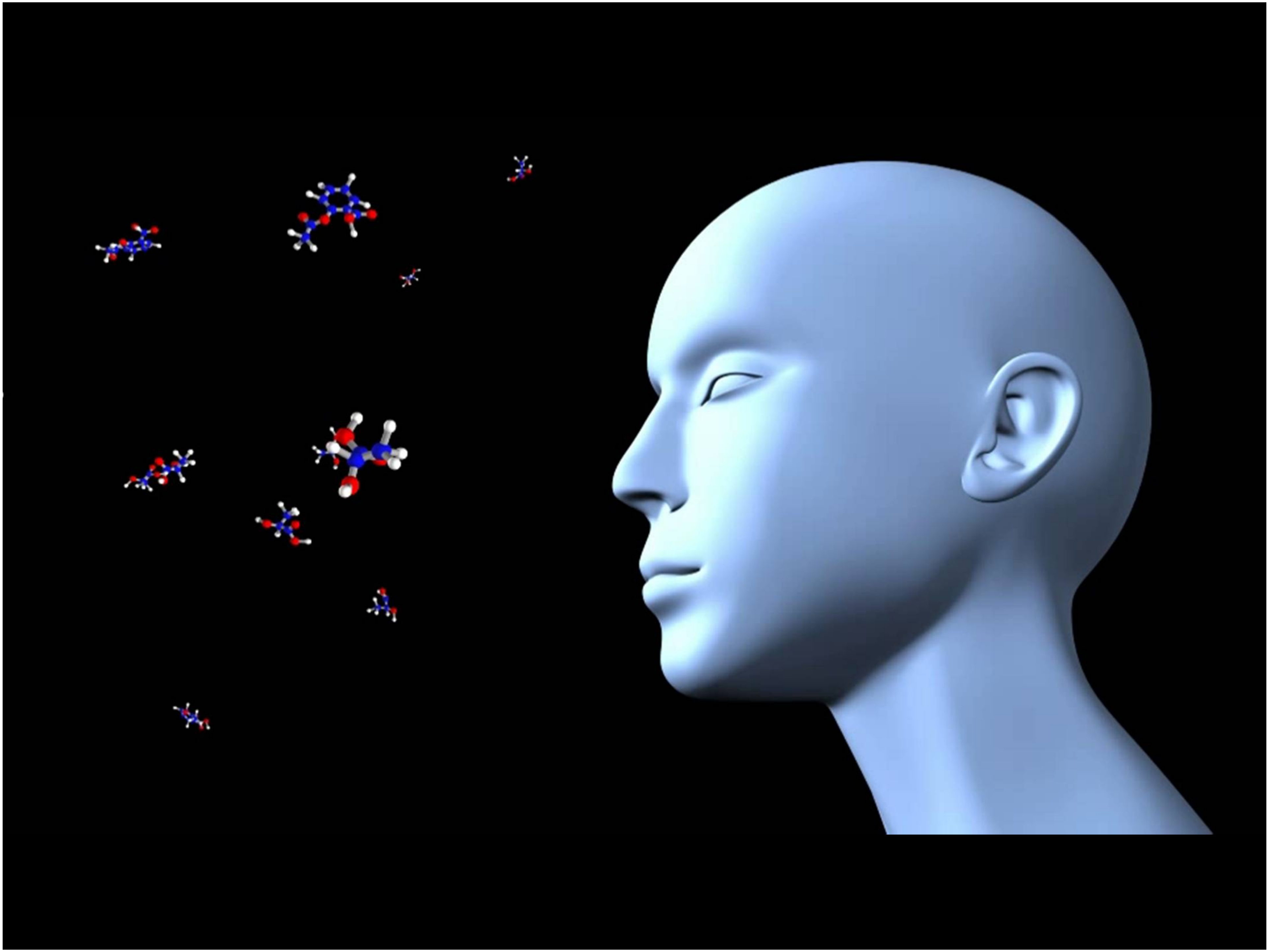
NEURAL RELATIVITY PRINCIPLE

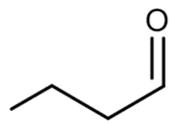
Alex Koulakov, *Cold Spring Harbor Laboratory*



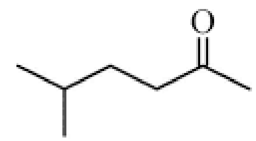
$\simeq$

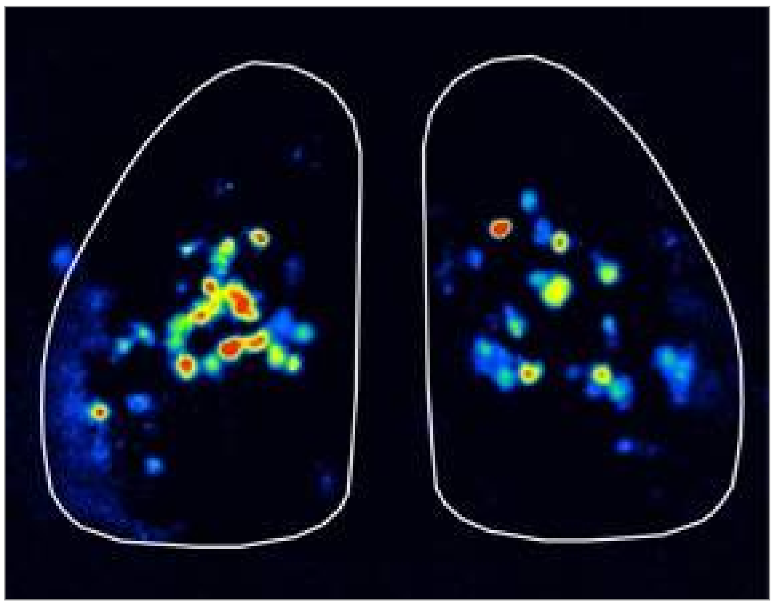
Odorants are represented by patterns of glomerular activation

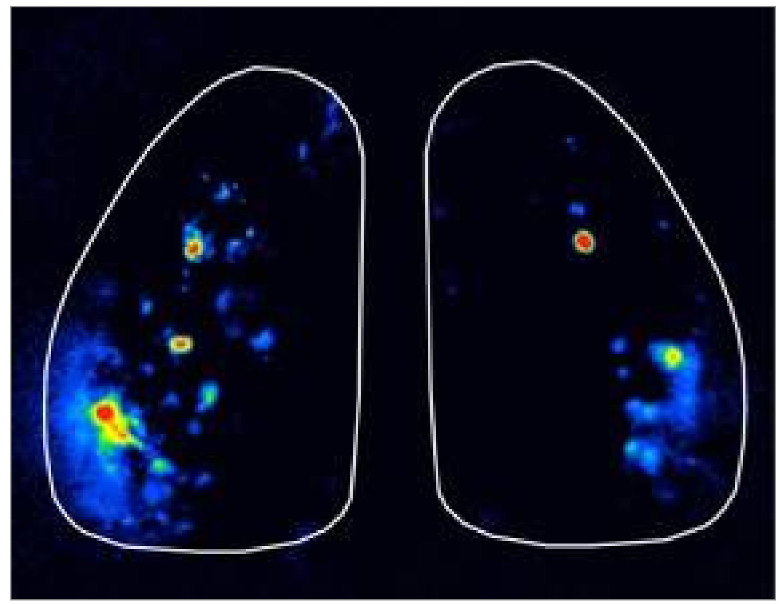
butyraldehyde



hexanone





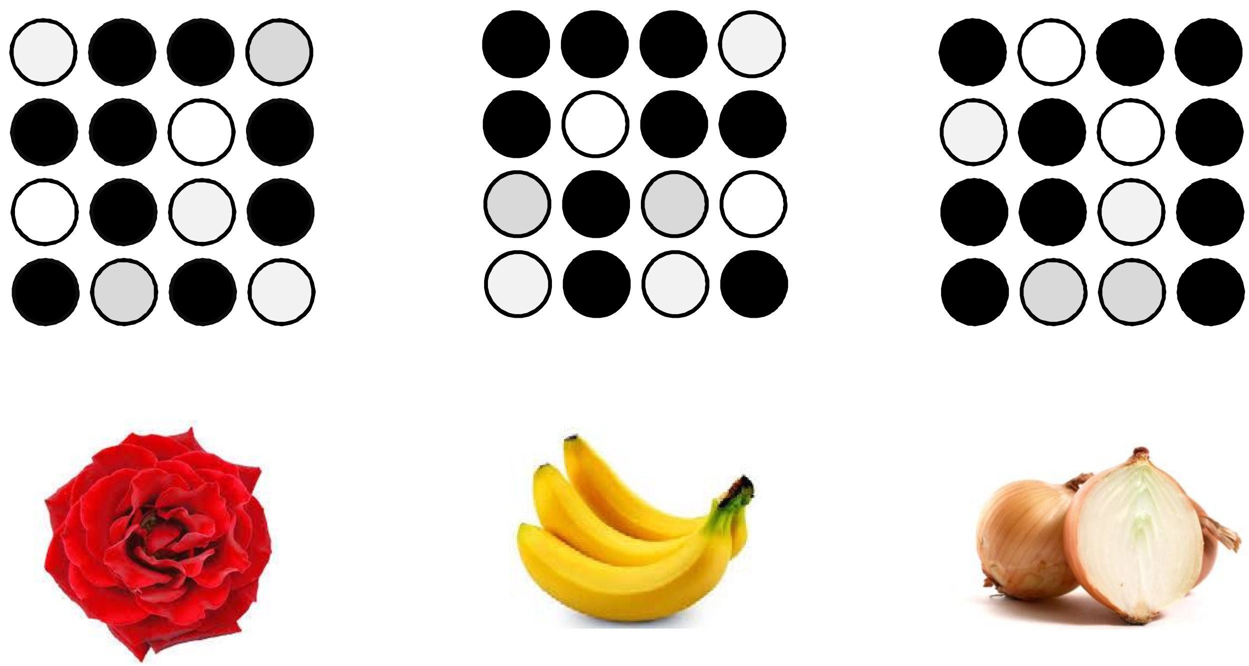


Odorant-Evoked SpH Signals
in the Mouse Olfactory Bulb

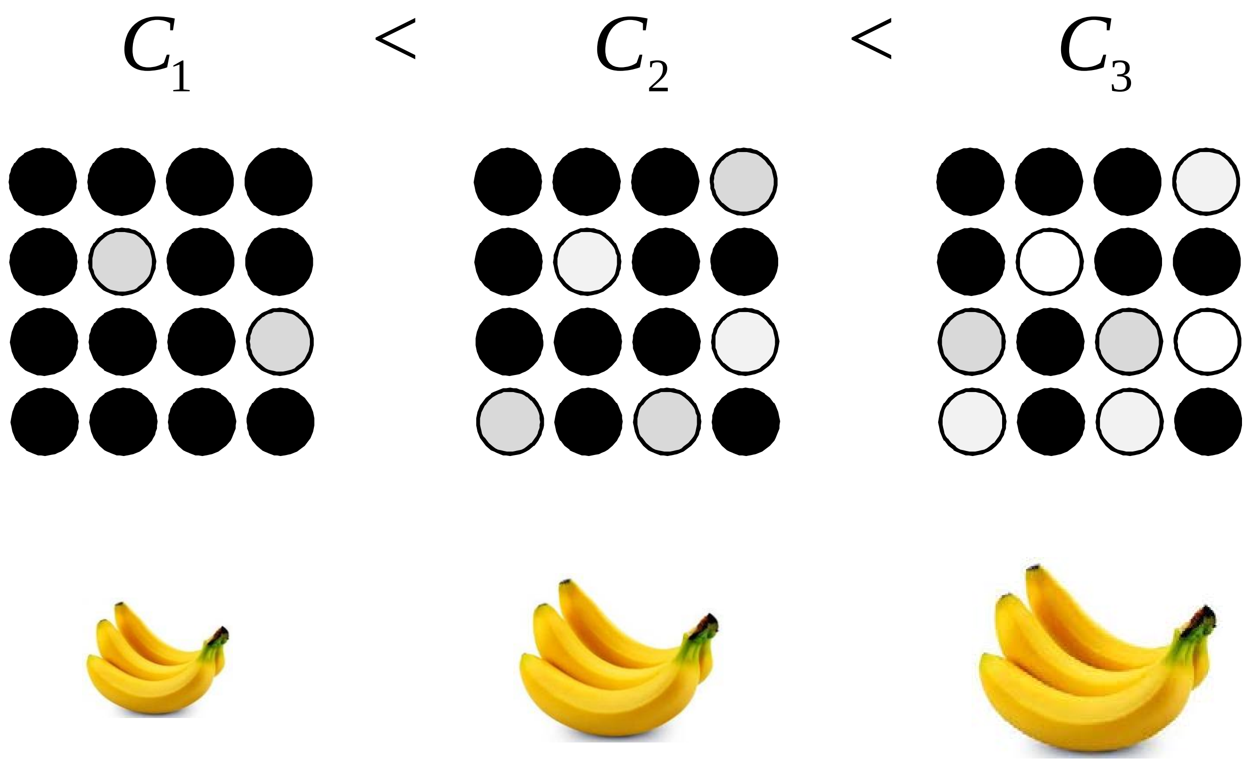
Bozza et.al., Neuron, 2004

Odorants are represented by patterns of glomerular activation

<u>Glomeruli in the olfactory bulb (OB)</u>



Odorant are represented by patterns of glomerular activation

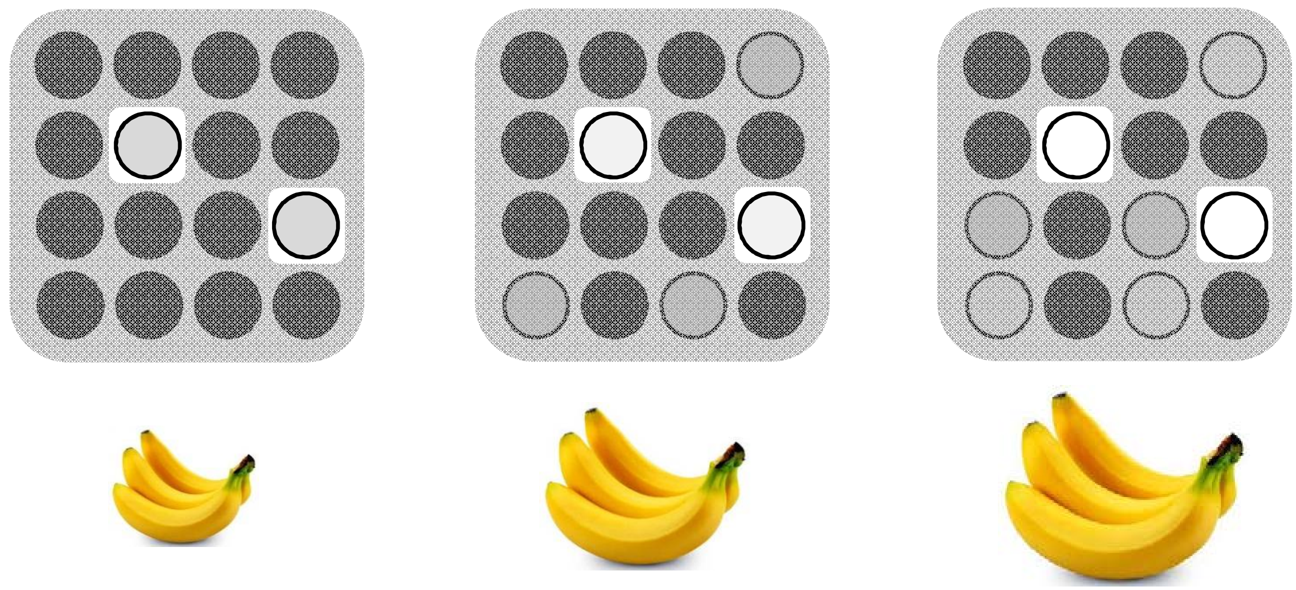


How can odor identity be constant?

Solution – primacy coding

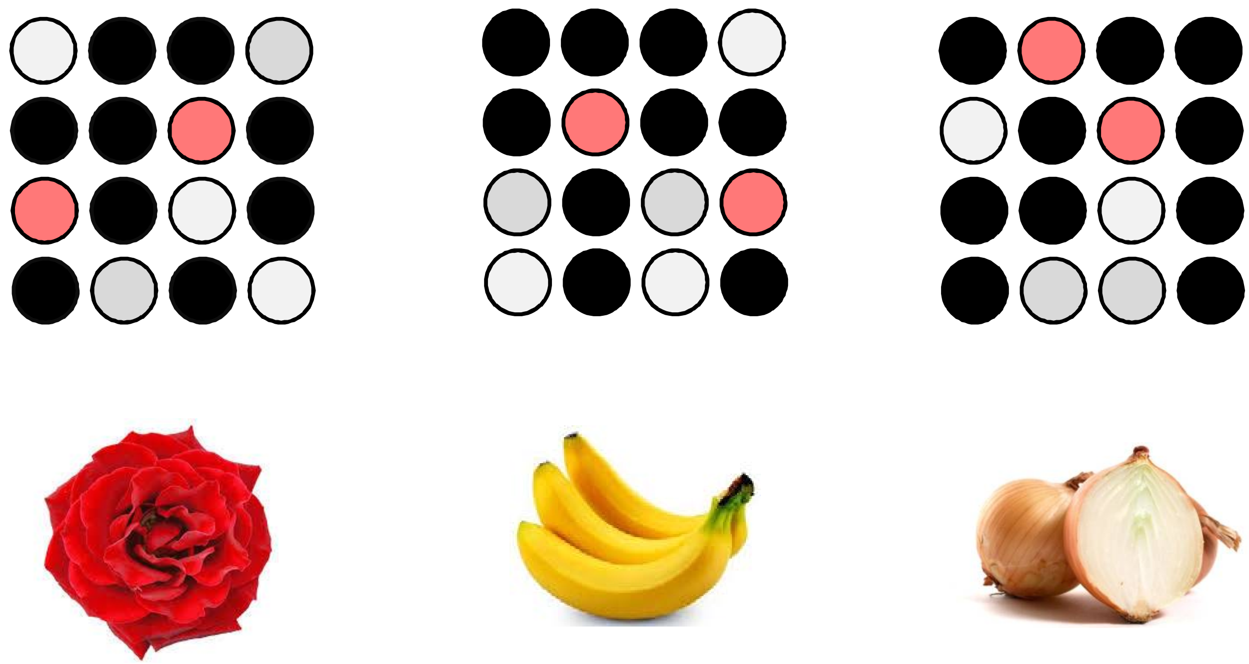
Template representing an odorant includes a very small number of glomeruli of highest affinity to the odorant (activated at the smallest concentration)

$$C_1 < C_2 < C_3$$



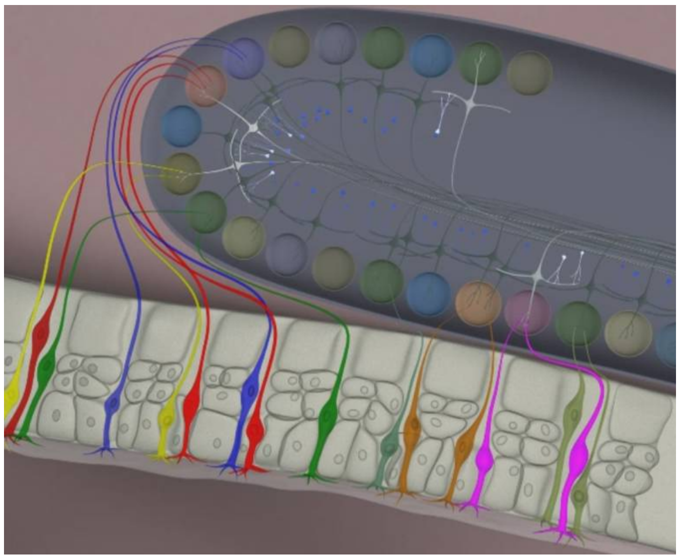
p (= 2) is an important parameter of the code

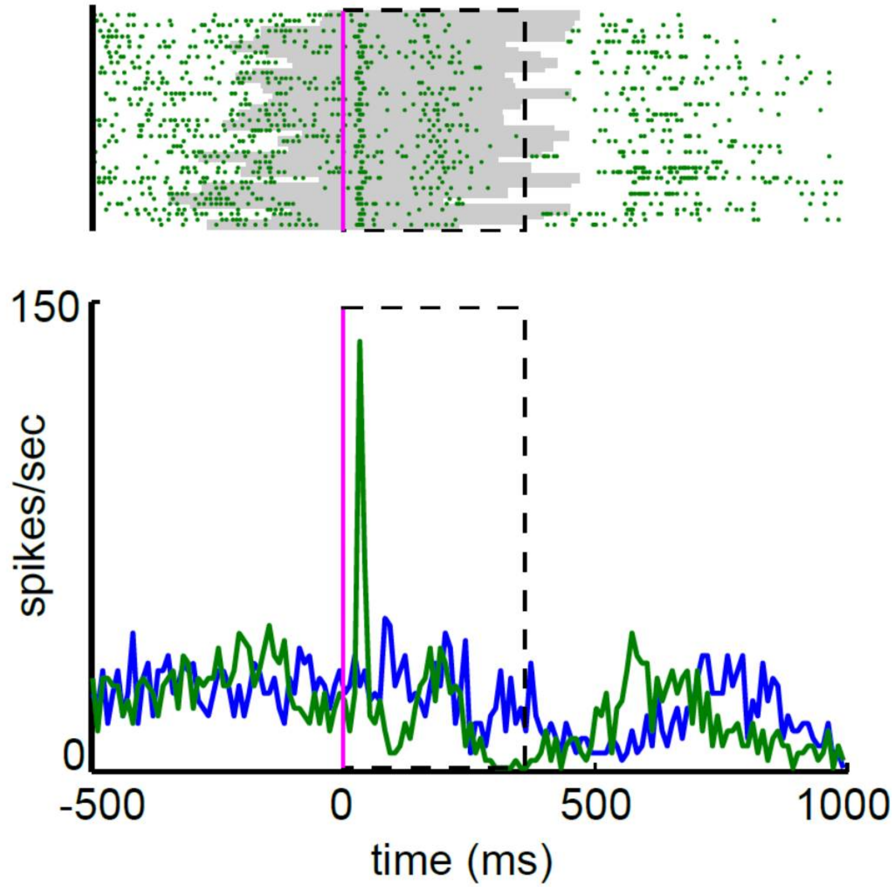
Different smells are represented by their ‘primacy’ glomeruli



Temporal codes

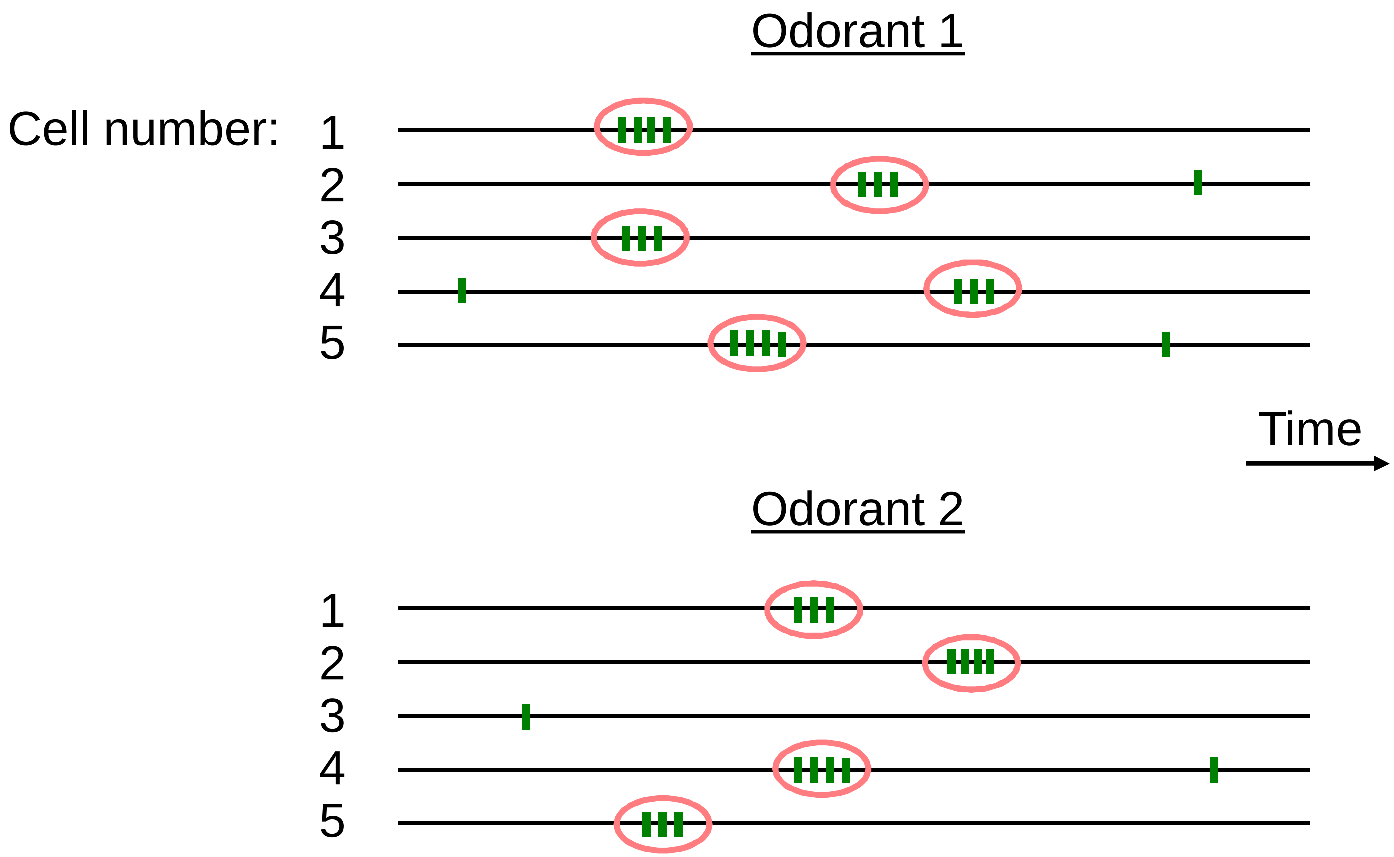
Temporal codes in the olfactory bulb



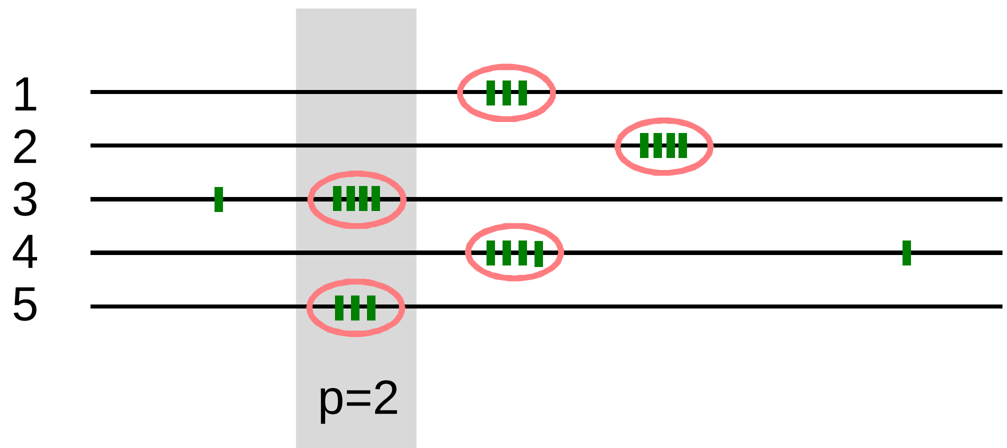


Cury and Uchida (2010)
Shusterman, Smear, Koulakov, and Rinberg (2011)

Odor identity is represented in the sequence of sharp events generated by MCs



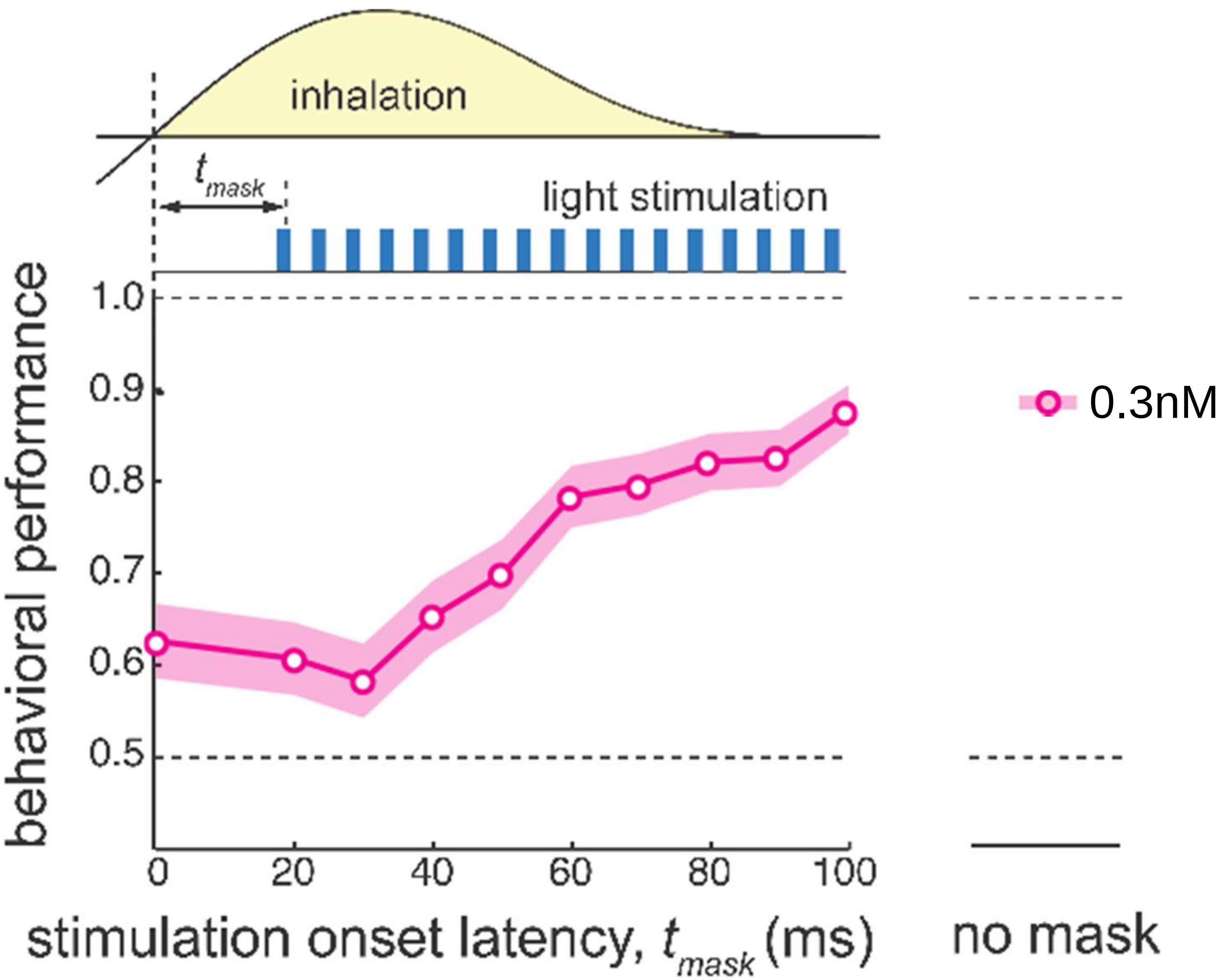
Primacy coding



First set of p active mitral cells determines odorant identity

Prediction: odor identity is determined early in the sniff cycle

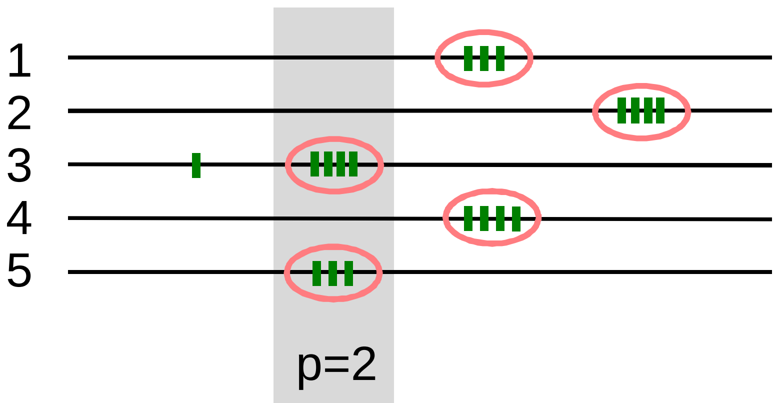
Smell A vs smell B



Chris Wilson (NYU)

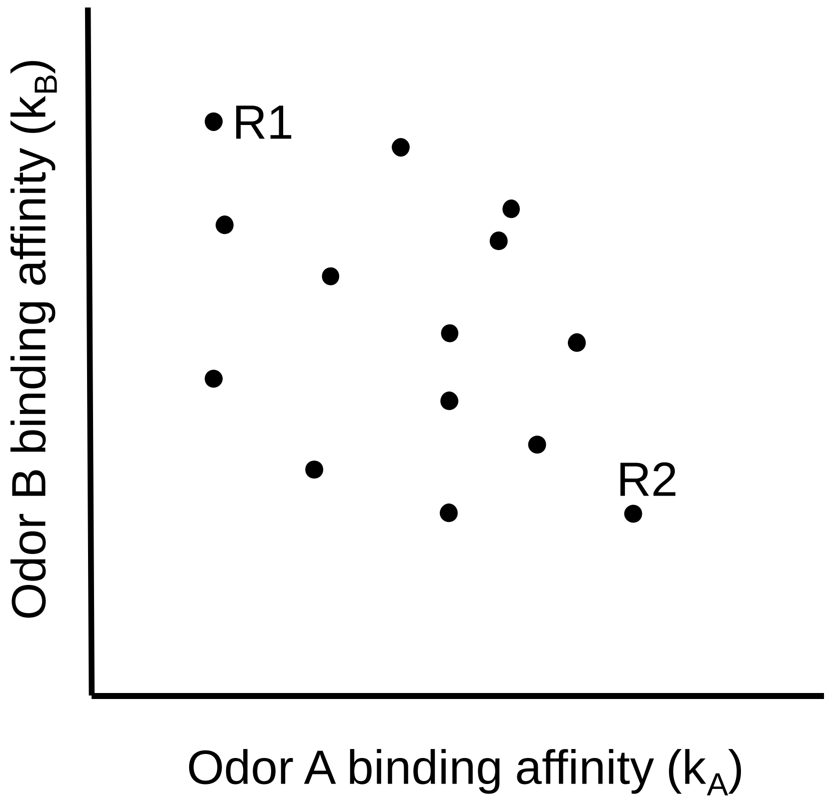
Dima Rinberg (NYU)

Primacy coding:
Shazam service for the brain?

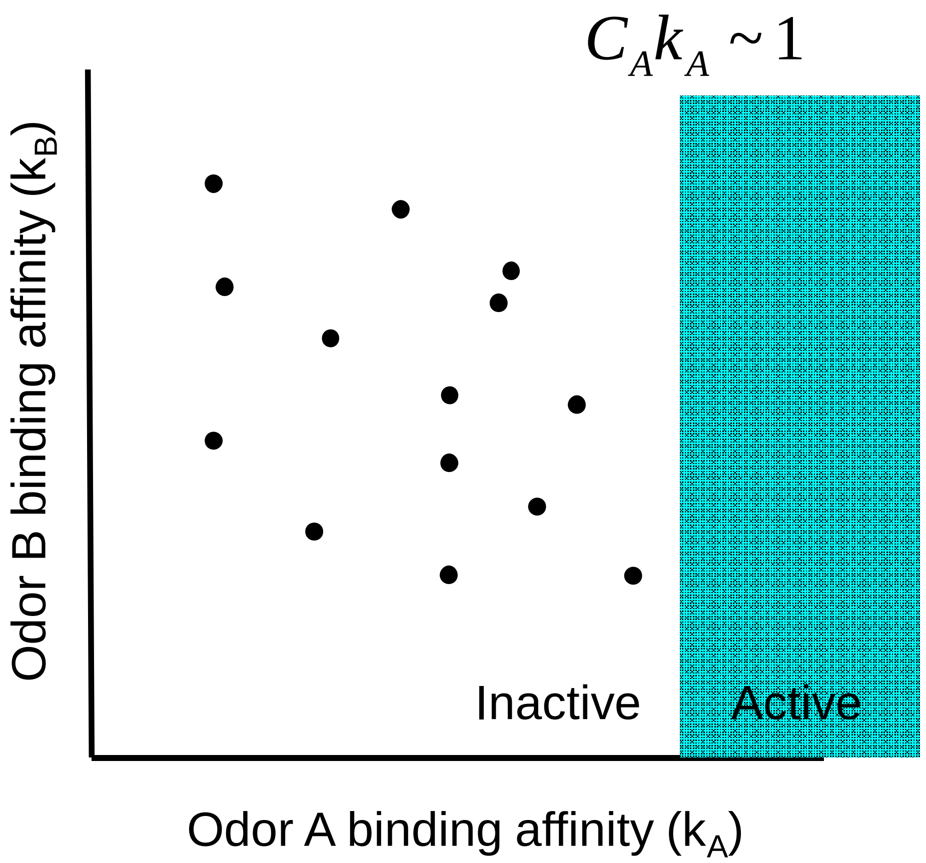


evolution of olfactory receptors

2D odorspace

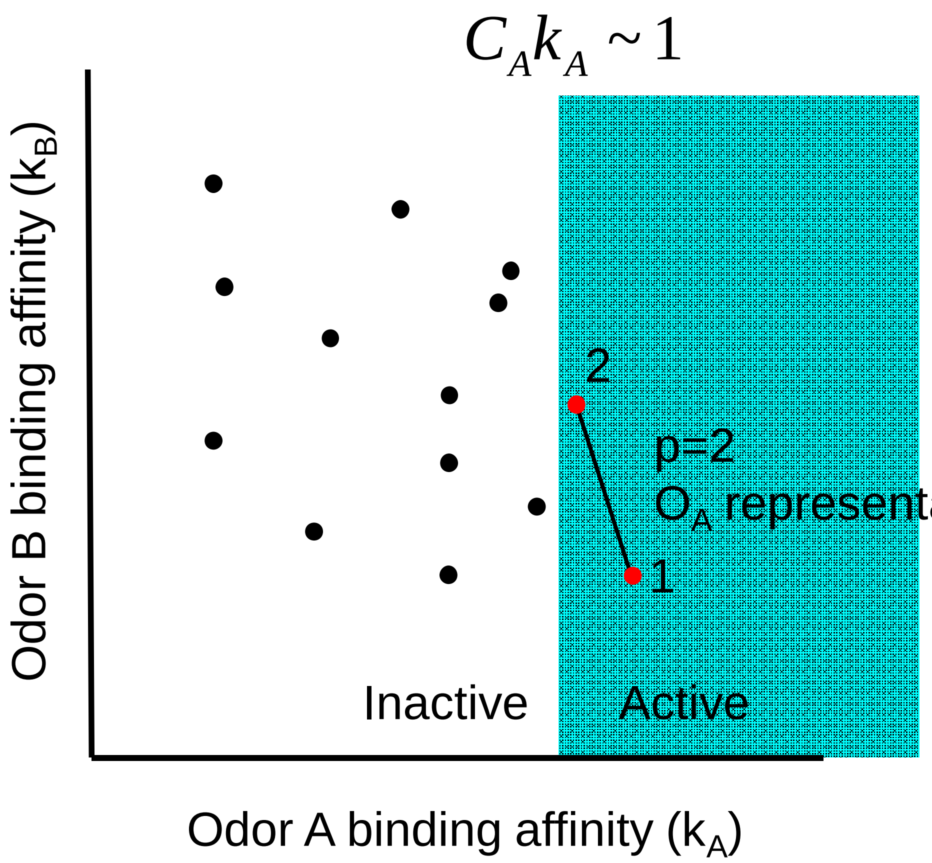


2D odorspace



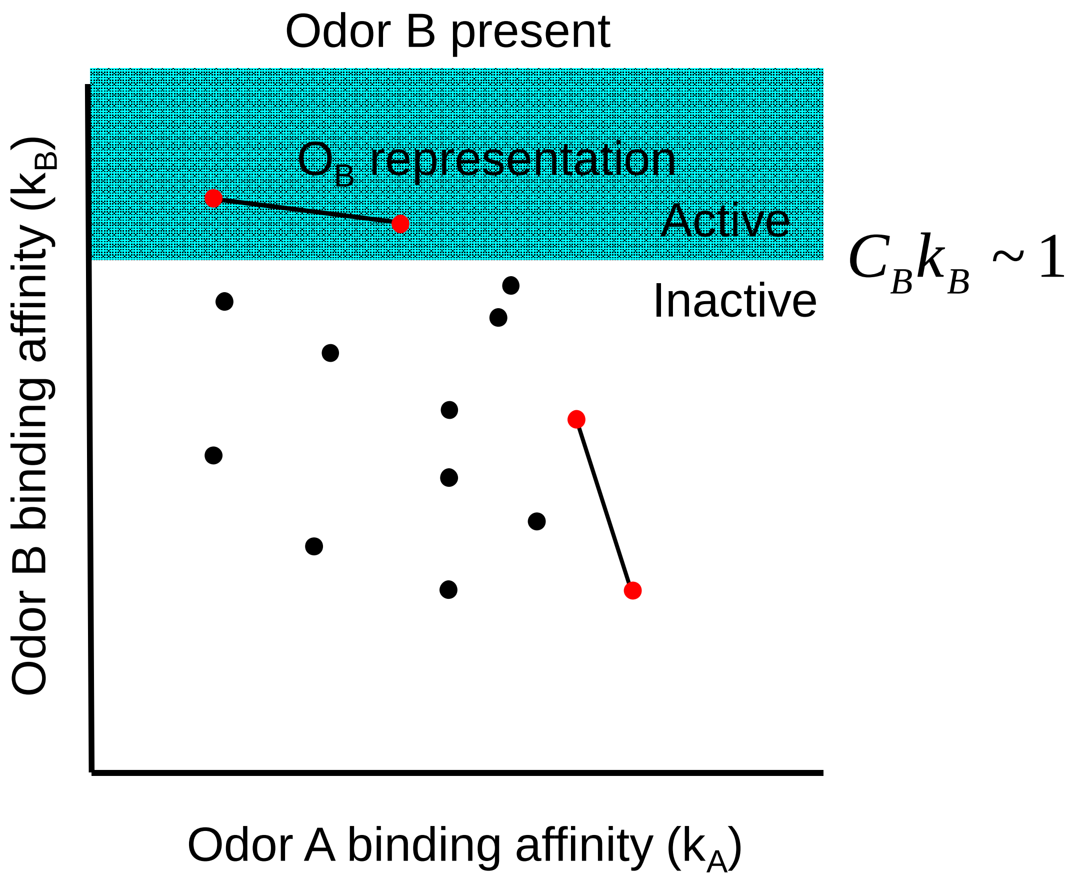
Odor A present

2D odorspace

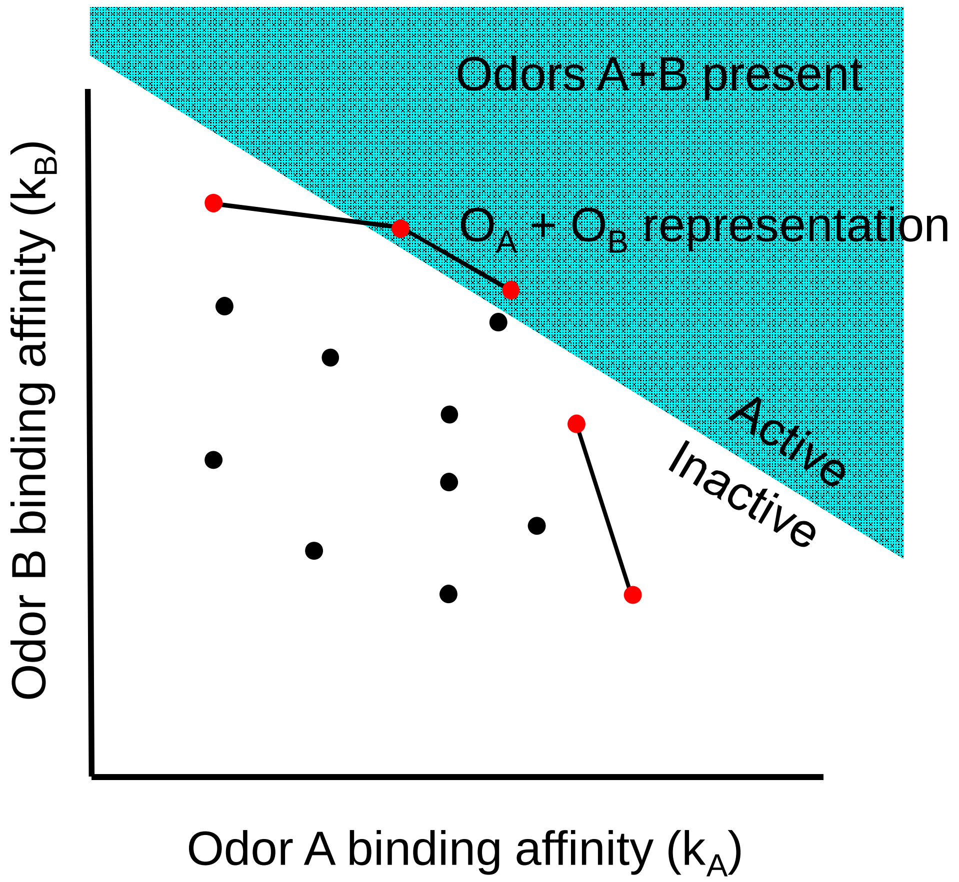


Odor A present

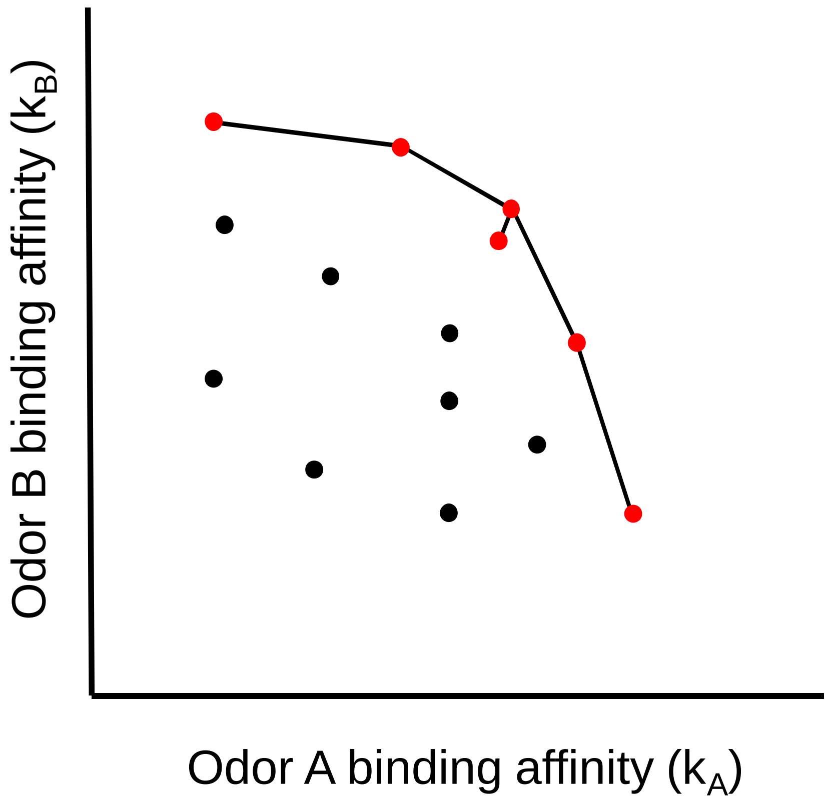
2D odorspace



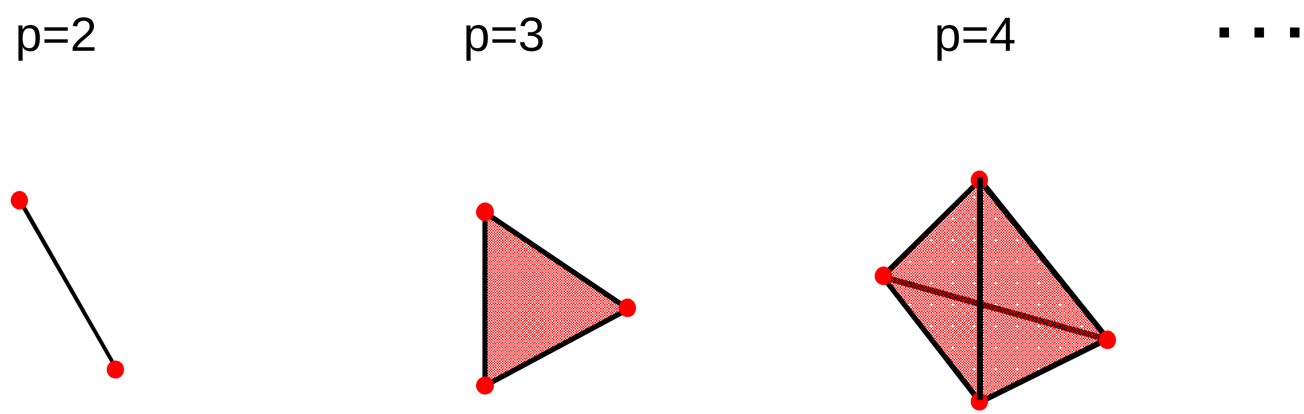
2D odorspace



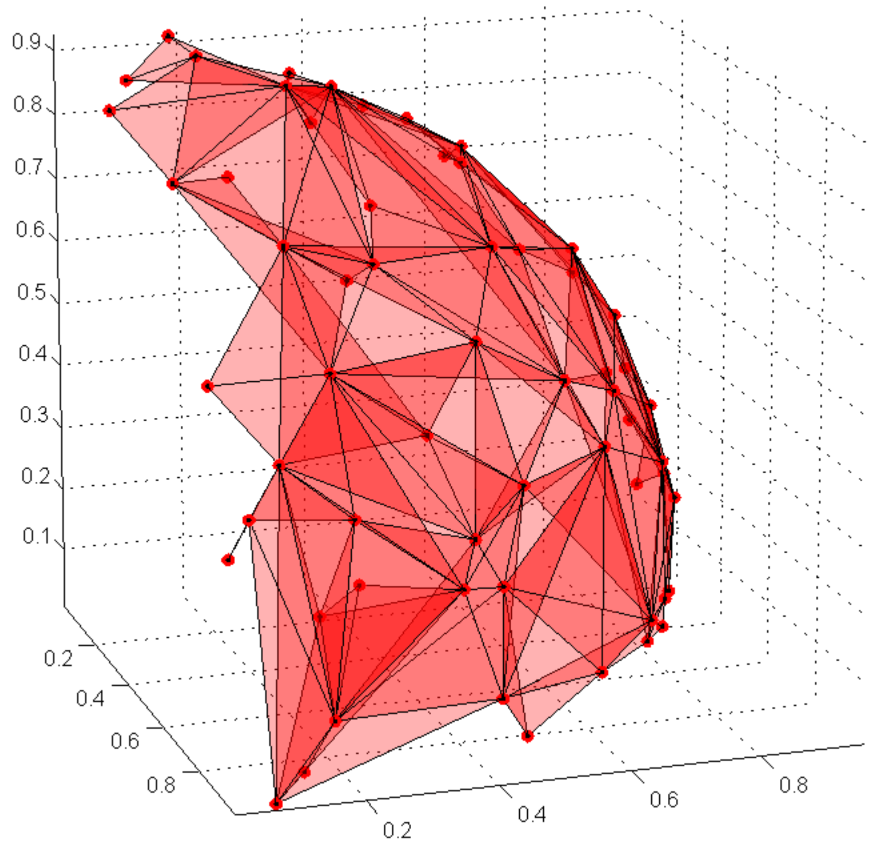
p=2 primacy model



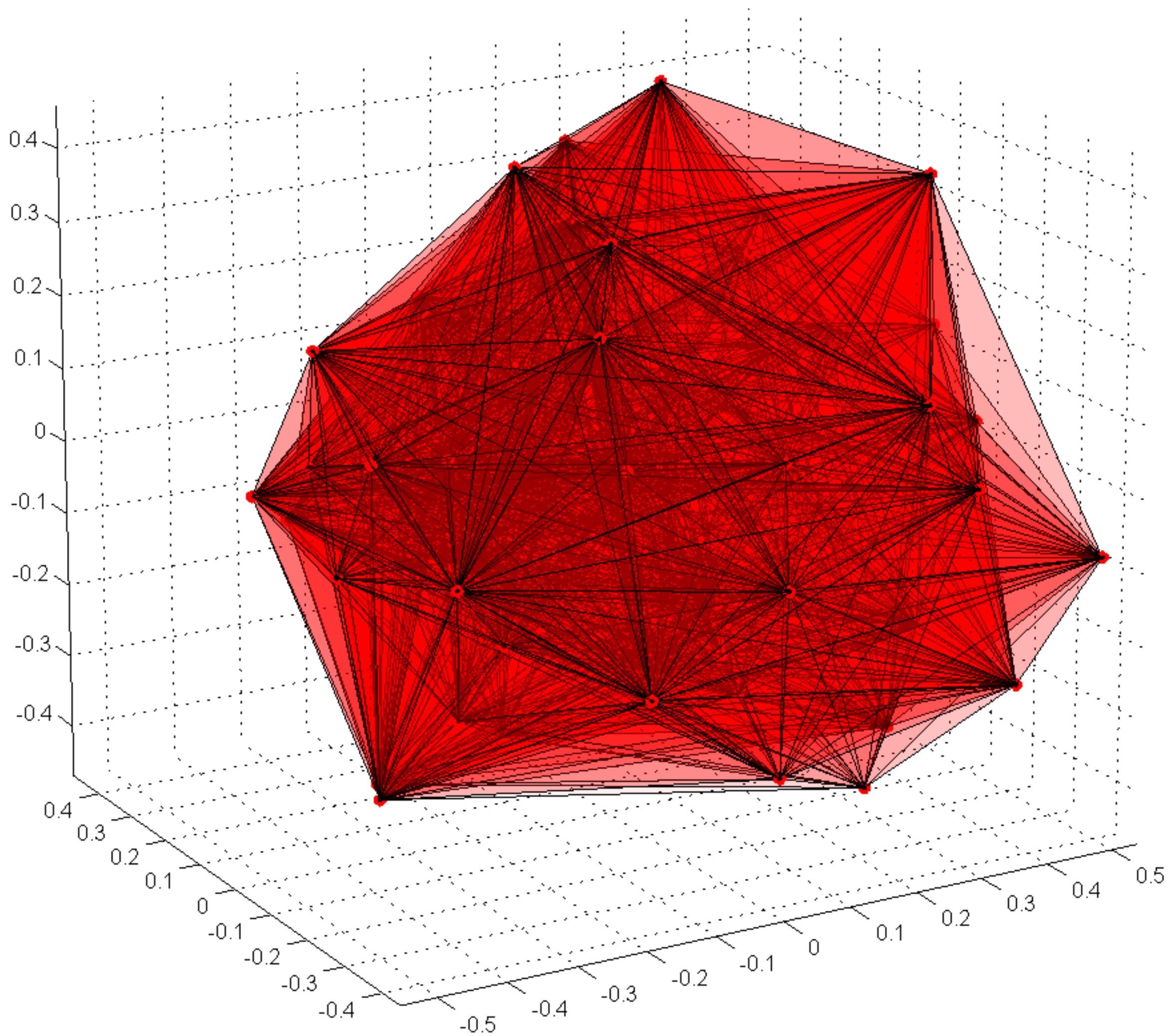
Individual odor identities are represented by simplexes



D=3, p=3 primacy hull

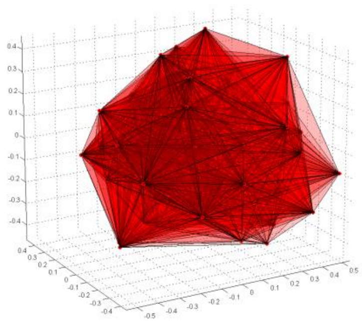


D=6, p=7 primacy hull



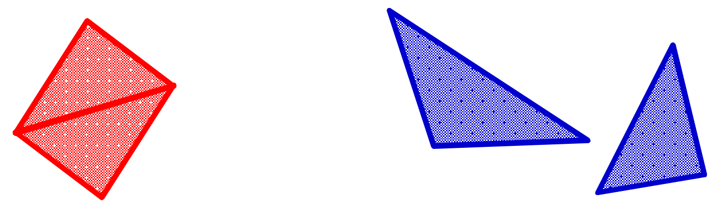
Prediction: Higher-order correlations in the response matrix

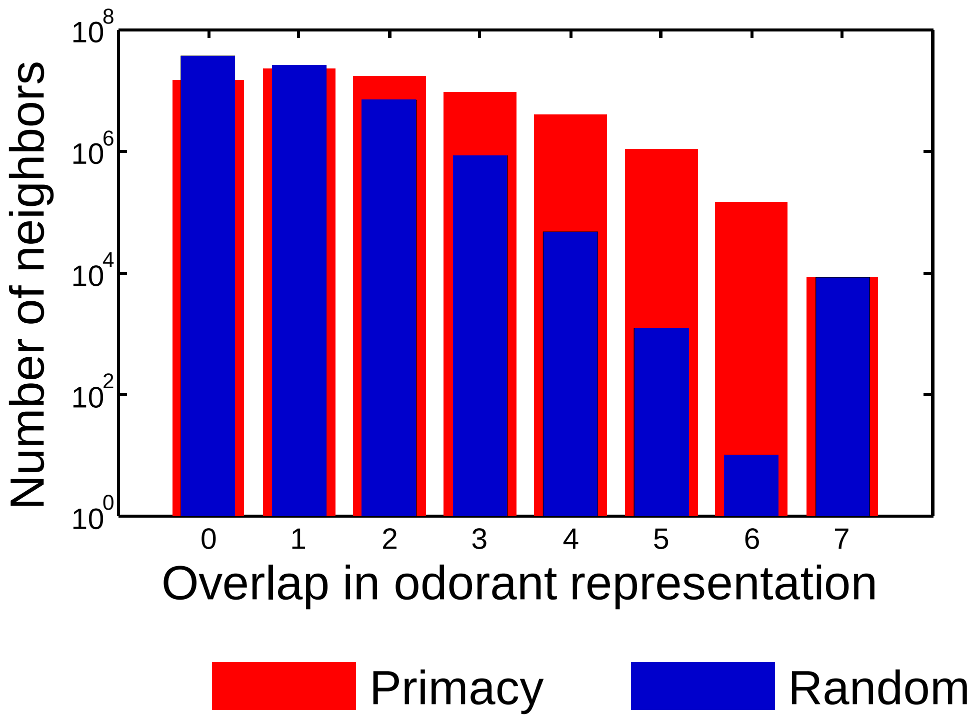
D=6, p=7
Primacy hull



Primacy

Random





Primacy structure in the response matrix

$\hat{R}_{or}$

Receptors or glomeruli

Odorants

6	4	1	2	**8**	**7**	3	5	**9**
7	6	4	**9**	5	1	**8**	3	2
8	**9**	1	**7**	3	4	6	5	2
2	**9**	4	**8**	3	**7**	6	1	5
2	3	5	**9**	4	1	**8**	**7**	6
6	1	**8**	3	**9**	2	**7**	5	4
9	**7**	6	2	4	1	5	**8**	3
6	1	2	3	**7**	**9**	**8**	5	4
5	**8**	**7**	3	**9**	4	2	1	6
8	5	3	1	**7**	**9**	6	2	4

p = 3

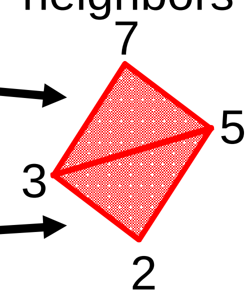
→

$\hat{S}_{or}$

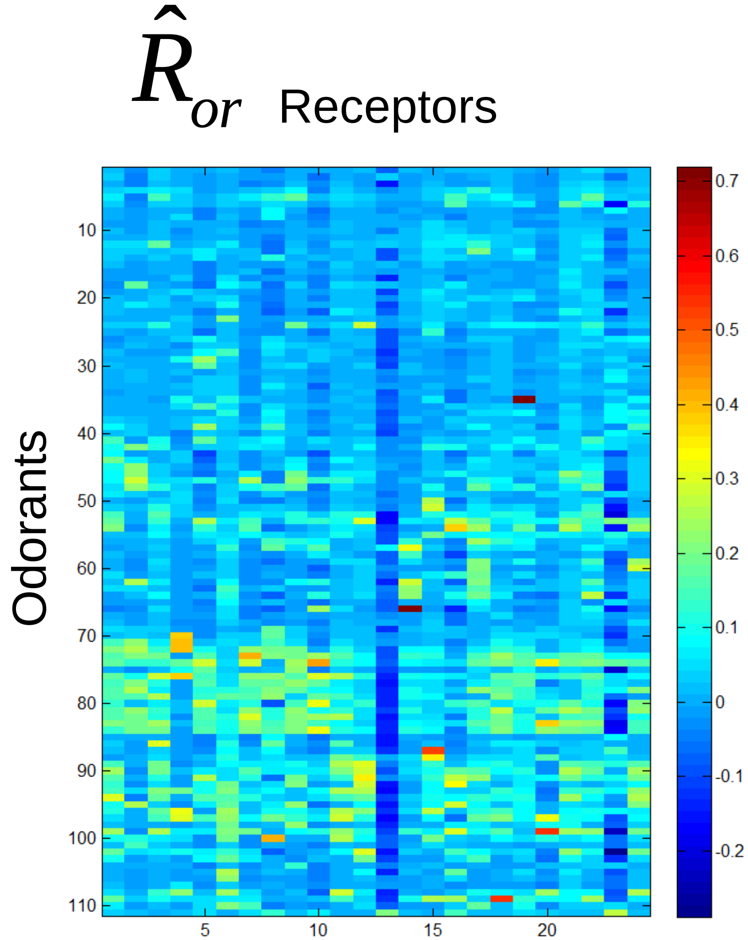
Receptors or glomeruli

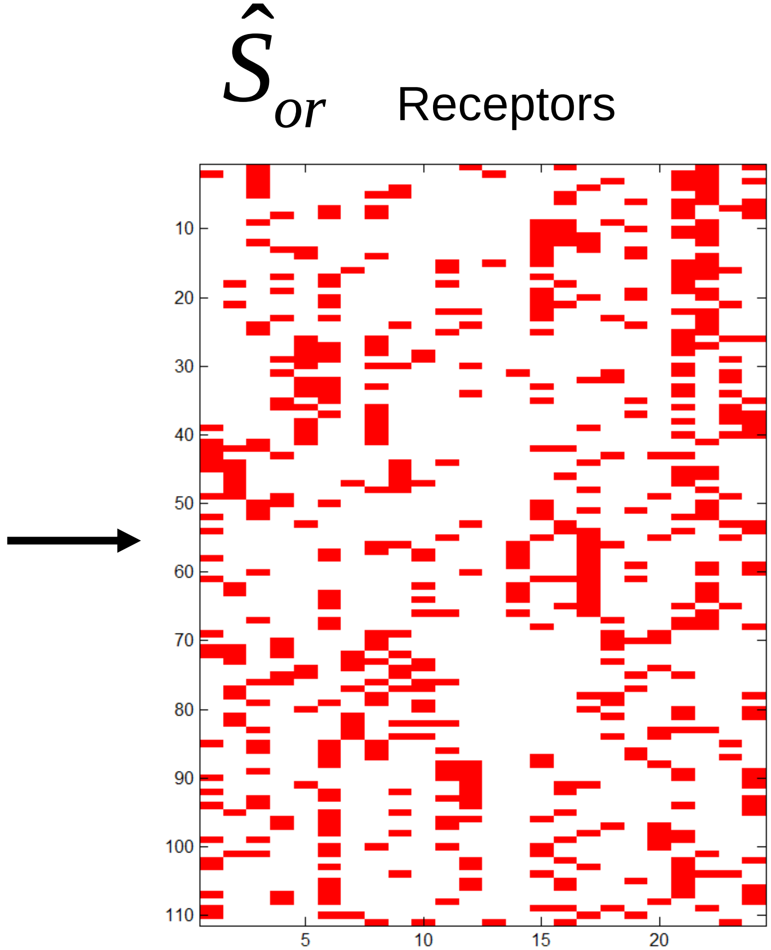
0	0	0	0	**1**	**1**	0	0	**1**
1	0	0	**1**	0	0	**1**	0	0
1	**1**	0	**1**	0	0	0	0	0
0	**1**	0	**1**	0	**1**	0	0	0
0	0	0	**1**	0	0	**1**	**1**	0
0	0	**1**	0	**1**	0	**1**	0	0
1	**1**	0	0	0	0	0	**1**	0
0	0	0	0	**1**	**1**	**1**	0	0
0	**1**	**1**	0	**1**	0	0	0	0
1	0	0	0	**1**	**1**	0	0	0
1	2	3	4	5	6	7	8	9

Nearest neighbors

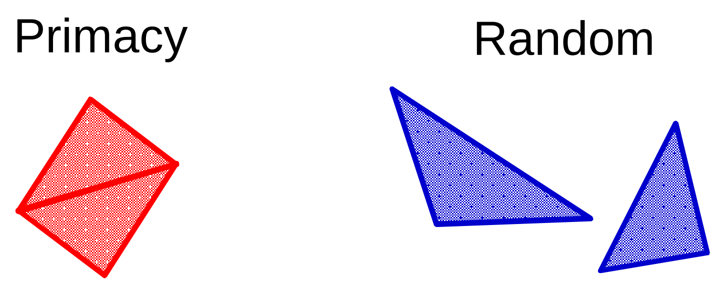


Fly data: Hallem and Carlson (2006)

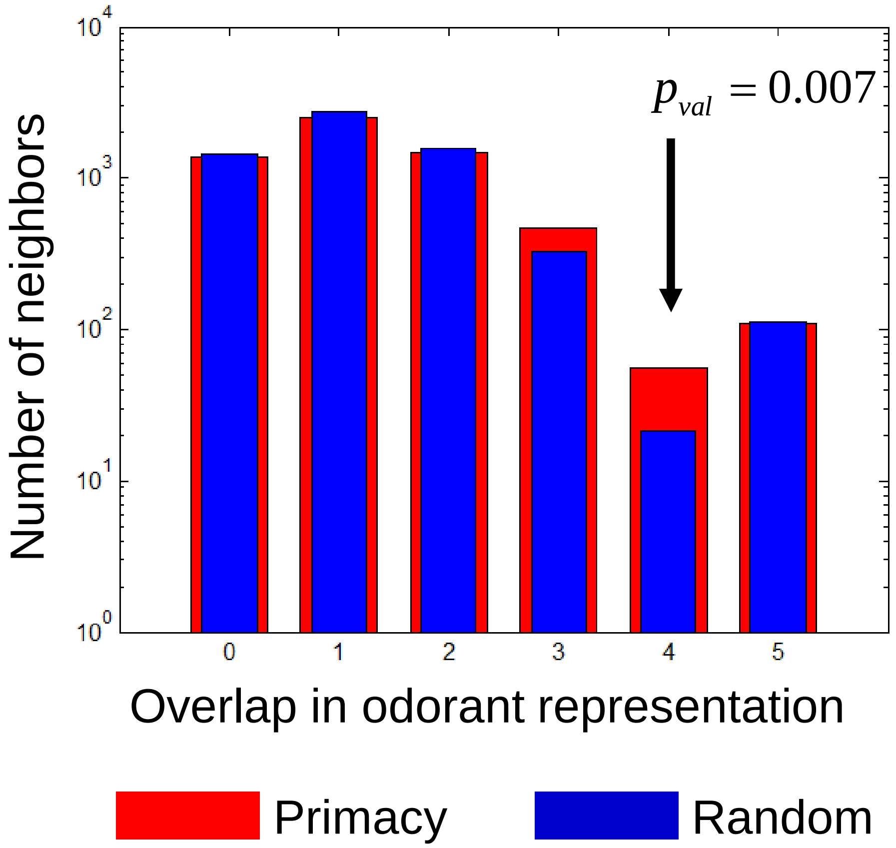




Number of nearest neighbors, p=5



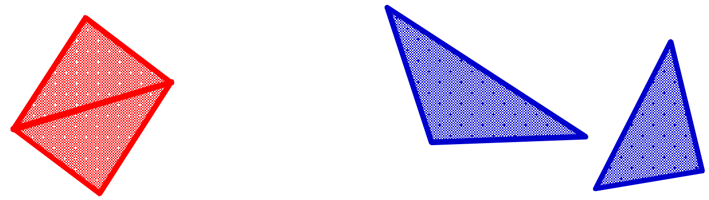
Hamza
Giaffar



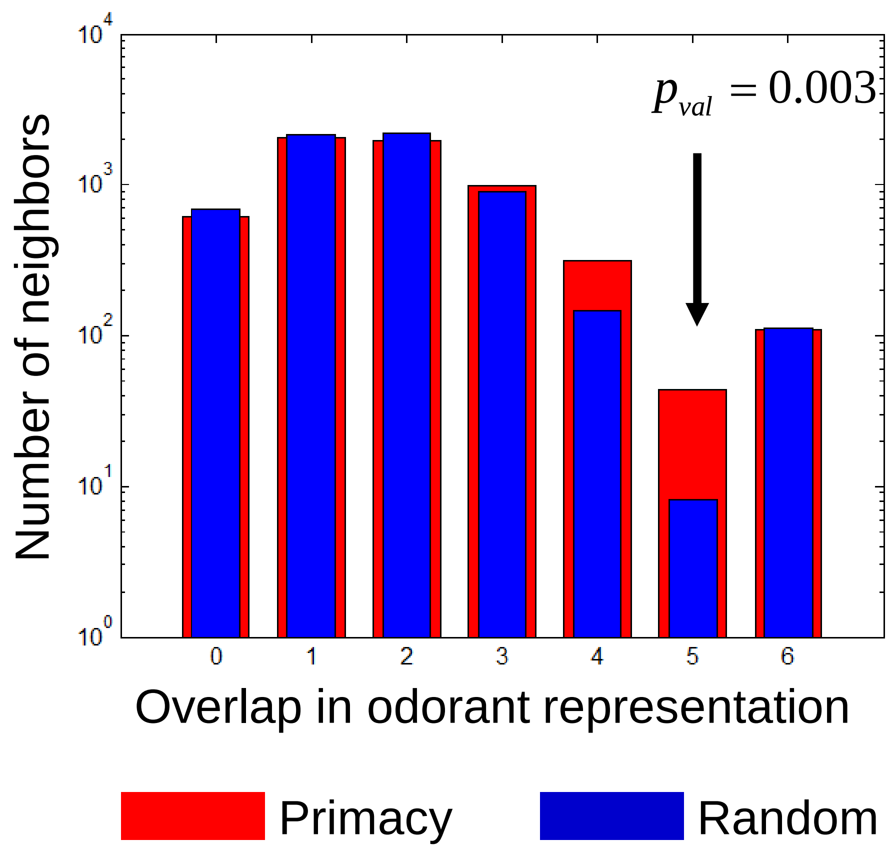
Number of nearest neighbors, p=6

Primacy

Random



Hamza
Giaffar



Conclusions
(OR evolution model)

- Primacy model predicts that OR affinities occupy a narrow shell called primacy hull.

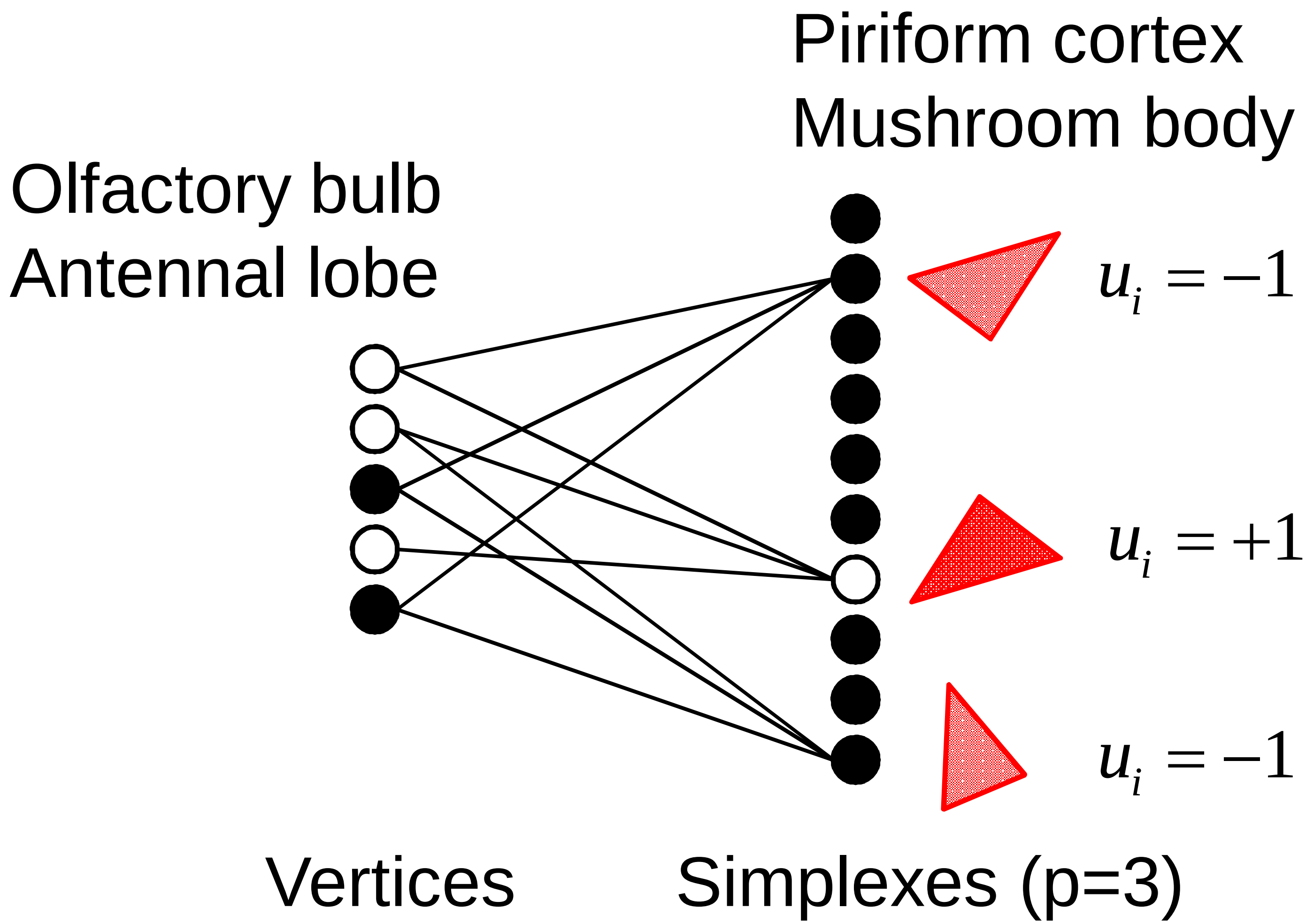
- Topmost p responses of olfactory receptors share substantial overlaps

- Increased overlaps are present in fly data (p=5)

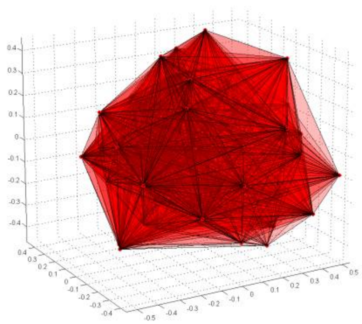
- These findings suggest substantial higher-order correlations in OR responses

Network models

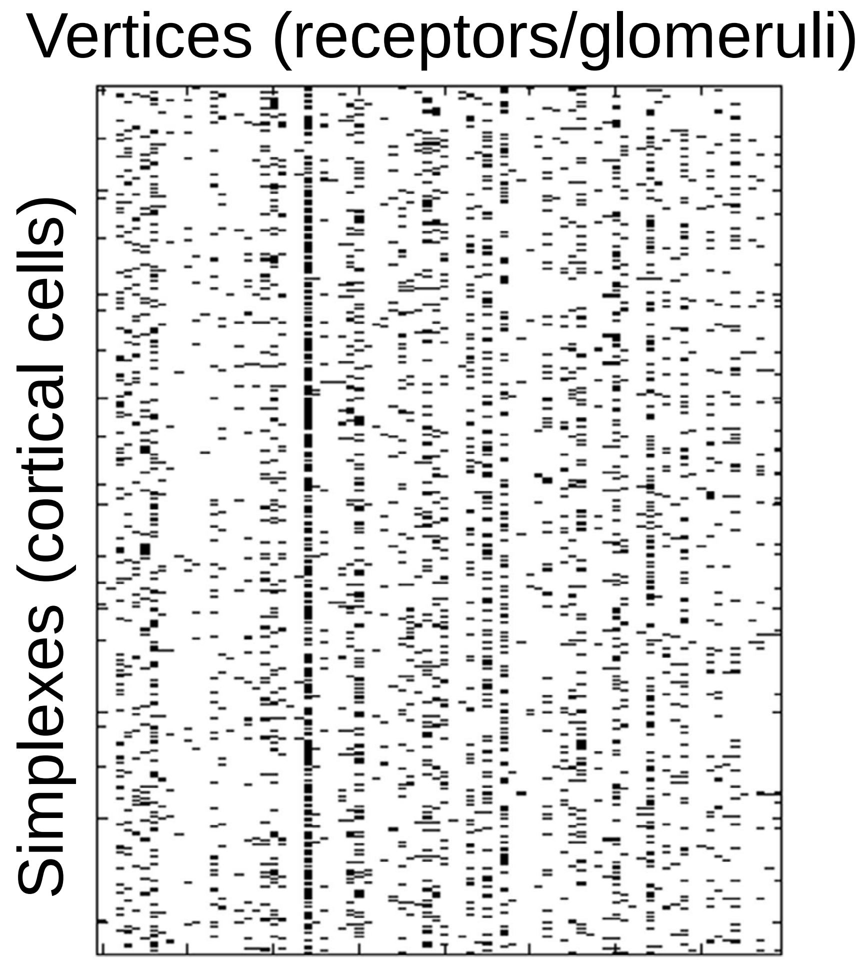
Expand, sparsen, and decorrelate



Connectivity between glomeruli and simplexes is given by the simplectic matrix



$$\hat{S} =$$

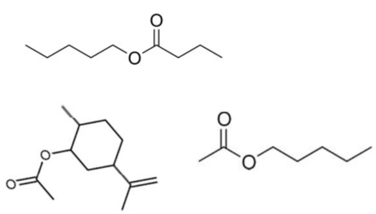


Dual networks

How does decoding work?

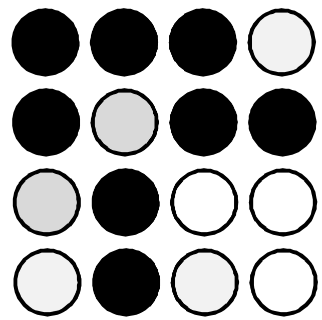
Stimulus

$\vec{x}$



Glomerular responses

$\vec{y} = K\vec{x}$



??

Cortical representation

$\tilde{x}$

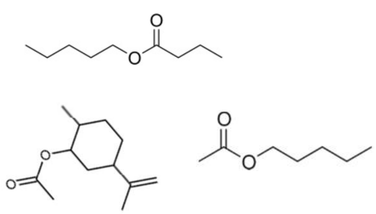
$$\tilde{x} \leftarrow \min_{y=K\tilde{x}} \left\| \tilde{x} \right\|_{\alpha}$$

α=1: Compressed sensing

Primacy (relativity) principle

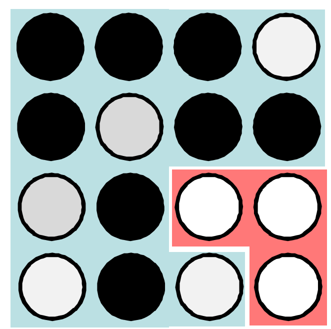
Stimulus

$\vec{x}$



Glomerular responses

$\vec{y} = K\vec{x}$



$\bar{P}$ P

??

Cortical representation

$\tilde{x}$

$$\tilde{x} \leftarrow \min \left\| \tilde{x} \right\|_{\alpha}$$

$$\sum_n S_{Pn} y_n \geq \sum_n S_{\bar{P}n} y_n$$

Non-parametric conditions:
Intensity invariance

Non-parametric problem:

$$\tilde{x} \leftarrow \min \|\tilde{x}\|_{\alpha}, \qquad \sum_n S_{Pn} y_n \geq \sum_n S_{\bar{P}n} y_n$$

Fix the scale:

$$\tilde{x} \leftarrow \min \|\tilde{x}\|_{\alpha}, \qquad \sum_n S_{Pn} y_n \geq \varepsilon \geq \sum_n S_{\bar{P}n} y_n$$

Single condition:

$$\tilde{x} \leftarrow \min \|\tilde{x}\|_{\alpha}, \qquad u_s(\sum_n S_{sn} y_n - \varepsilon) \geq 0$$

$$u_s = \begin{cases} +1, & s \in P \\ -1, & s \in \bar{P} \end{cases}$$

Primary problem is difficult to implement:

$$\tilde{x} \leftarrow \min \left\| \tilde{x} \right\|_{\alpha}, \quad u_s \left(\sum_n S_{sn} y_n - \varepsilon \right) \geq 0 \qquad u_s = \begin{cases} +1, & s \in P \\ -1, & s \in \overline{P} \end{cases}$$

$$y_n = \sum_m K_{nm} \tilde{x}_m$$

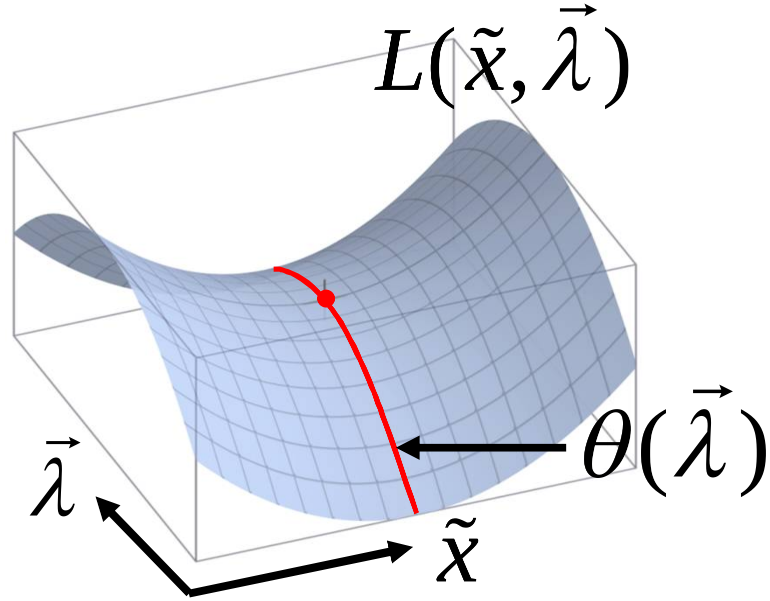
Lagrangian (Karush-Kuhn-Tucker):

$$L(\tilde{x}, \vec{\lambda}) = \left\| \tilde{x} \right\|_{\alpha} - \sum_s \lambda_s u_s \left(\sum_n S_{sn} y_n - \varepsilon \right) \qquad \lambda_n \geq 0$$

Duality: Lagrange coefficients become variables

Dual cost-function:

$$\theta(\vec{\lambda}) = \min L(\tilde{x}, \vec{\lambda})$$



Dual problem:

$$\vec{\lambda} \leftarrow \max \theta(\vec{\lambda})$$

$$\lambda_n \geq 0$$

$$\overset{\tilde{x} = \tilde{x}(\vec{\lambda})}{\Longleftrightarrow}$$

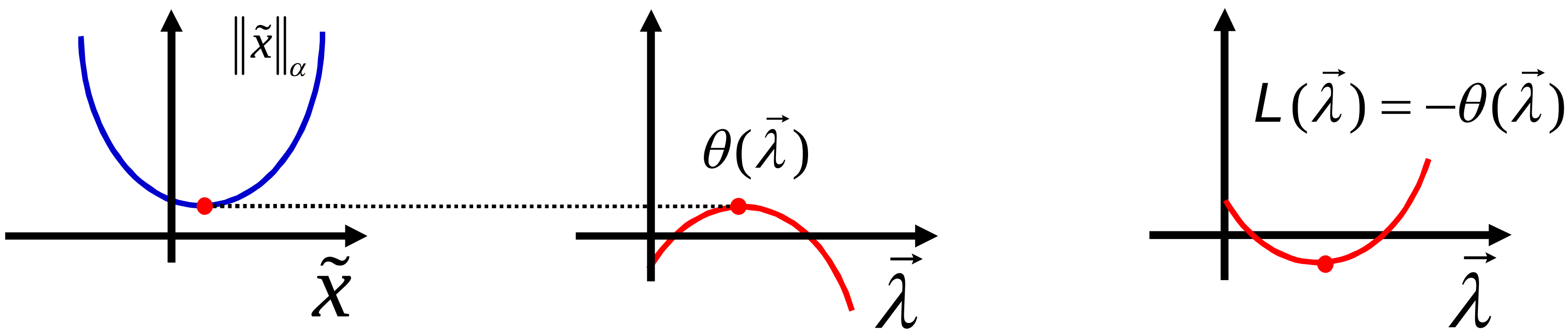
Primal problem:

$$\tilde{x} \leftarrow \min \|\tilde{x}\|_\alpha ,$$

+ a bunch of very complex inequalities

Dual problem can be easily solved by a neural network

<u>Primal problem:</u> <u>Dual problem:</u> <u>Network Lyapunov function:</u>



+ a bunch of very complex inequalities

$\lambda_n \geq 0$

$\lambda_n \geq 0$

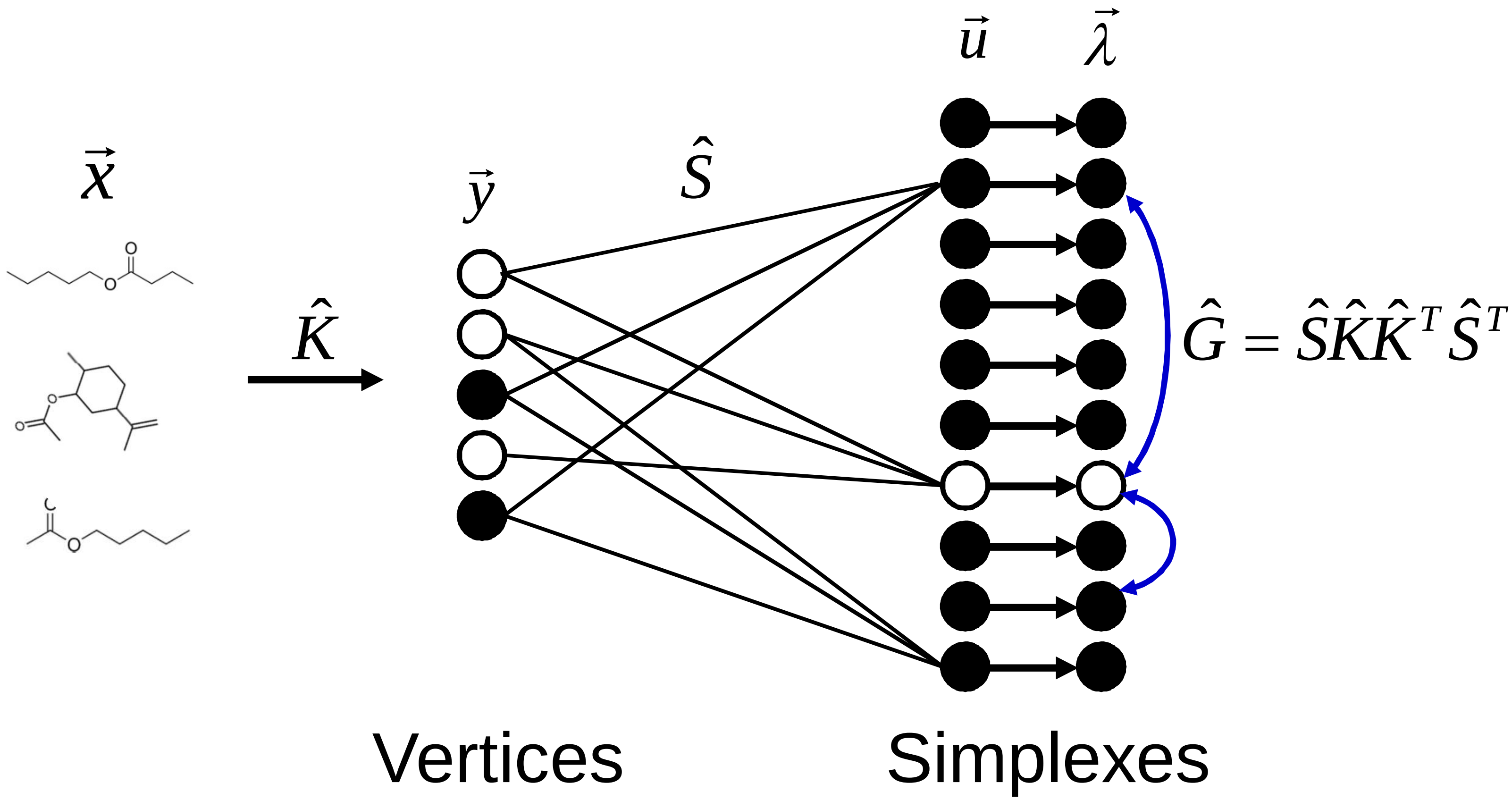
$$L(\vec{\lambda}) = -\varepsilon \sum_s u_s \lambda_s - \frac{1}{2} \sum_{sq} \lambda_s u_s G_{sq} u_q \lambda_q$$

$$\hat{G} = \hat{S}\hat{K}\hat{K}^T\hat{S}^T$$

Feedforward inputs

Feedback

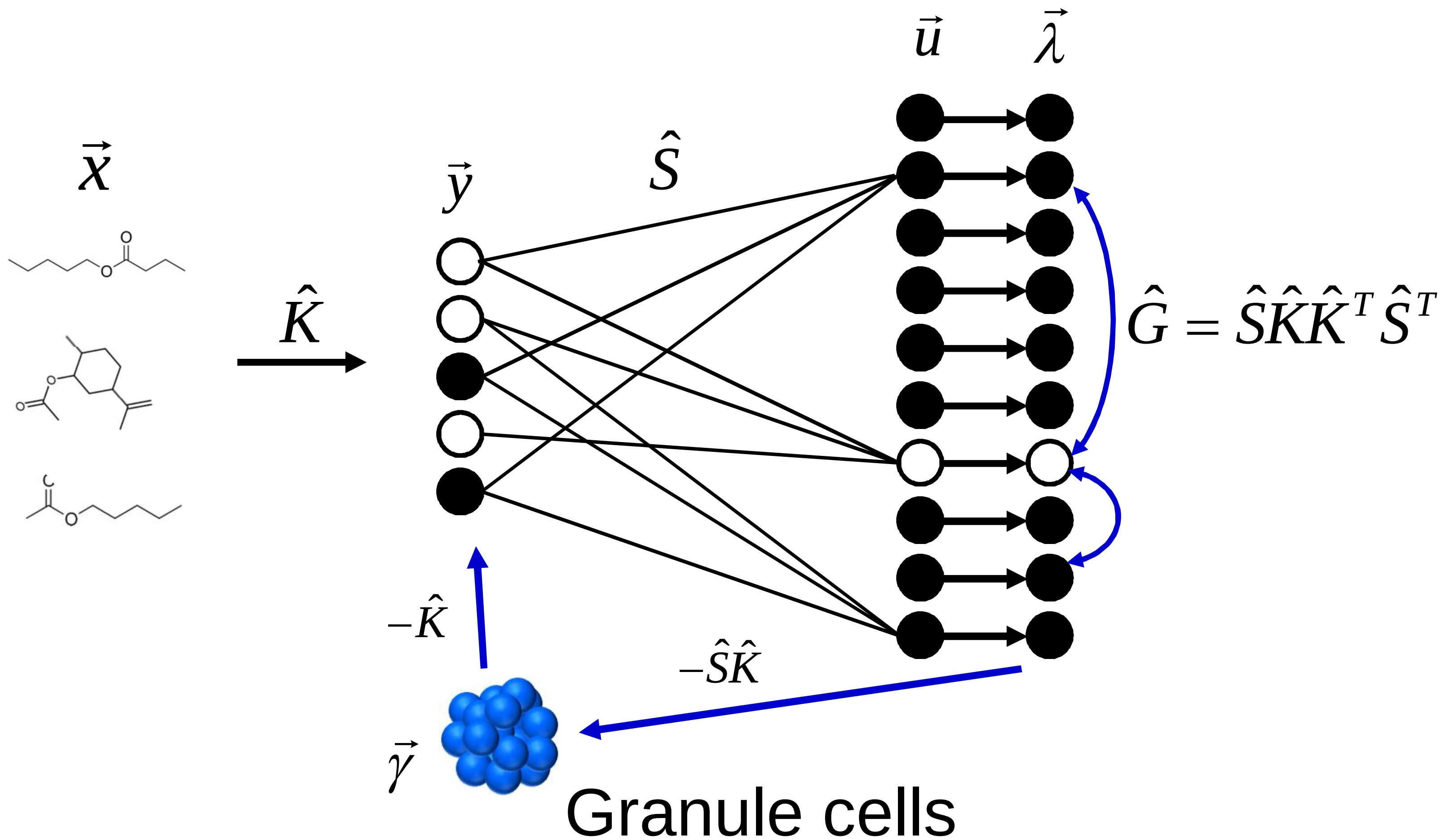
Dual network



Non-negativity constraint, $x_n \geq 0$

$$L(\tilde{x},\vec{\lambda}) = \|\tilde{x}\|_\alpha - \sum_s \lambda_s u_s (\sum_n S_{sn} y_n - \varepsilon) - \sum_n \gamma_n x_n$$

$$\lambda_n, \gamma_n \geq 0$$



Features of dual networks:

- Operate with Lagrange-Karush-Kuhn-Tucker multipliers rather than with original stimulus variables
- Rely on inequalities -> intensity-invariant encoding
- Implement inequalities easily $(\lambda_n \geq 0)$
- Sparse activity vectors
- New set of inequalities -> new set of λ-s -> new cell type

Conclusions:

- Primacy model: small number of receptors activated first code for odorant identity

- More general idea – neural relativity – the implementation of invariant stimulus percepts in dual networks.

Thanks to:

Collaborators:

Olfaction
- Dima Rinberg (NYU)
- Roman Shusterman (Haifa)
- Florin Albeanu (CSHL)
- Steve Shea (CSHL)
- Venki Murthy (Harvard)
- John Lisman (Braindeis)

Lab Members
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- Yi Wei
- Daniel Kepple
- Hamza Giaffar

Animation
- Dancing-lemon-studio.com

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THE SWARTZ FOUNDATION

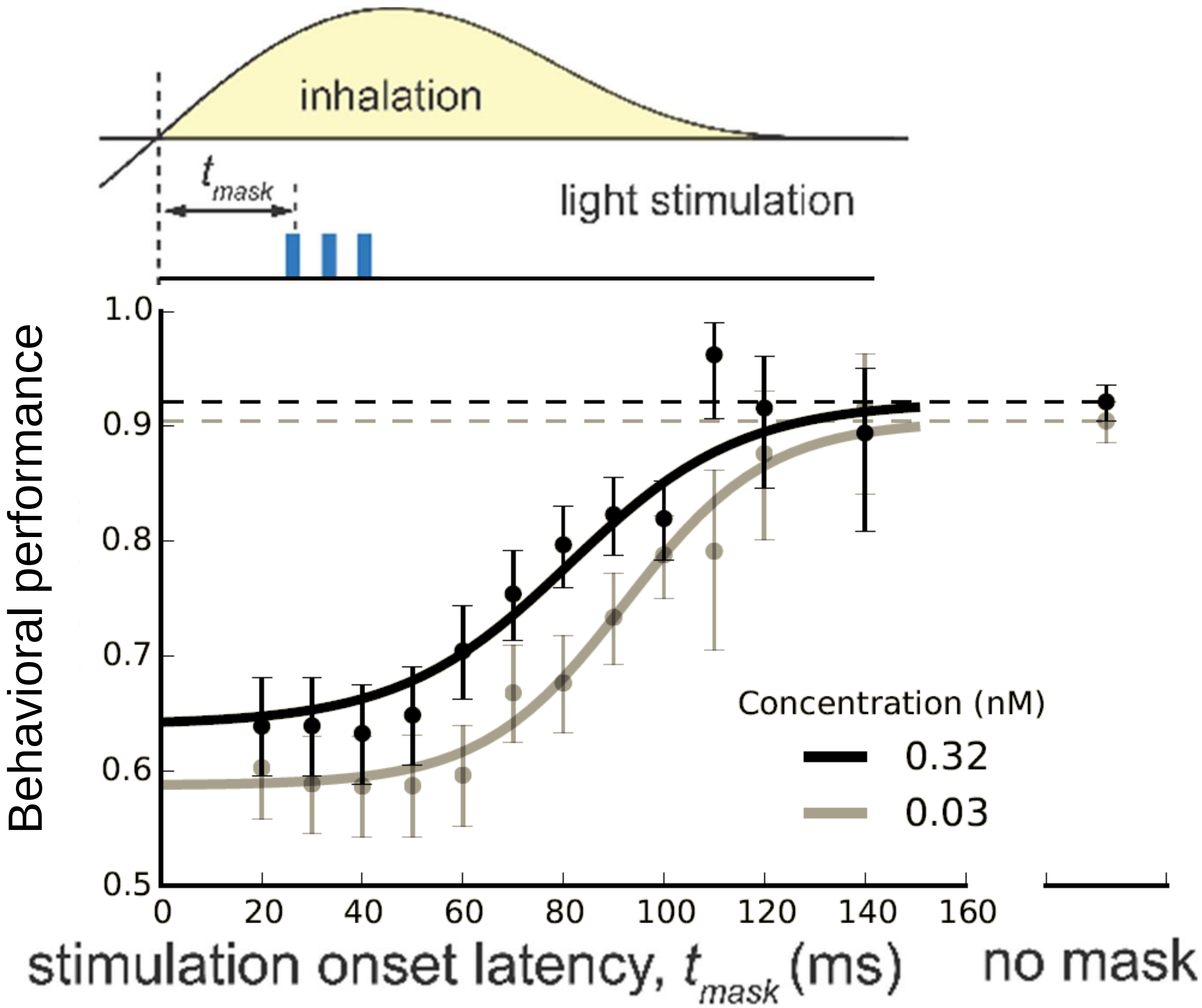
NIMH
National Institute of Mental Health

National Eye Institute
NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE ON AGING
National Institutes of Health

NYSTEM NEW YORK STATE STEM CELL SCIENCE

Smell A vs smell B

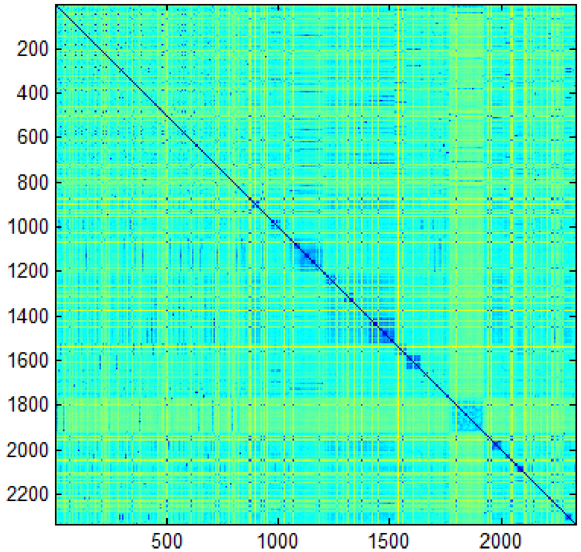


Chris Wilson (NYU)

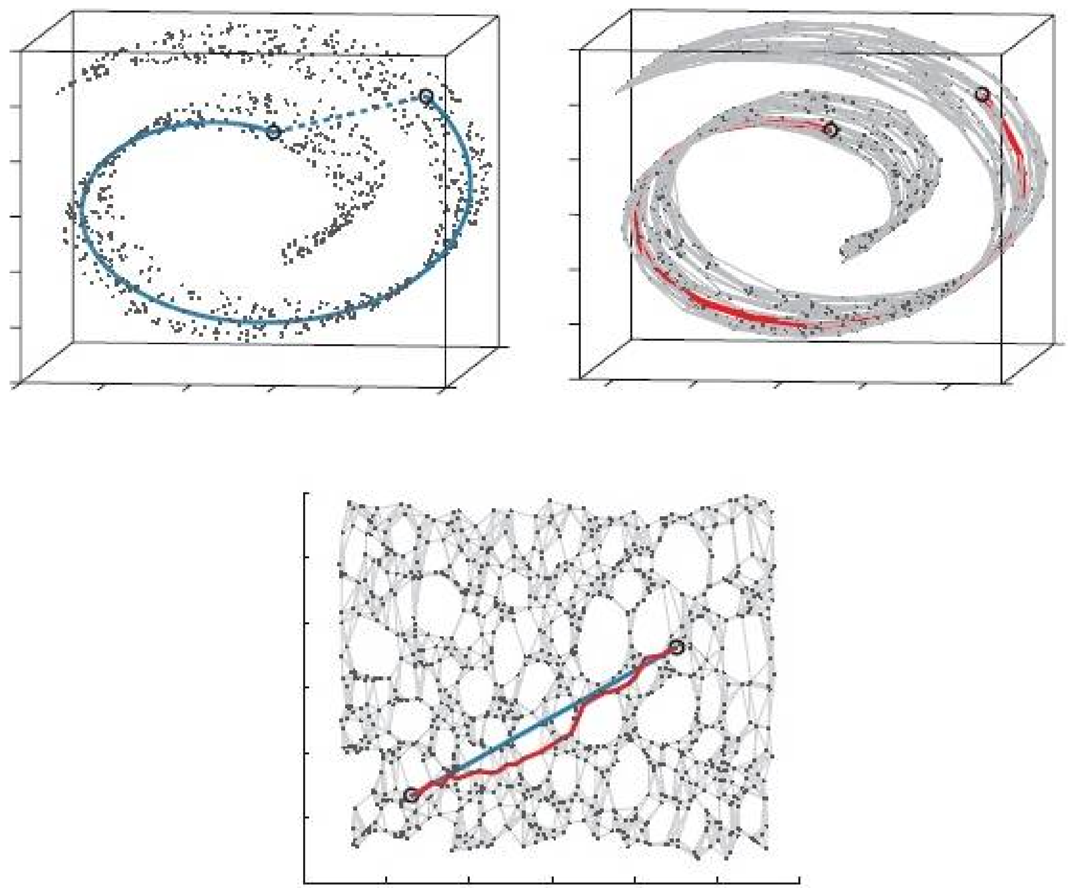
Dima Rinberg (NYU)

Mouse+human OR Isomap algorithm

OR – OR distance matrix

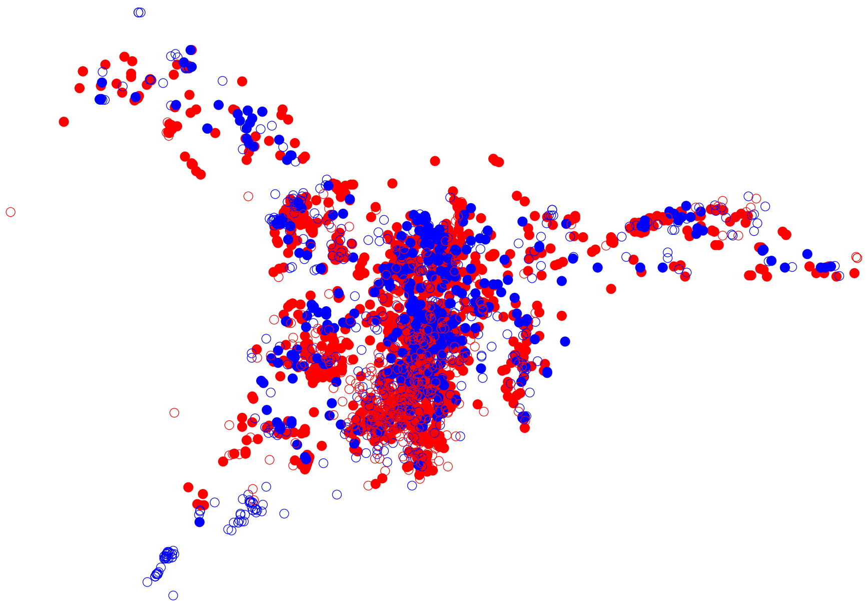


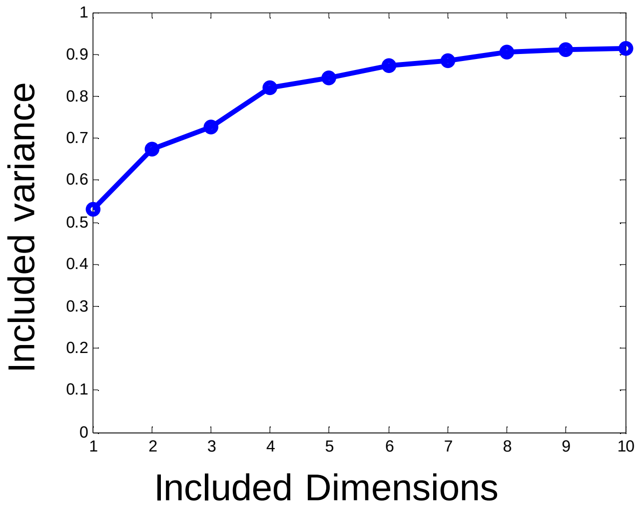
Isomap algorithm



Tenenbaum, de Silva and Langford (2000)

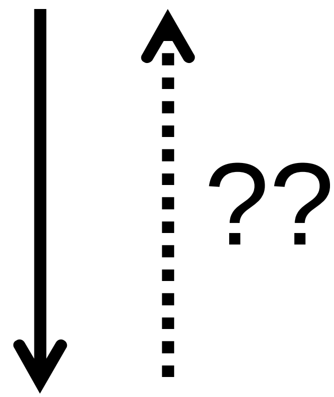
Mouse+human OR Isomap space





Can primacy model provide insight into the emergence of low-dimensional olfactory manifolds?

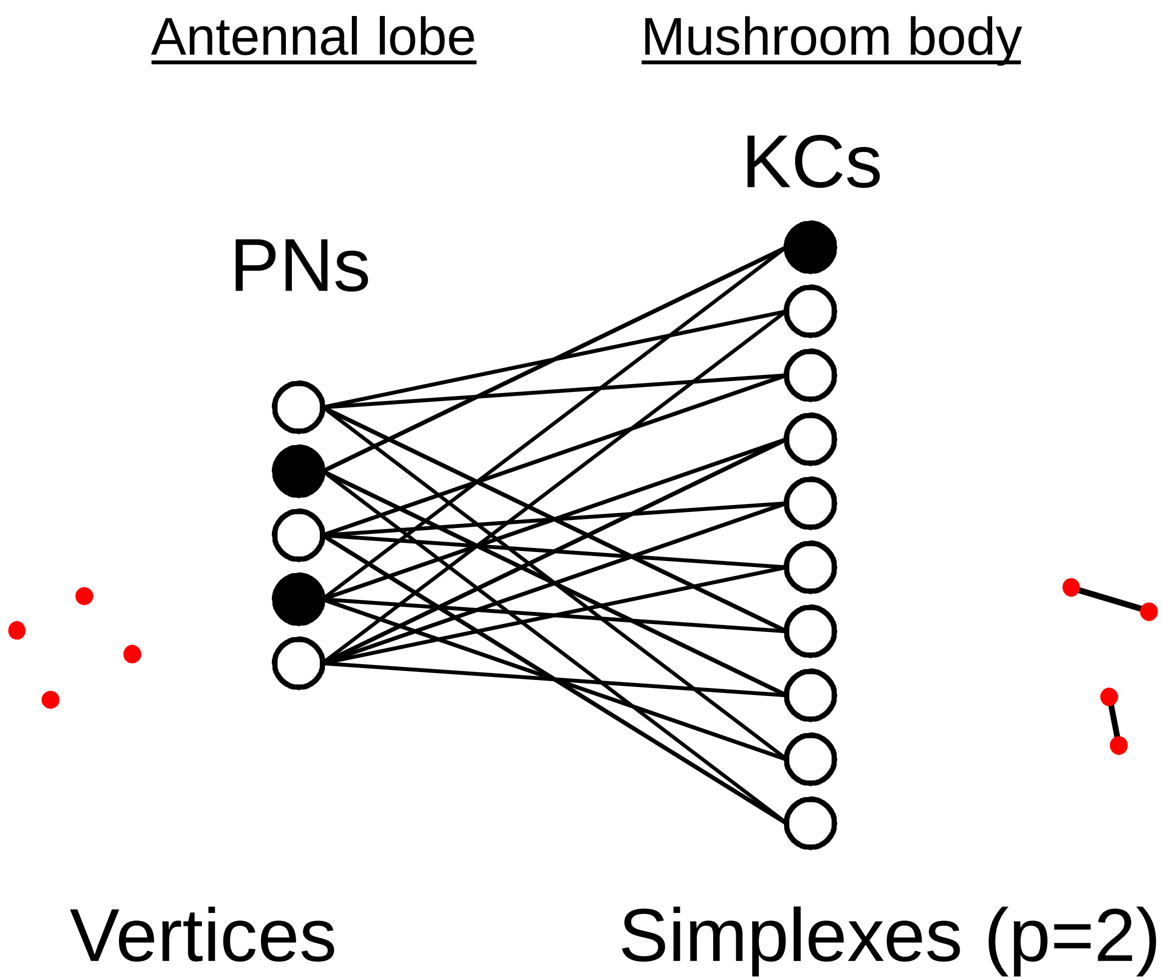
Dimension of olfactory space, D



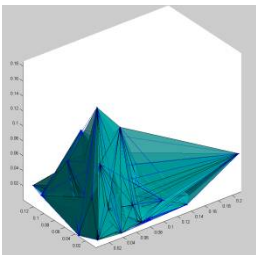
Primacy model (p~D)

Primacy and connectivity

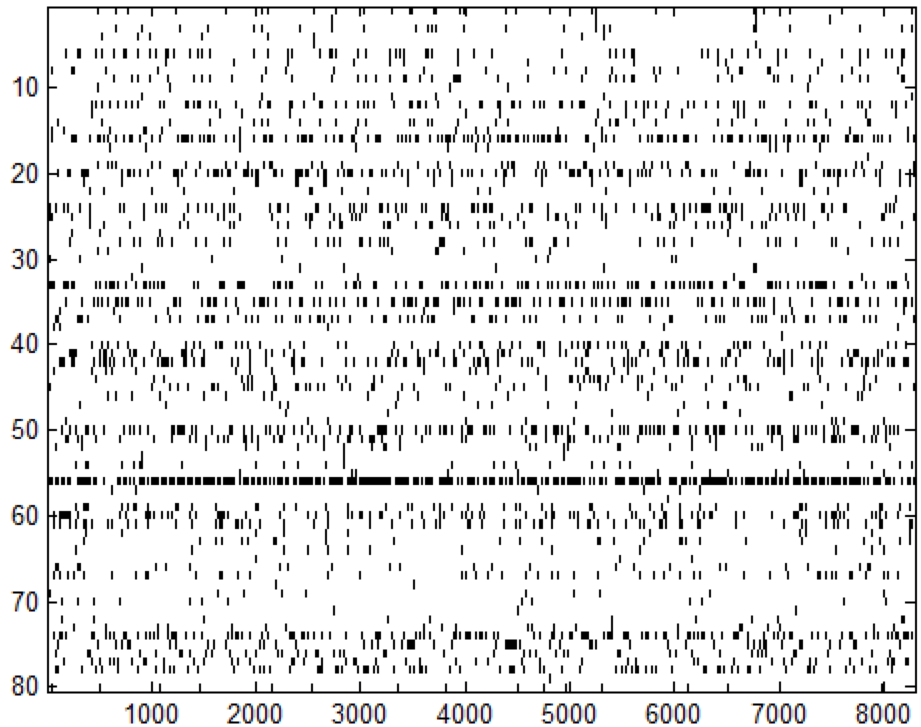
Fly olfactory system



Connectivity between glomeruli (PN, vertices) and KC (simplexes) looks random

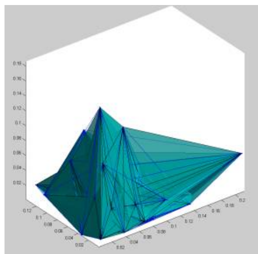


Vertices
(glomeruli)

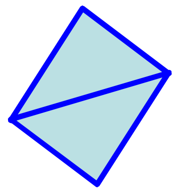


Simplexes
(kenyon cells)

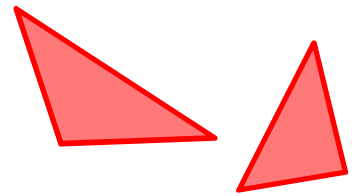
Higher-order correlations in connectivity

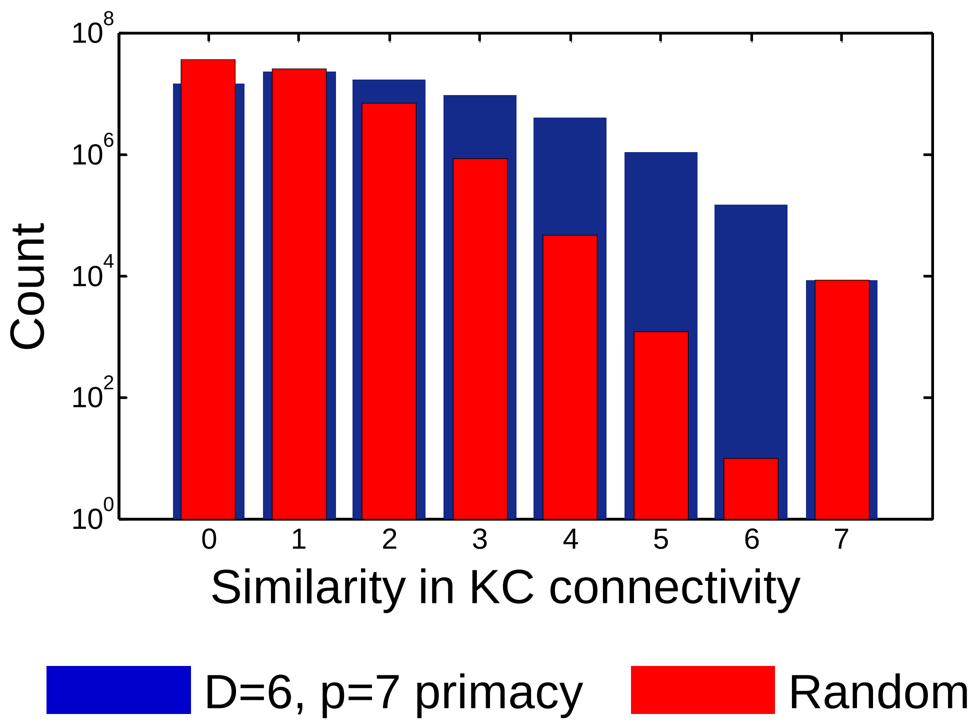


Primacy



Random





Conclusions:

- Primacy model: small number of receptors activated first code for odorant identity

- Primacy code favors the representation of low-dimensional olfactory manifolds

- The network architecture based on sparse connectivity between AL and MB is ideal for implementing primacy coding

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