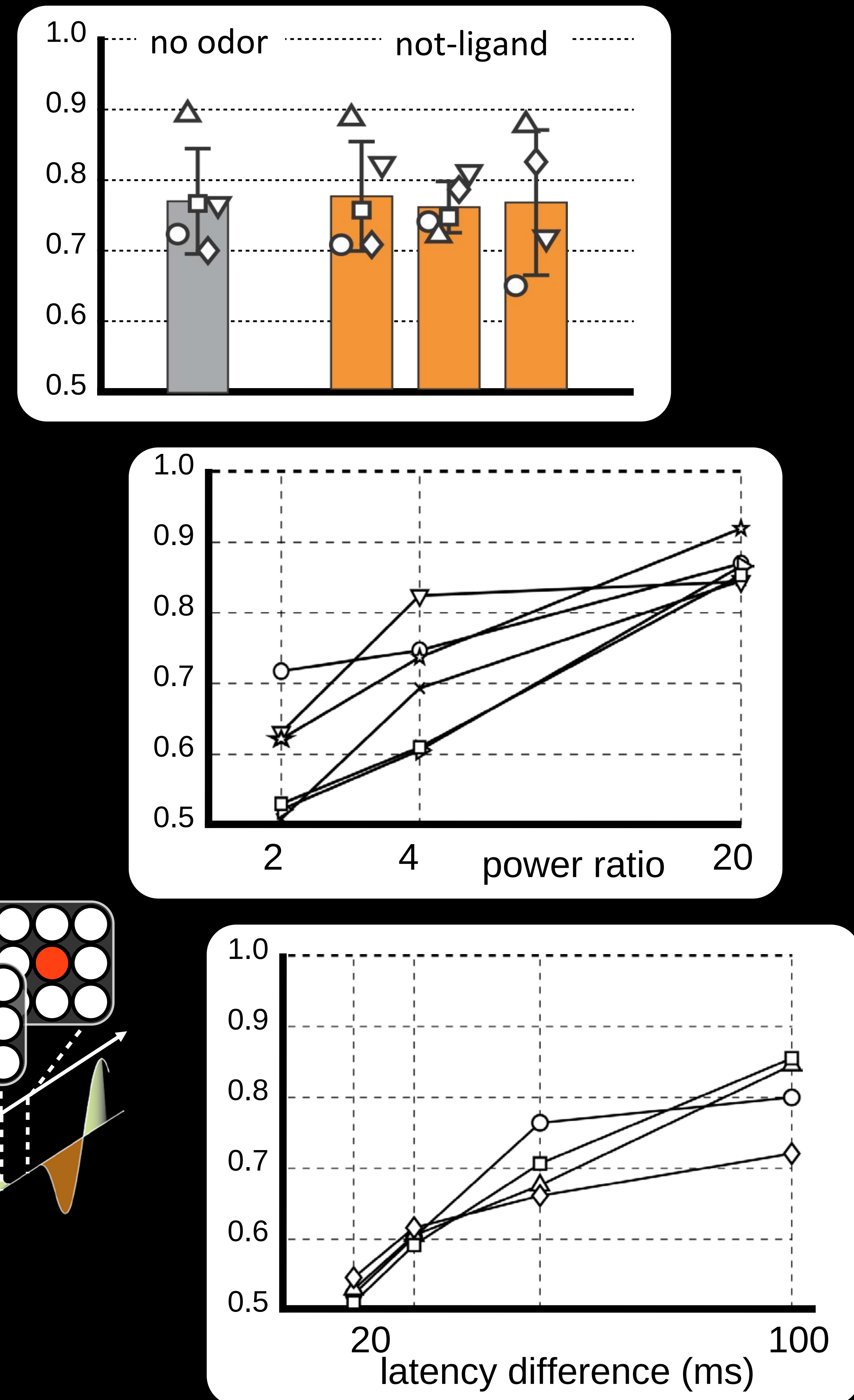

vs
vs
vs
fraction correct
1.0
0.9
0.8
0.7
0.6
0.5
Carvone
Hexanal
Octanoic Acid
Methyl Salicylate
Ethyl Tiglate
Methyl Benzoate
no odor
not-ligand
ligand


vs
go
no-go
20 mW
20 mW
20 mW
10 mW
5 mW
1 mW
no-go power (mW)
10
5
1
1.0
0.9
0.8
0.7
0.6
0.5
fraction correct
2
4
8
16
power ratio

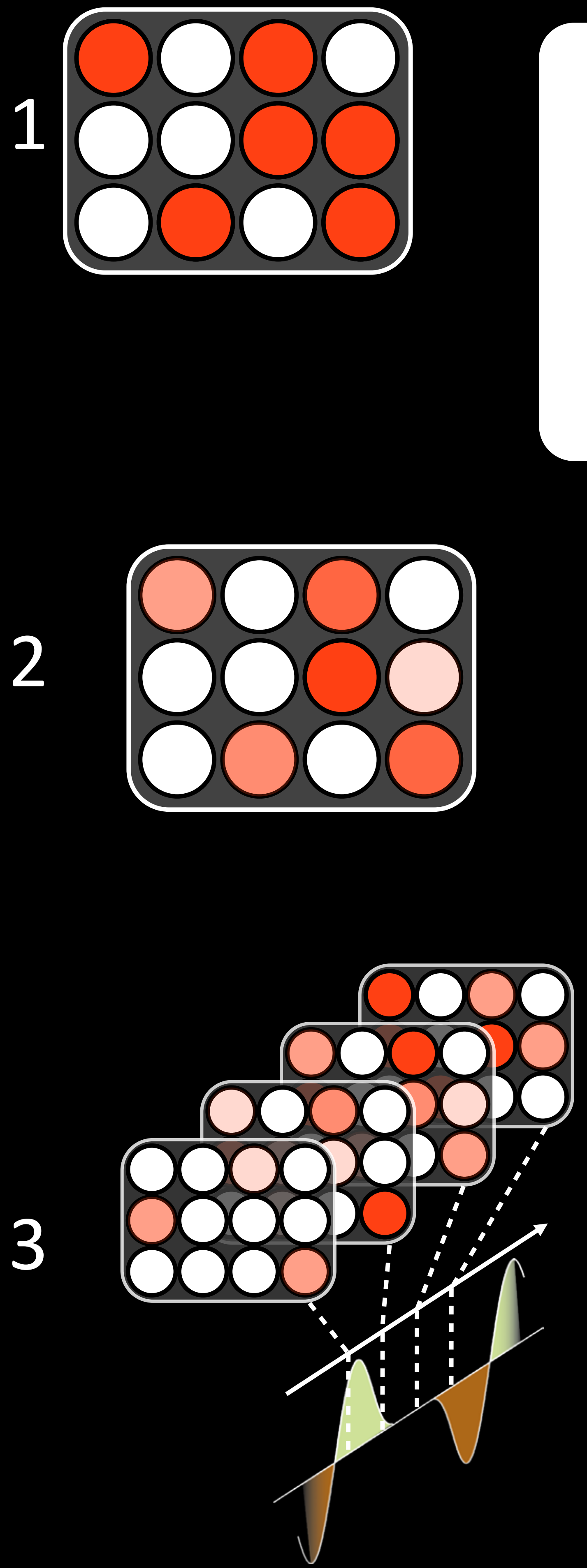


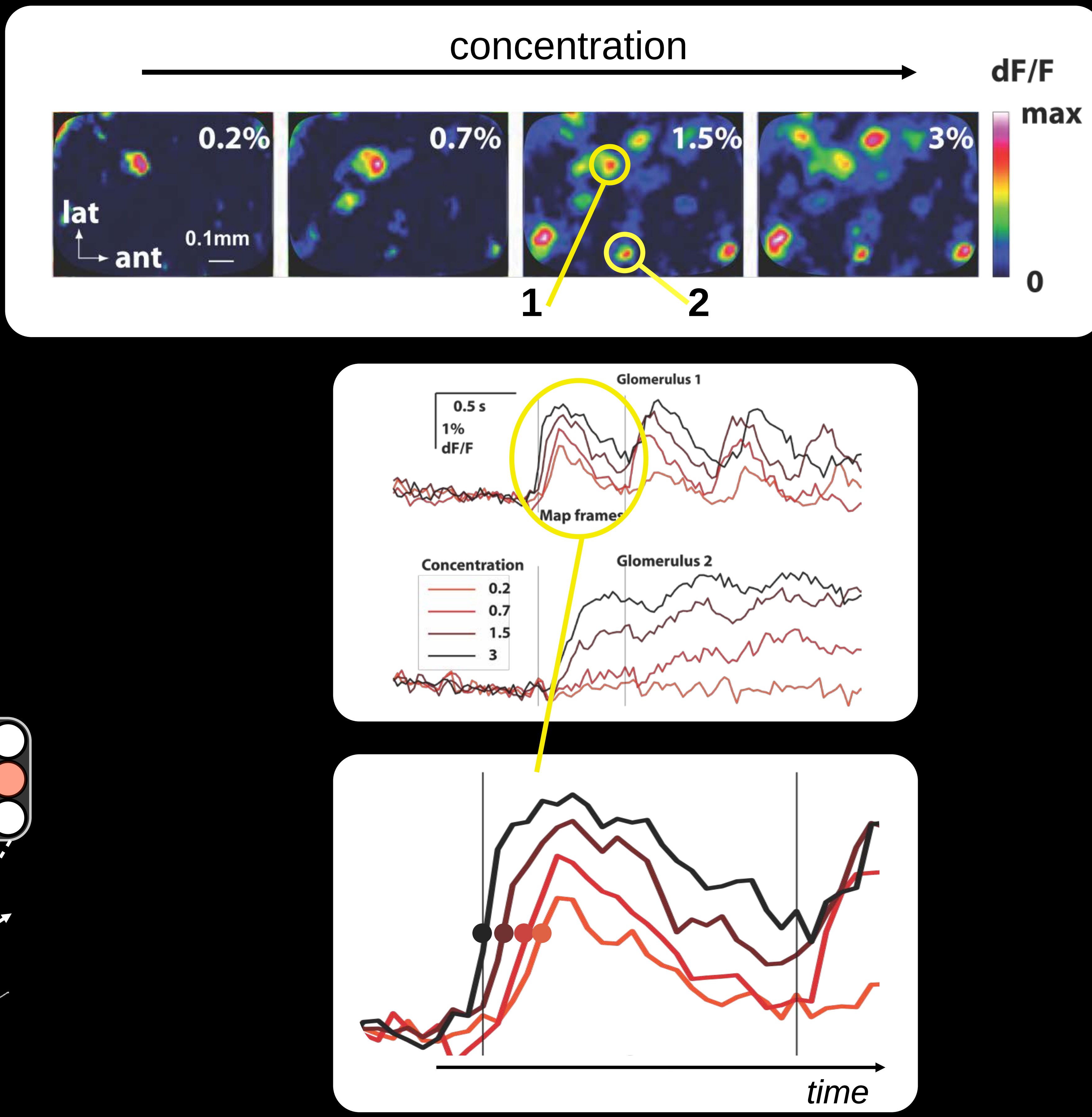
vs
100 ms
25 ms
15 ms
100 ms
go
no-go
fraction correct
latency difference (ms)
1.0
0.9
0.8
0.7
0.6
0.5
0
20
40
60
80
100



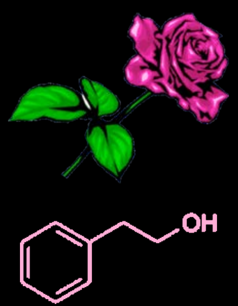


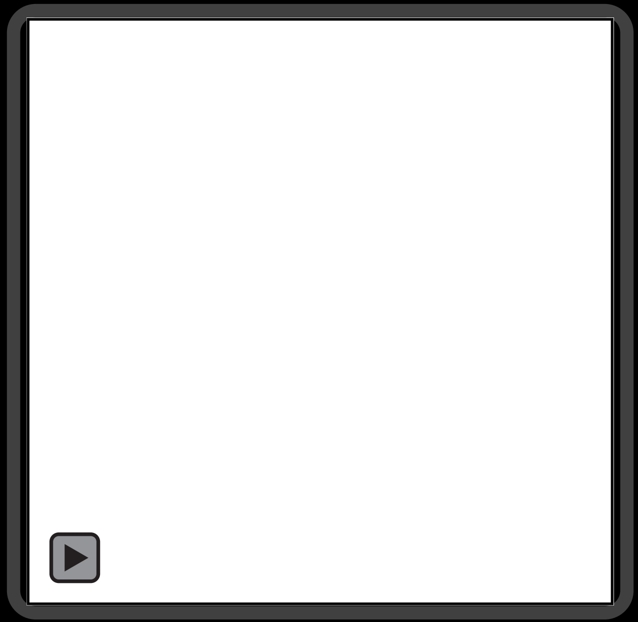
Smear, M., Resulaj, A., Zhang, J., Bozza, T. & Rinberg, D.
Nat Neurosci **16,** 1687–1691 (2013).





H. Spors, M. Wachowiak, L.B. Cohen, & R.W. Friedrich. **Temporal dynamics and latency patterns of receptor neuron input to the olfactory bulb**. *J Neurosci* **26,** 1247–1259 (2006).





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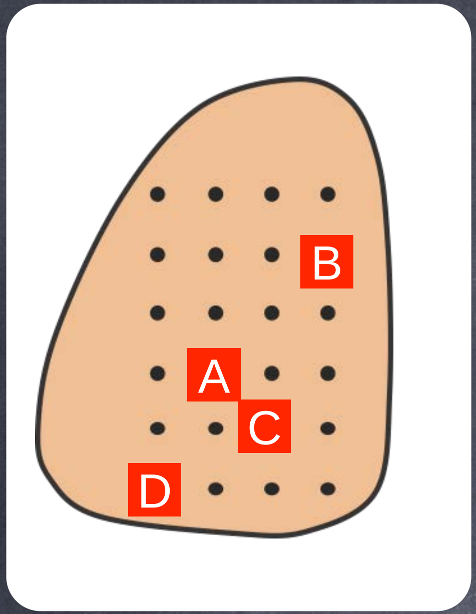
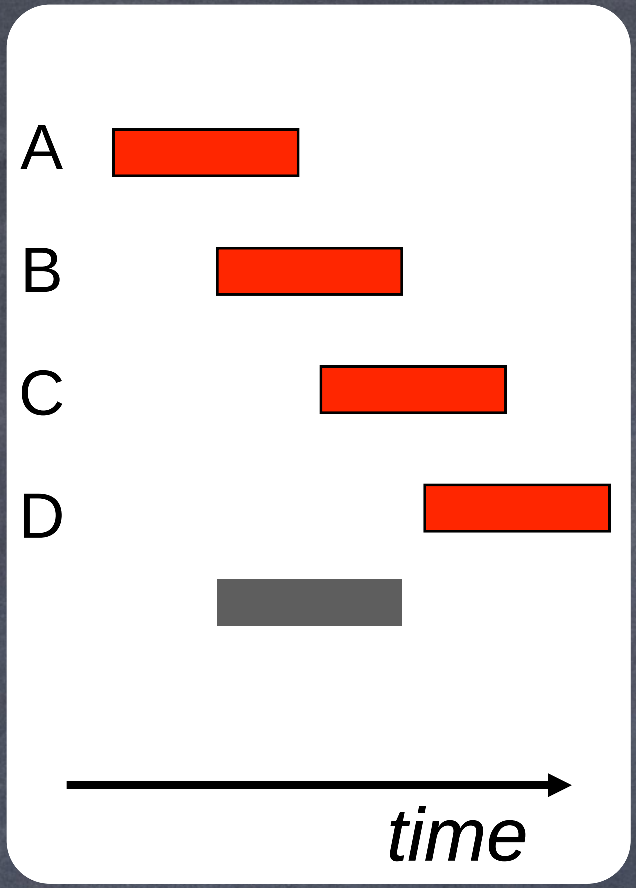
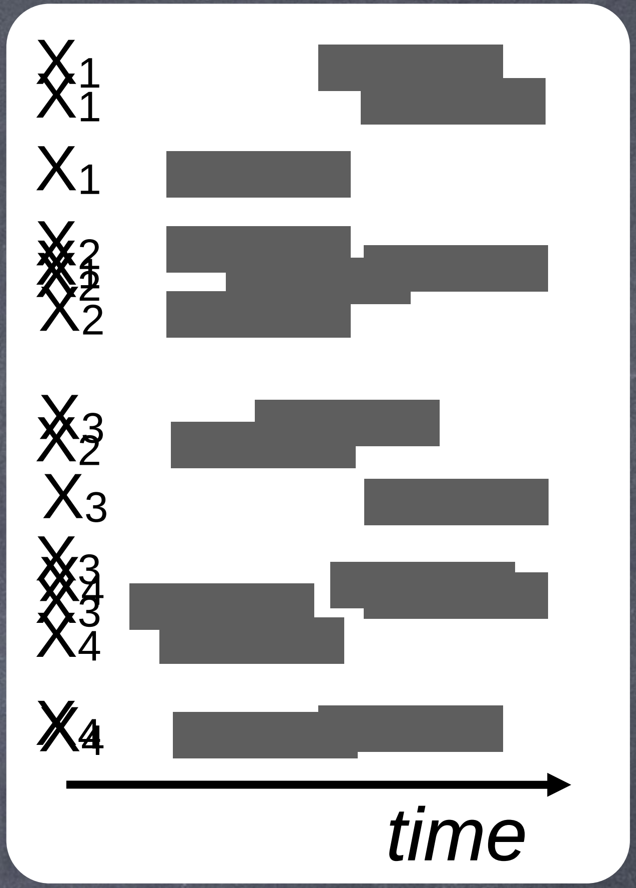


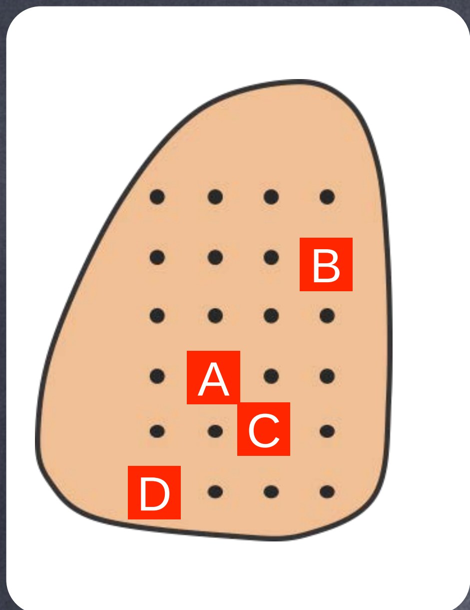


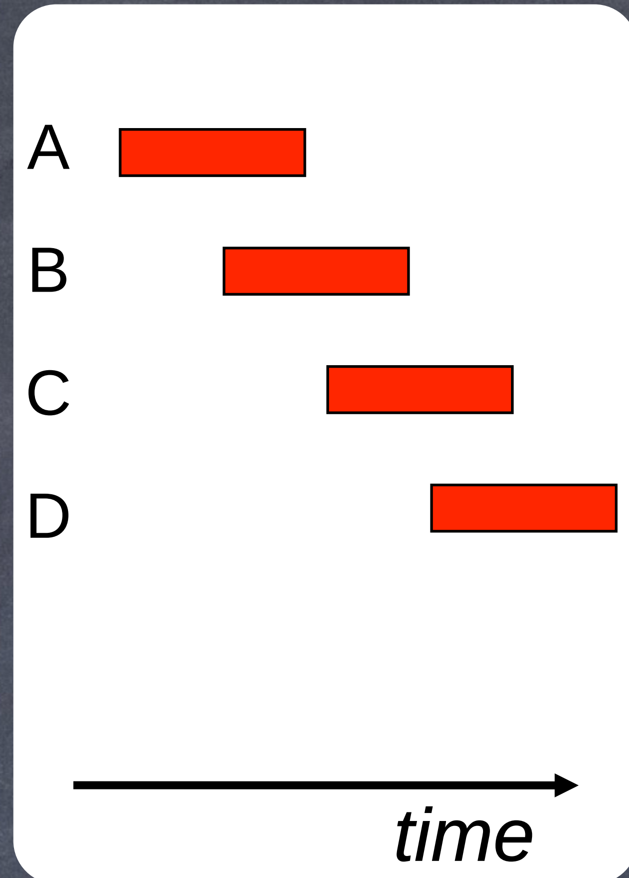
target

VS



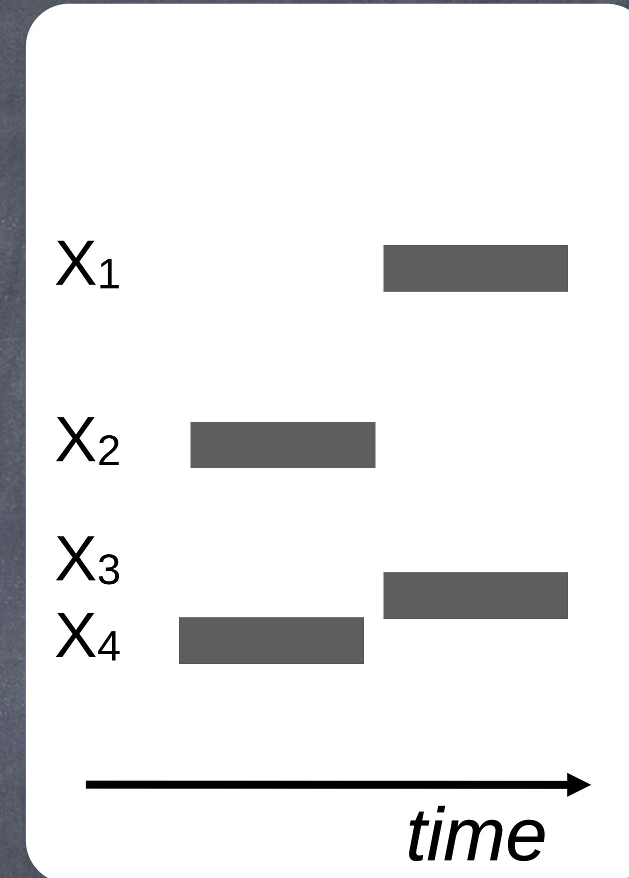
non-target



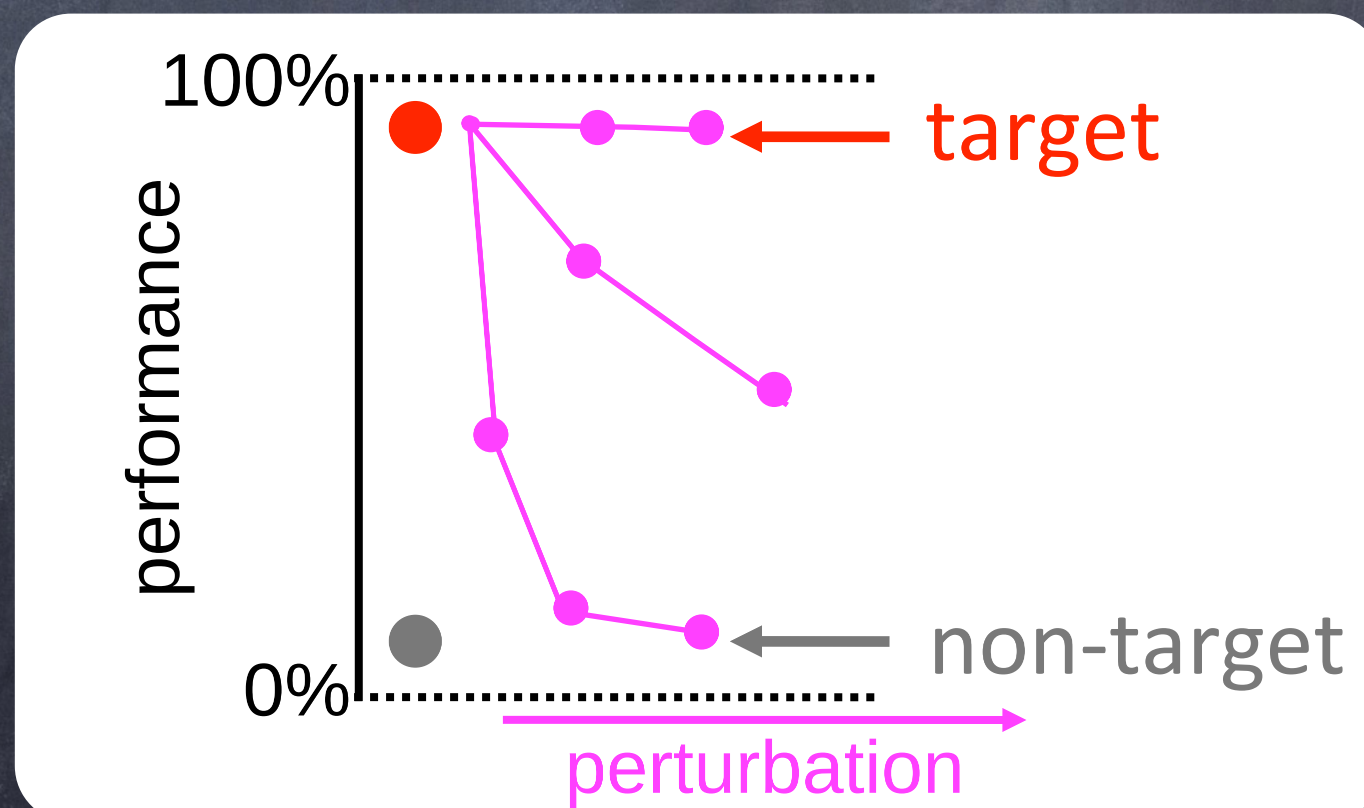


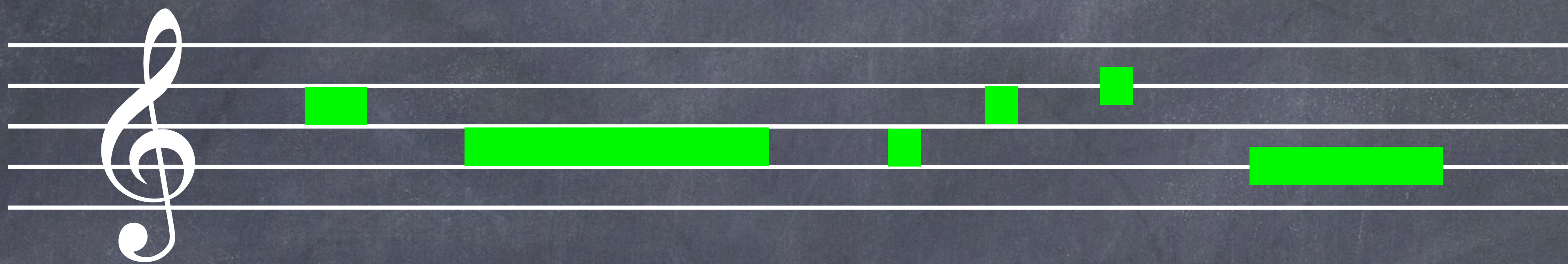
target

VS



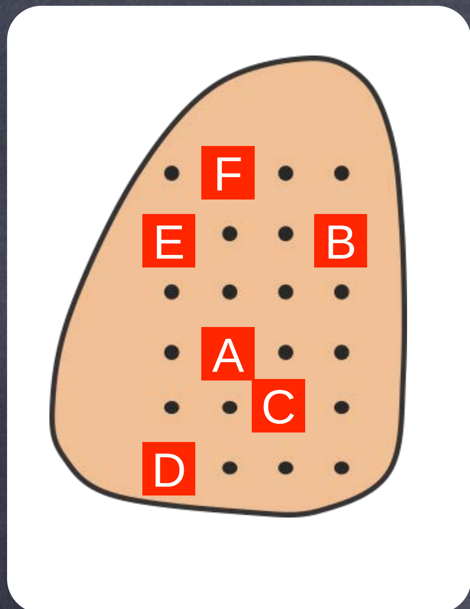
non-target

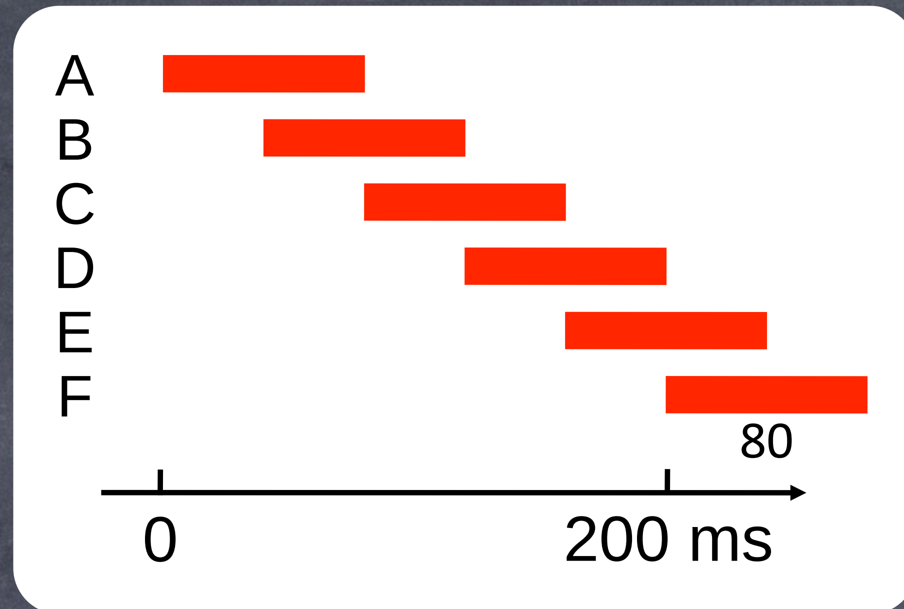




“Hey Jude”

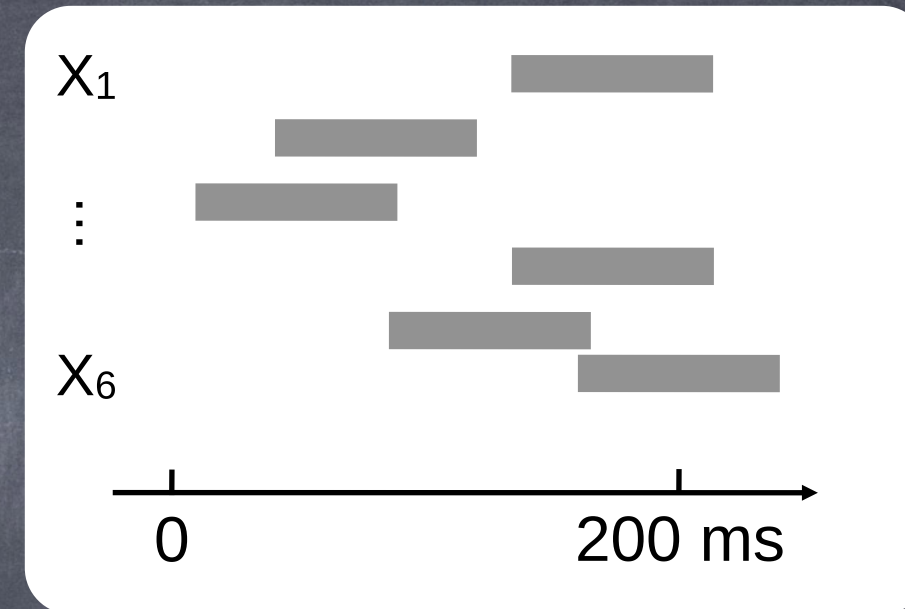
“Hey Jude”



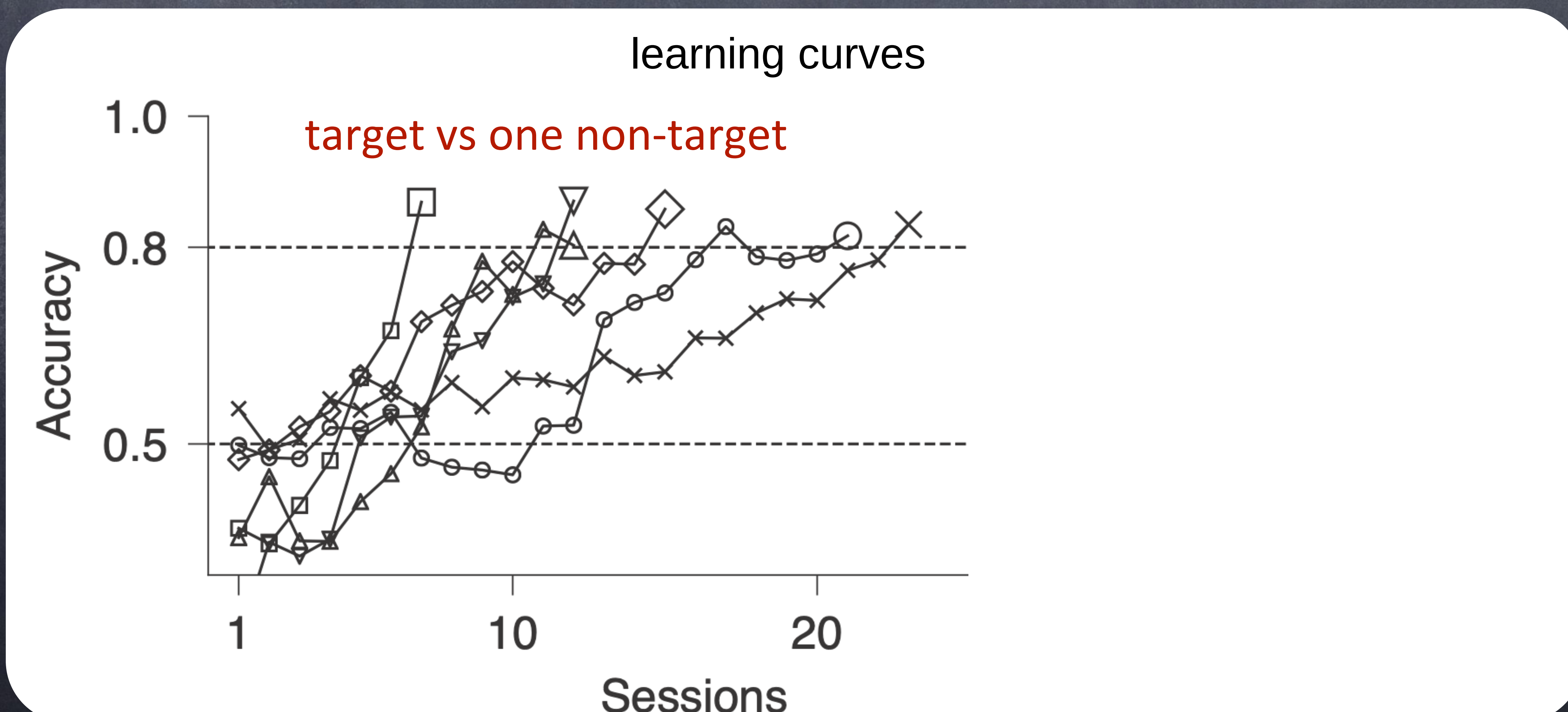


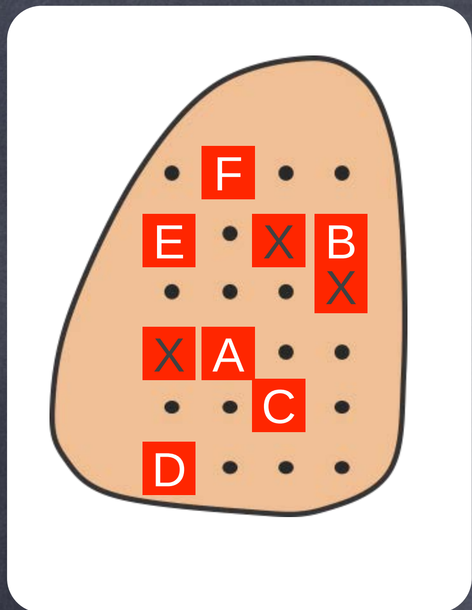
target

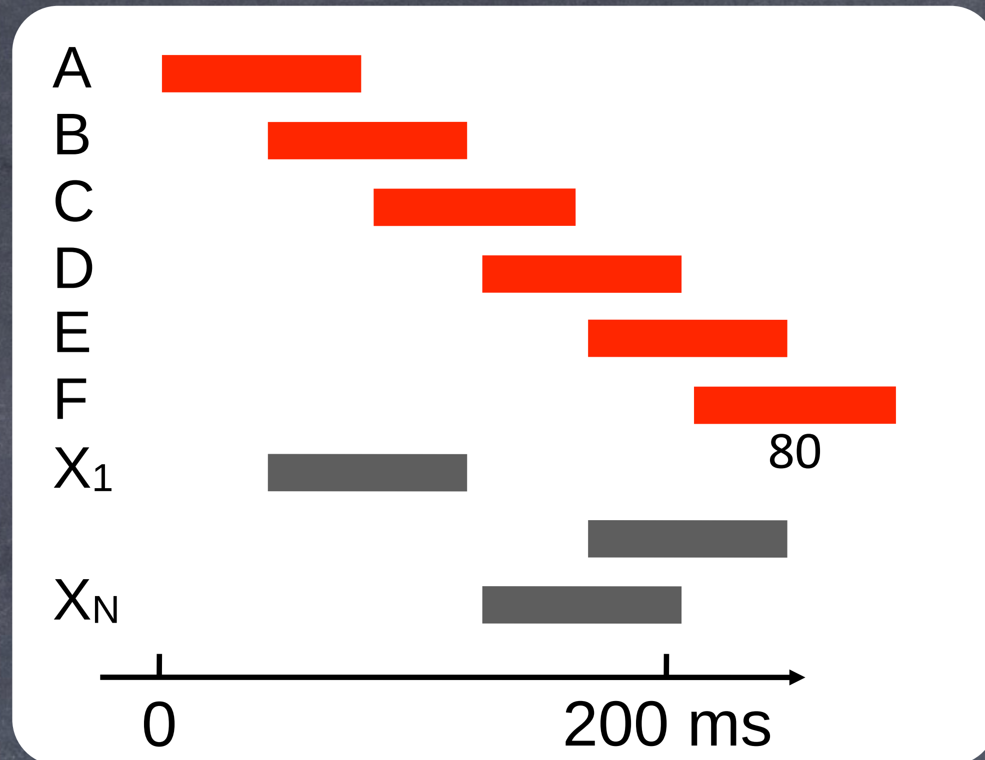
VS

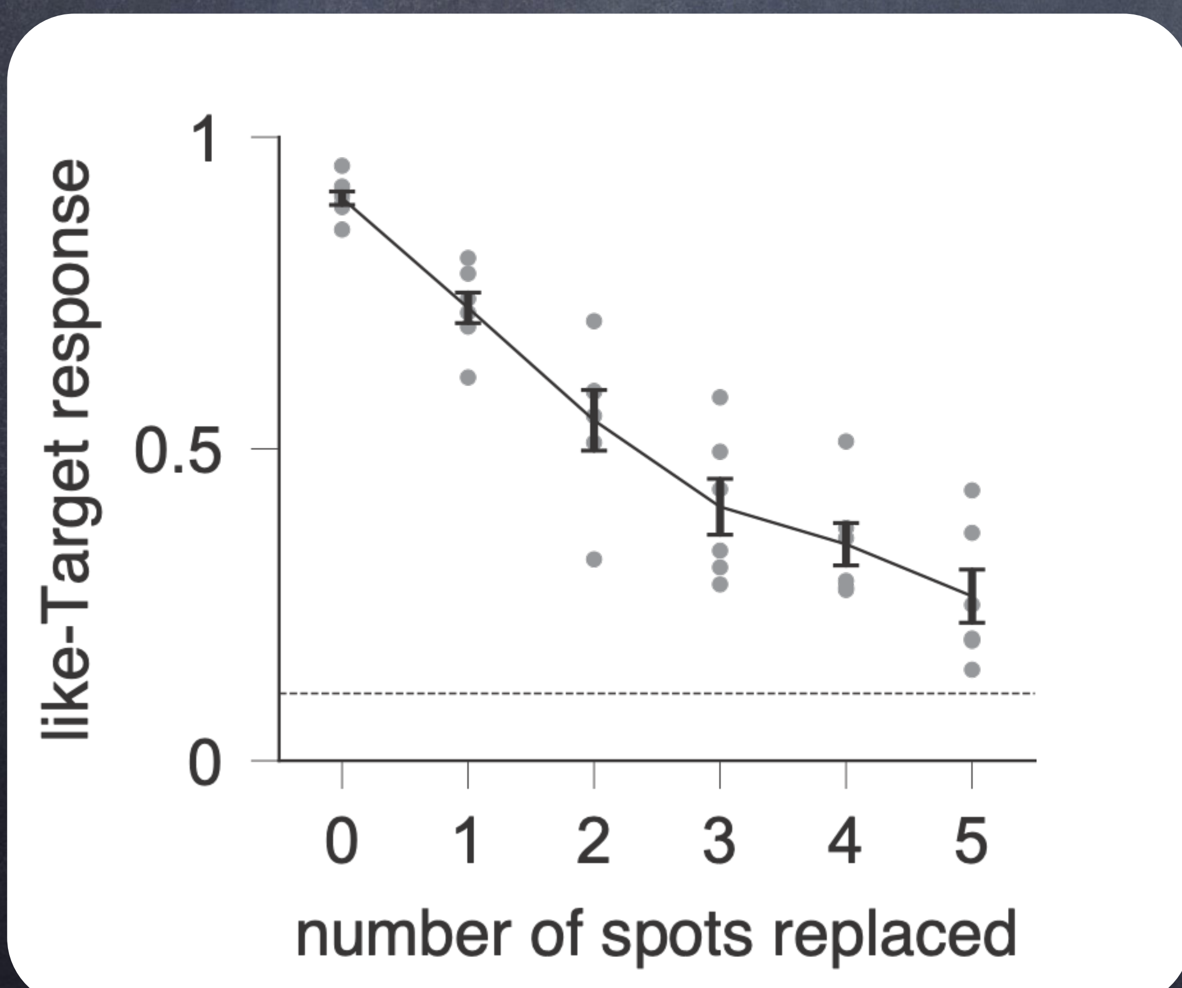


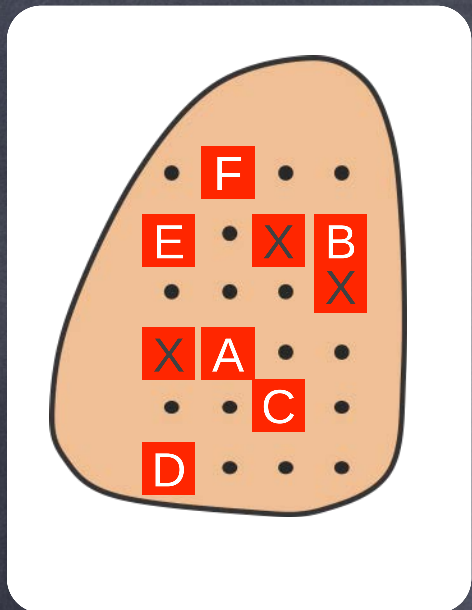
non-targets

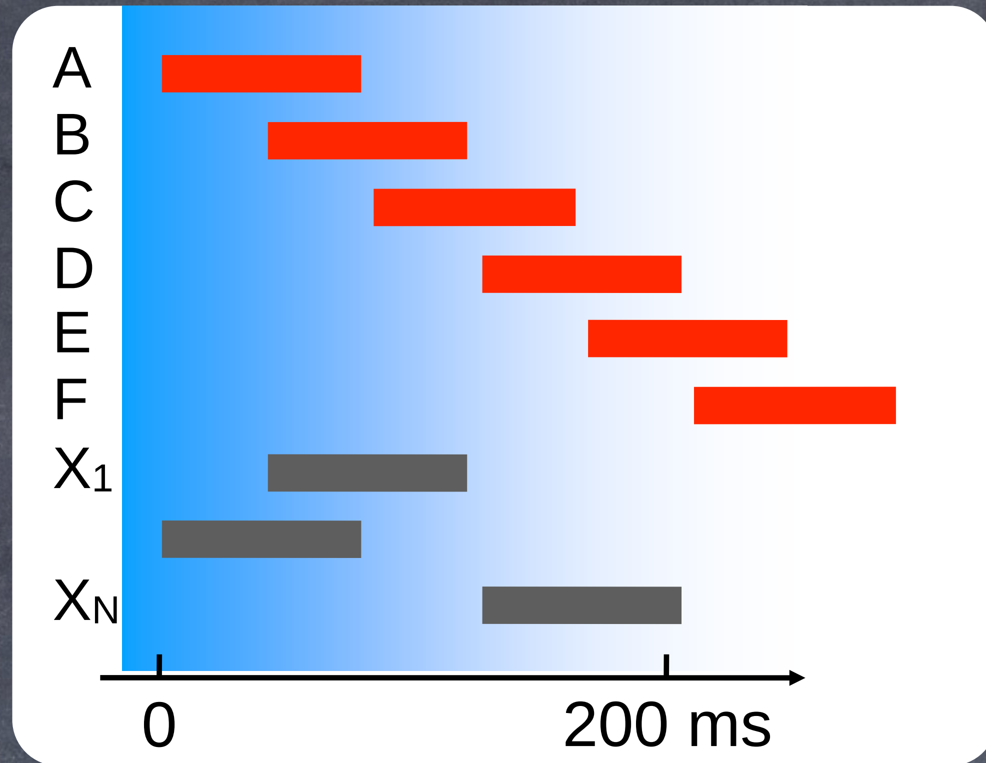



F
E
X
B
X
X
A
C
D


A
B
C
D
E
F
80
X1
XN
0
200 ms

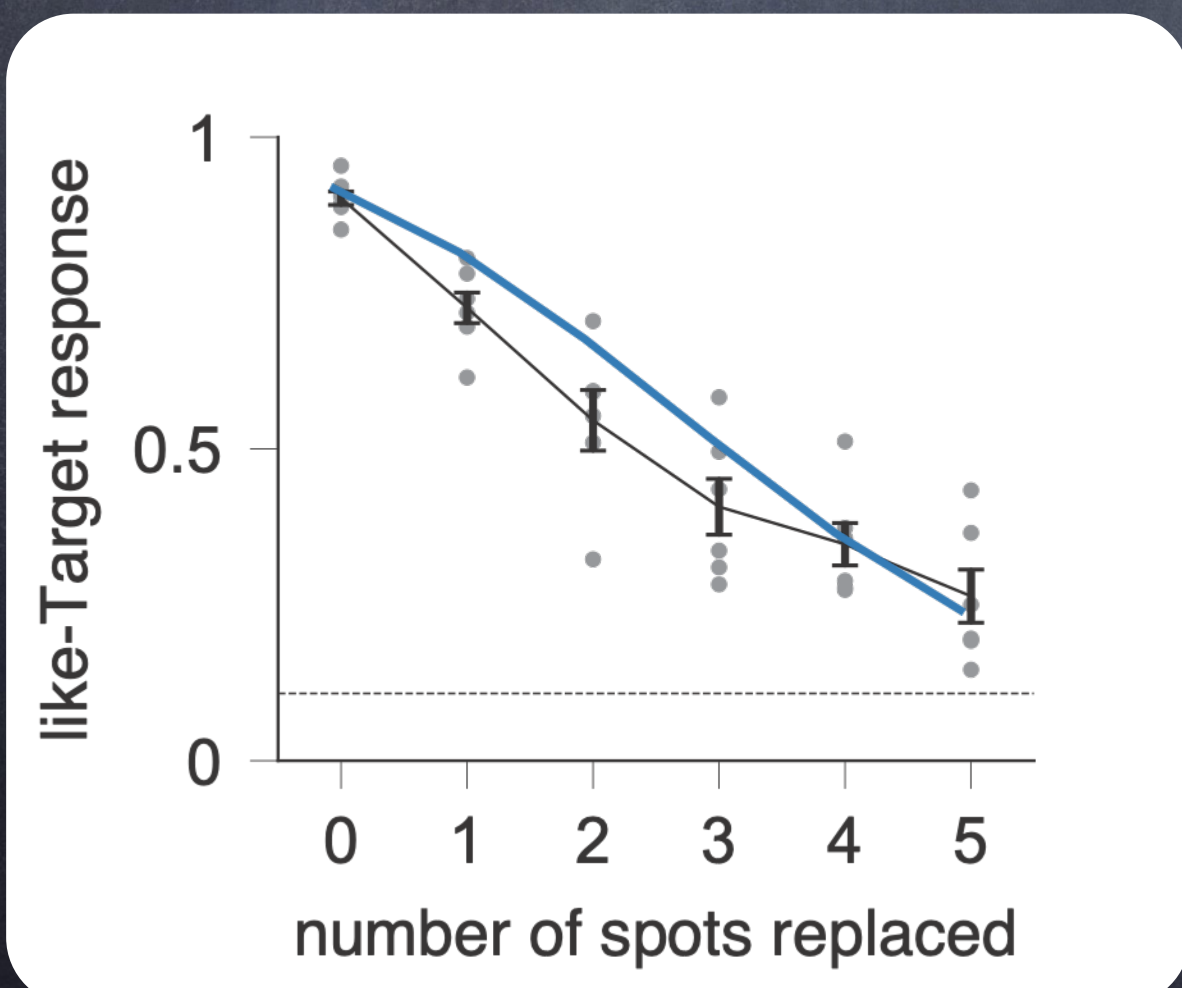

like-Target response
1
0.5
0
0
1
2
3
4
5
number of spots replaced

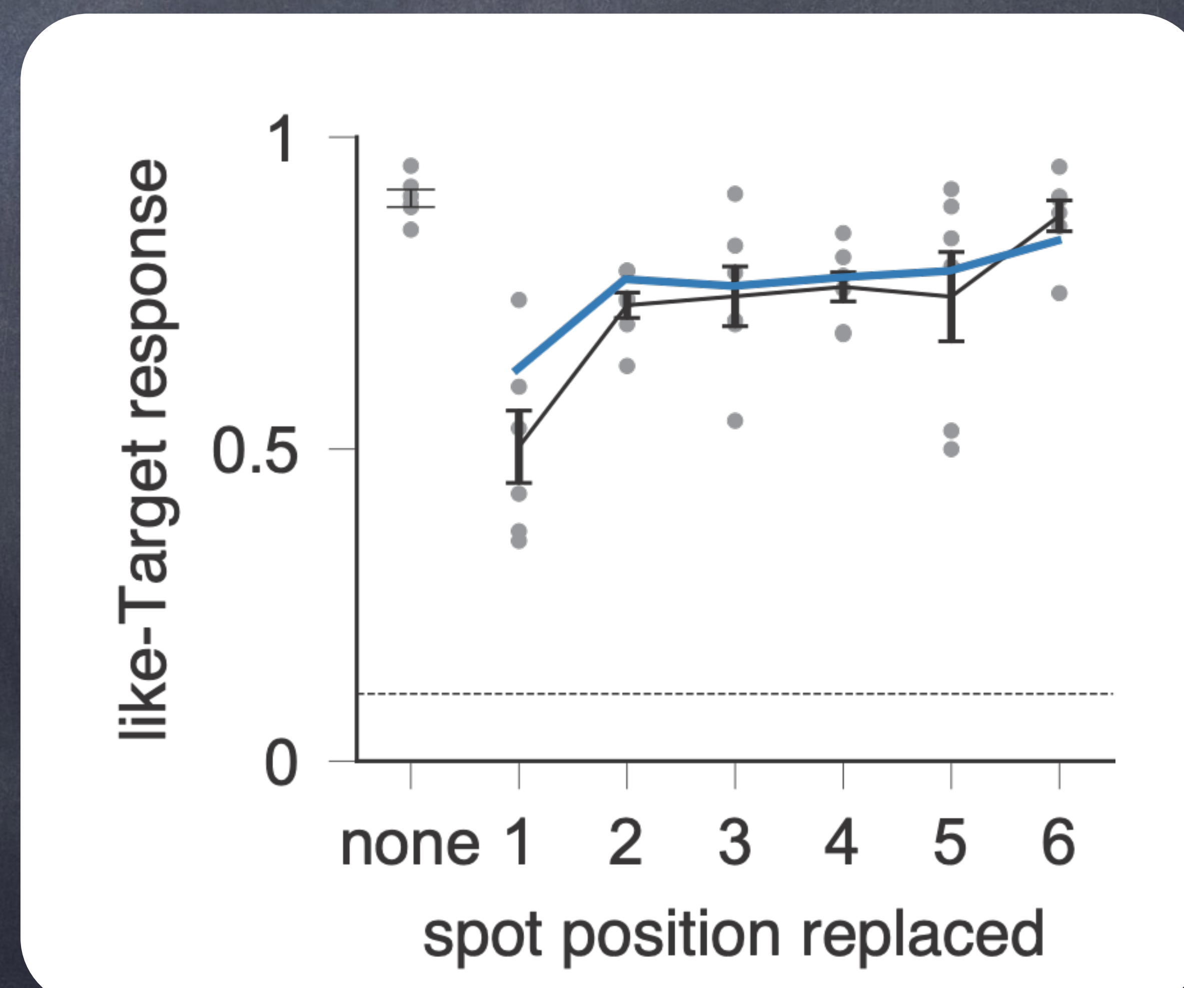


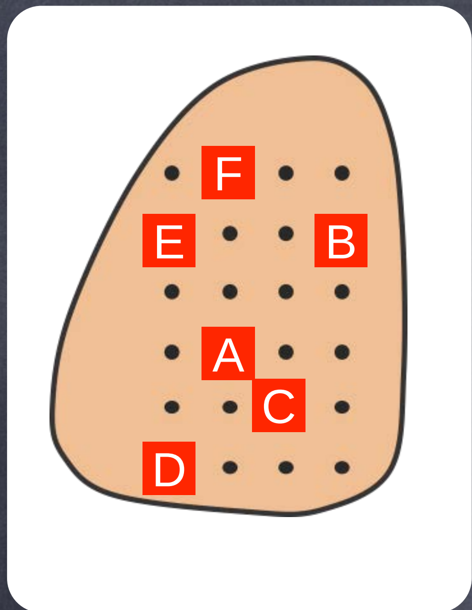


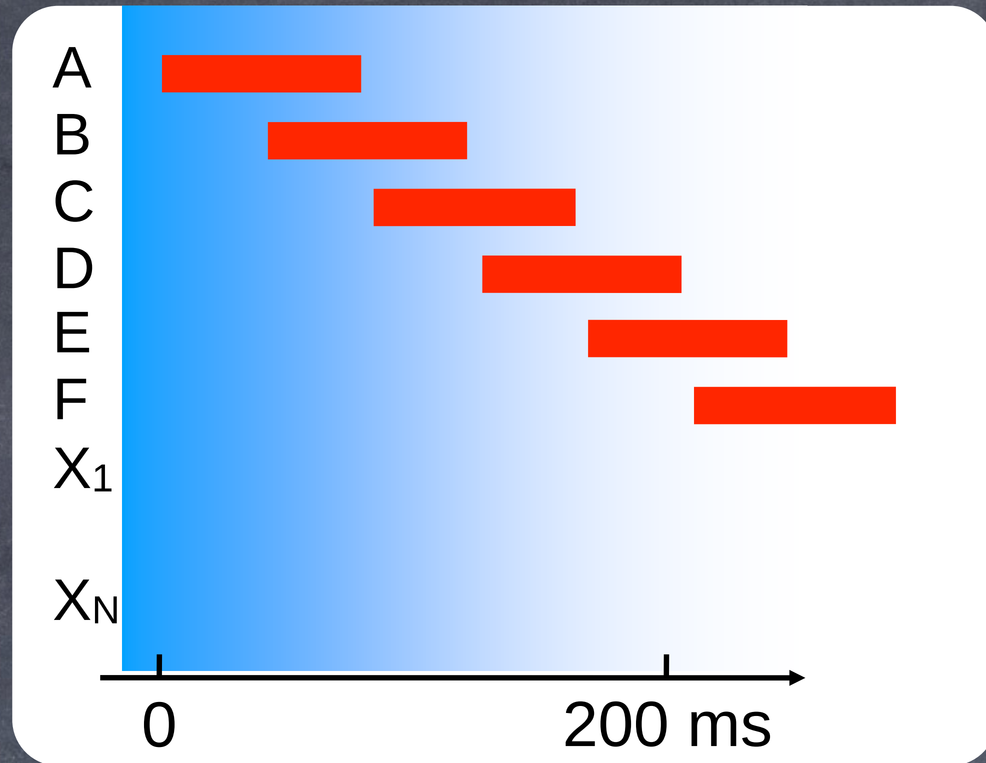
$$x_i = \begin{cases} 1, & \textit{replace} \\ 0, & \textit{same} \end{cases}$$

$$\text{logit}(p) = \beta_0 + \sum_i \beta_i x_i + \sum_{i,j} \gamma_{i,j} x_i x_j$$

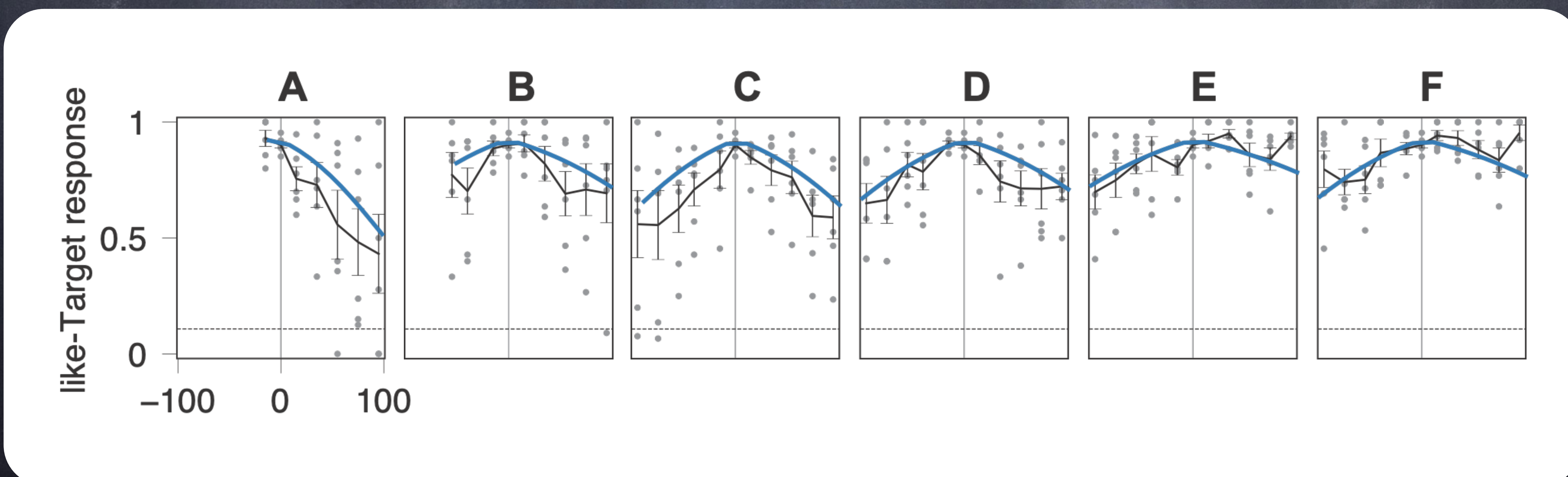


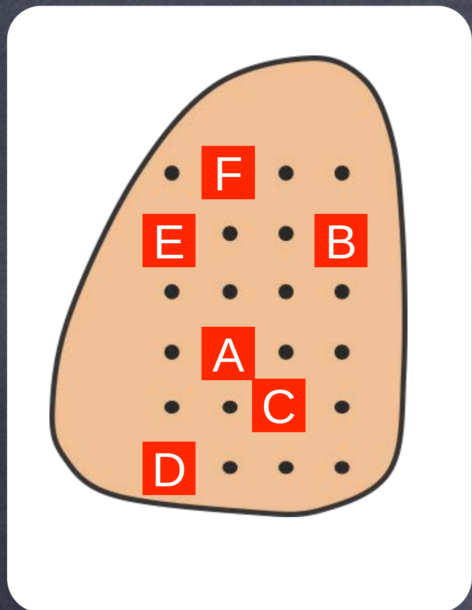


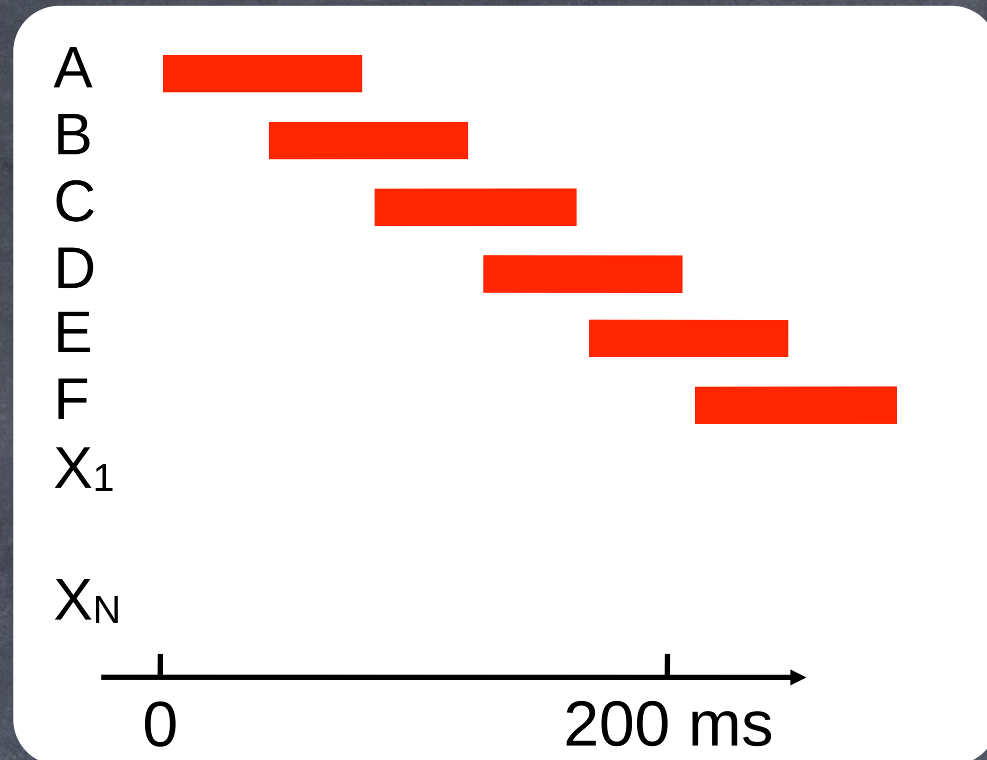




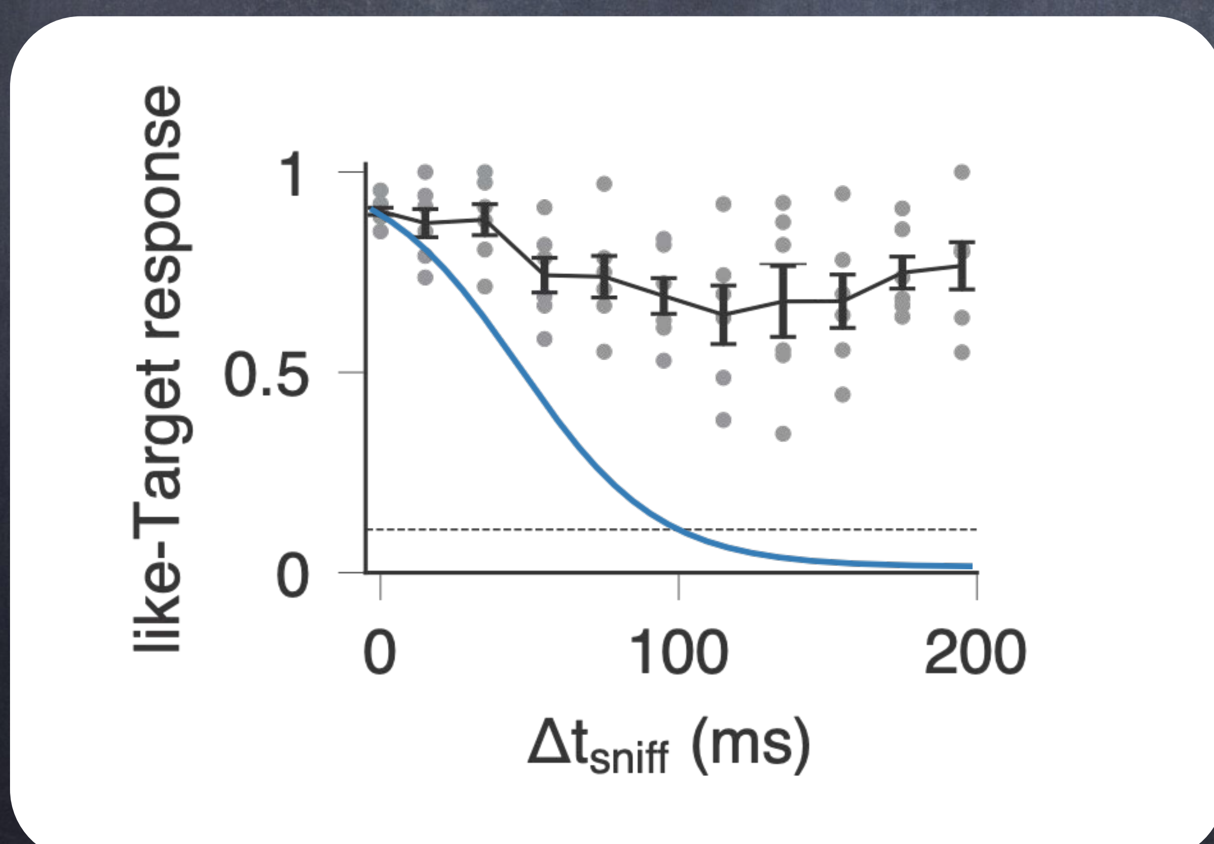
$$\text{logit}(p) = \beta_0 + \sum_{i,\Delta t_i>0} \beta_i^+ |\Delta t_i| + \sum_{i,\Delta t_i<0} \beta_i^- |\Delta t_i|$$

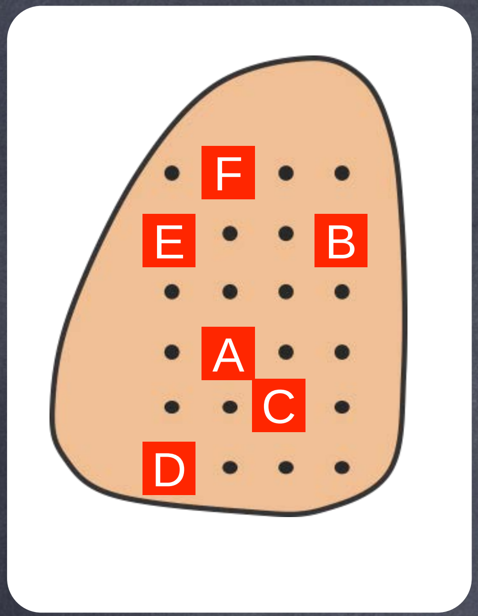


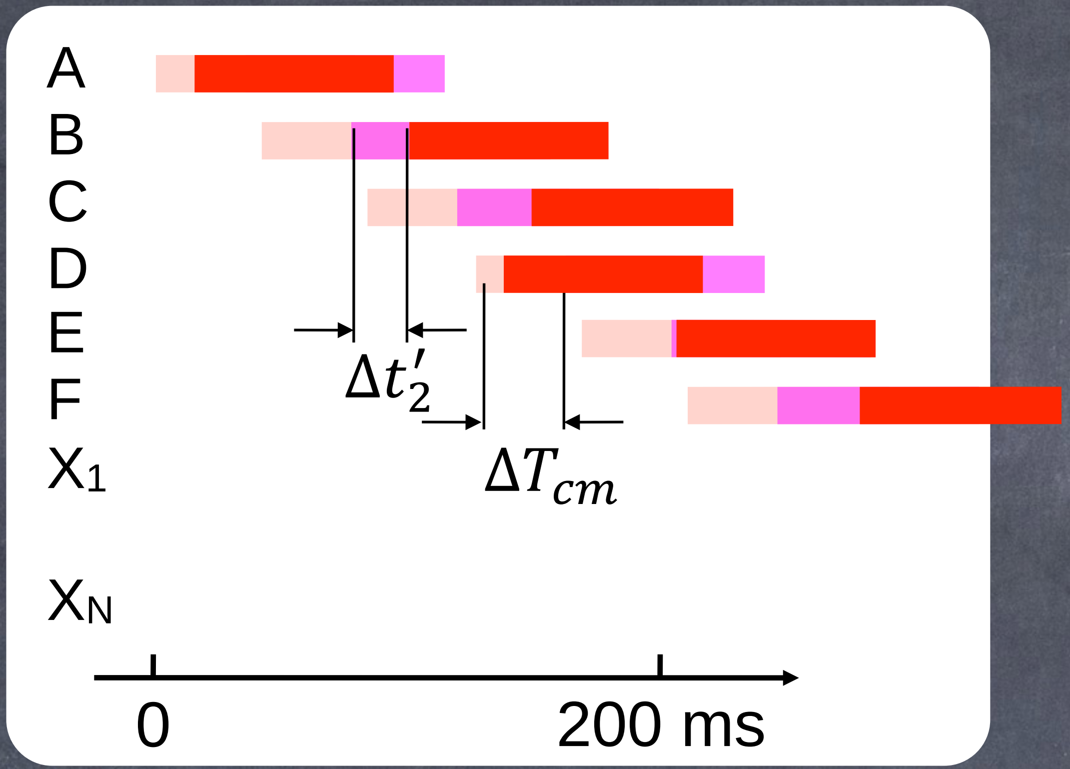




$$\text{logit}(p) = \beta_0 + \sum_{i,\Delta t_i > 0} \beta_i^{+} |\Delta t_i| + \sum_{i,\Delta t_i < 0} \beta_i^{-} |\Delta t_i|$$

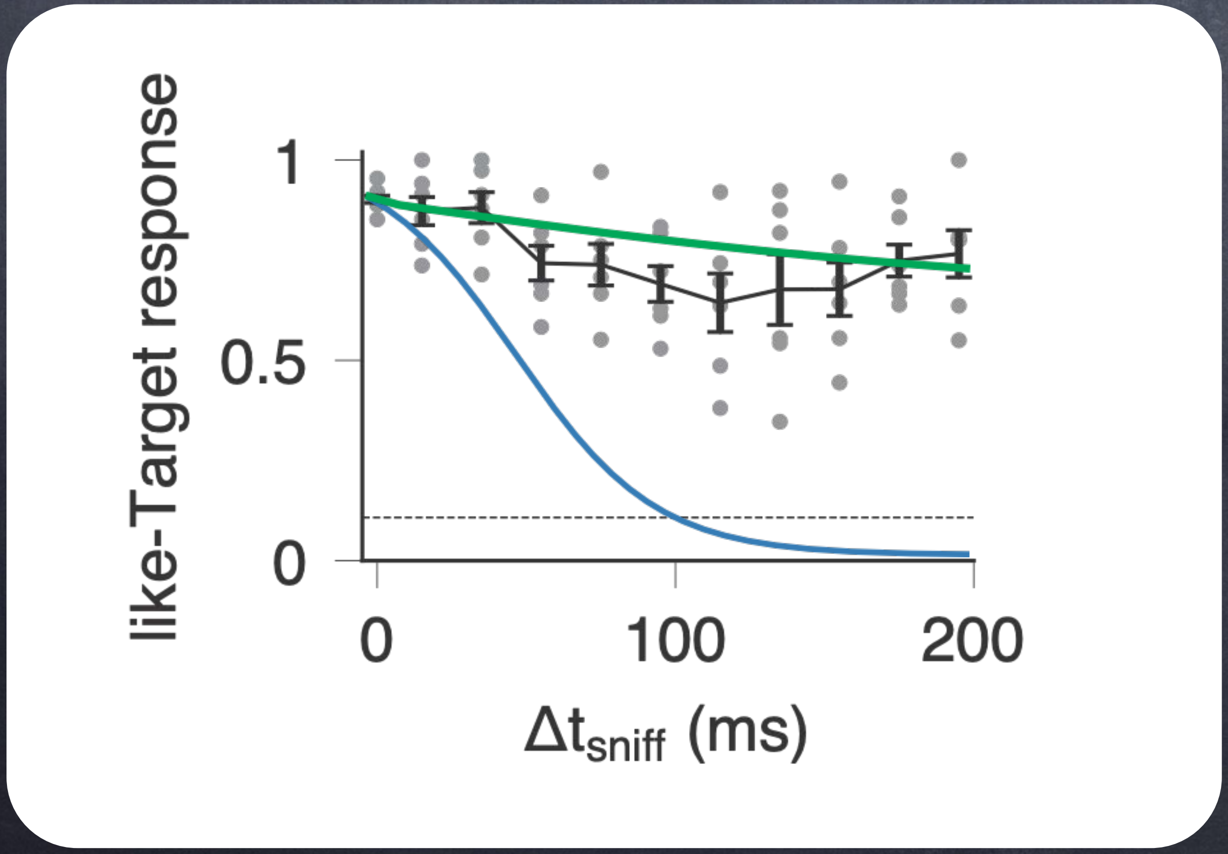


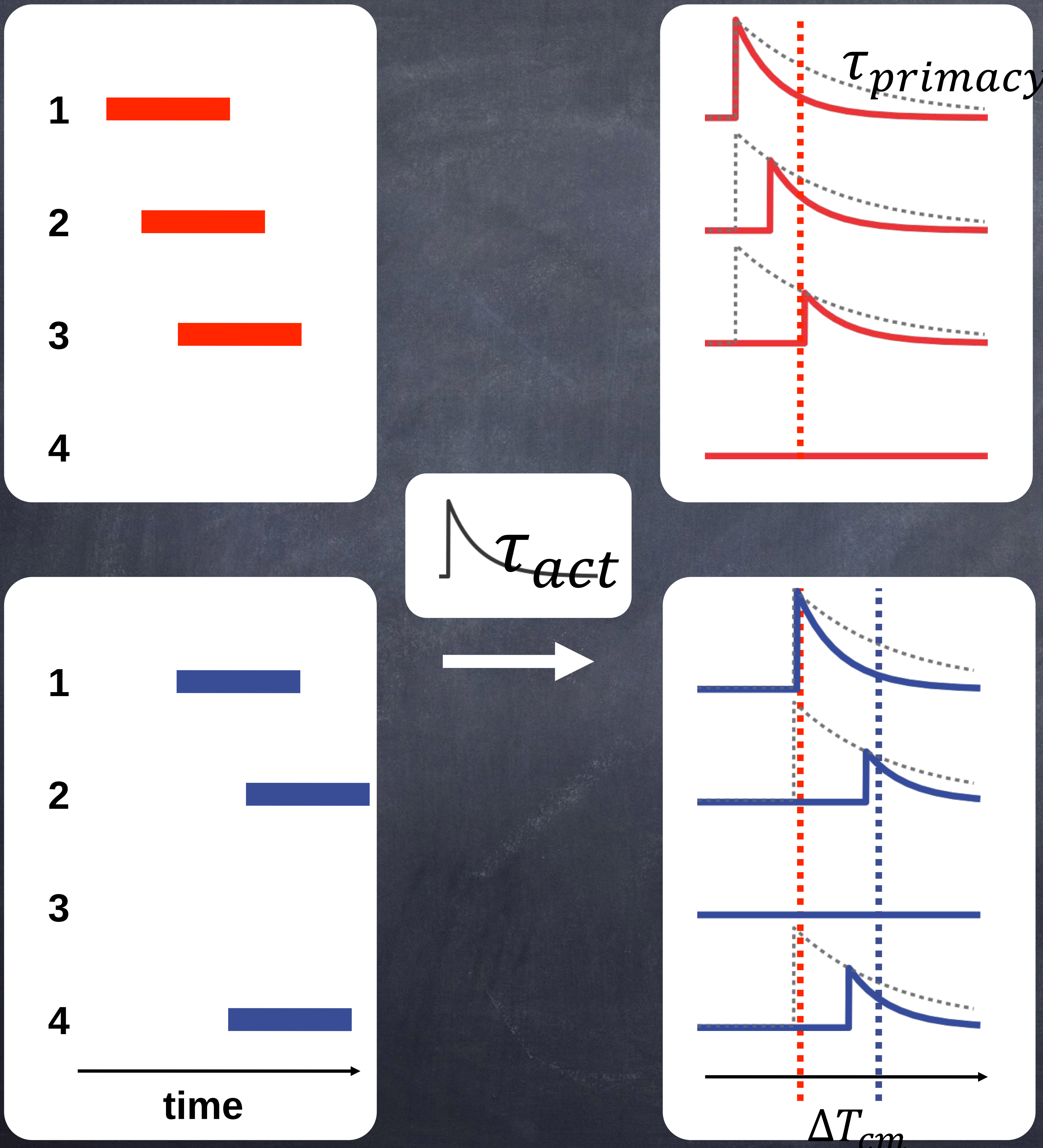




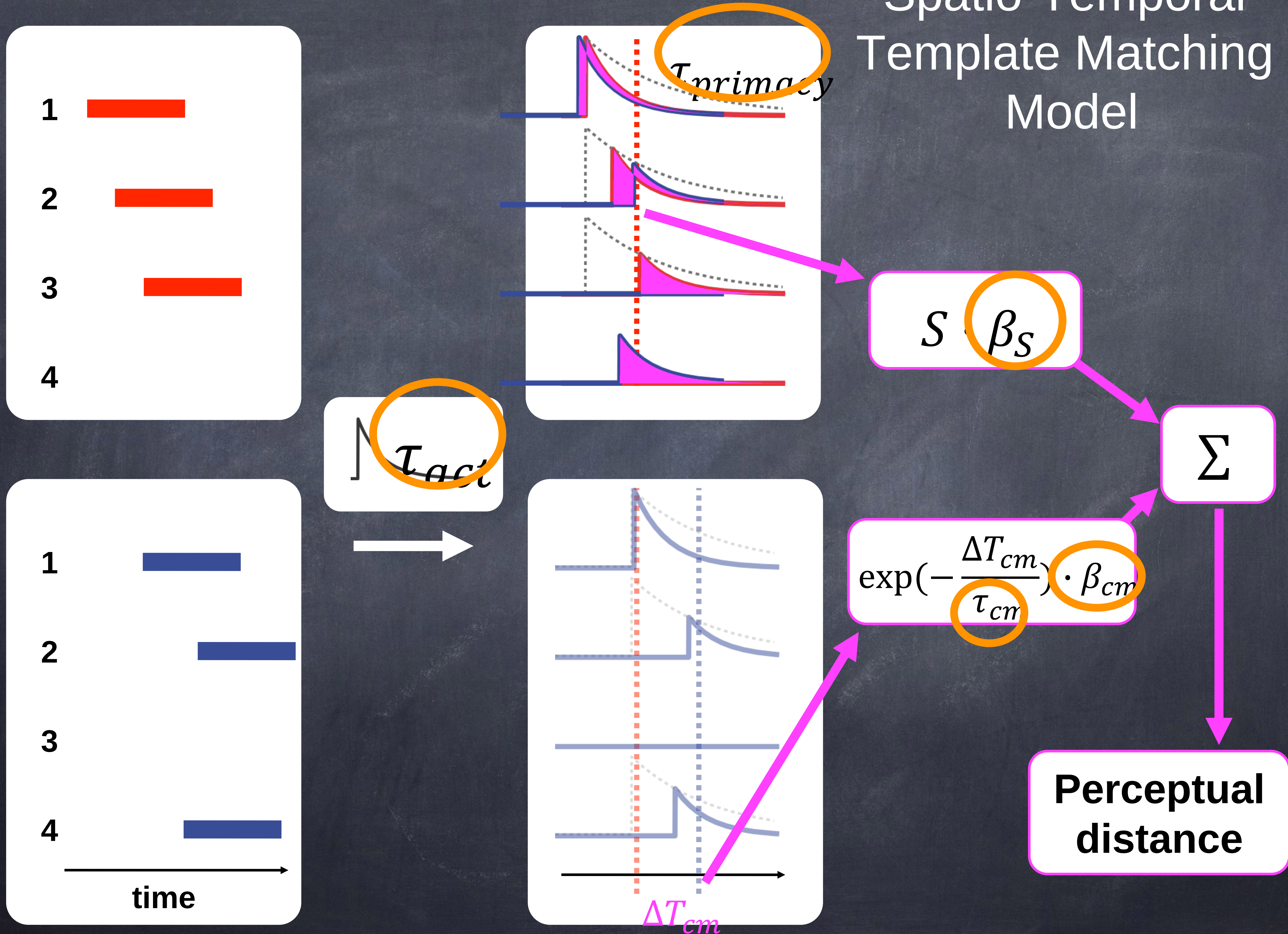
$$\Delta t_i = \Delta T_{cm} + \Delta t'_i$$

$$\mathrm{logit}(p) = \beta_0 + \beta_{cm}\Delta T_{cm} + \sum_{i,\Delta t'_i>0} \beta_i^+ |\Delta t'_i| + \sum_{i,\Delta t'_i<0} \beta_i^- |\Delta t'_i|$$

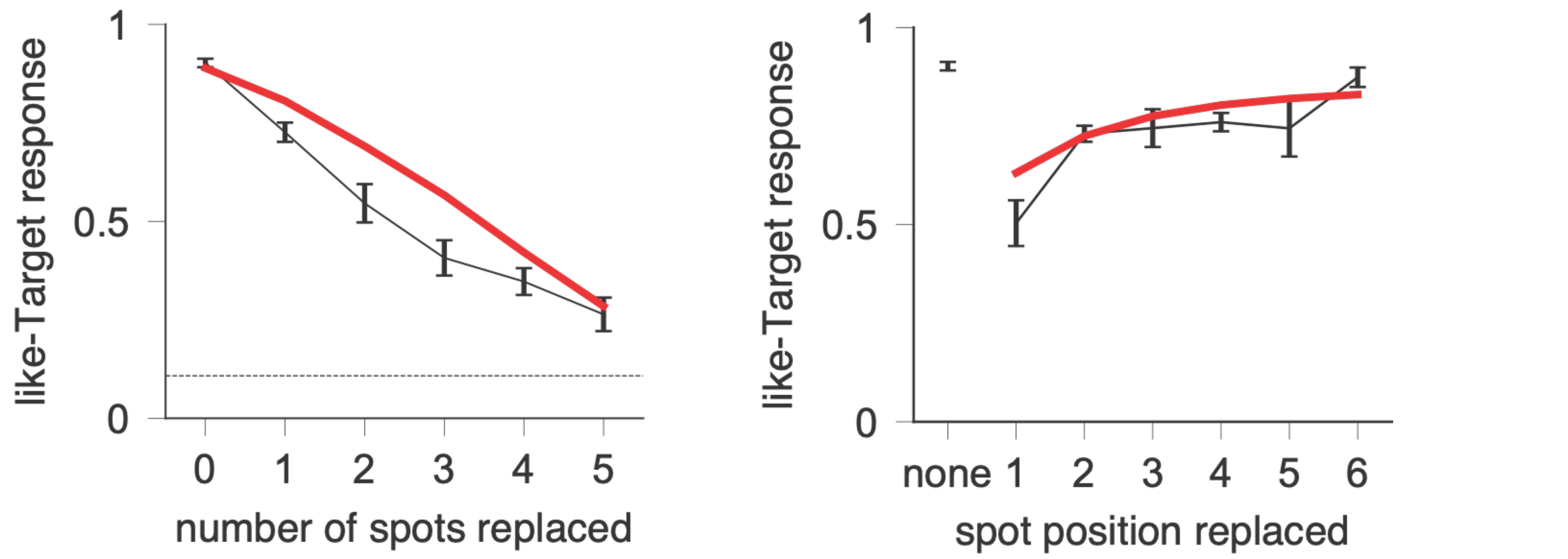



1
2
3
4
$\tau_{primacy}$
τ_{act}
1
2
3
4
time
ΔT_{cm}

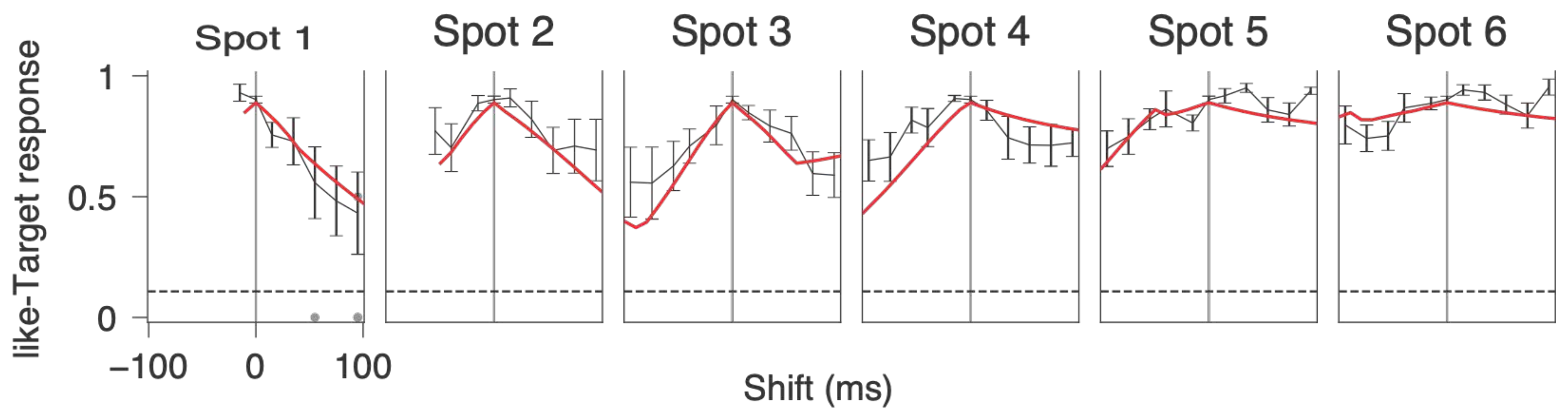
Spatio-Temporal Template Matching Model

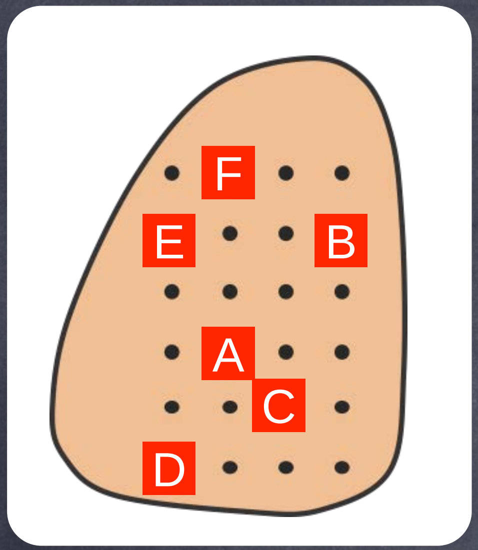


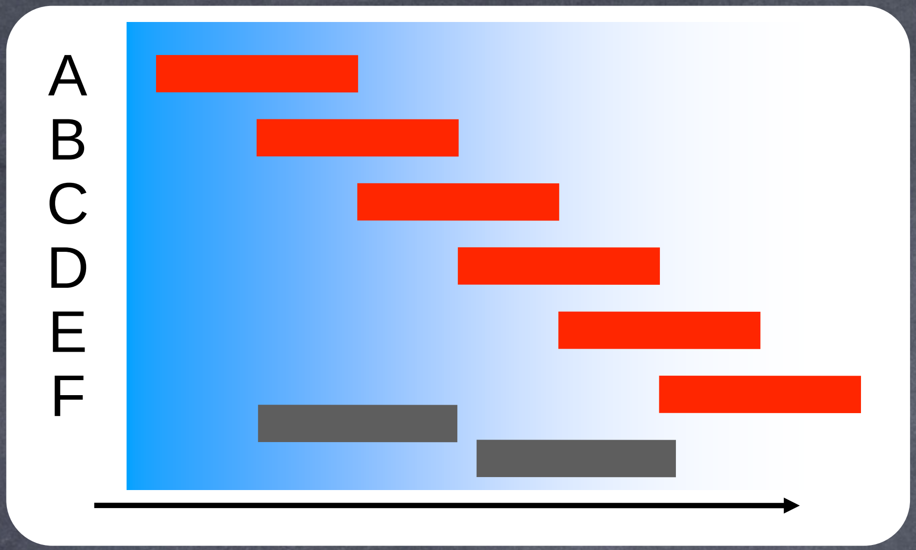
Spatial perturbations



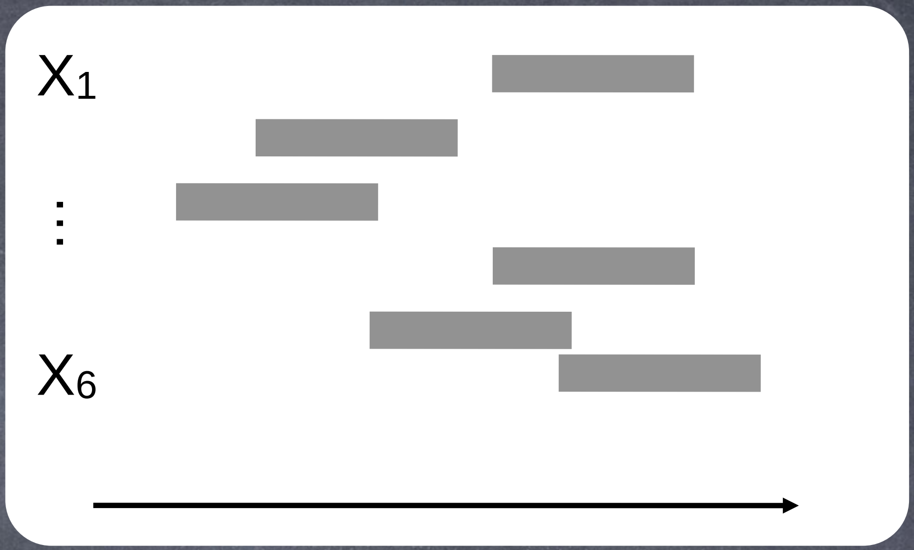
Temporal perturbations



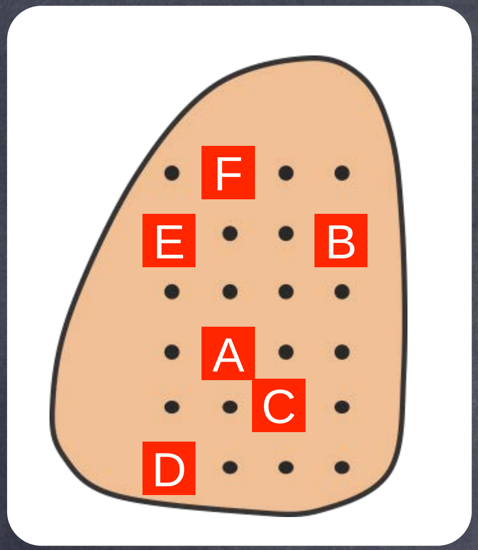


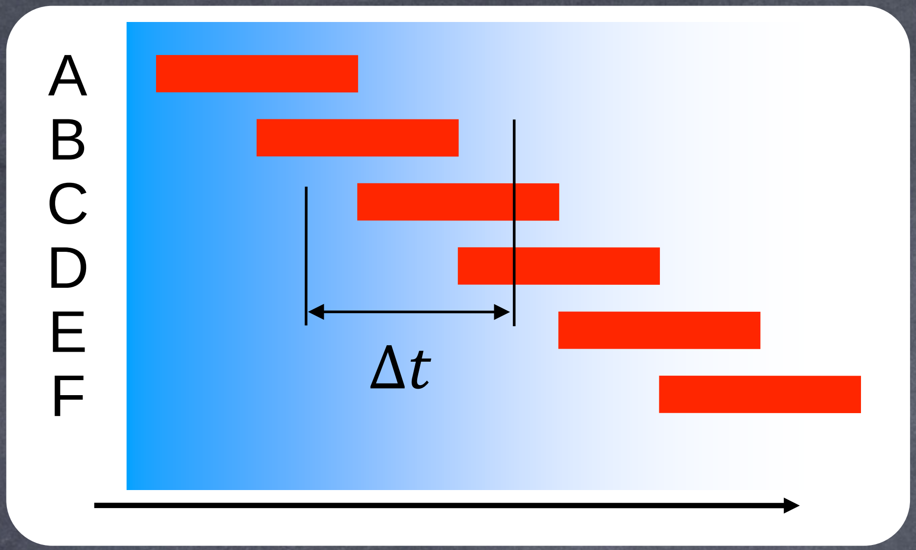


VS

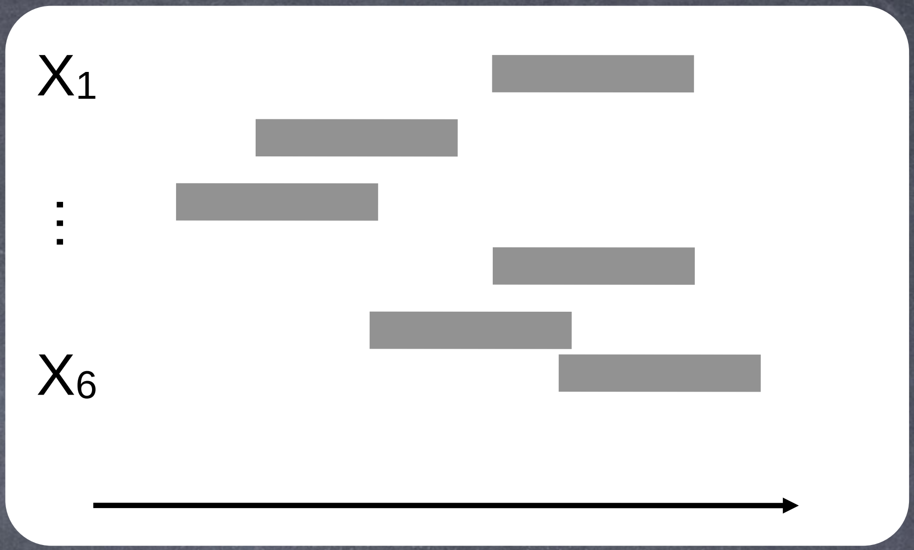


- Earlier spots are more relevant than later - Primacy effect
- Spatial channels are independent

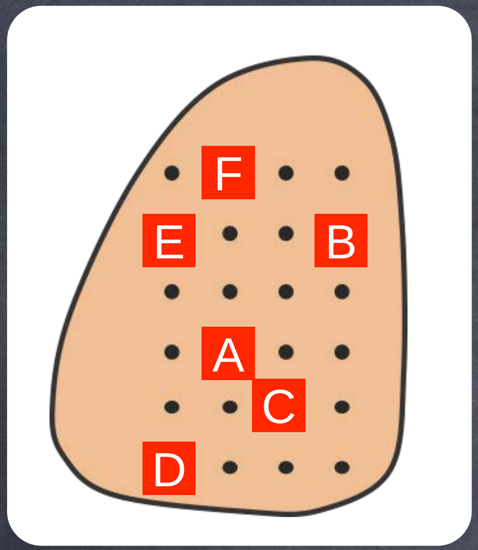


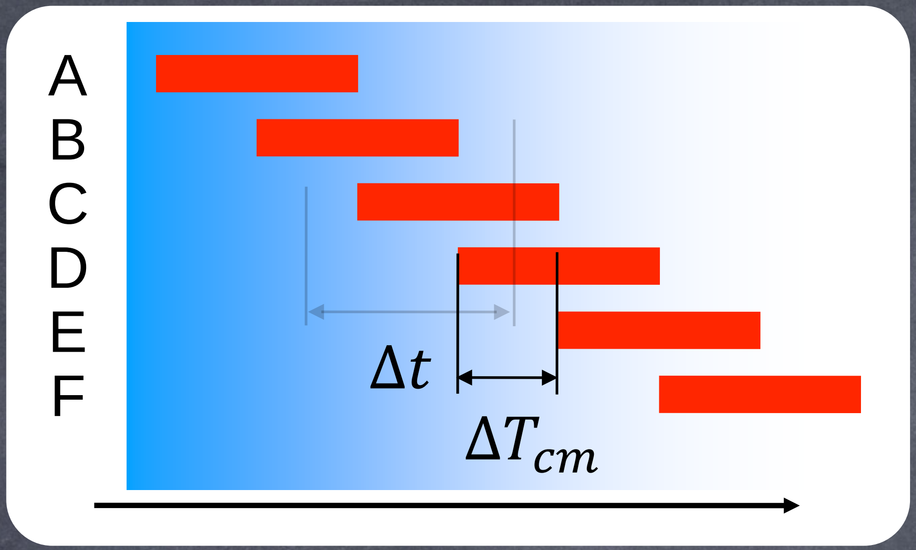


VS

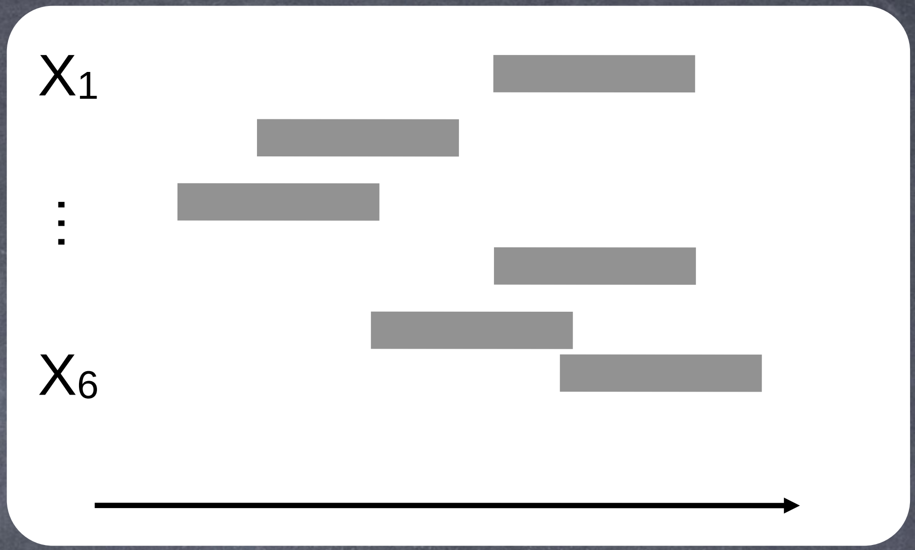


- Earlier spots are more relevant than later - Primacy effect
- Spatial channels are independent
- Strong sensitivity to relative timing



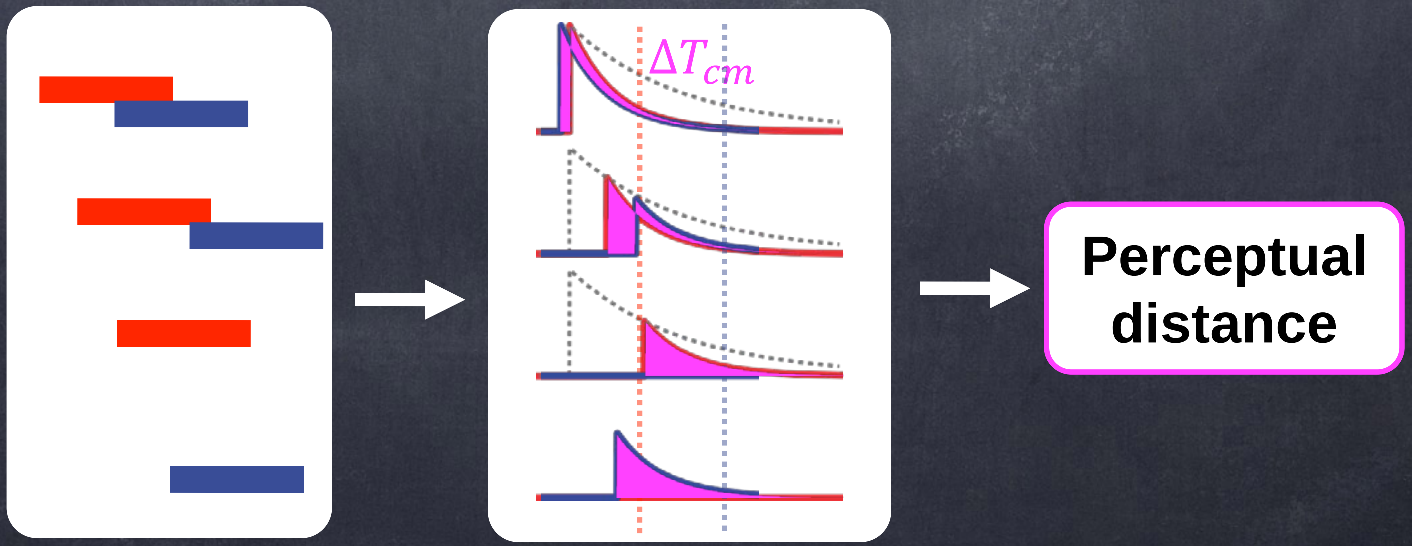


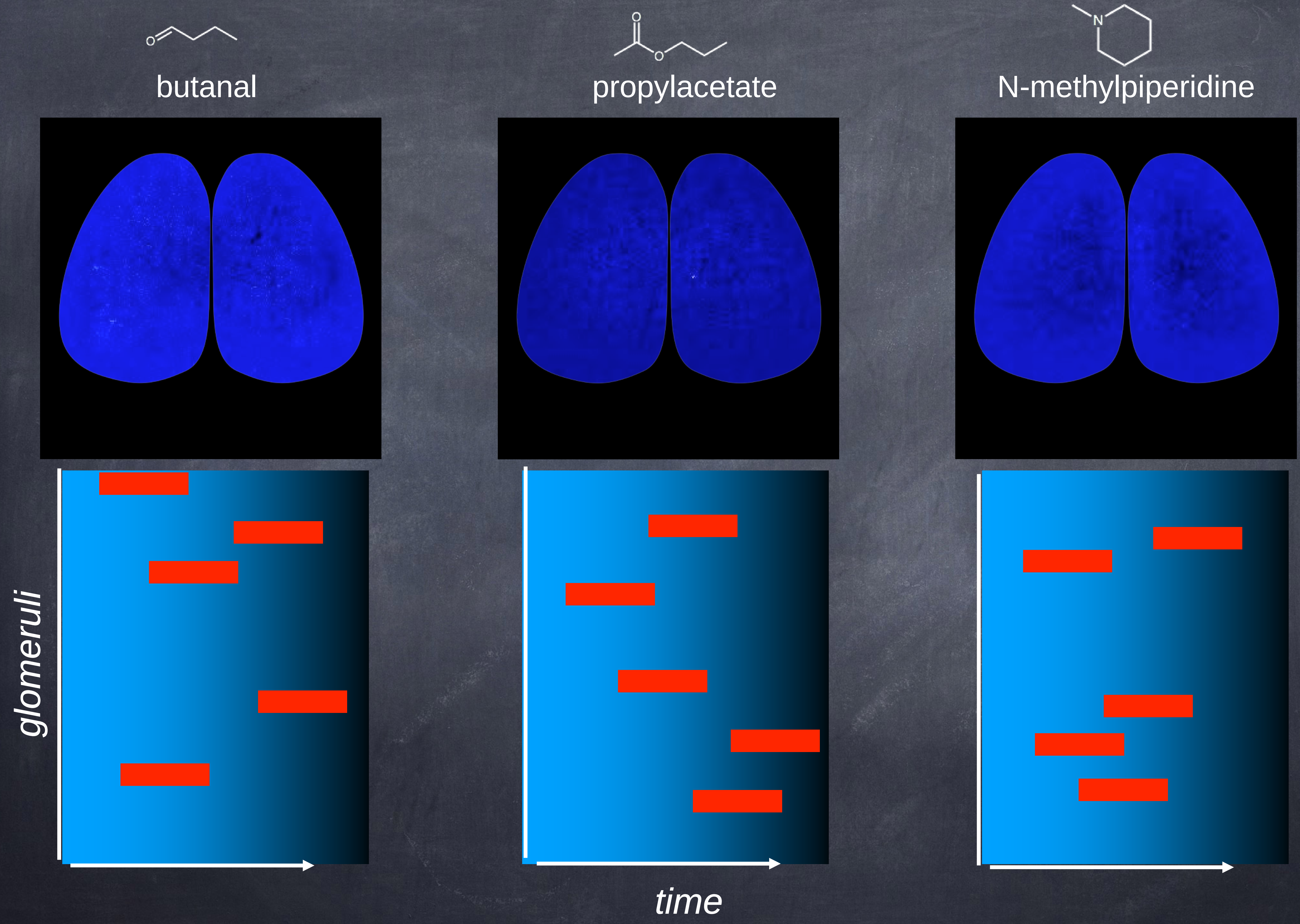
VS



- Earlier spots are more relevant than later - Primacy effect
- Spatial channels are independent
- Strong sensitivity to relative timing
- Weak sensitivity to the global shift relative to the sniff cycle

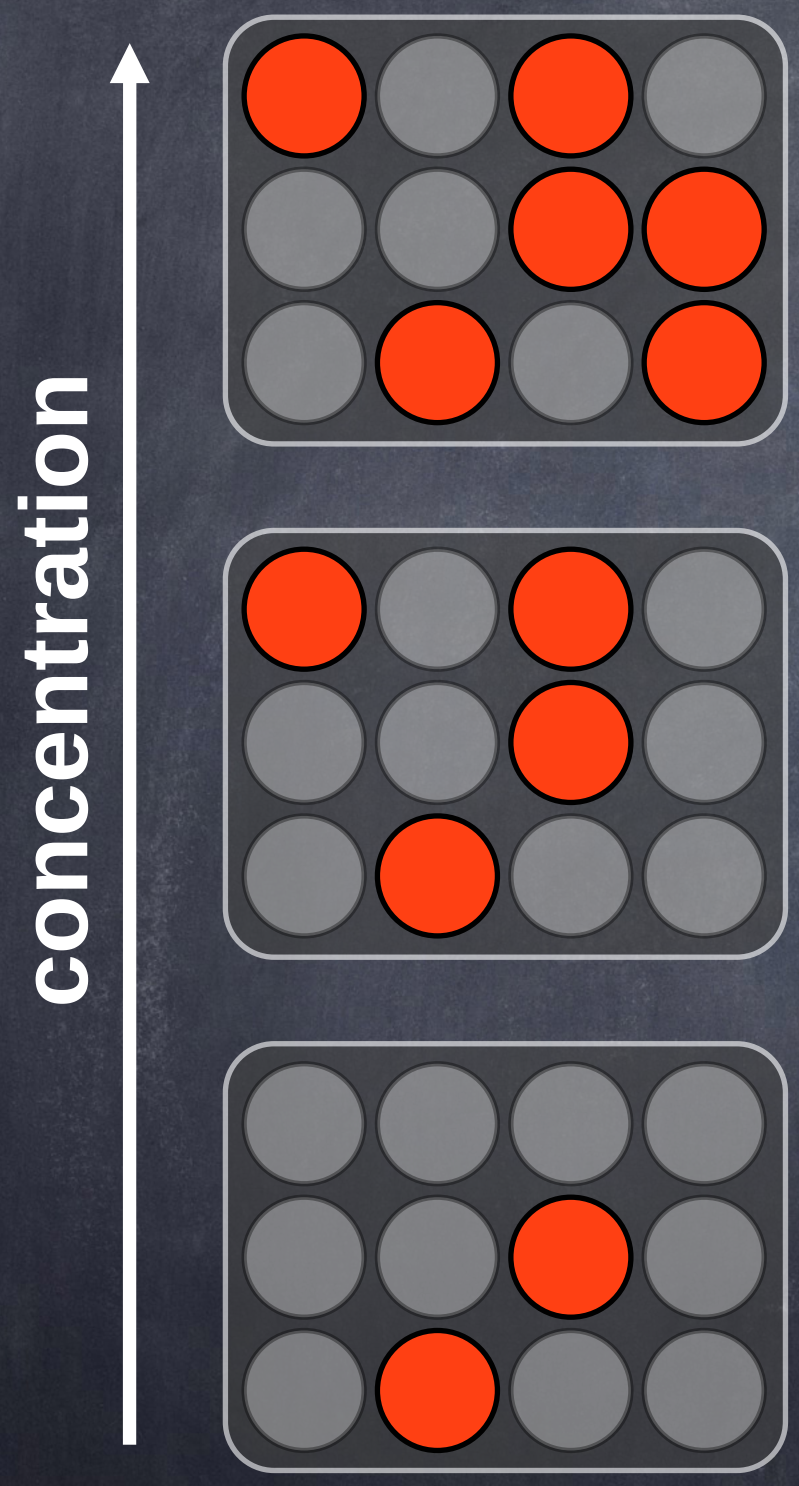
Spatio-Temporal Template Matching Model

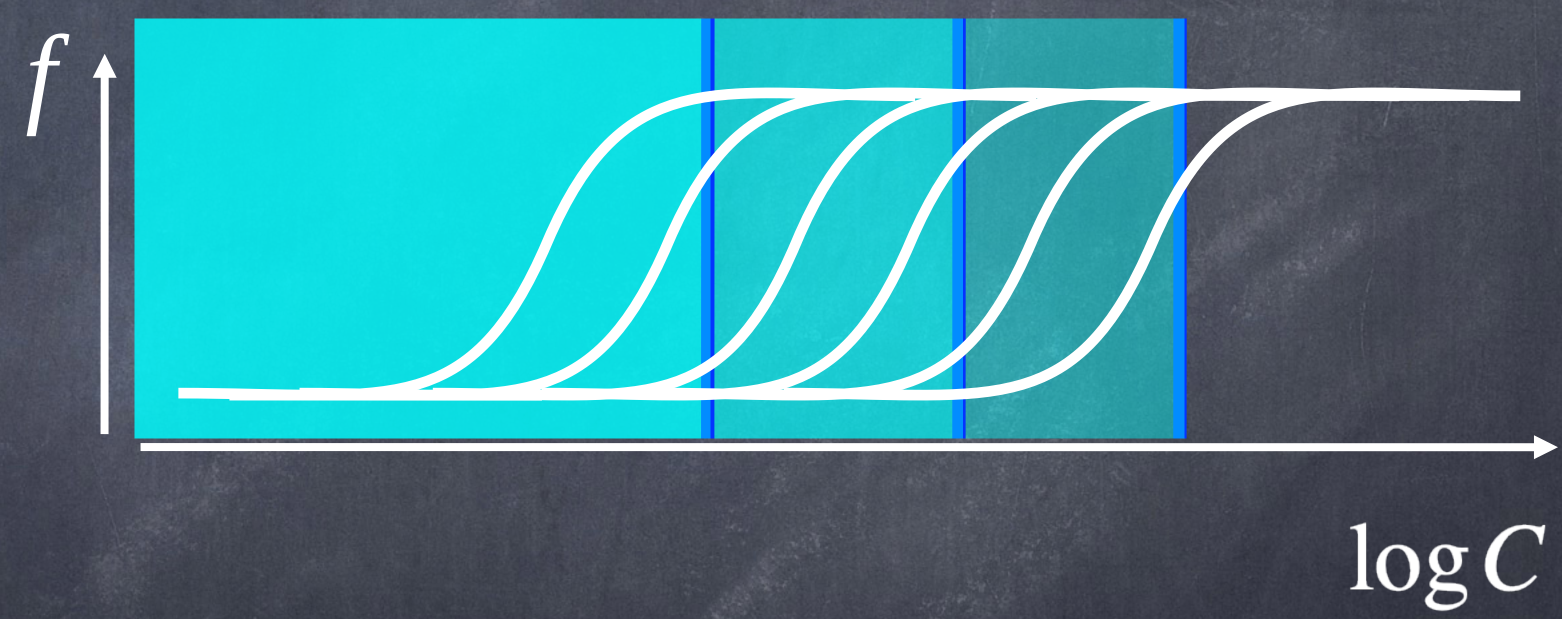



butanal
propylacetate
N-methylpiperidine
glomeruli
time

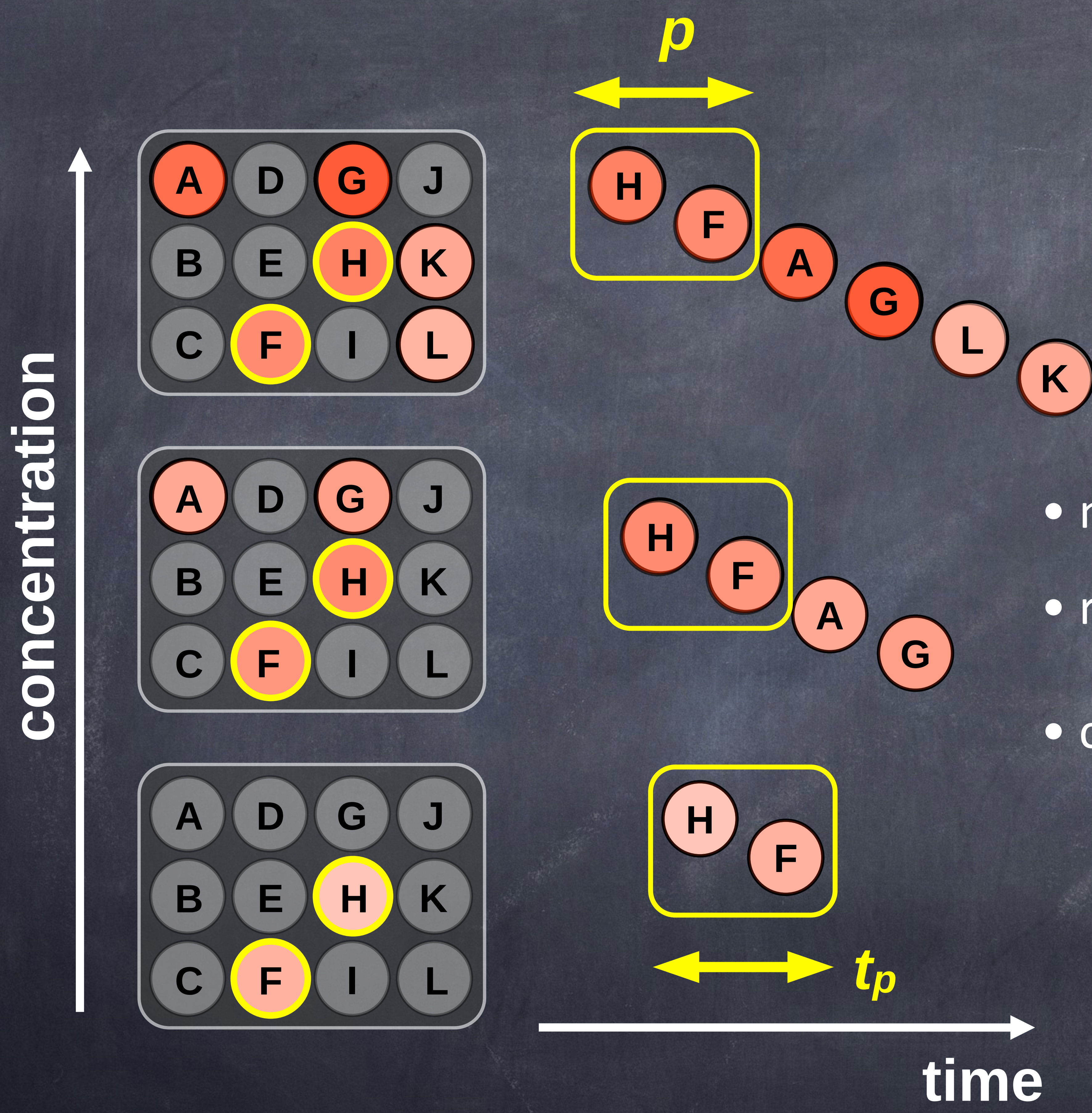

Intensity

receptor ligand interaction

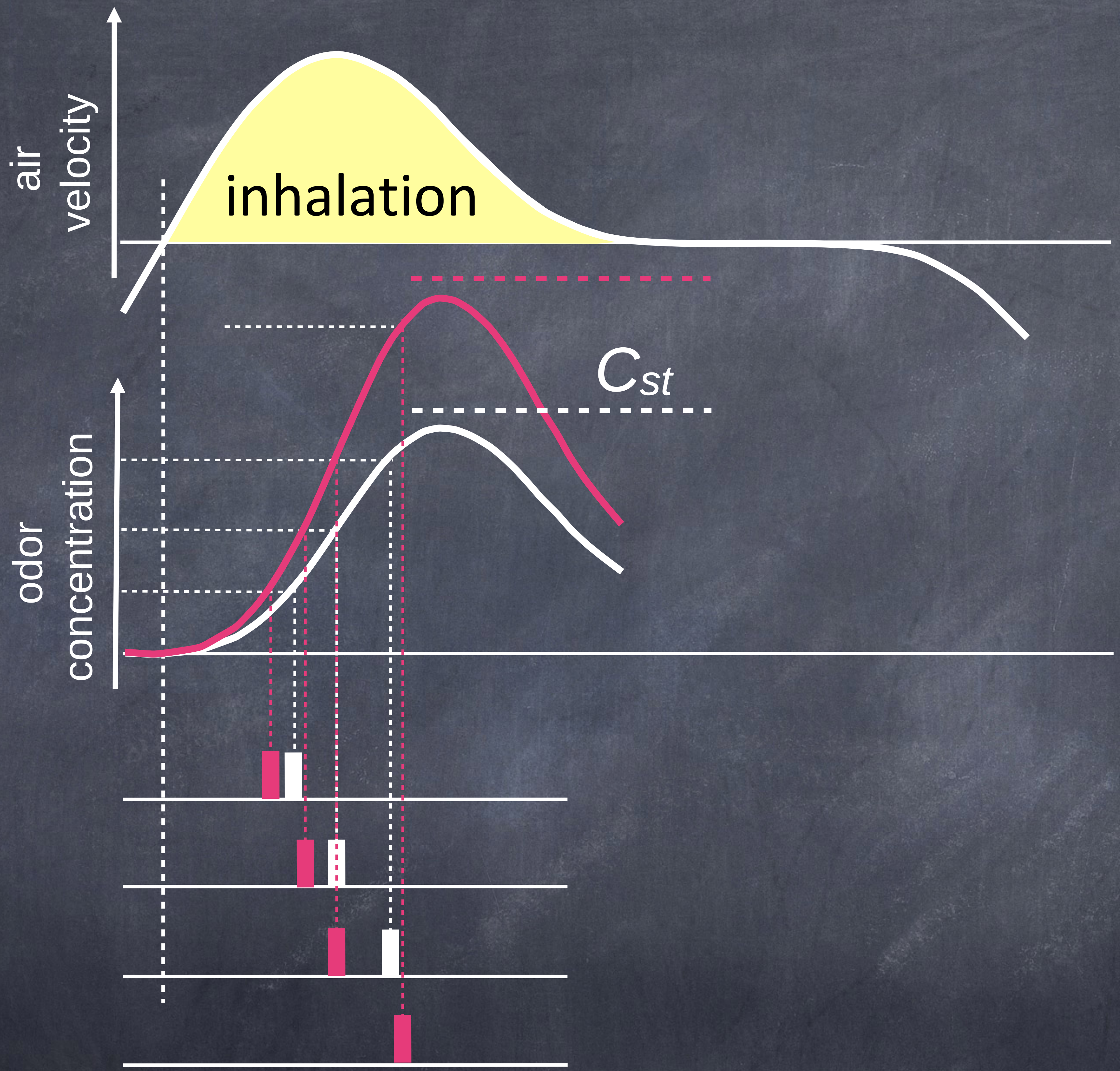




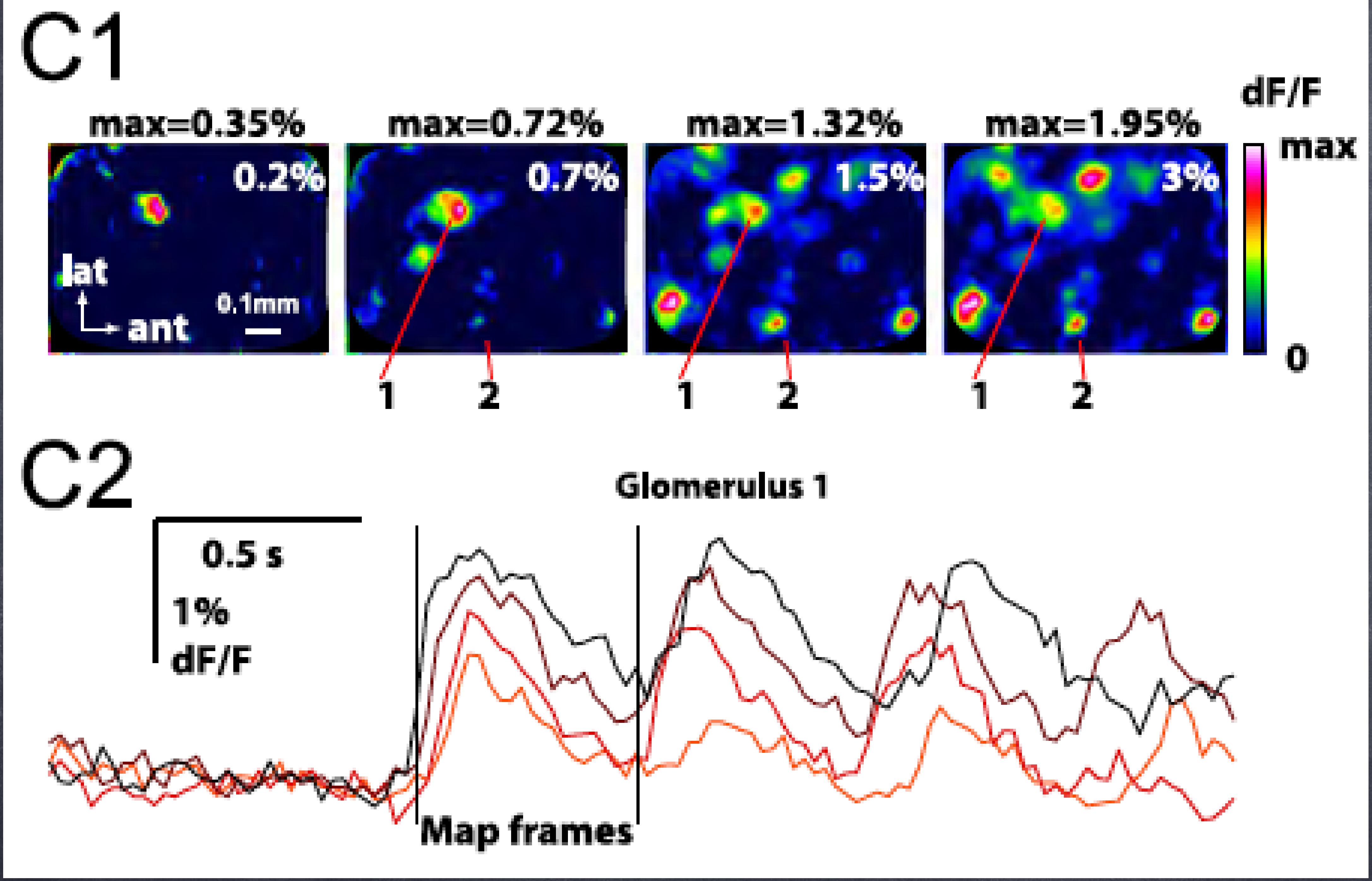
Primacy coding



- concentration invariance
- neural mechanisms
- reading the code
- code features
- window of relevant information

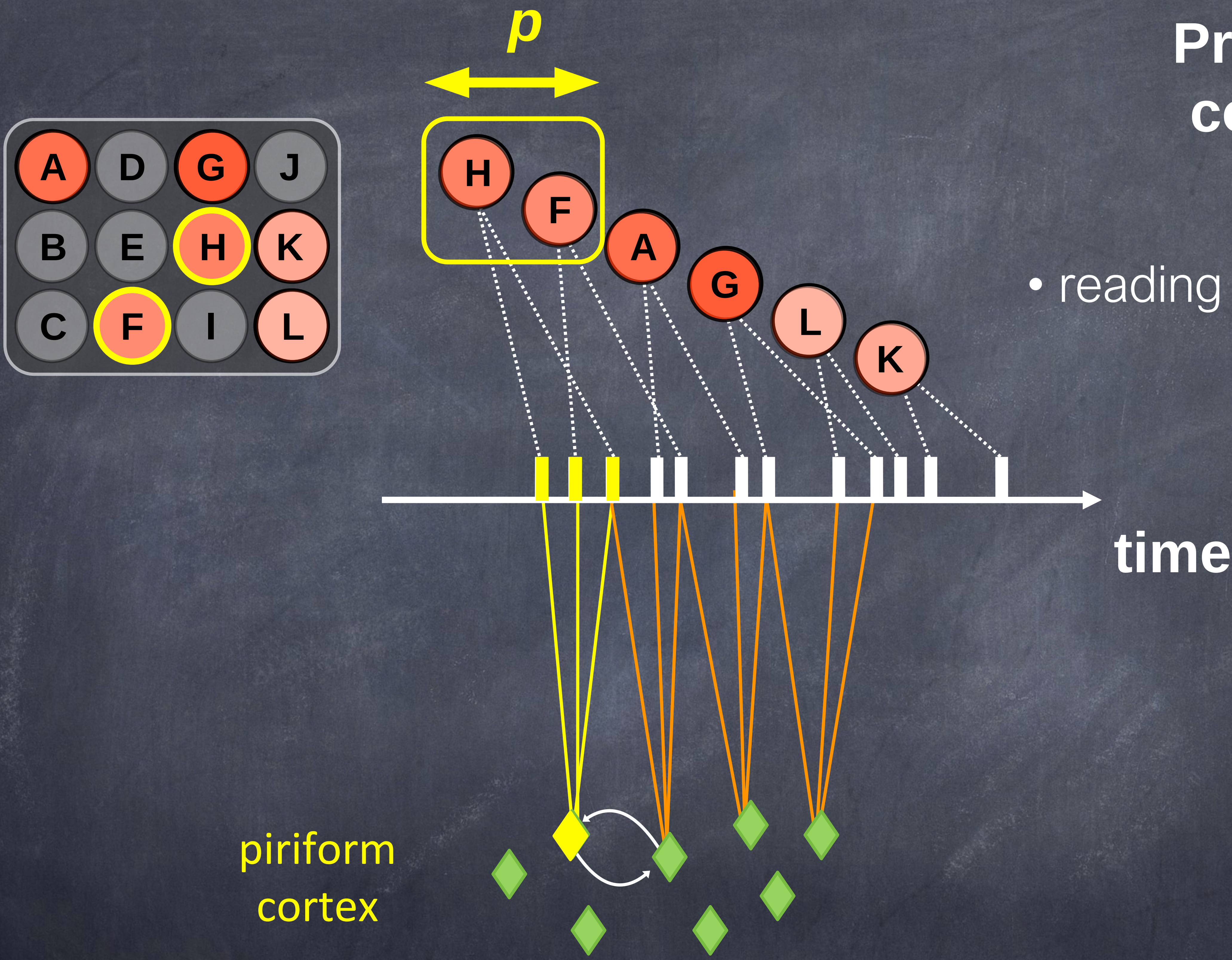


air velocity
inhalation
C_{st}
odor concentration

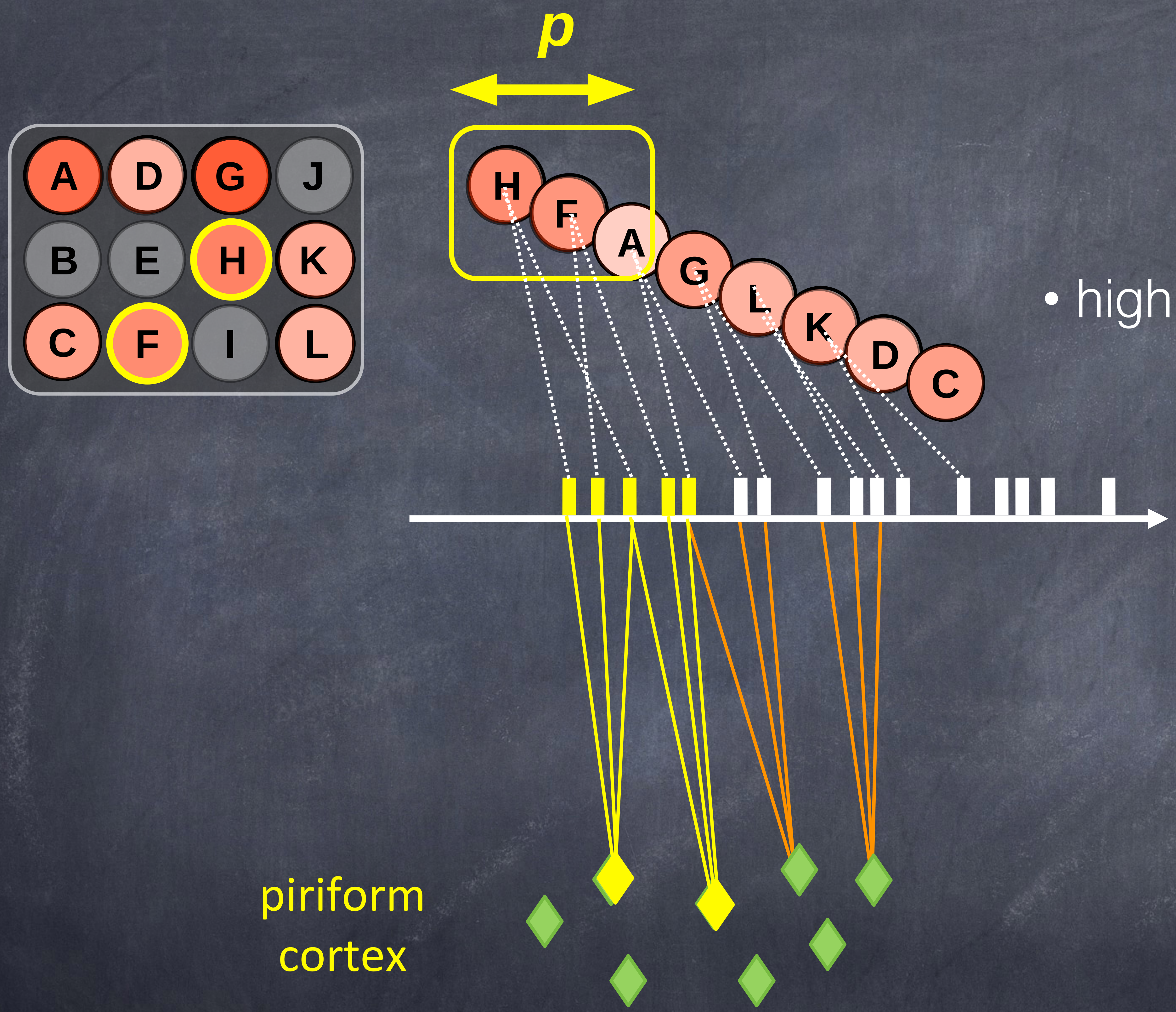

C1
dF/F
max=0.35%
max=0.72%
max=1.32%
max=1.95%
max
0.2%
0.7%
1.5%
3%
lat
ant
0.1mm
0
1
2
1
2
1
2
C2
Glomerulus 1
0.5 s
1%
dF/F
Map frames

Primacy coding

- reading the code



Primacy coding



- high concentrations

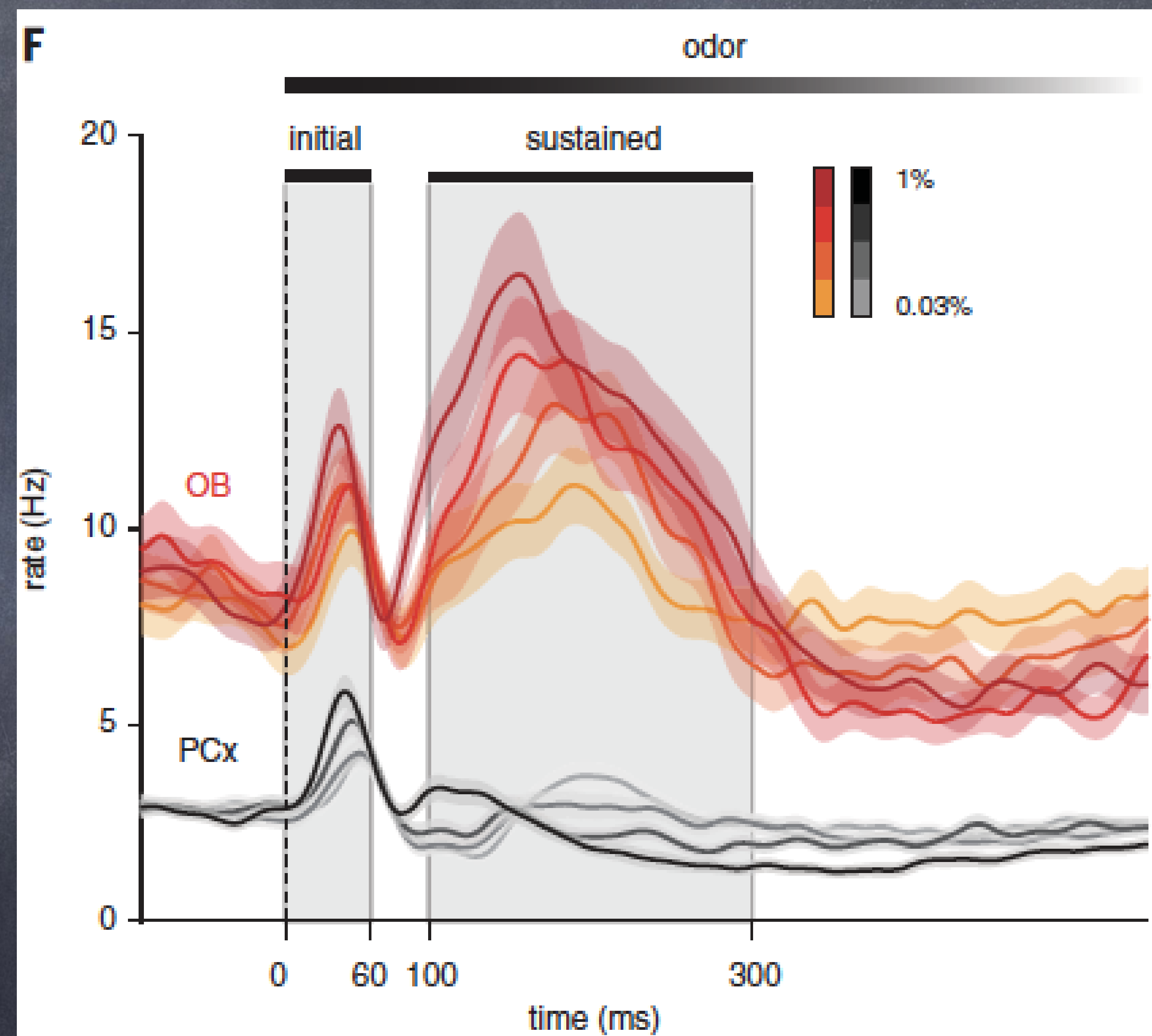
RESEARCH ARTICLE

Science, 2018

NEUROSCIENCE

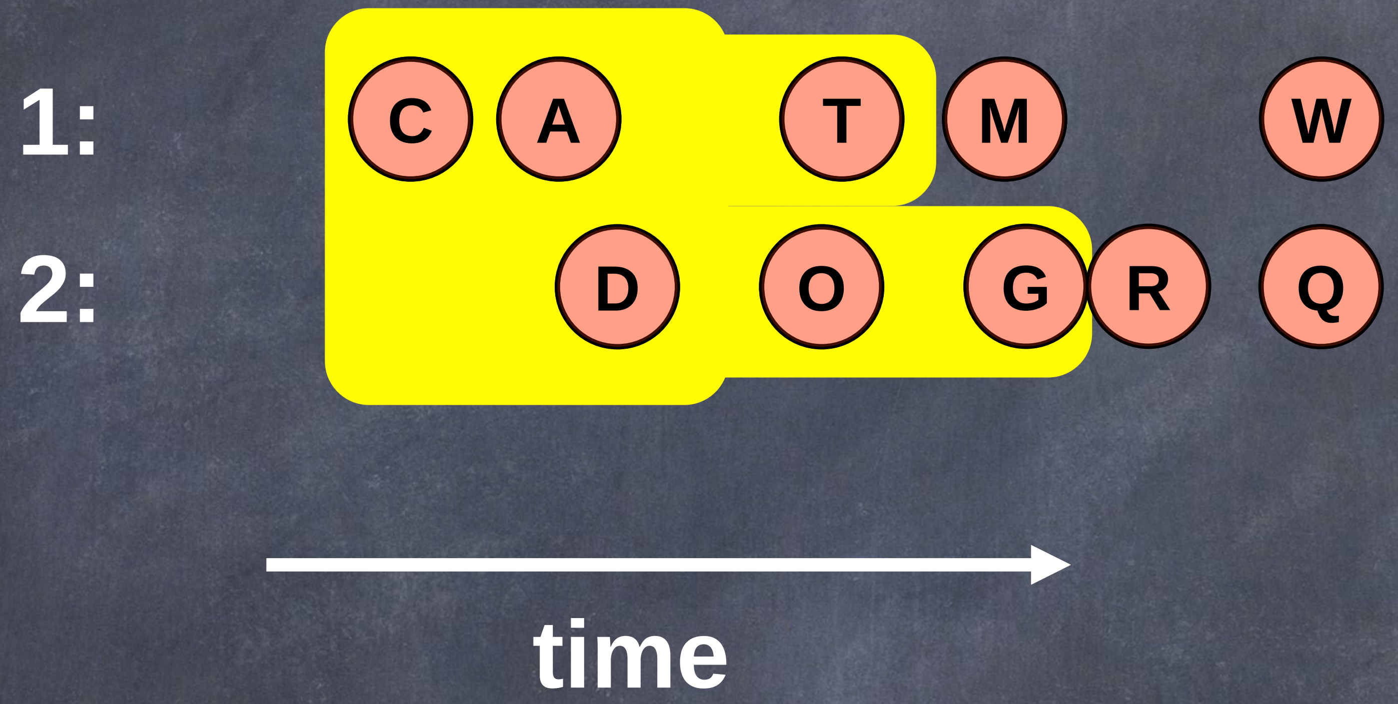
Recurrent cortical circuits implement concentration-invariant odor coding

Kevin A. Bolding and Kevin M. Franks*



Primacy coding

- mixtures



frontiers
IN SYSTEMS NEUROSCIENCE

Odor concentration invariance by chemical ratio coding

Naoshige Uchida[†] **and Zachary F. Mainen**[*]

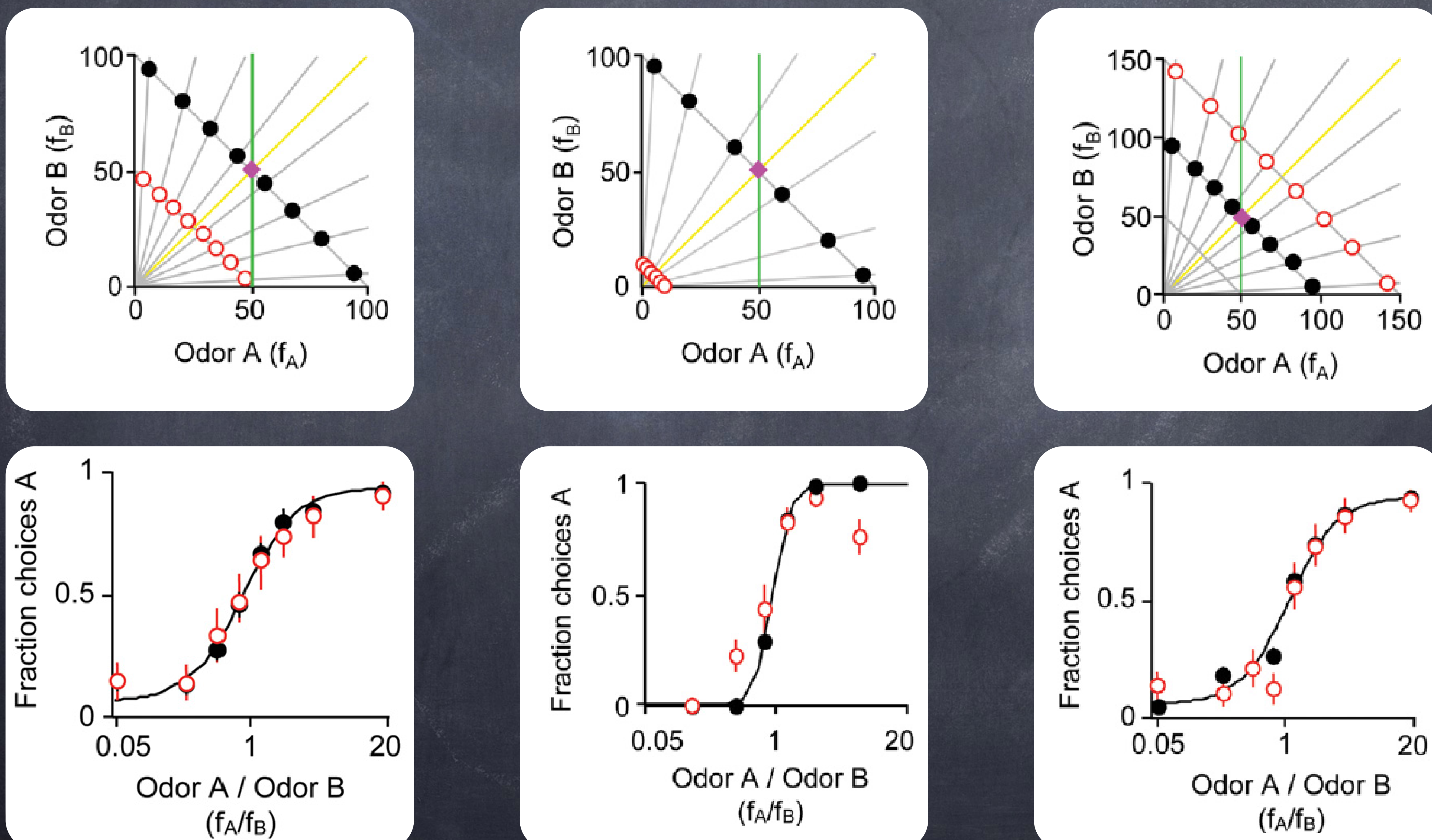
Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA

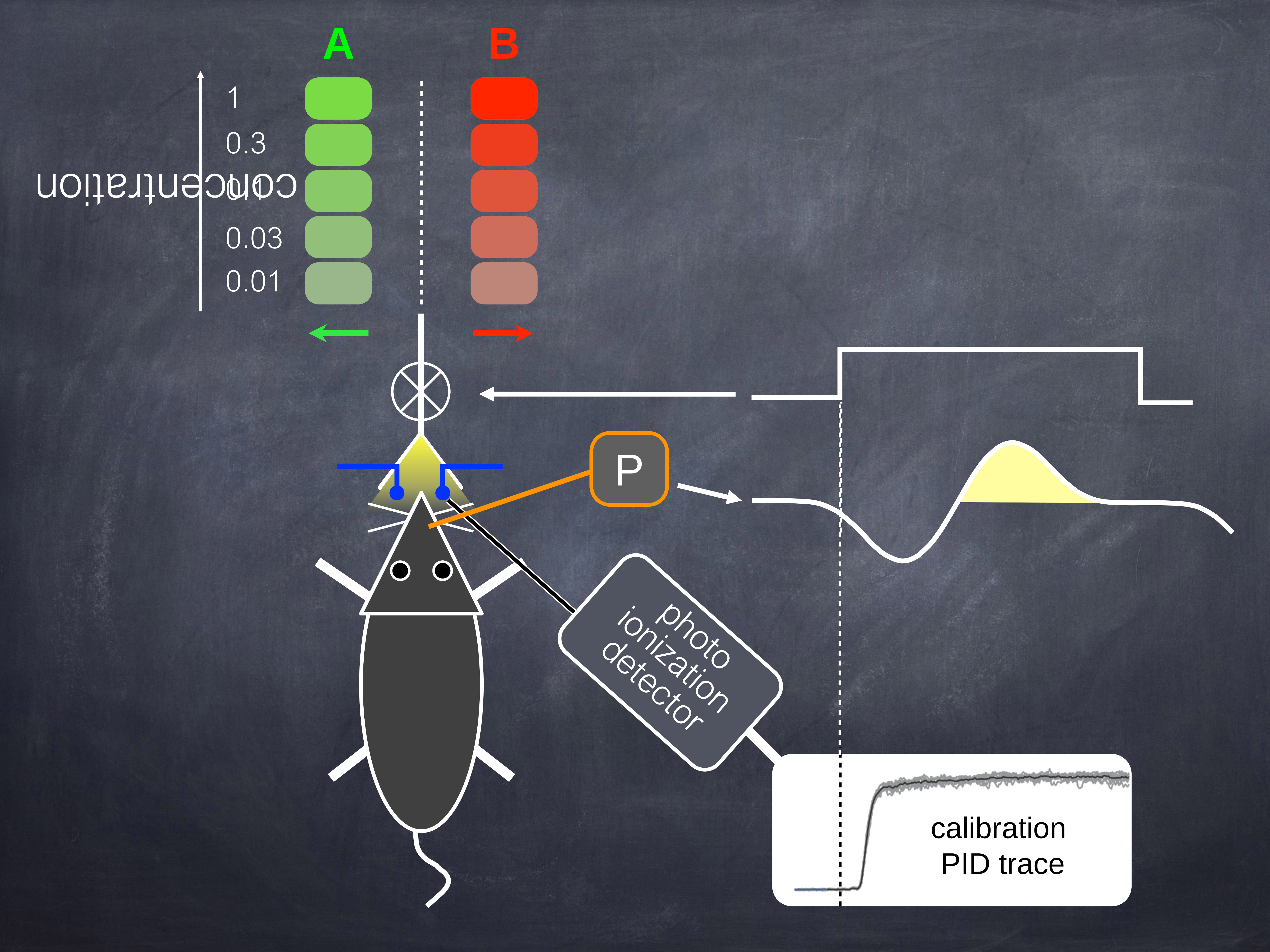
frontiers
IN SYSTEMS NEUROSCIENCE

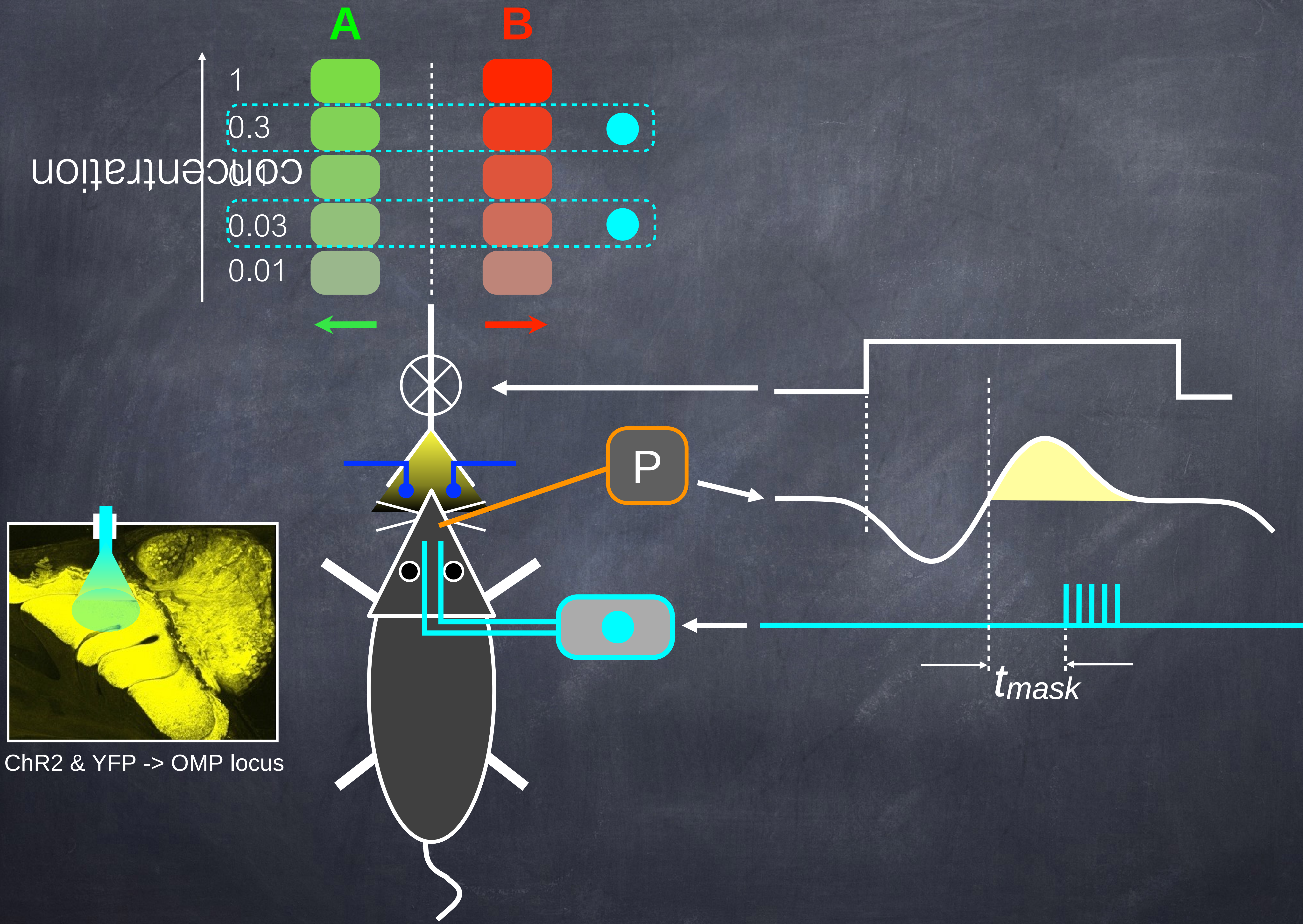
Odor concentration invariance by chemical ratio coding

Naoshige Uchida† **and Zachary F. Mainen***

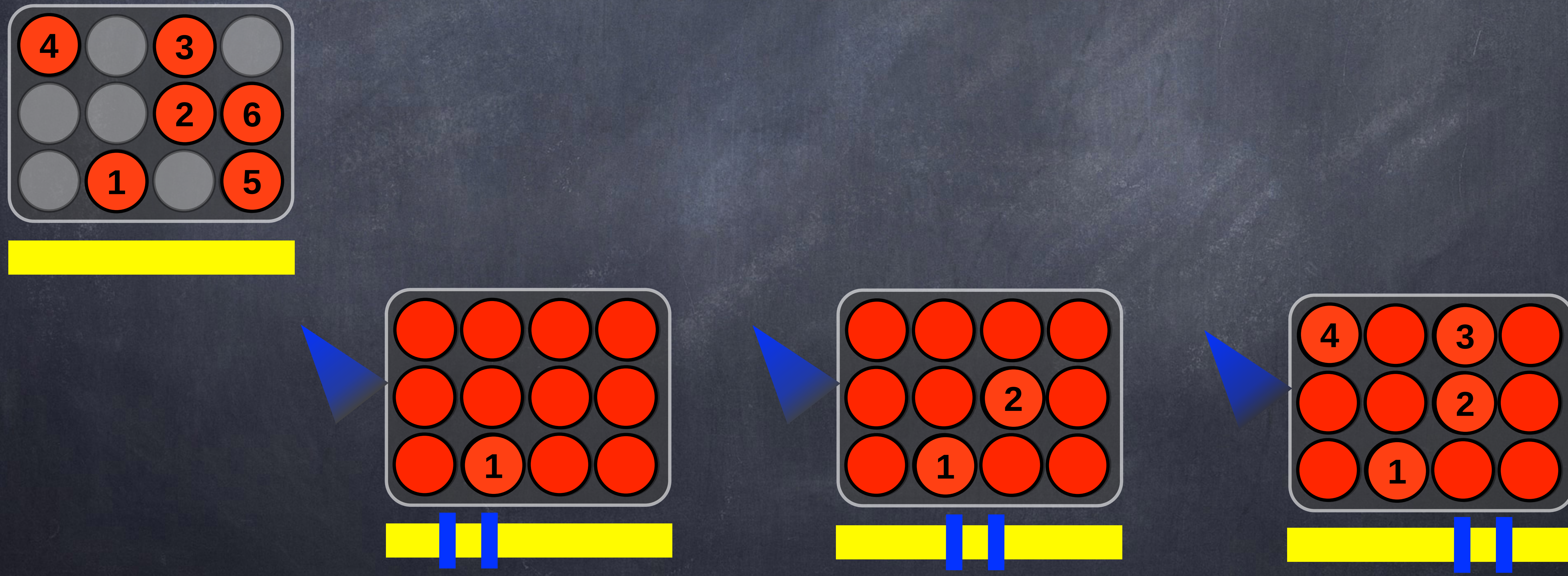
Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA

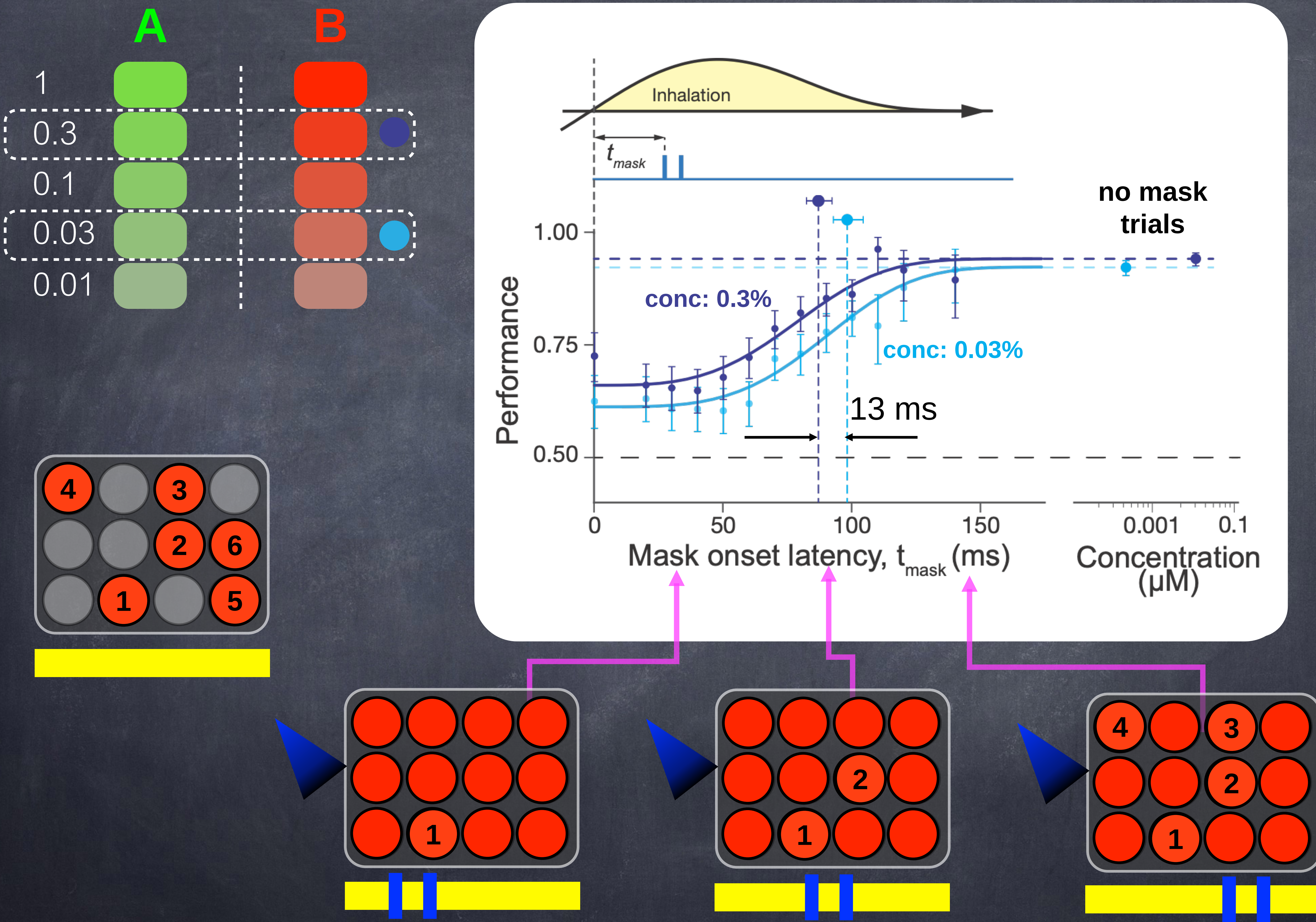


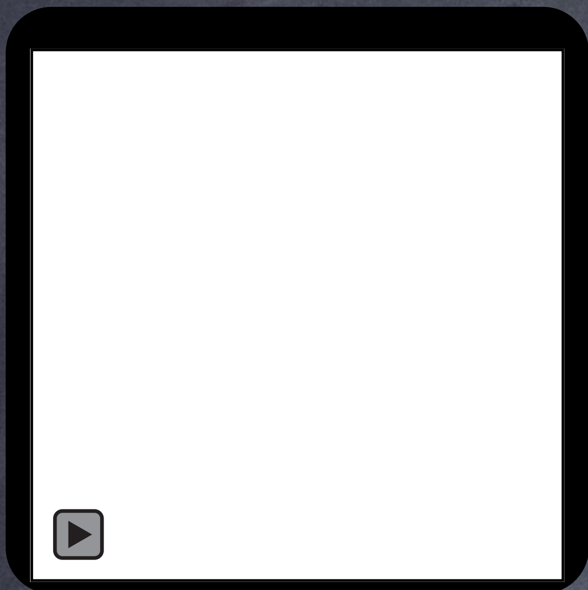

A
B
1
0.3
0.03
0.01
concentration
P
photo
ionization
detector
calibration
PID trace

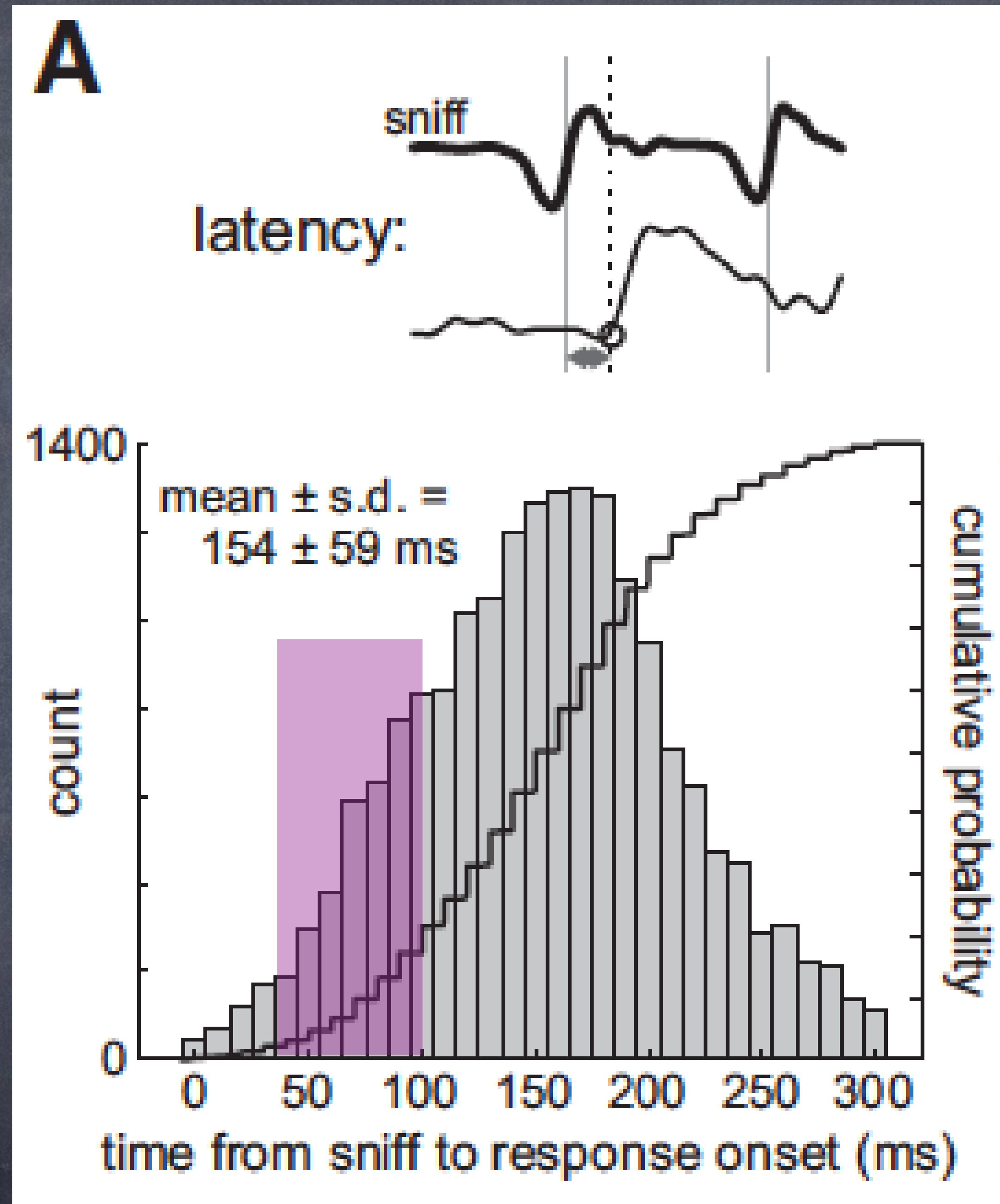


A
B
concentration
1
0.3
0.03
0.01
P
t_{mask}
ChR2 & YFP -> OMP locus


4
3
2
6
1
5
1
2
1
4
3
2
1

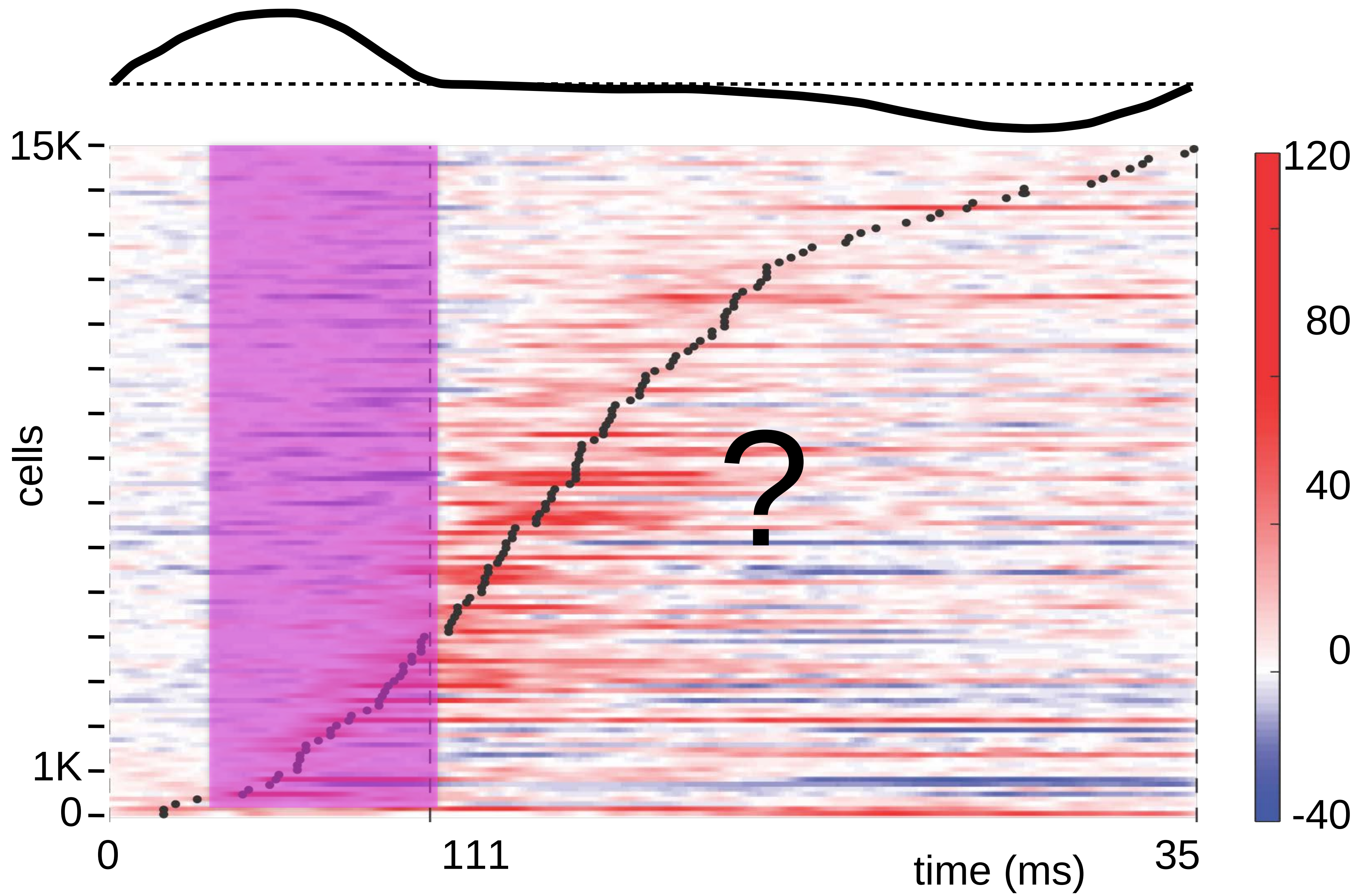

A
B
1
0.3
0.1
0.03
0.01
Inhalation
t mask
no mask trials
1.00
0.75
0.50
Performance
conc: 0.3%
conc: 0.03%
13 ms
0
50
100
150
0.001
0.1
Mask onset latency, t mask (ms)
Concentration (μM)
4
3
2
6
1
5
1
2
1
4
3
2
1



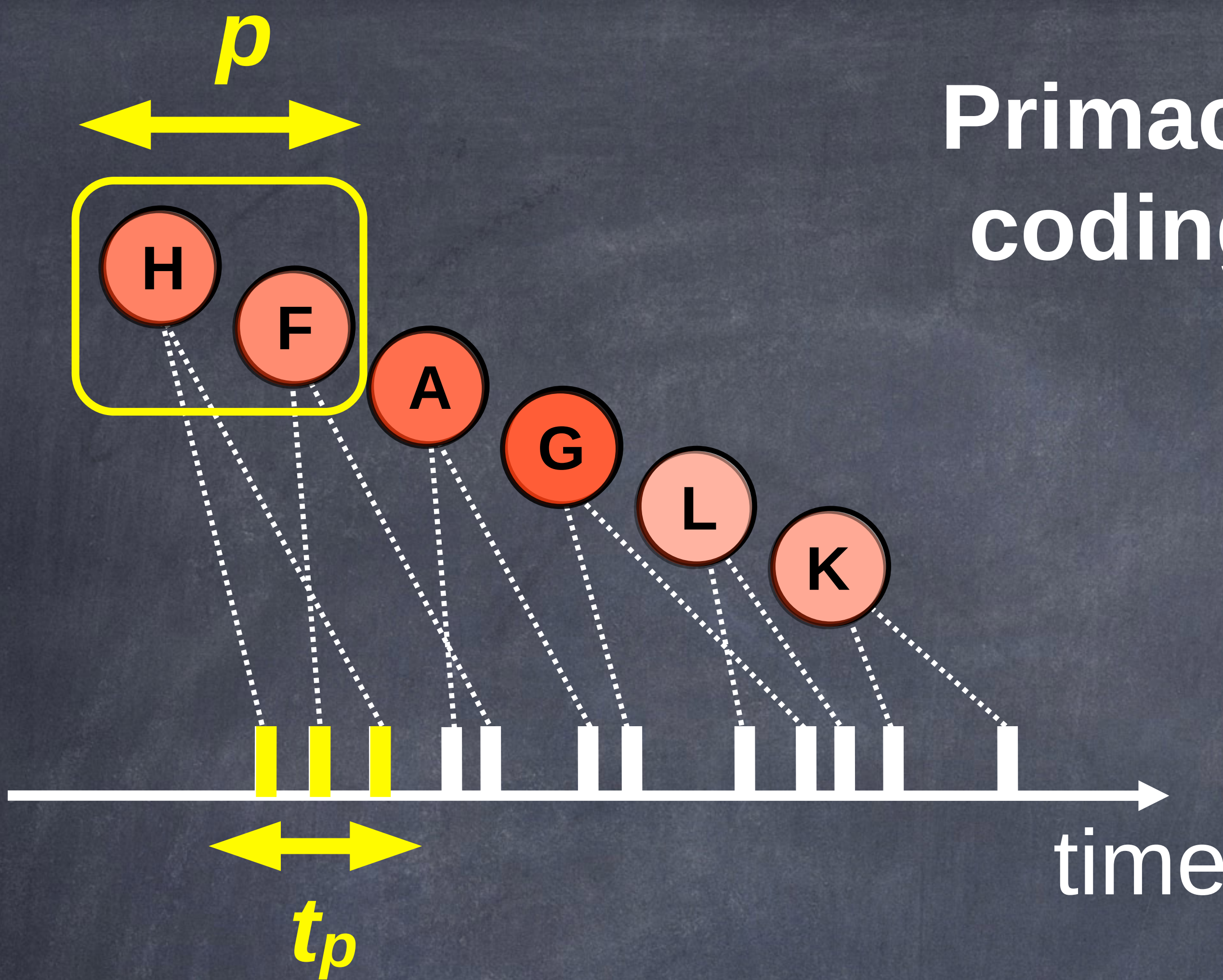


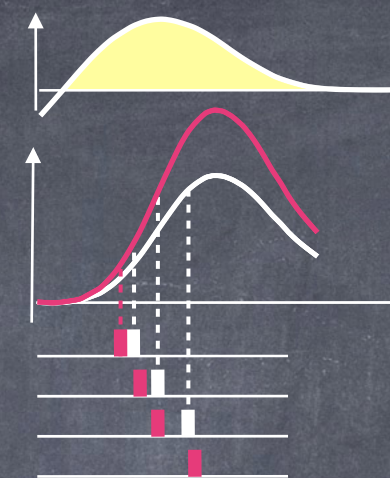
R Carey, et. al.,
J. Neurophysiol. 2009

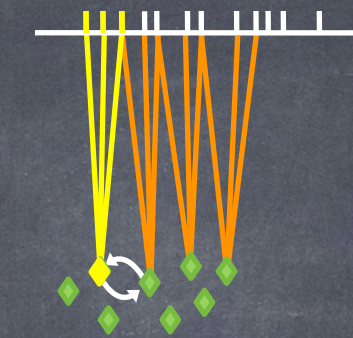
~50.000 M/T cells
~15.000 excitatory responses

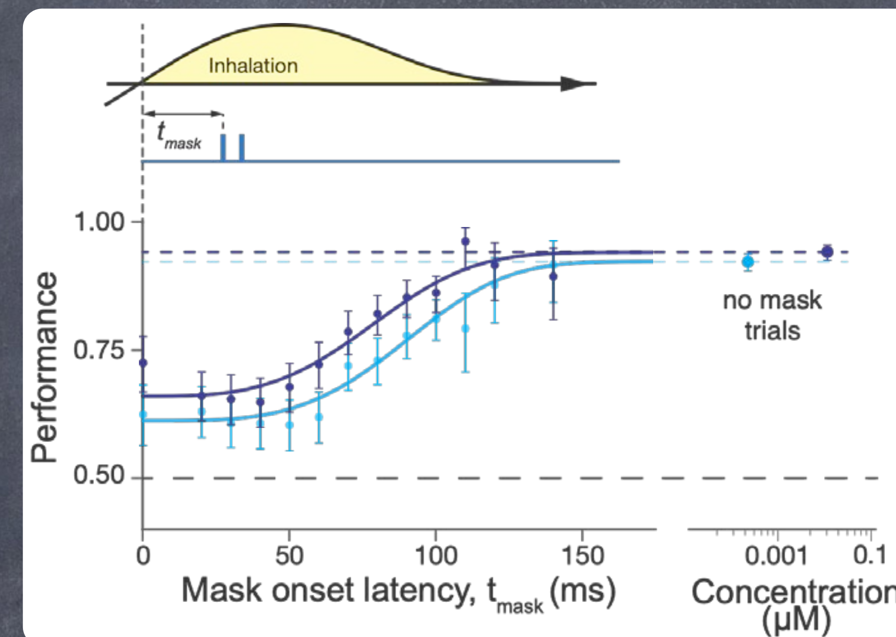


Primacy coding







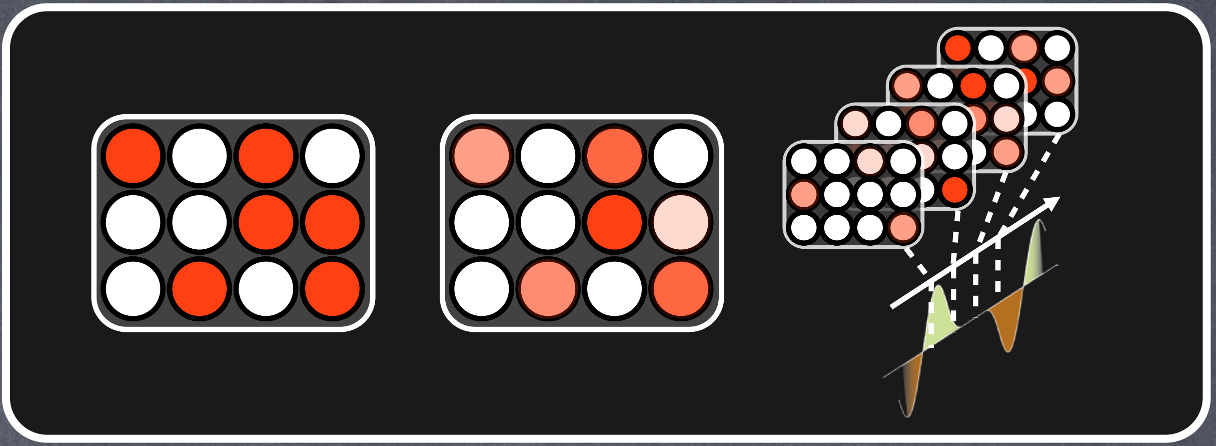


- concentration invariance
- mechanisms for forming the code
- mechanisms for reading the code
- the code is consistent with some known behavioral phenomena

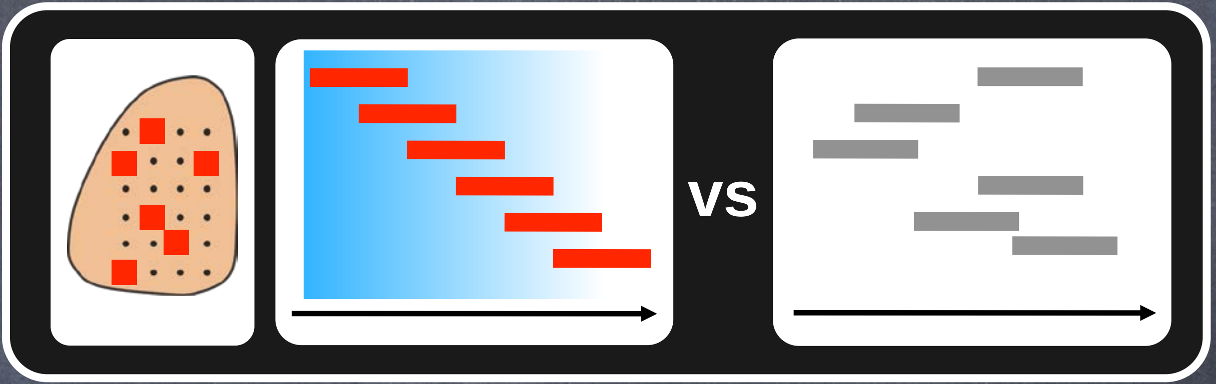
=> small temporal window is relevant for behavior

$\vec{S} \rightarrow \vec{N} \rightarrow B$

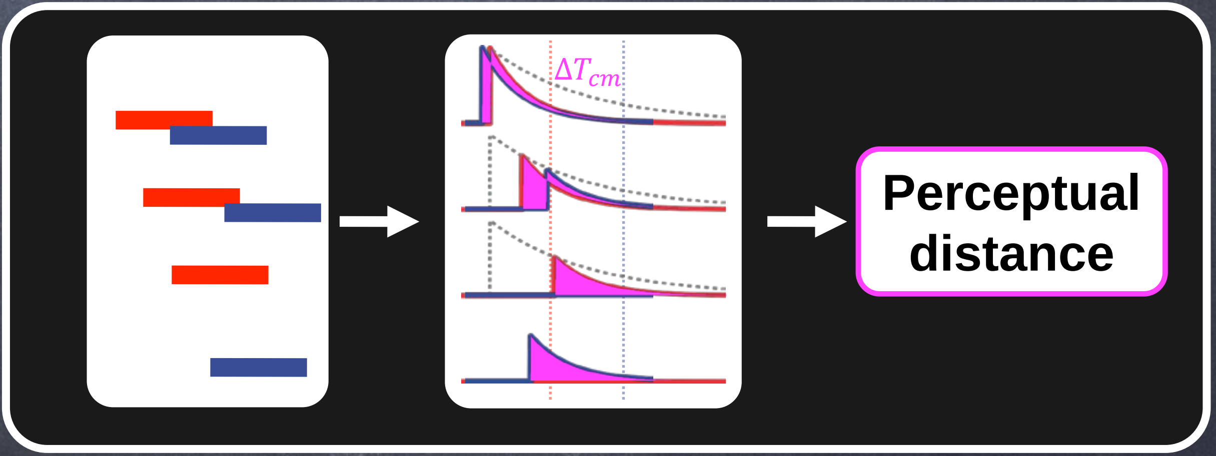
- Multiple coding features are perceptually accessible



- Paradigm for evaluation of behavioral relevance of coding features



- Spatial-temporal template matching model for perceptual distances



- Primacy coding for concentration invariance