A proposed role for cortical feedback in the identification of odors in complex olfactory scenes

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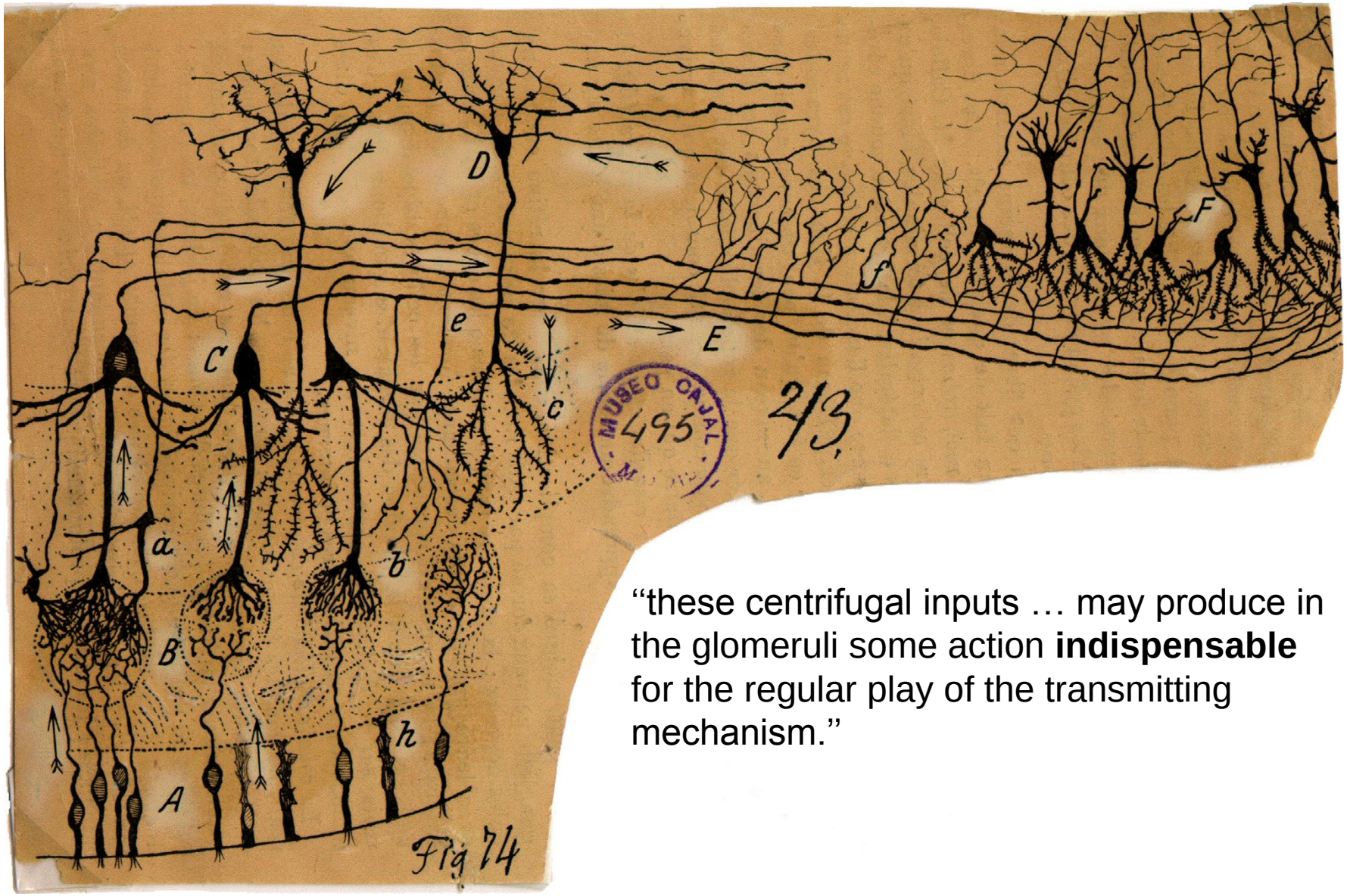
What is the role of cortical feedback?



“these centrifugal inputs … may produce in the glomeruli some action **indispensable** for the regular play of the transmitting mechanism.”

Cajal , 1894

Outline

1. Odor identification problem in complex scenes
2. Reformulation of the problem as estimation of odor presences
   - Solution is unique
   - Solution estimate the sources present under challenging conditions
3. Recursive implementation of the algorithm
4. Experimental characterization of cortical feedback and the effect of cortical input on bulbar output

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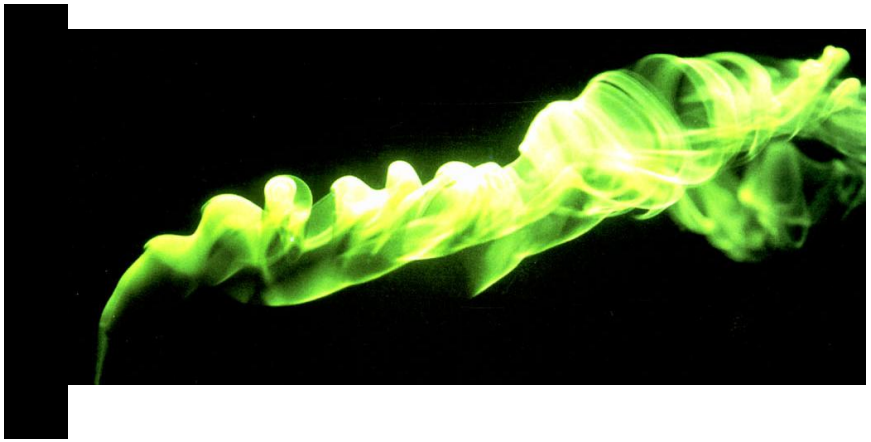
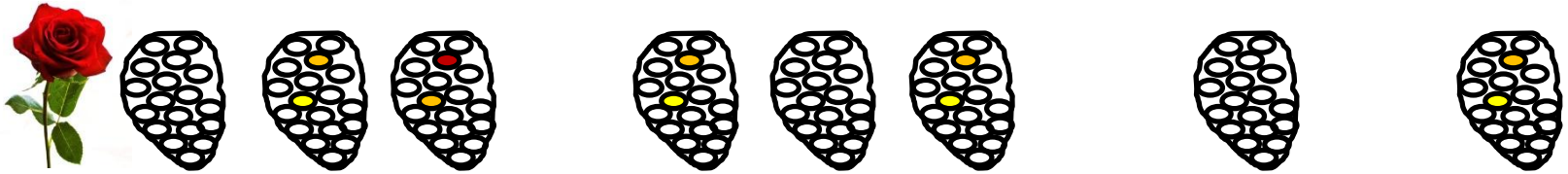
Statement of the odor recognition problem

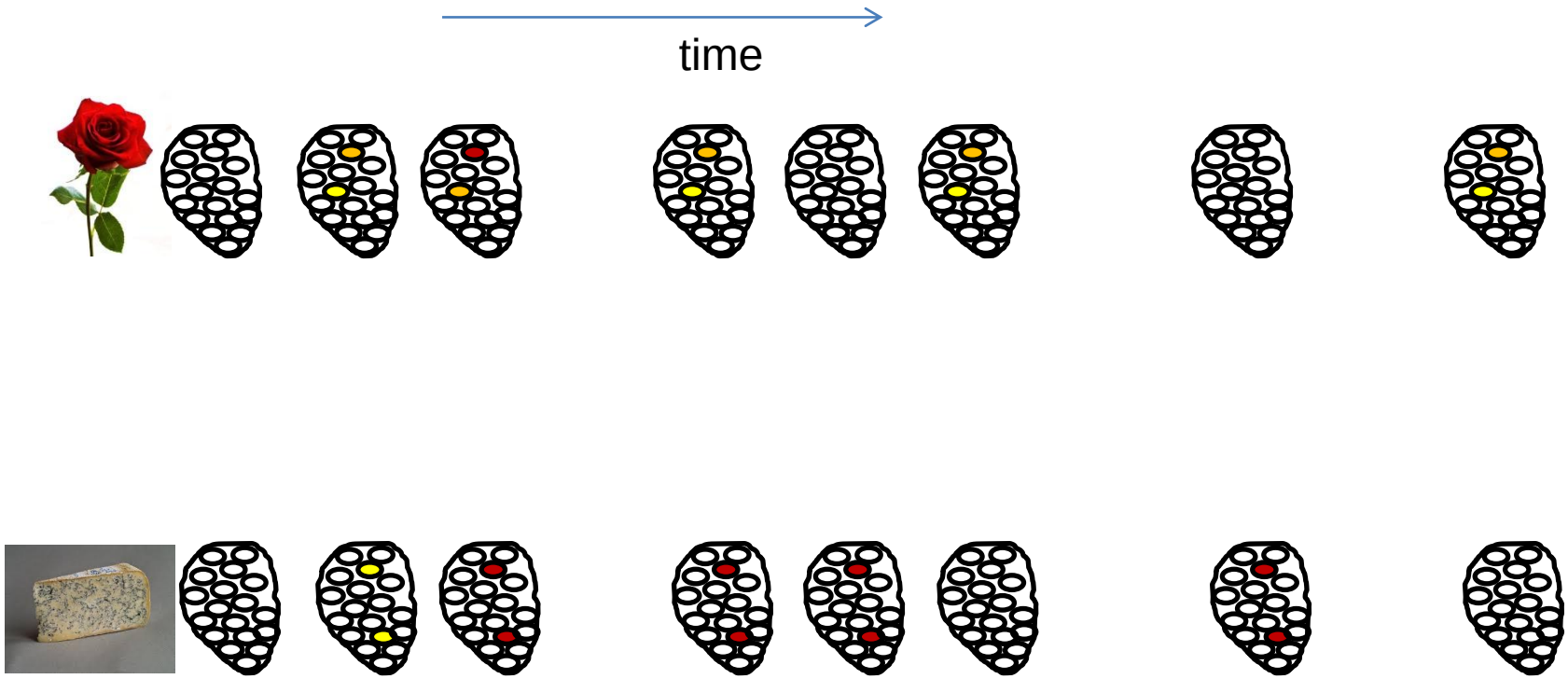


Nagel and Wilson , 2011

time

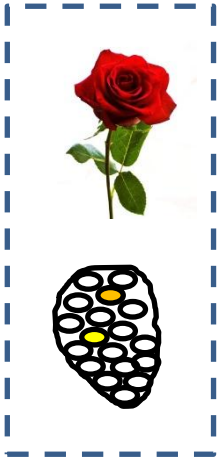


Different odors have different glomerular patterns and different fluctuations in time

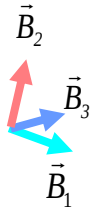


Mixtures of time-varying signals create a complex olfactory scene

Representation of odors as vectors

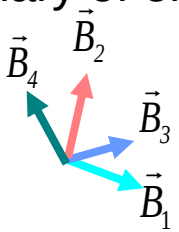


Dictionary of elements

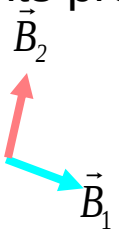


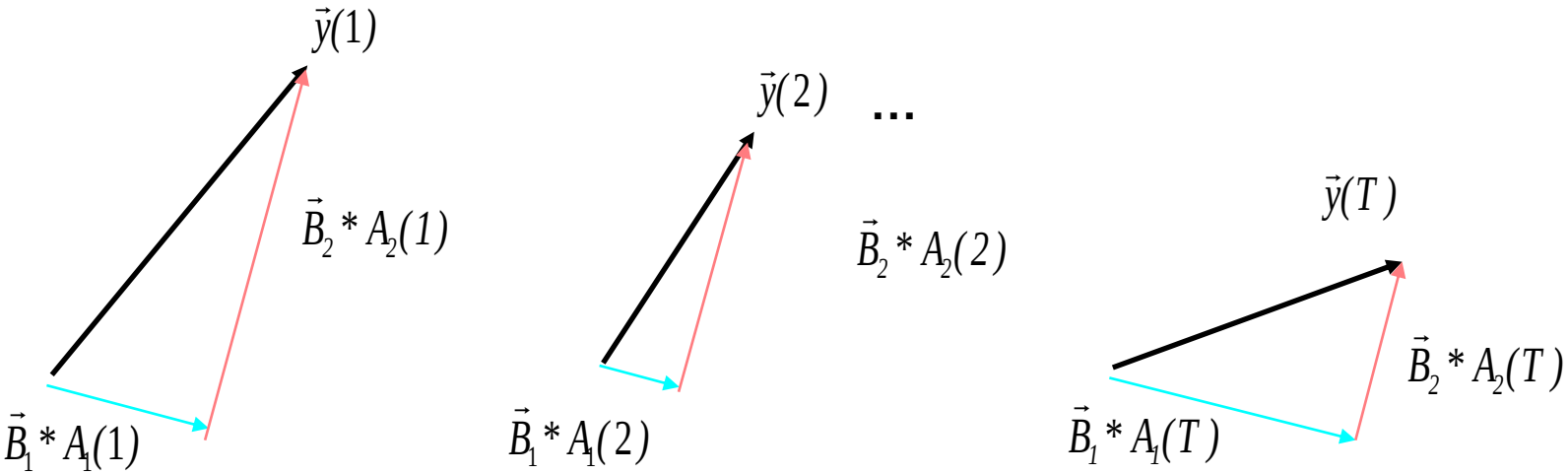
The observed signal is a combination of few elements

Dictionary of elements



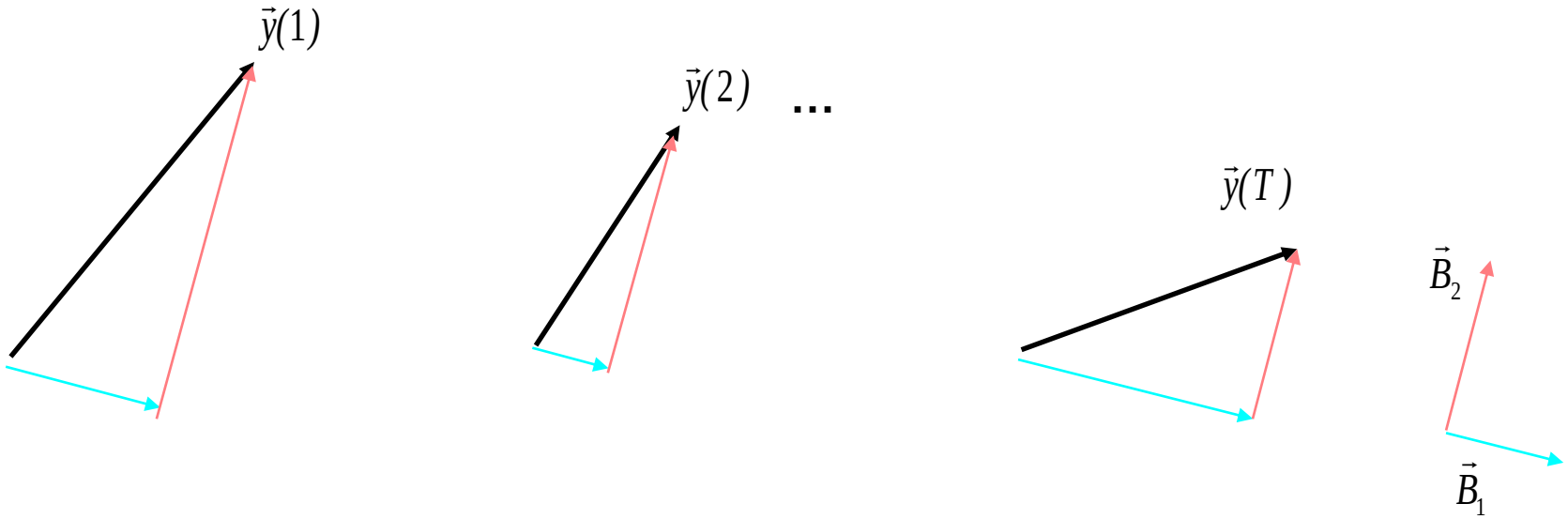
Elements present





Different approaches for parameter estimation

1) Find the independent (or uncorrelated)component (ICA, PCA) that create the signal and choose the dictionary elements that match the identified components.



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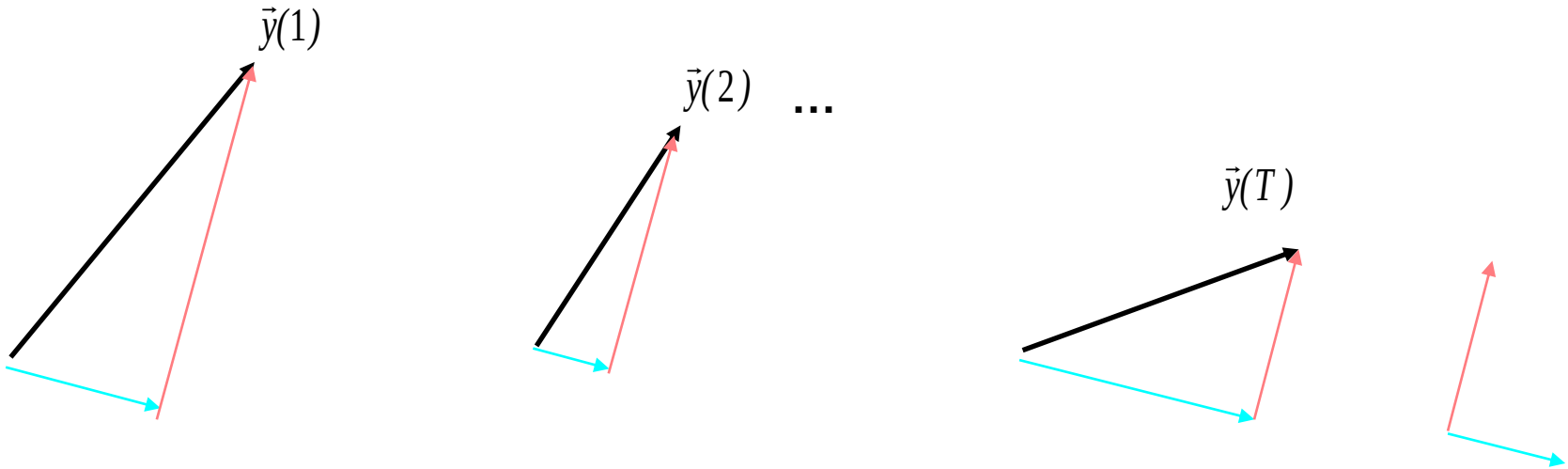
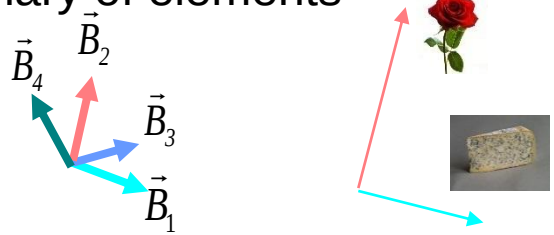
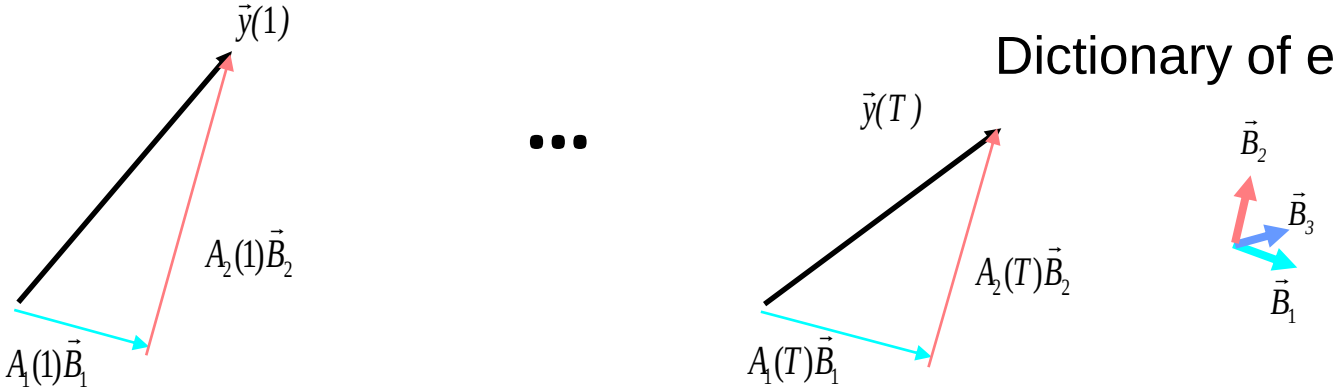


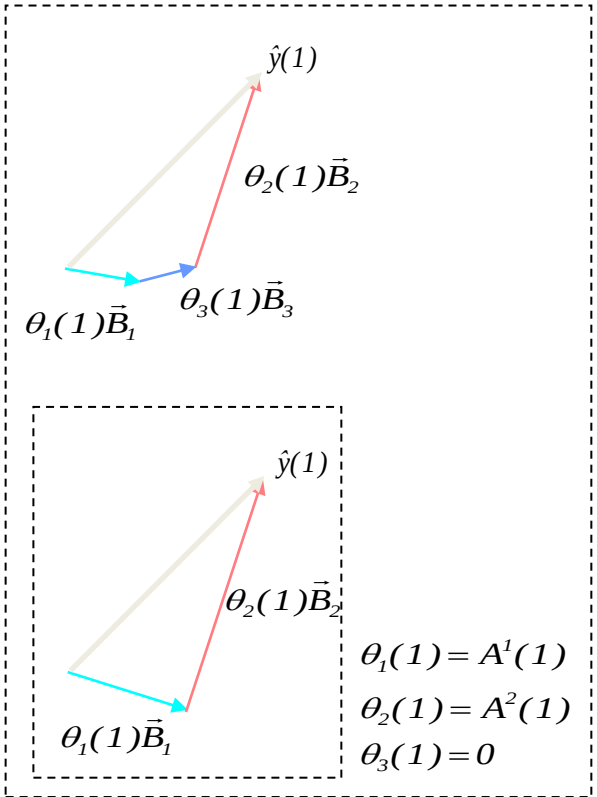
Dictionary of elements



2)Minimize the estimation error using the sparsest solution



Dictionary of elements



Single solution is found by adding a sparseness constraint

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Reformulation of the estimation problem

$$A_i(t)$$

Time-varying amplitude of each dictionary element

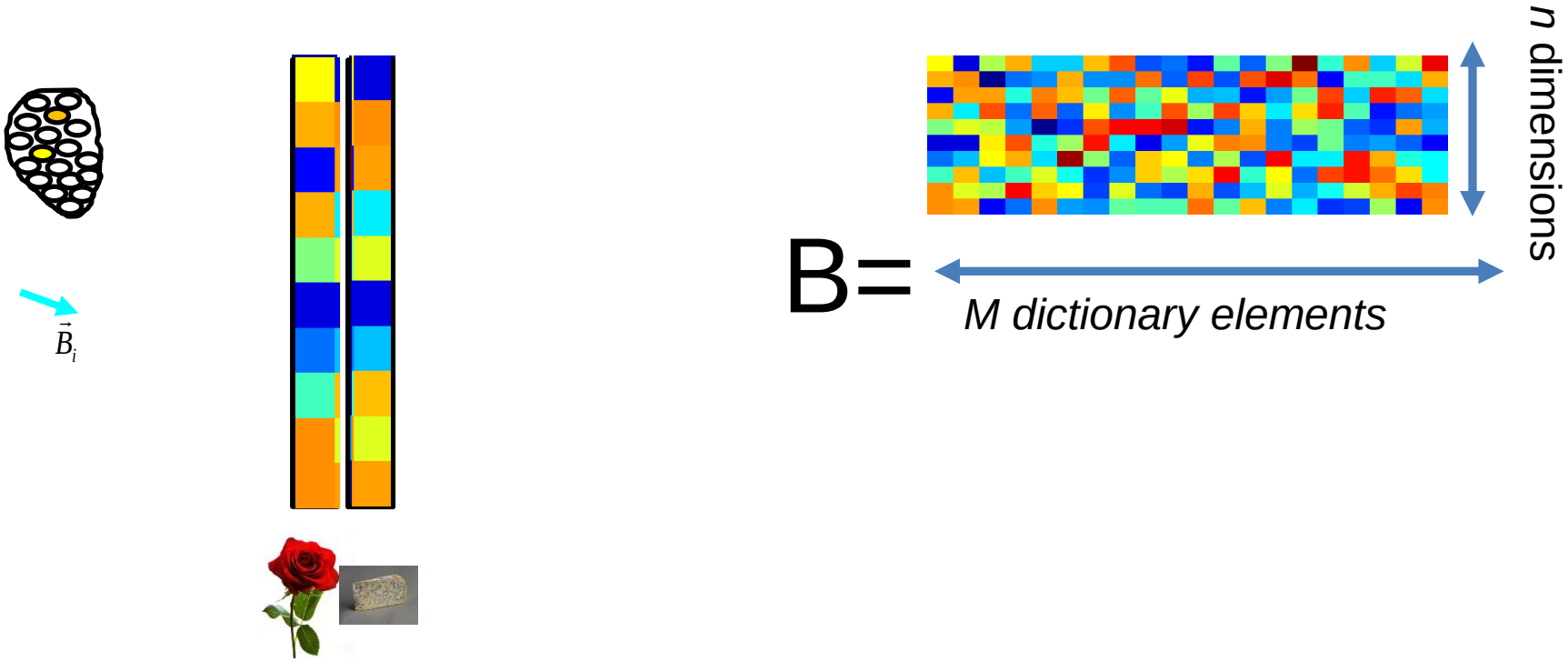
Time invariant component

Time-varying component

1, if element *i* is present

0, if element i is not present in a scene

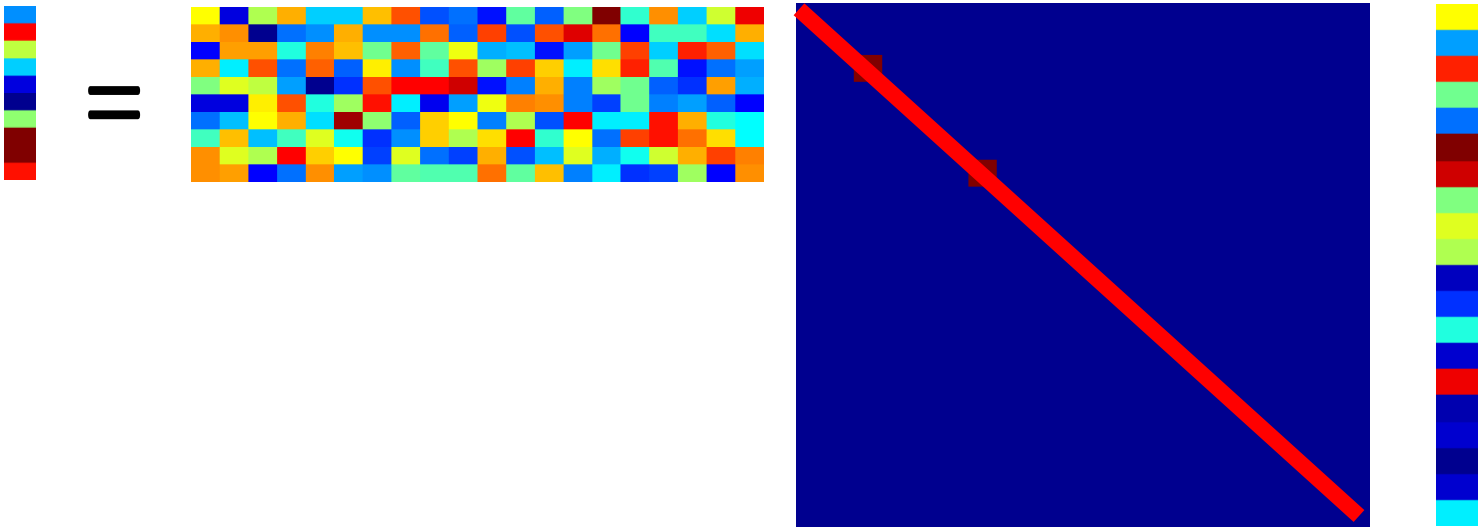
Estimation of the time-varying component



In general, M>>n

Estimation of the time varying component

$\hat{y}(t)$ B Θ $\hat{A}(t)$



Estimation of the time varying component

By calculating the estimated square error:

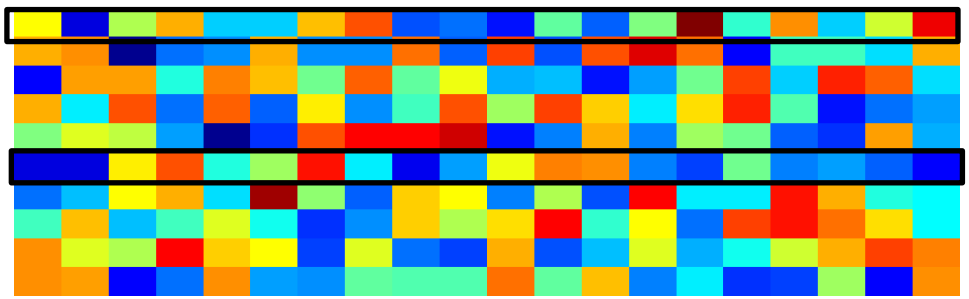
$$C = \left(\vec{y}(t) - \hat{y}(t)\right)^T \left(\vec{y}(t) - \hat{y}(t)\right)$$

And taking the derivative we obtain:

$$\hat{A}(t) = B^T \left(BB^T\right)^{-1} y(t) \approx B^T y(t)$$

"Glomerule" 1

"Glomerule" 4

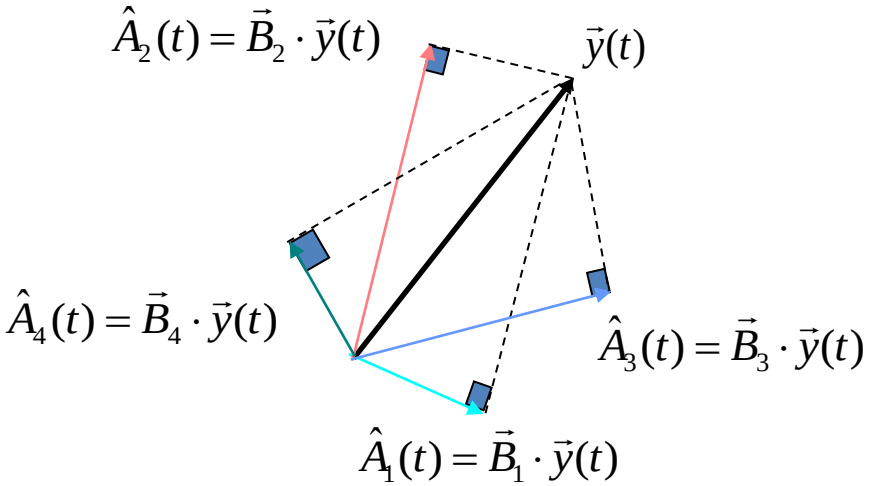


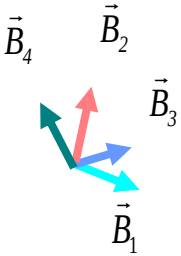
$$\left(BB^T\right)^{-1} \approx I$$

if glomerular are uncorrelated

Estimation of the time varying component

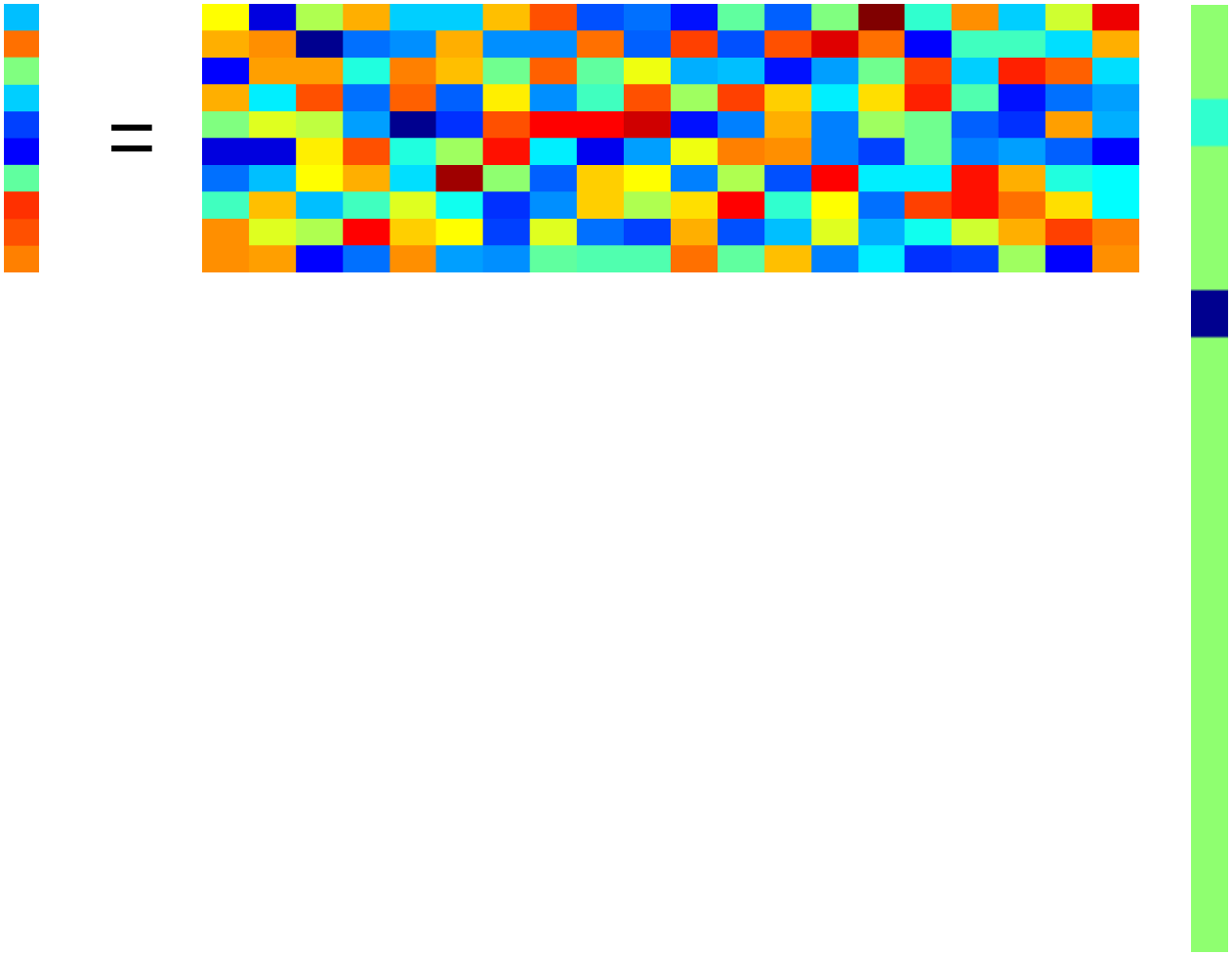
$$\hat{A}(t) \approx B^T y(t)$$





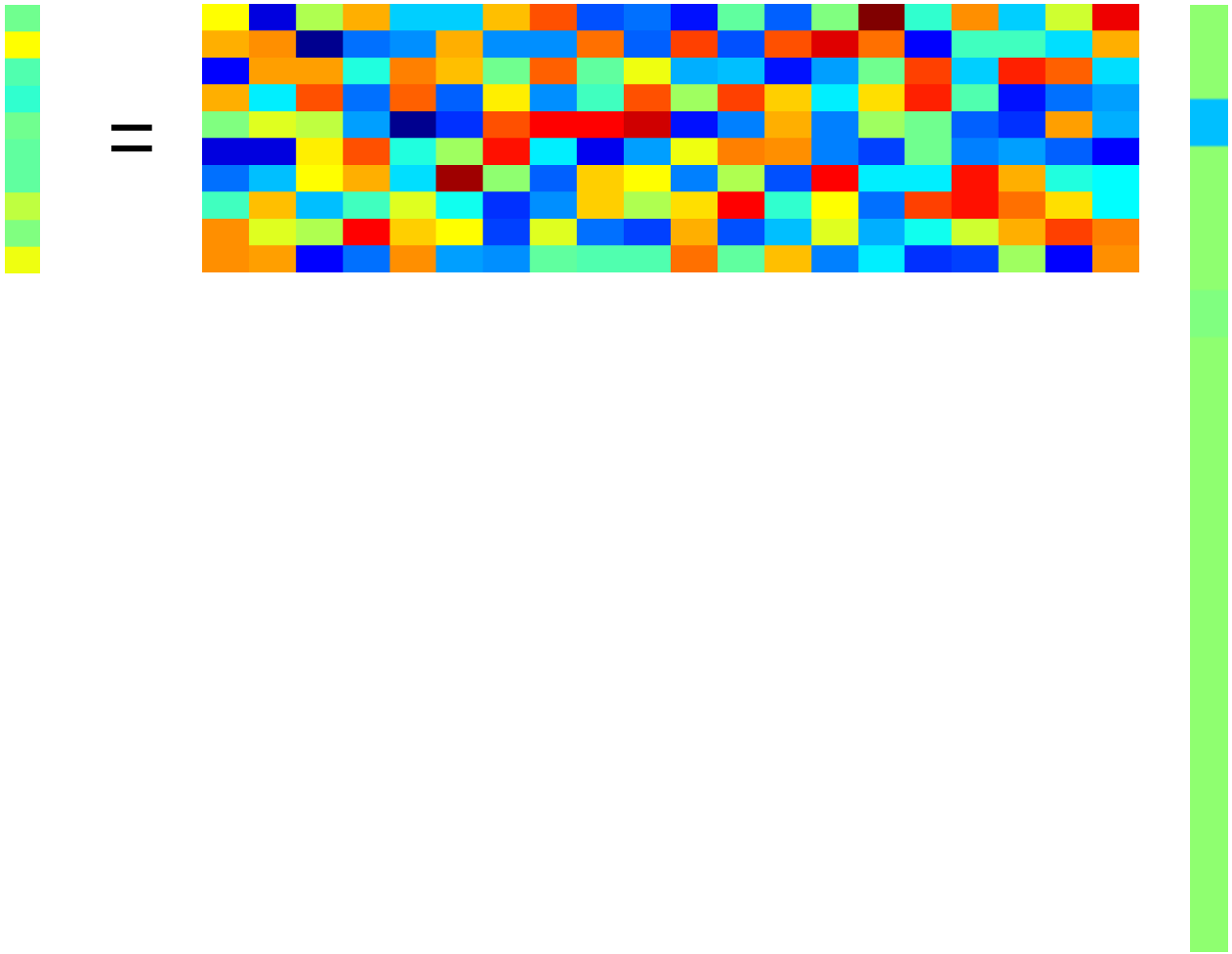
We can find a sparse solution at each time step

$\vec{y}(1)$ B $\theta(1)$



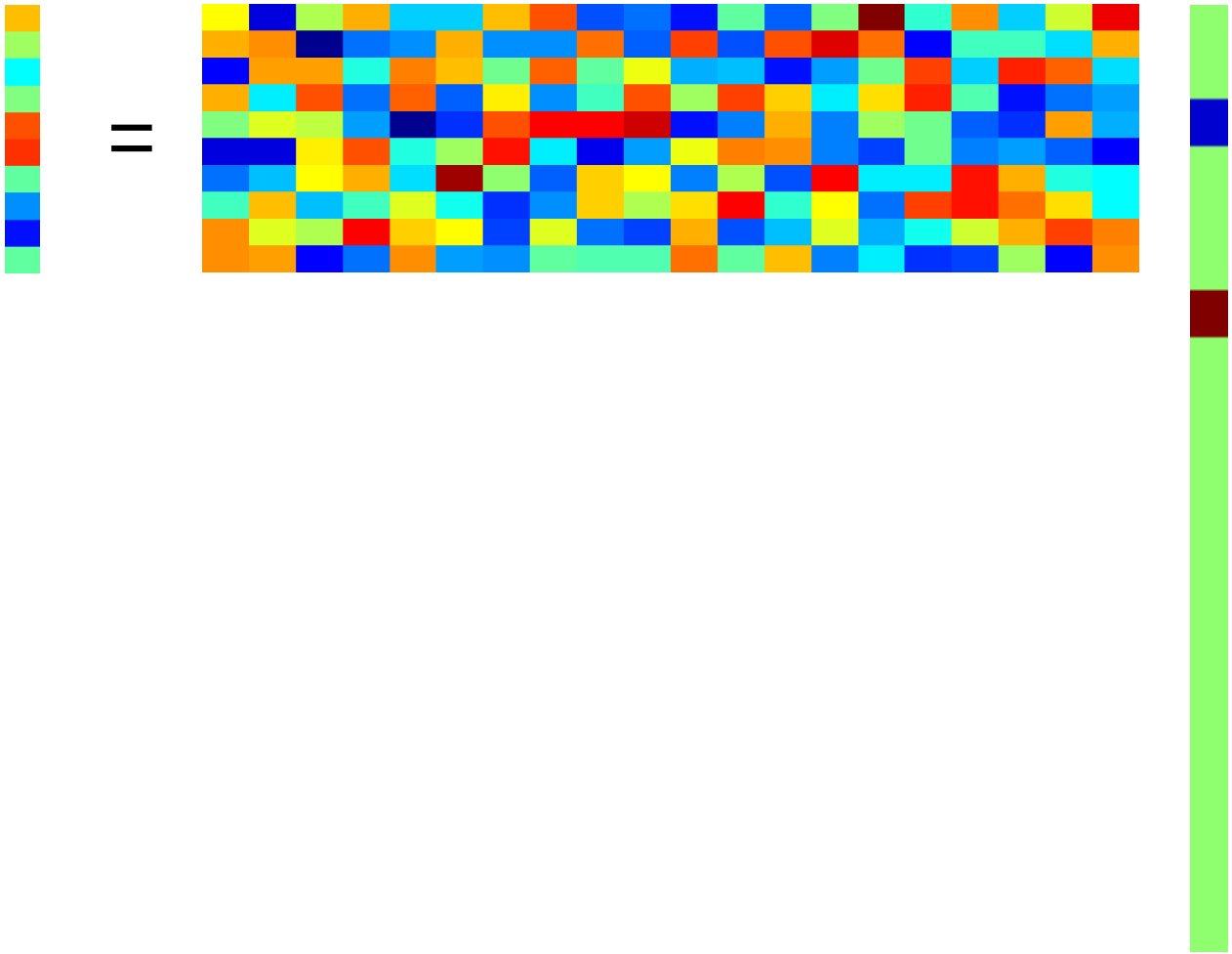
We can find a sparse solution at each time step

$\vec{y}(2)$ $\quad$ B $\quad$ $\theta(2)$



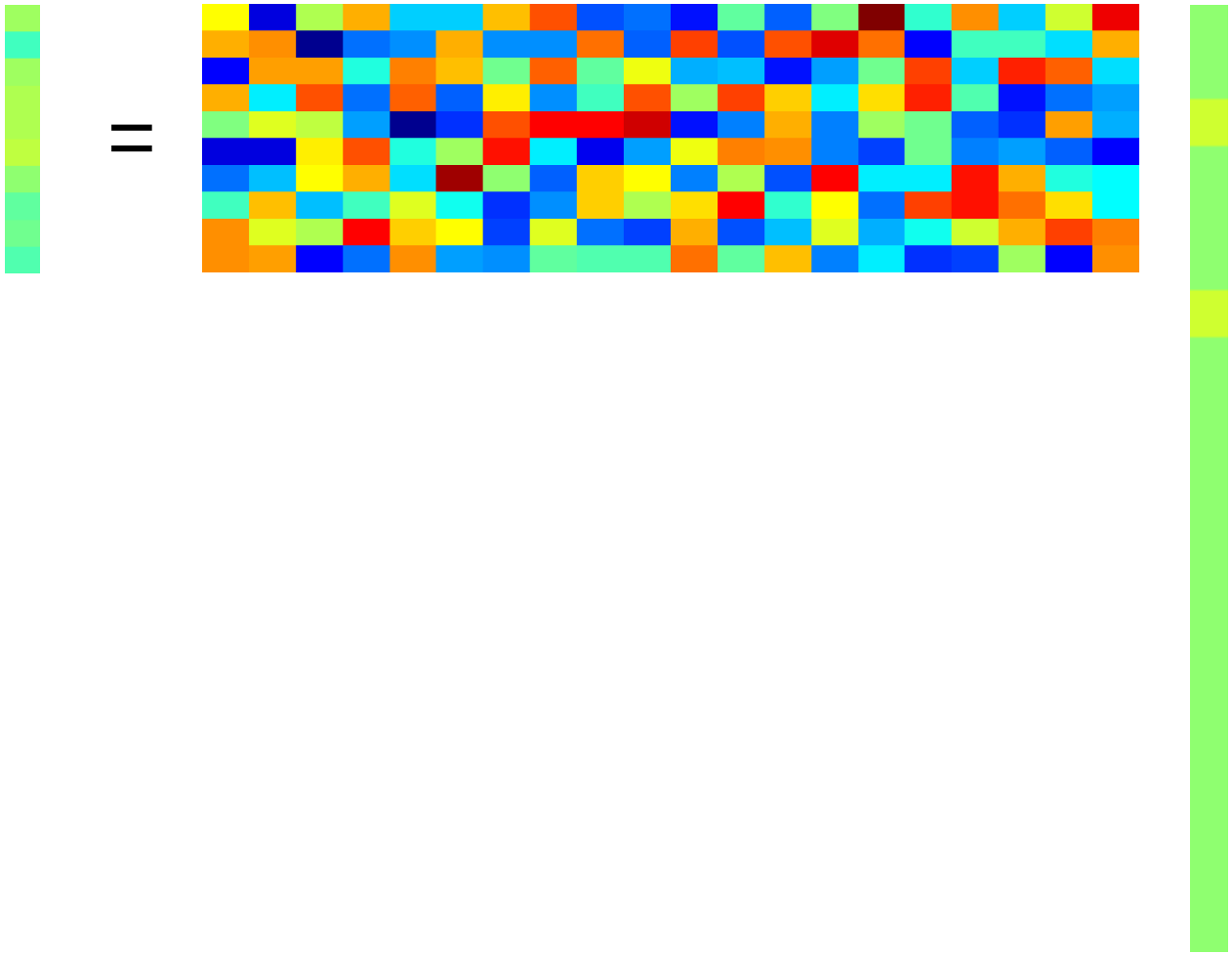
We can find a sparse solution at each time step

$\vec{y}(3)$ B $\theta(3)$



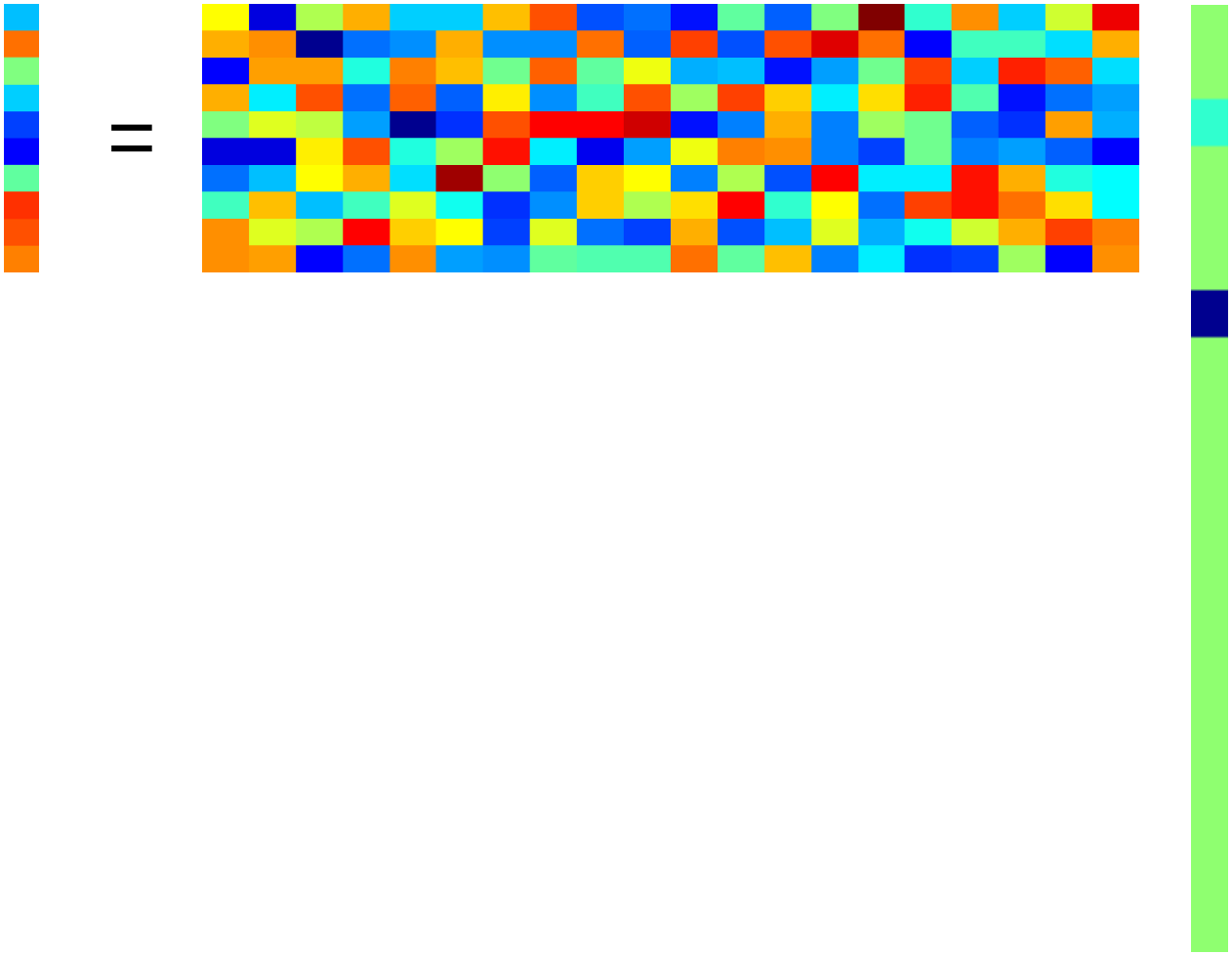
We can find a sparse solution at each time step

$\vec{y}(4)$ $\quad$ B $\quad$ $\theta(4)$



We find a single solution for all time steps

$\vec{y}(1)$ B $\theta(1)$



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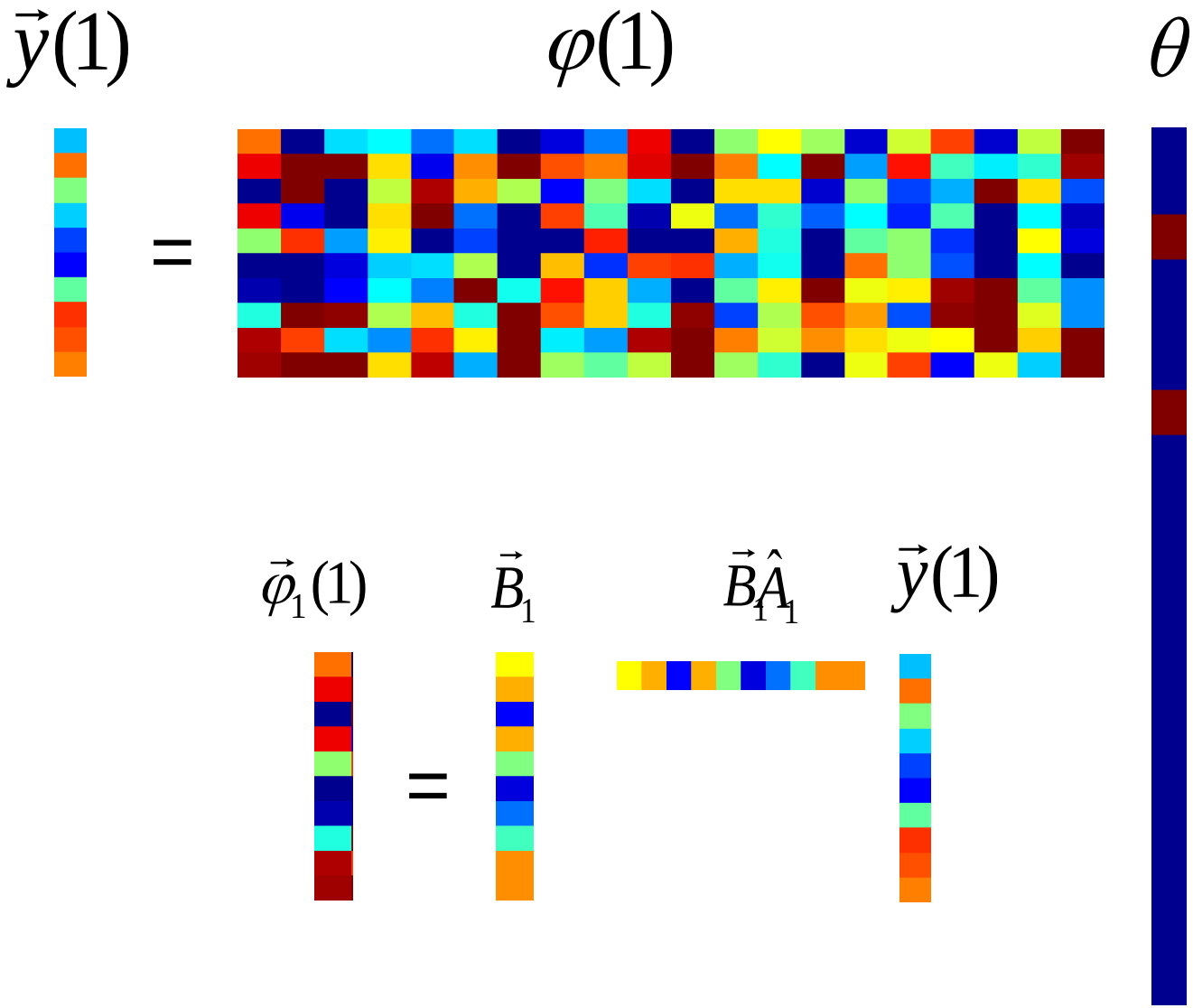
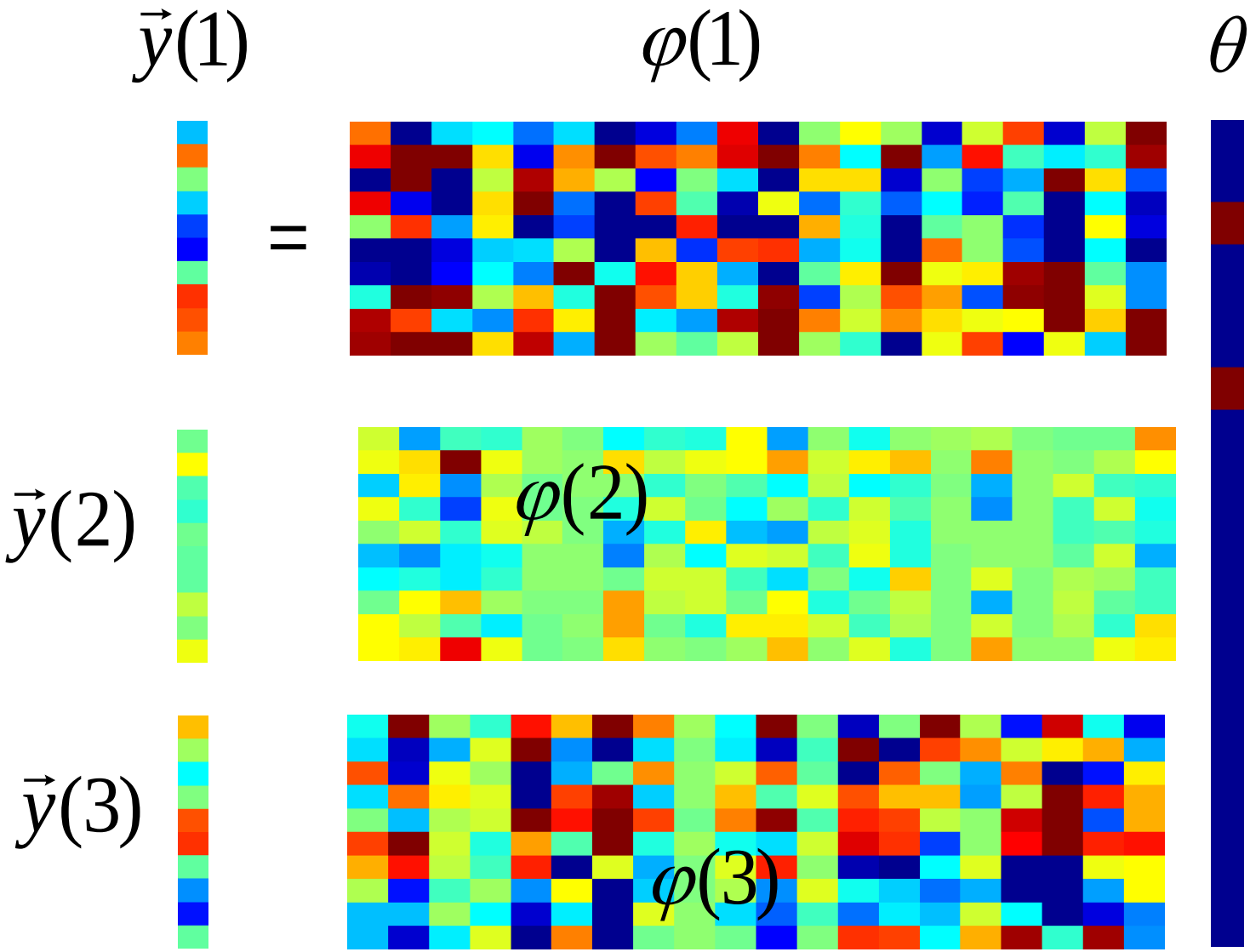
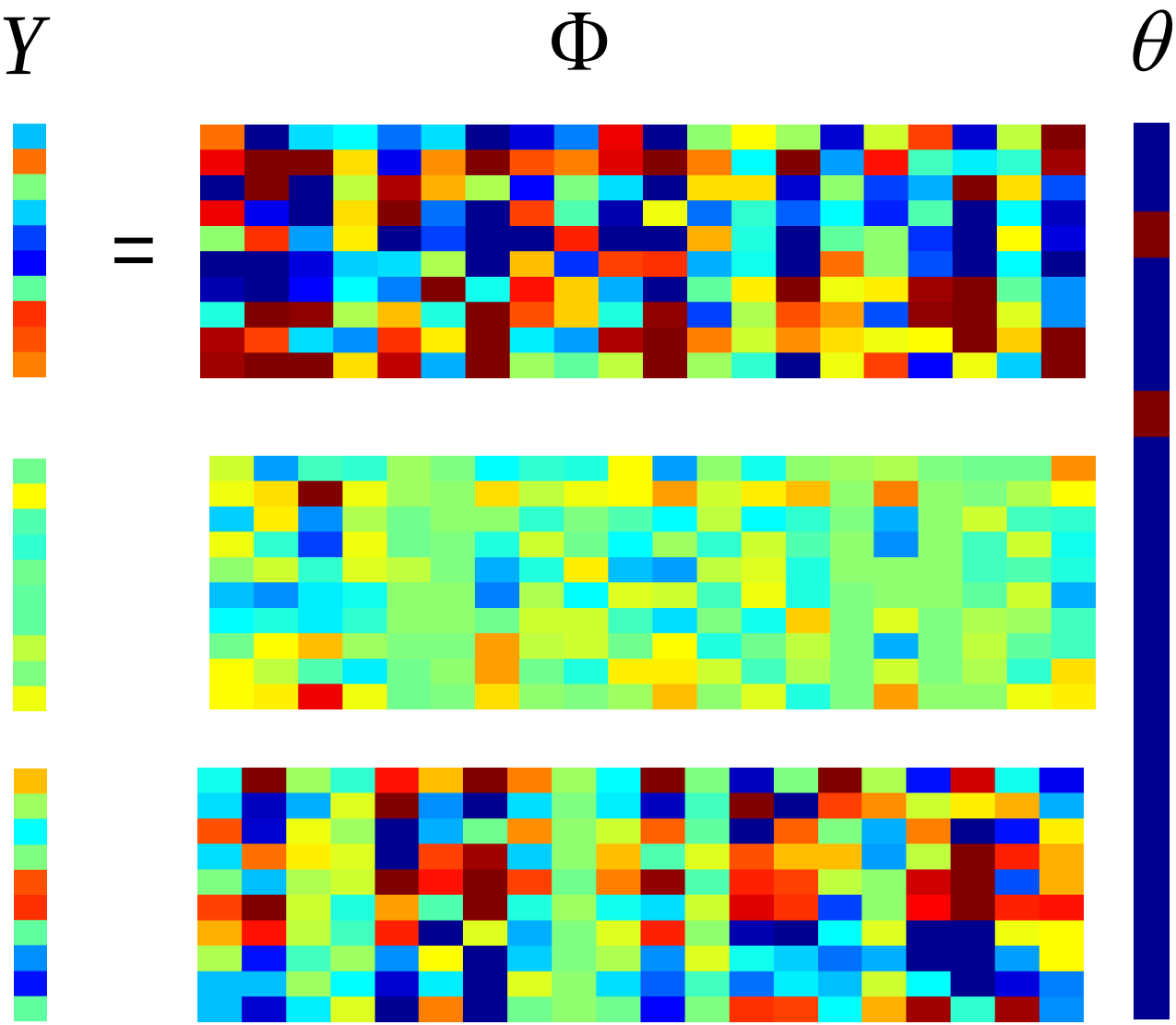


We find a single solution for all time steps



We find a single solution for all time steps



We find a single solution for all time steps

$$Y = \Phi\theta$$

The solution is given by

$$\theta = \left(\Phi^T\Phi\right)^{-1}\Phi^T Y$$

☺

Otazu and Leibold, *PLoS One*, 2011

However, in order for the solution to be unique, we require

$$\left(\Phi^T\Phi\right)$$

to be invertible. Under which conditions is it invertible?

☹

The matrix $\Phi^T\Phi$ is positive definite

$$x^T\left(\Phi^T\Phi\right)x > 0$$ For all vectors x

The single elements of $\Phi^T\Phi$ *are:* $$\left(\Phi^T\Phi\right)_{i,j} = \sum_{t=1}^{T}\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(\vec{y}(t)\cdot\vec{B}_j\right)\left(\vec{B}_i\cdot\vec{B}_j\right)$$

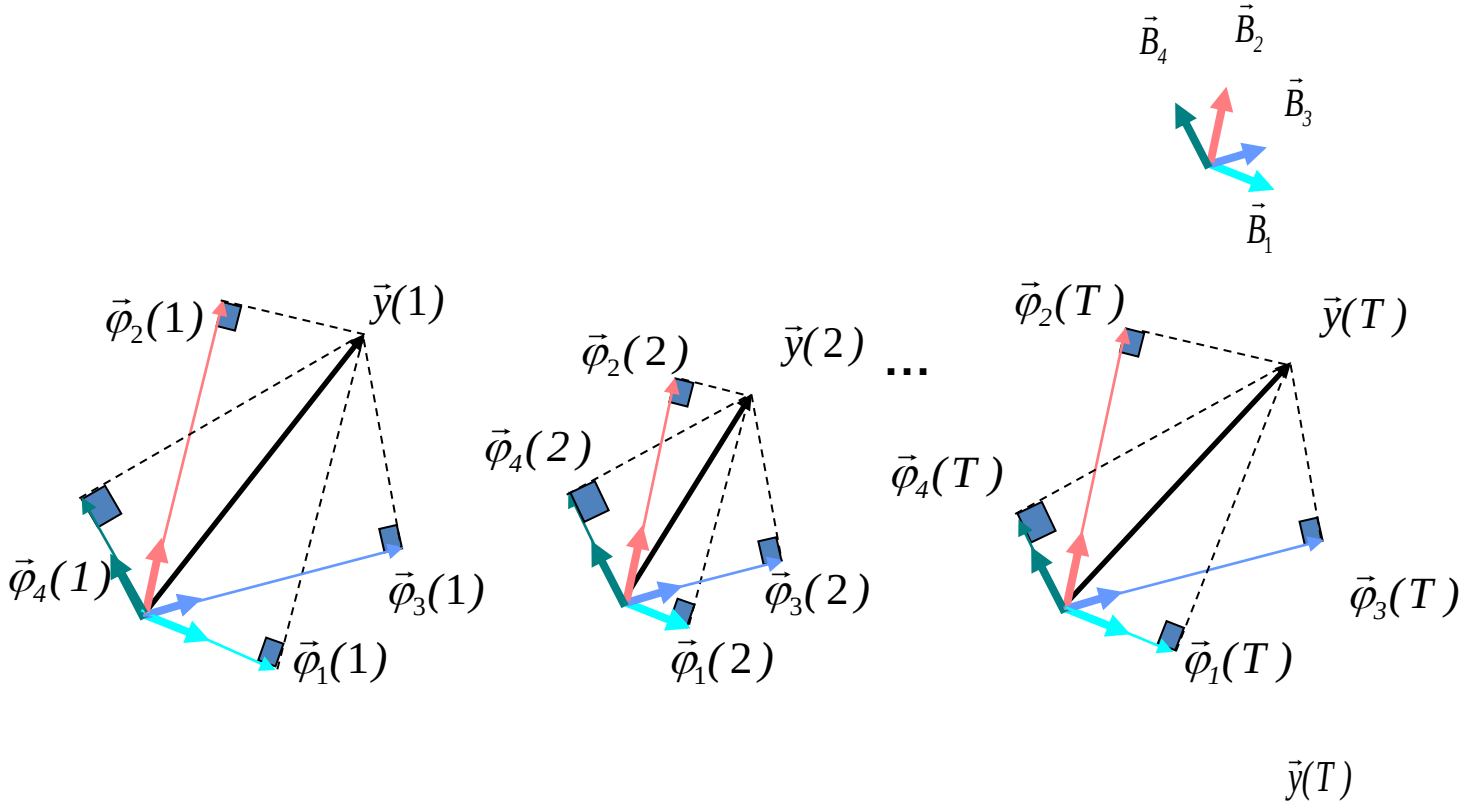
$$x^T\left(\Phi^T\Phi\right)x = \sum_{t=1}^{T}\sum_{i=1}^{N}\sum_{j=1}^{N} x_i x_j\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(\vec{y}(t)\cdot\vec{B}_j\right)\left(\vec{B}_i\cdot\vec{B}_j\right)$$

$$= \sum_{t=1}^{T}\sum_{m=1}^{M}\left(\sum_{i=1}^{N}\frac{(x_i)}{\sqrt{2}}\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(B_{m,i}\right)\right)^2 + \sum_{t=1}^{T}\sum_{i=1}^{N}(x_i)^2\left(\vec{y}(t)\cdot\vec{B}_i\right)^2\left(\frac{1}{2}\right) > 0$$

- All the eigenvalues of $\Phi^T\Phi$ are positive, as long as we consider only dictionary elements $\vec{B}_i$ where $\vec{y}(t)\cdot\vec{B}_i > 0$, for any t
- No zero eigenvalues, therefore, $\Phi^T\Phi$ is invertible
- Solution is unique

Corrected Projections Algorithm (CPA)

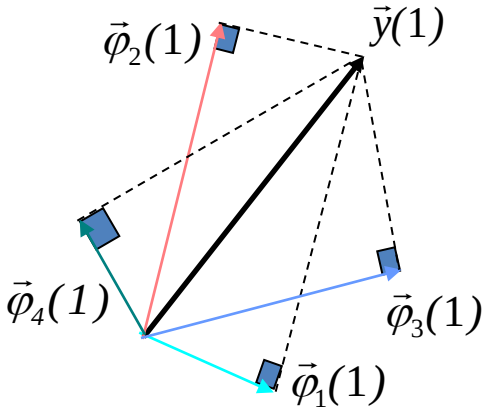
1) Calculate the projections

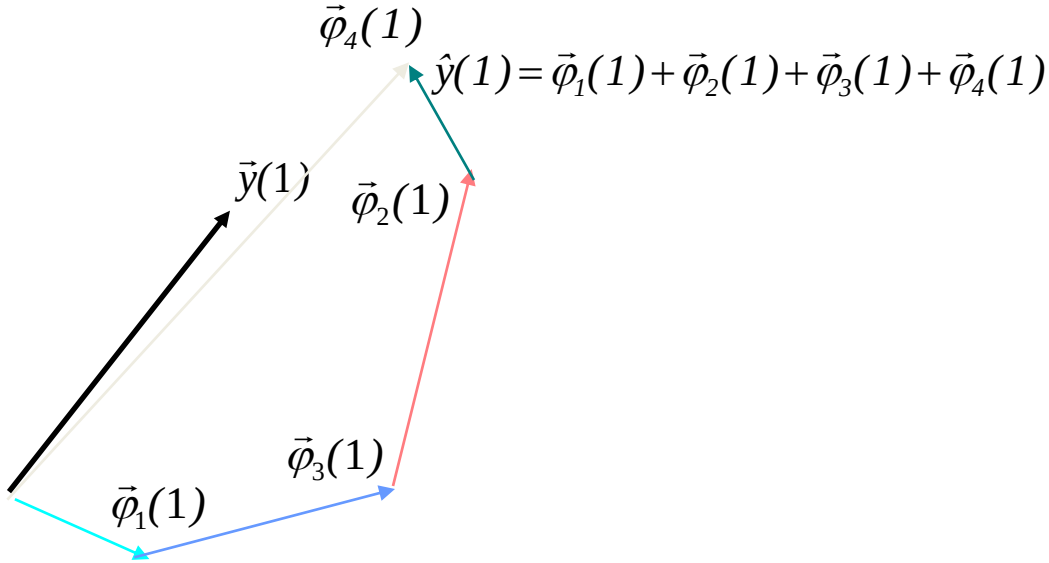


Otazu and Leibold, *PLoS One*, 2011

Corrected Projections Algorithm (CPA)

2) Use the projections to create an estimate of the observed signal





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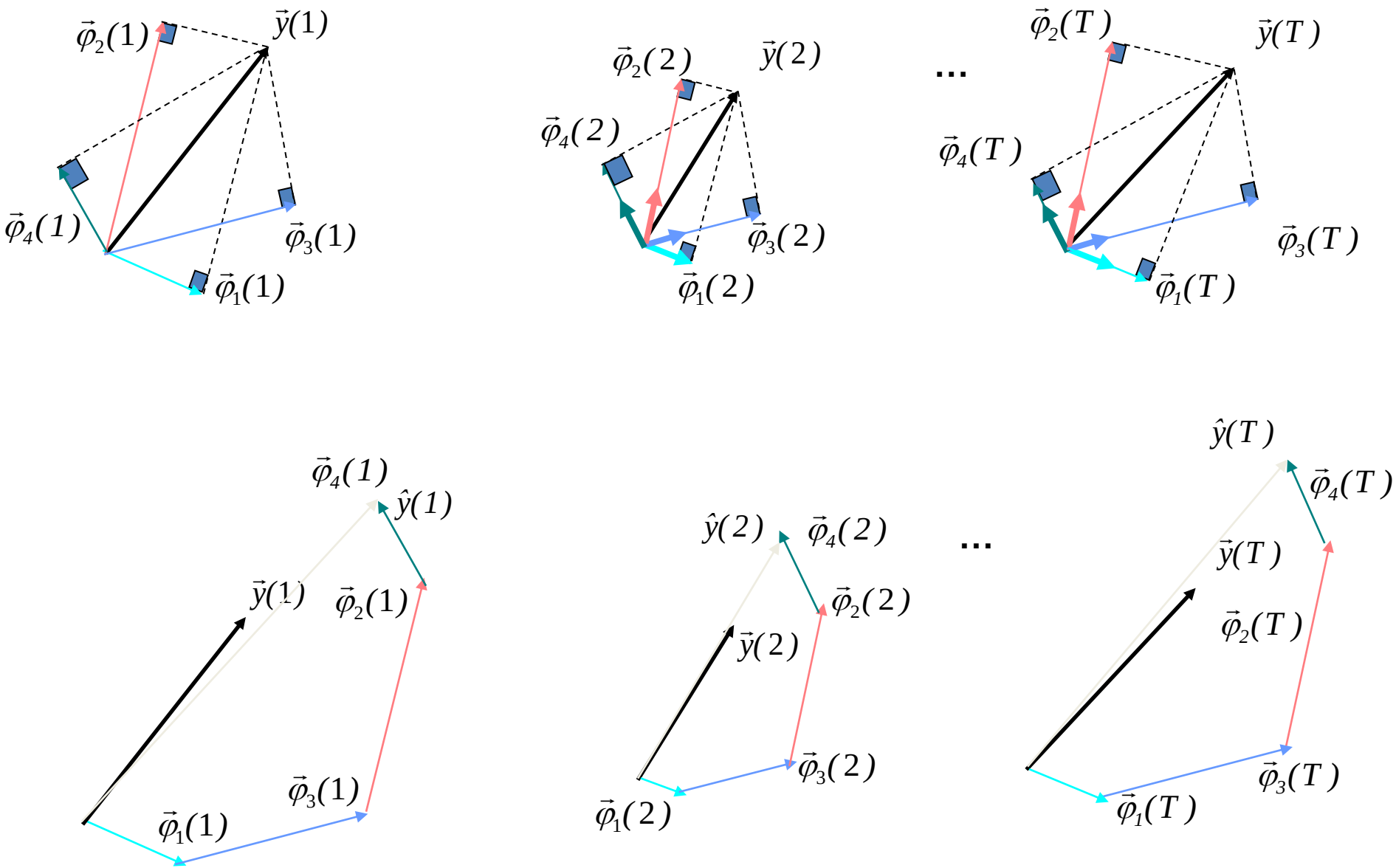
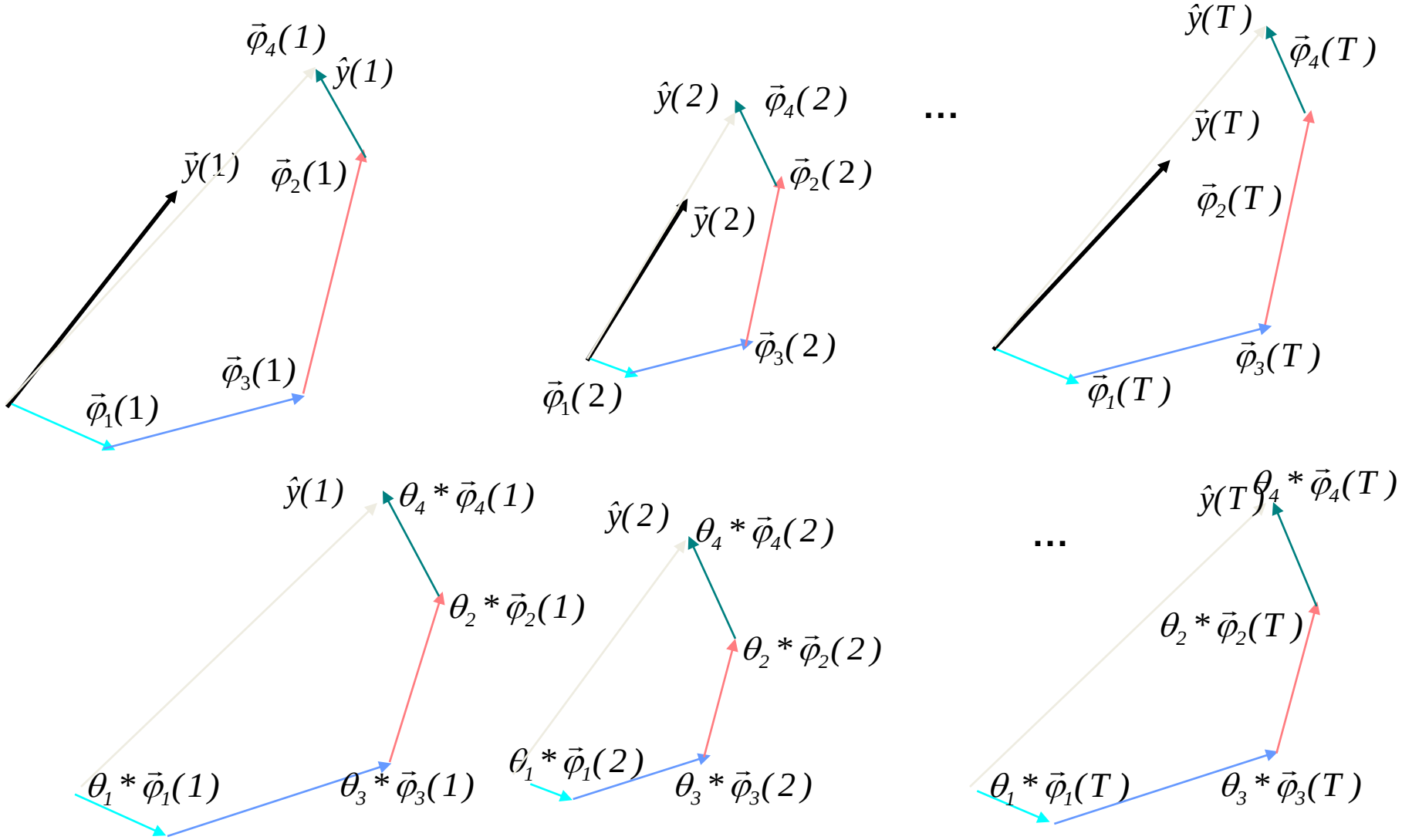


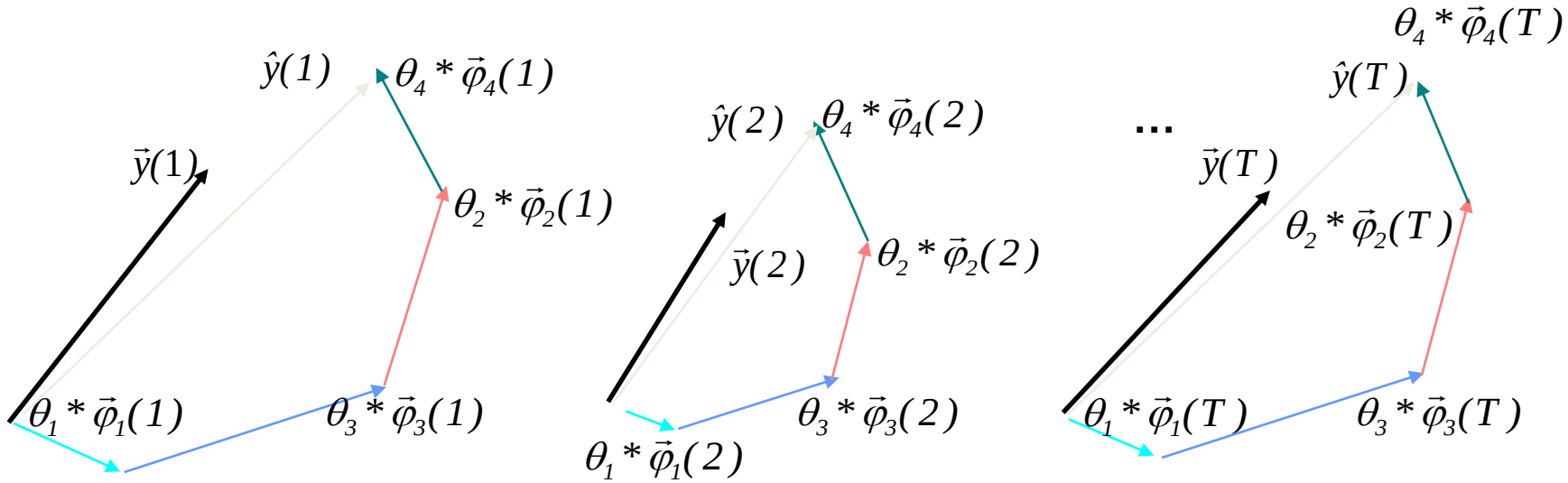
Corrected Projections Algorithm (CPA)

3) Correct the projections by a factor ϑ



Corrected Projections Algorithm (CPA)

3) Find the θ *that minimize the error between the estimate and the observed signal*



Otazu and Leibold, *PLoS One*, 2011

Minimal error is given if the sources present are orthogonal

Model of the olfactory scene

$$\vec{y}(t) = A_1(t)\vec{B}_1 + A_2(t)\vec{B}_2$$

Lets assume that $\overrightarrow{\boldsymbol{B_1}}$ and $\overrightarrow{\boldsymbol{B_2}}$ are orthogonal, that is:

$$\vec{B}_1 \cdot \vec{B}_2 = 0$$

CPA creates its estimate using the projections

$$\hat{y}(t) = \theta_1(\vec{y}(t)\cdot\vec{B}_1)\vec{B}_1 + \theta_2(\vec{y}(t)\cdot\vec{B}_2)\vec{B}_2 + \ldots + \theta_n(\vec{y}(t)\cdot\vec{B}_n)\vec{B}_n$$

$$\hat{y}(t) = \theta_1\left(A_1(t)\vec{B}_1\cdot\vec{B}_1 + A_2(t)\cancel{\vec{B}_2\cdot\vec{B}_1}\right)\vec{B}_1 + \theta_2\left(A_1(t)\cancel{\vec{B}_1\cdot\vec{B}_2} + A_2(t)\vec{B}_2\cdot\vec{B}_2\right)\vec{B}_2$$

$$+ \ldots + \theta_n(\vec{y}(t)\cdot\vec{B}_n)\vec{B}_n$$

$$\hat{y}(t) = \theta_1 A_1(t)\vec{B}_1 + \theta_2 A_2(t)\vec{B}_2 + \ldots + \theta_n(\vec{y}(t)\cdot\vec{B}_n)\vec{B}_n$$

If we choose then θ_1=1, θ_2=1, and θ_k=0, if $k \neq 1,2$

$$\hat{y}(t) = A_1(t)\vec{B}_1 + A_2(t)\vec{B}_2 = \vec{y}(t)$$

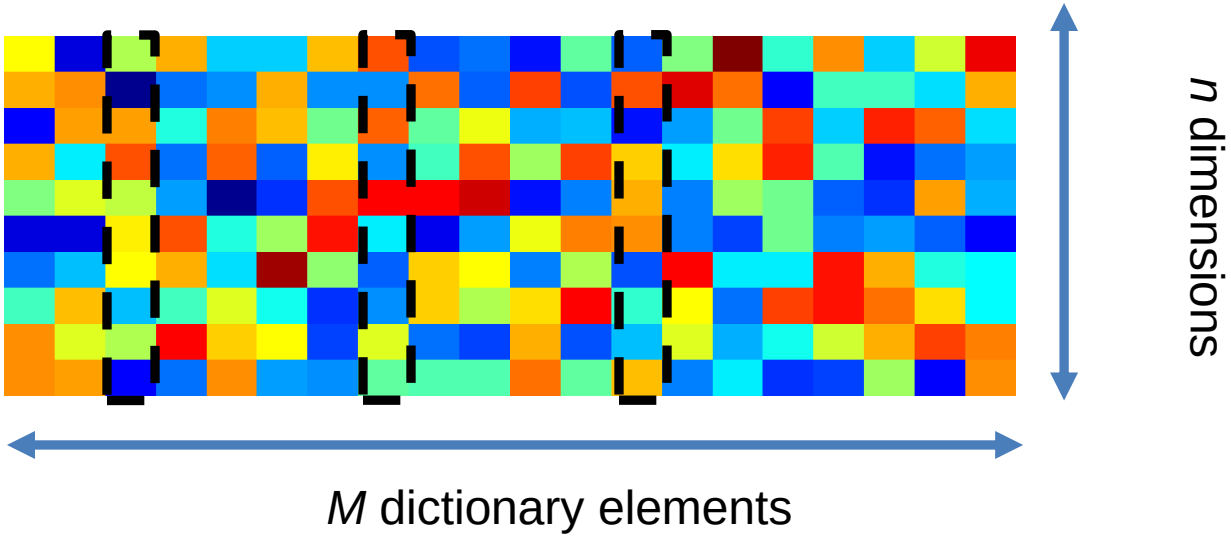
Therefore

$$\left|\hat{y}(t) - \vec{y}(t\right|^2 = 0$$

Then θ_1=1, θ_2=1, and θ_k=0, if $k \neq 1,2$ *is the solution*

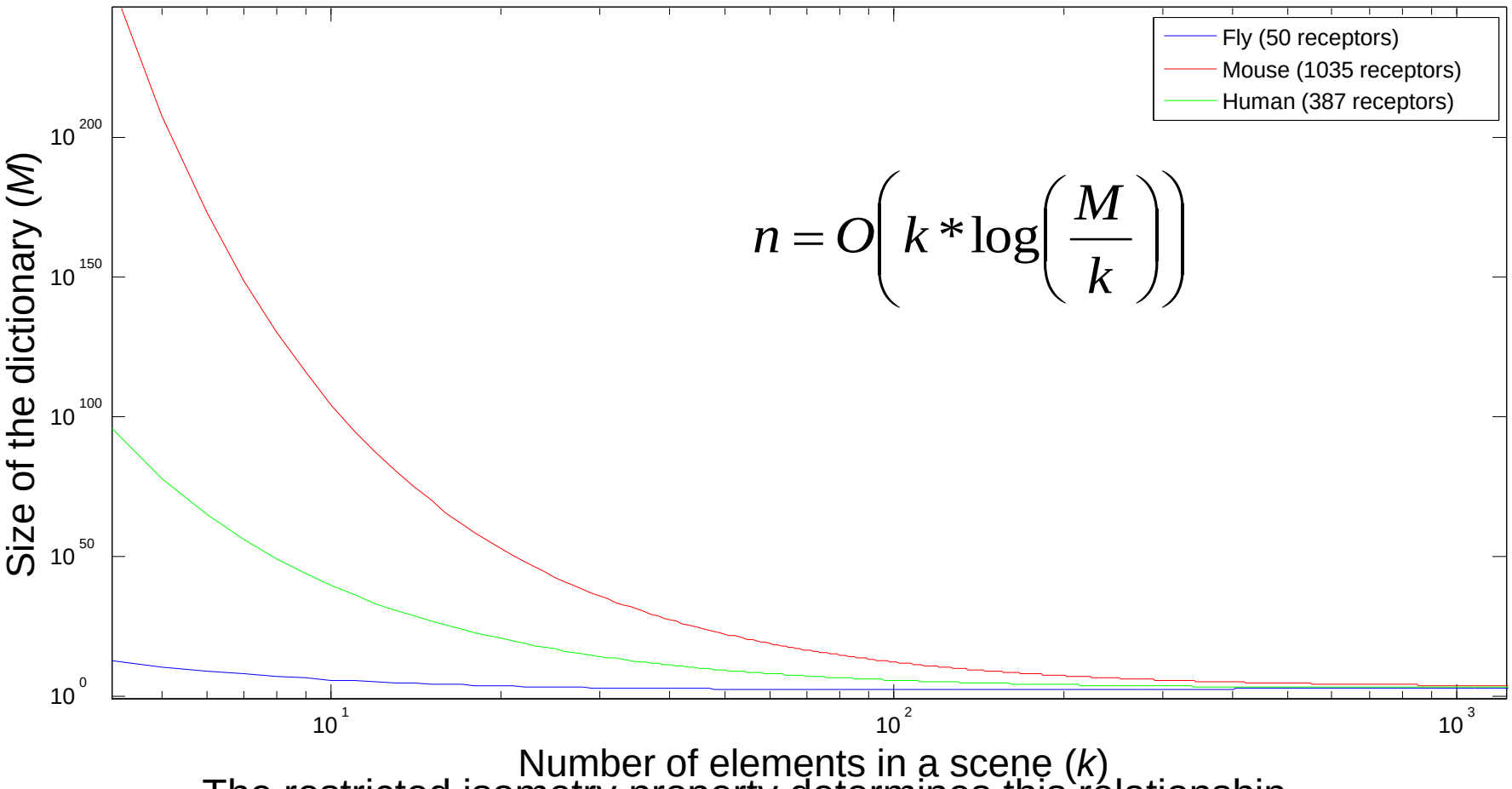
Matrices taken from a random ensemble satisfy the restricted isometry property (RIP)

B



$$n = O\left(k * \log\left(\frac{M}{k} \right) \right)$$

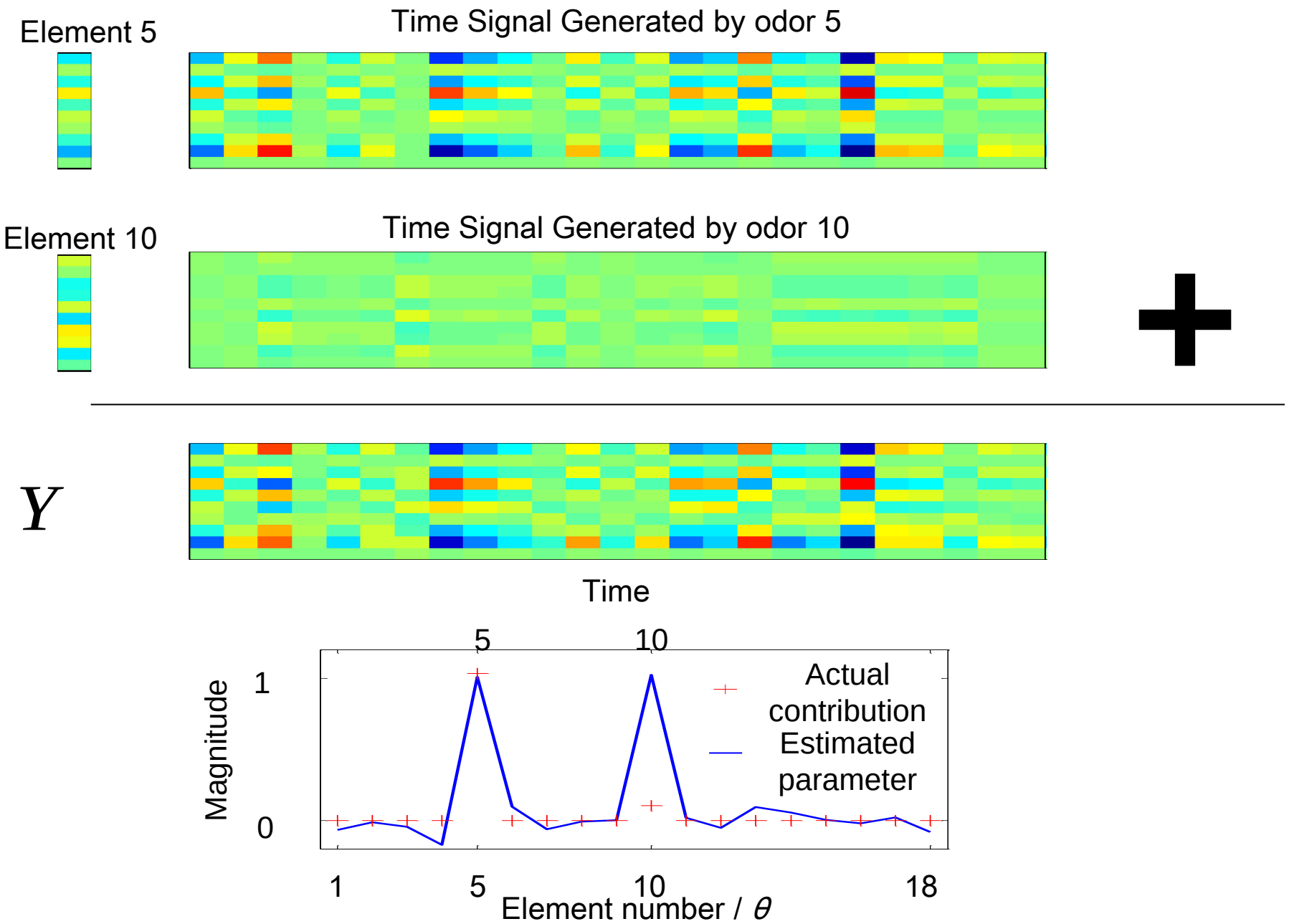
The number of receptors determine the complexity of the scene and the maximum size of the dictionary



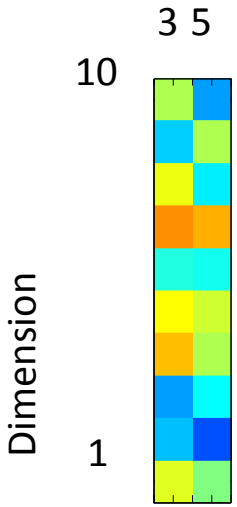
The restricted isometry property determines this relationship

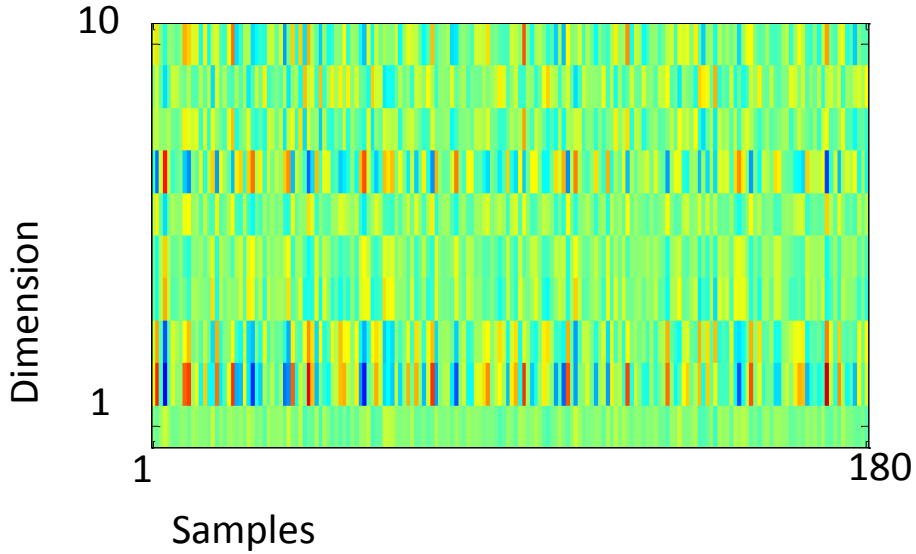
50 different volatile components in leaf litter, V. A. Isidorov1 et al, 2010

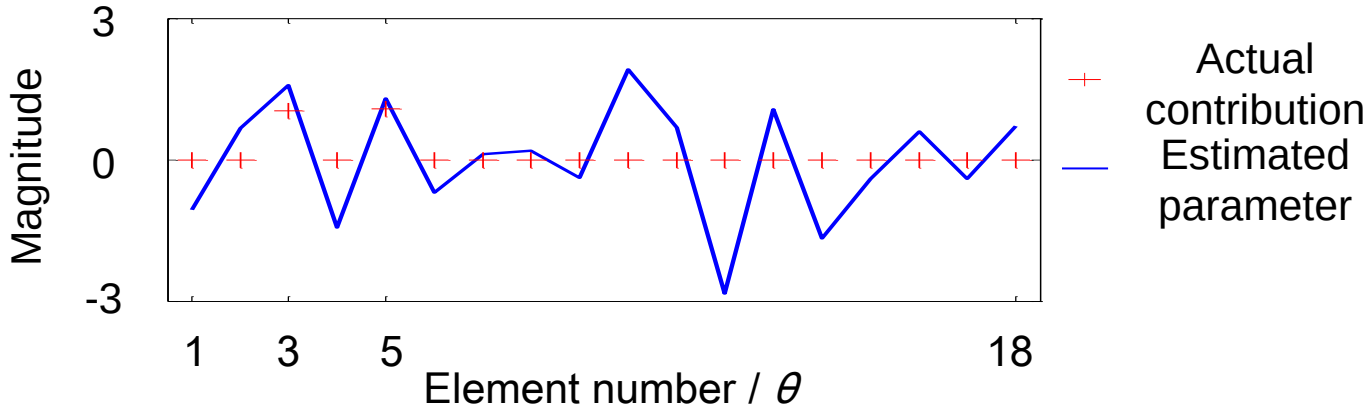
Amplitude invariant identification of sources



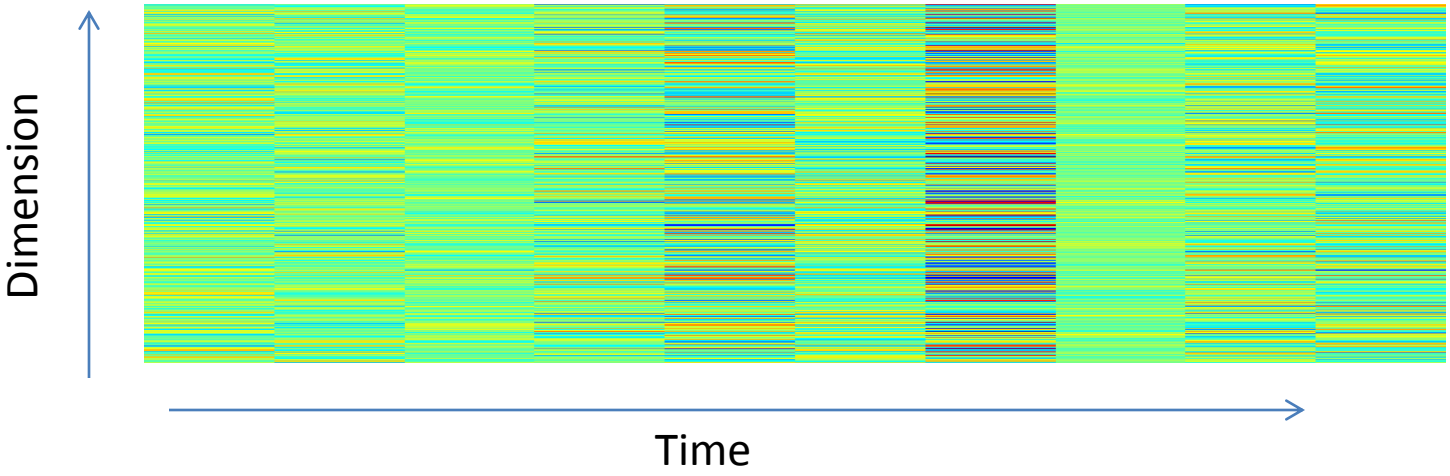
Solution is not exact for very similar vectors (needle in a haystack problem)



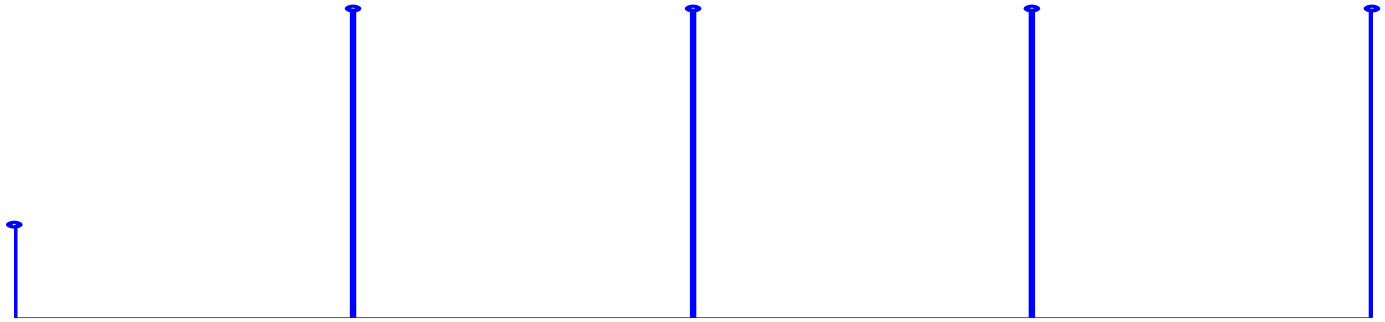




CPA identifies sources under challenging conditions

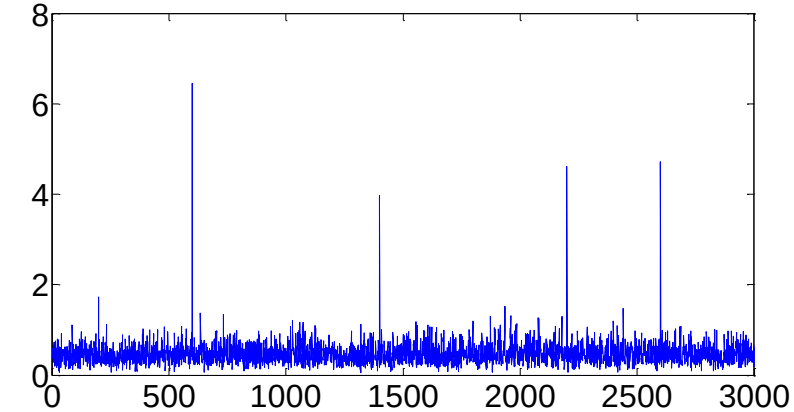


450 dimensions
Dictionary size =3000
5 elements present
Additive gaussian noise of twice the amplitude of the signal

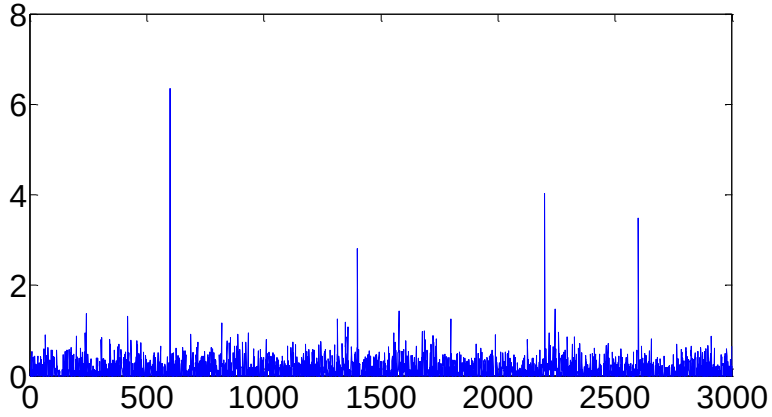


CPA identifies sources under challenging conditions

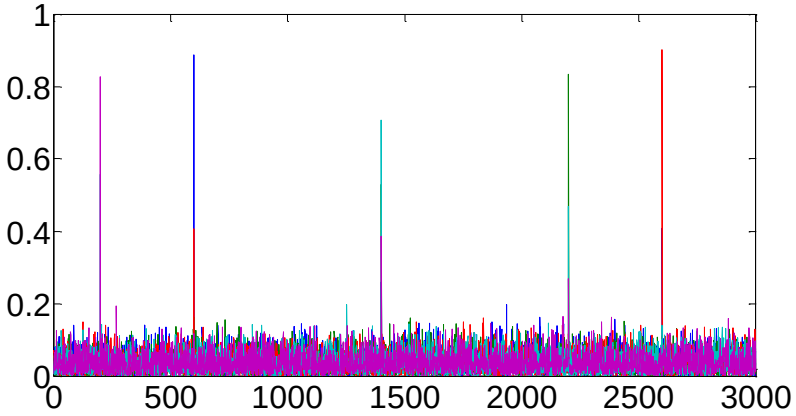
Template matching



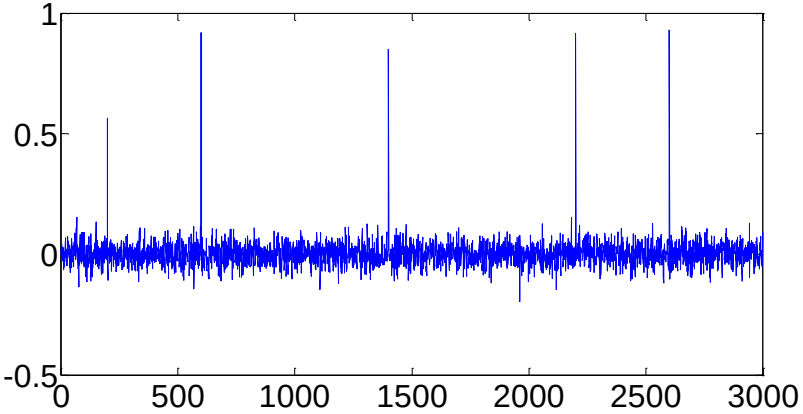
Matching pursuit (≈L1 optimization)



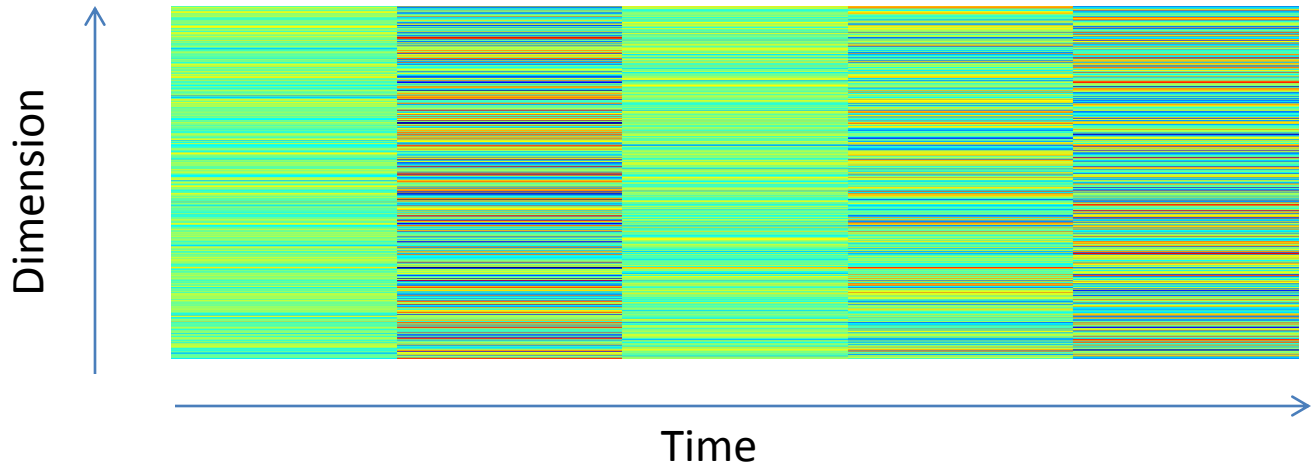
PCA (blind separation)



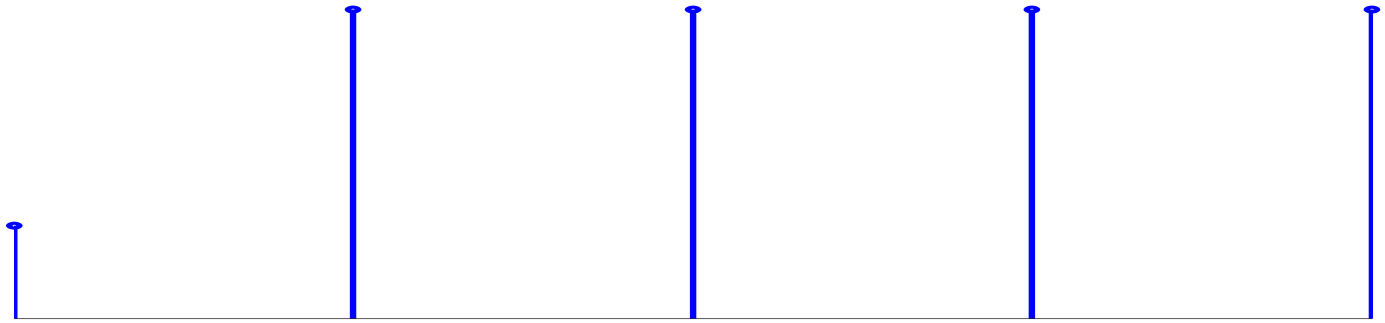
CPA



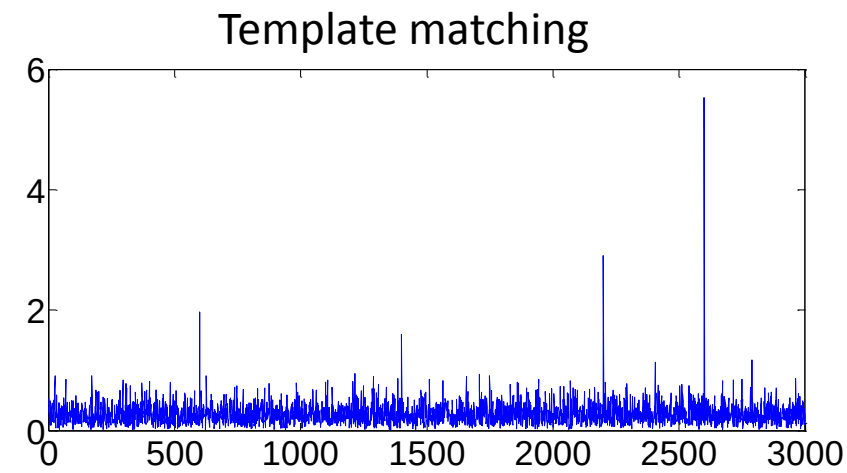
CPA identifies sources under challenging conditions

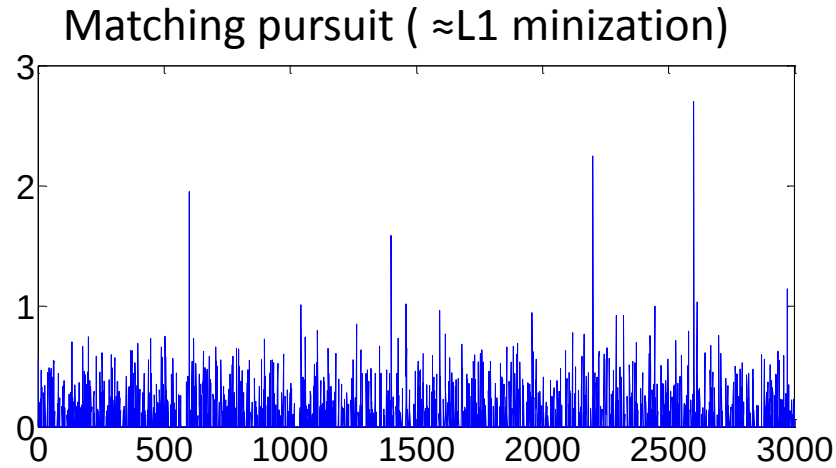


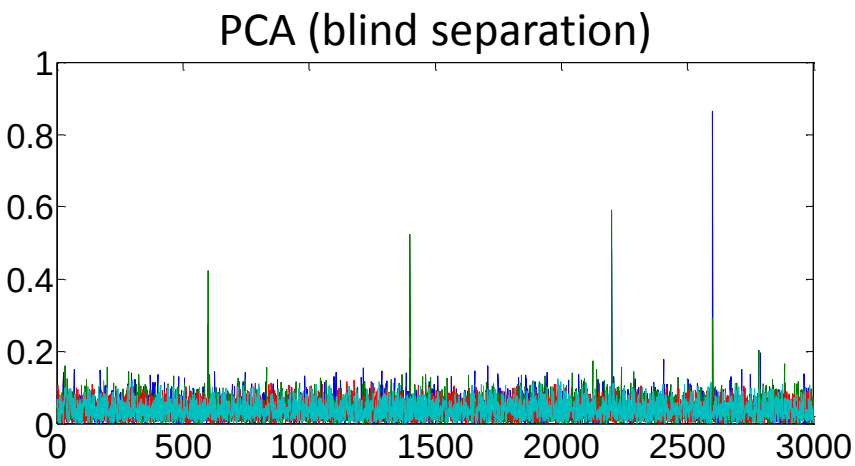
450 dimensions
Dictionary size =3000
5 elements present
Additive gaussian nose of twice the amplitude of the signal

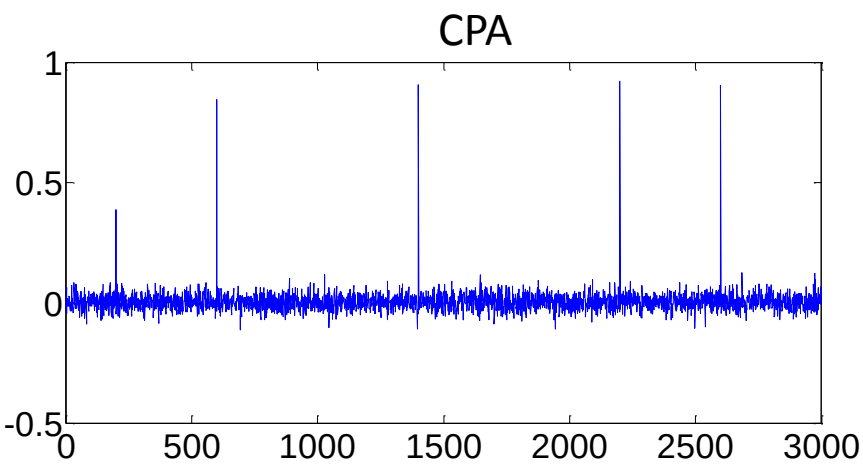


CPA identifies sources under challenging conditions

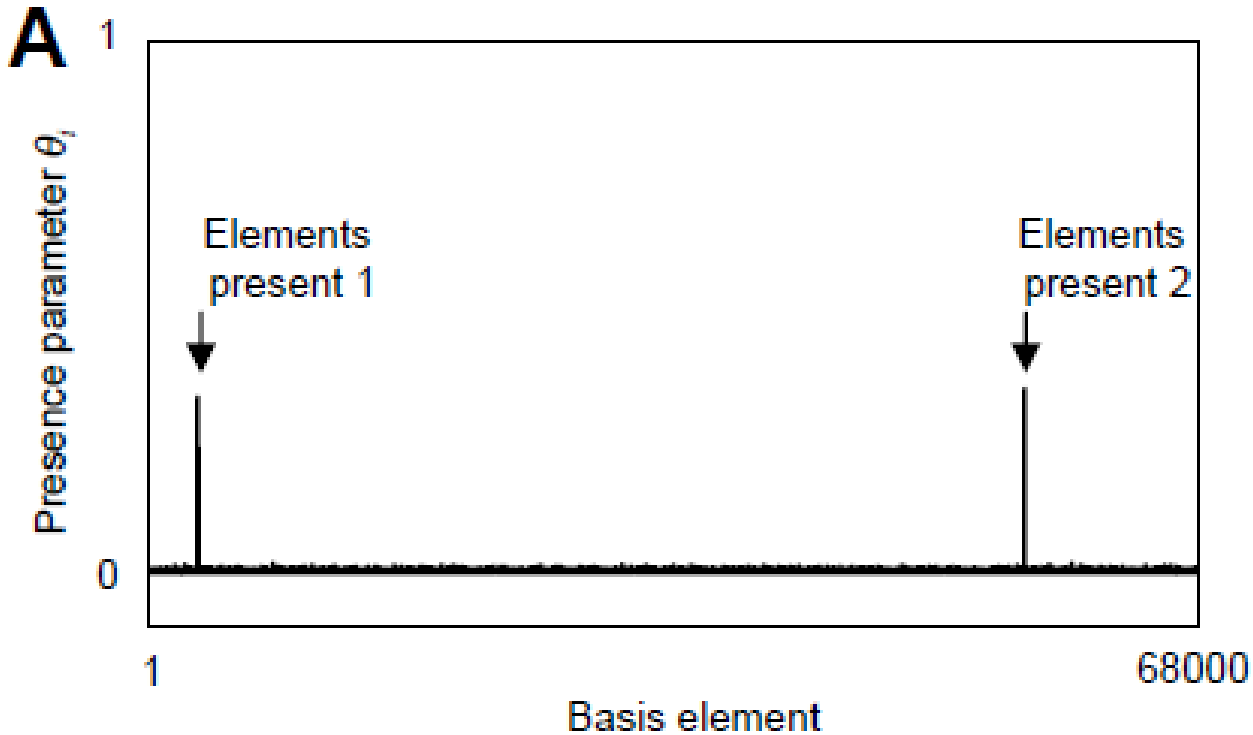








CPA can use very large dictionaries



400 dimensions
68000 dictionary elements
7 time samples

Otazu and Leibold, *PLoS One*, 2011

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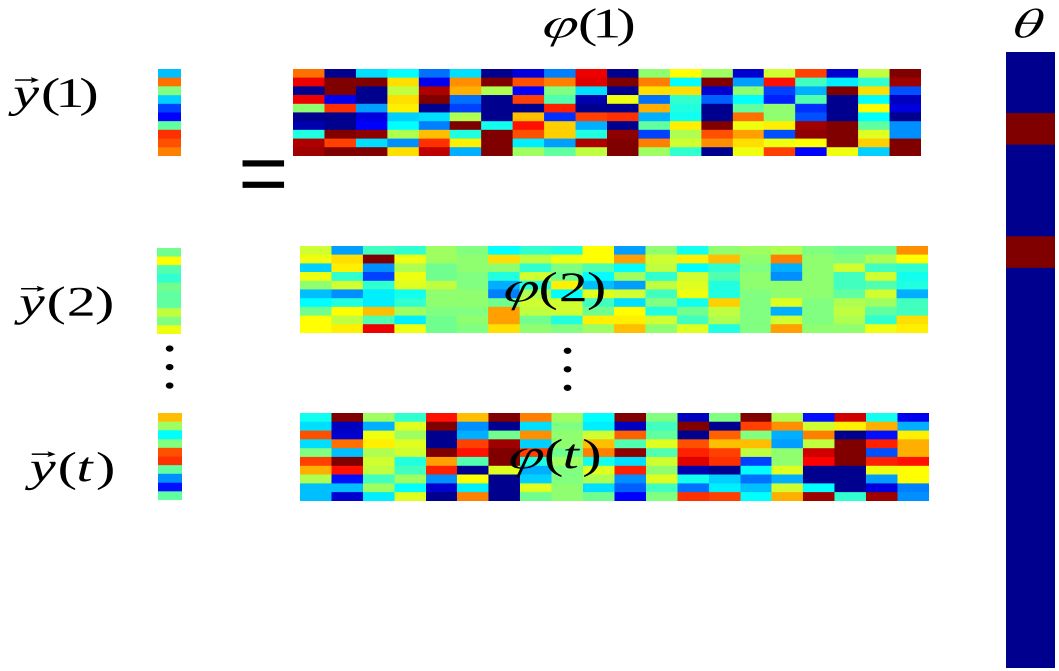
1. Odor identification problem in complex scenes
2. Reformulation of the problem as estimation of odor presences
   - Solution is unique
   - Solution estimate the sources present under challenging conditions
3. Recursive implementation of the algorithm
4. Experimental characterization of cortical feedback and the effect of cortical input on bulbar output

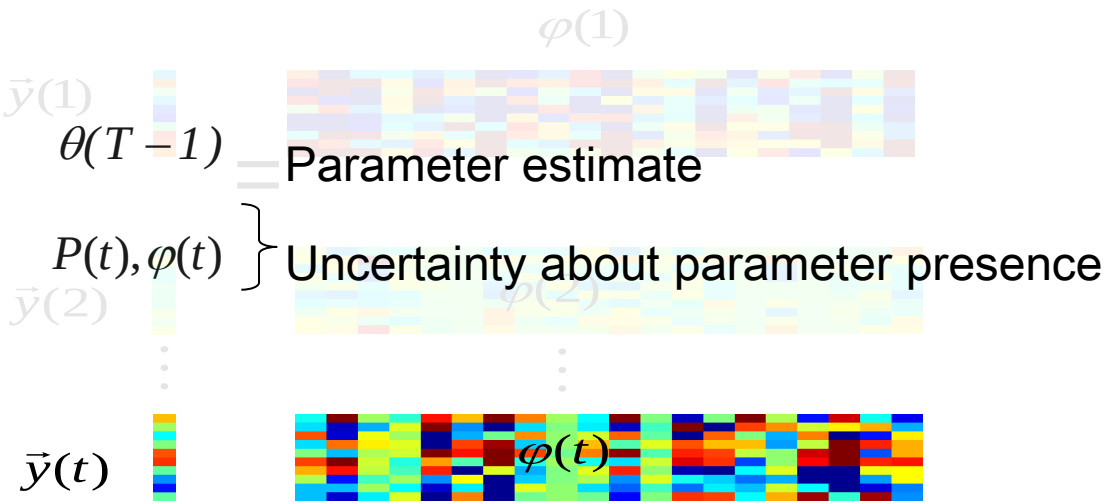
Standard CPA computation can be simplified



$$Y = \Phi\theta \qquad \theta = \left(\Phi^T\Phi\right)^{-1}\Phi^T Y$$

$(\Phi^T\Phi)$ is M by M

Iterative CPA (iCPA) process each observation when it arrives



$$\boldsymbol{P}(T) = \boldsymbol{P}(T-1) - \boldsymbol{P}(T-1)\boldsymbol{\varphi}^T(T)(\boldsymbol{I} + \boldsymbol{\varphi}(T)\boldsymbol{P}(T-1)\boldsymbol{\varphi}^T(T))^{-1}\boldsymbol{\varphi}(T)\boldsymbol{P}(T-1)$$

$$\hat{y}(T) = \boldsymbol{\varphi}(T)\vec{\Theta}(T-1)$$

$$\theta(T) = \theta(T-1) + \underbrace{P(T)\varphi(T)\overbrace{*(\vec{y}(T) - \hat{y}(T))}^{\text{Estimation error}}}_{\Delta\theta(T)}$$

iCPA have variables of different dimensionality and different dynamics

$$\boldsymbol{P}(T) = \boldsymbol{P}(T-1) - \boldsymbol{P}(T-1)\boldsymbol{\varphi}^T(T)(\boldsymbol{I} + \boldsymbol{\varphi}(T)\boldsymbol{P}(T-1)\boldsymbol{\varphi}^T(T))^{-1}\boldsymbol{\varphi}(T)\boldsymbol{P}(T-1)$$

$$\hat{y}(T) = \boldsymbol{\varphi}(T)\theta(T-1)$$

$$\theta(T) = \theta(T-1) + P(T)\varphi(T) * (\vec{y}(T) - \hat{y}(T))$$

Largest dimension variables (order M by M): P

Second dimension variables (order N by M): φ

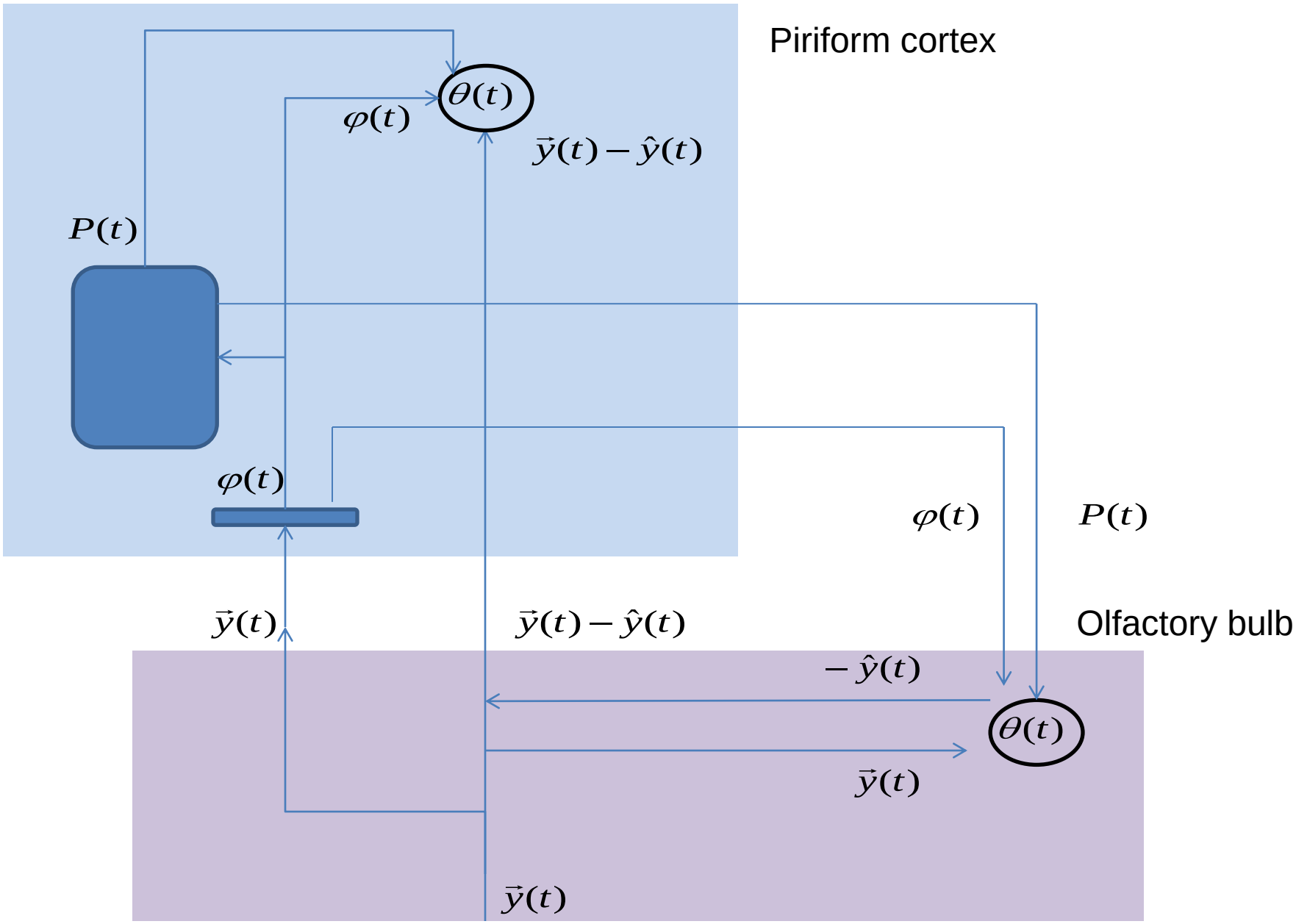
M>>N

Third largest variable (order M by 1): θ

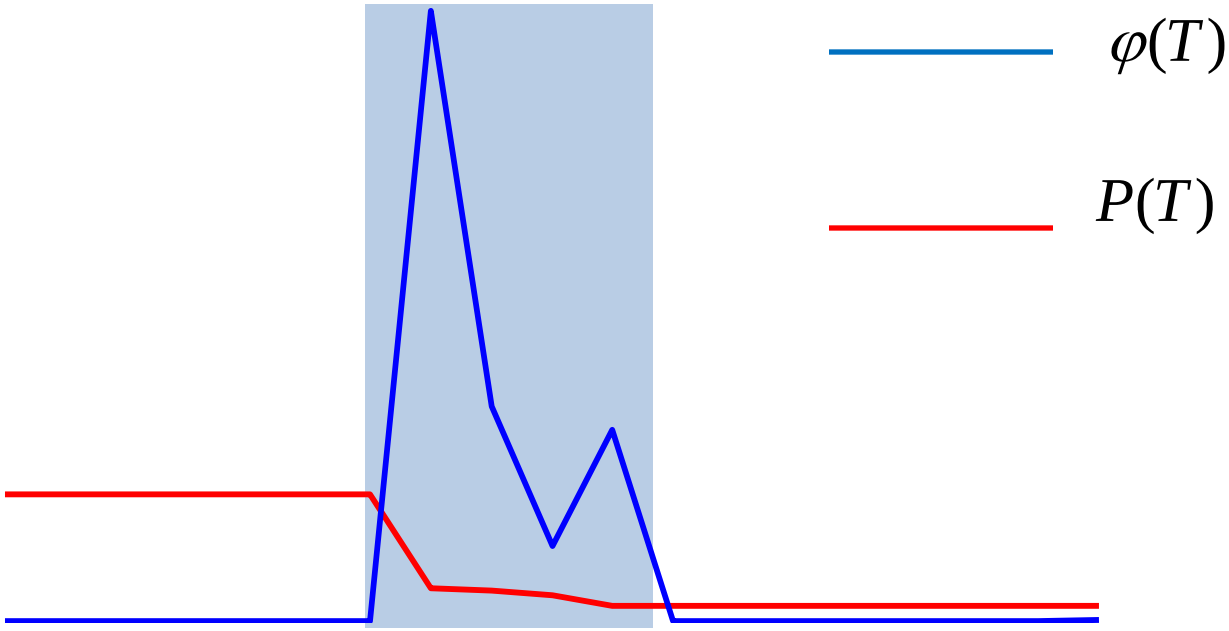
Smalles variable (order N by 1): $\vec{y}\,(t)$, $\hat{y}(t)$

2 variables for temporal integration: P, θ

Possible iCPA implementation in piriform/olfactory bulb circuit

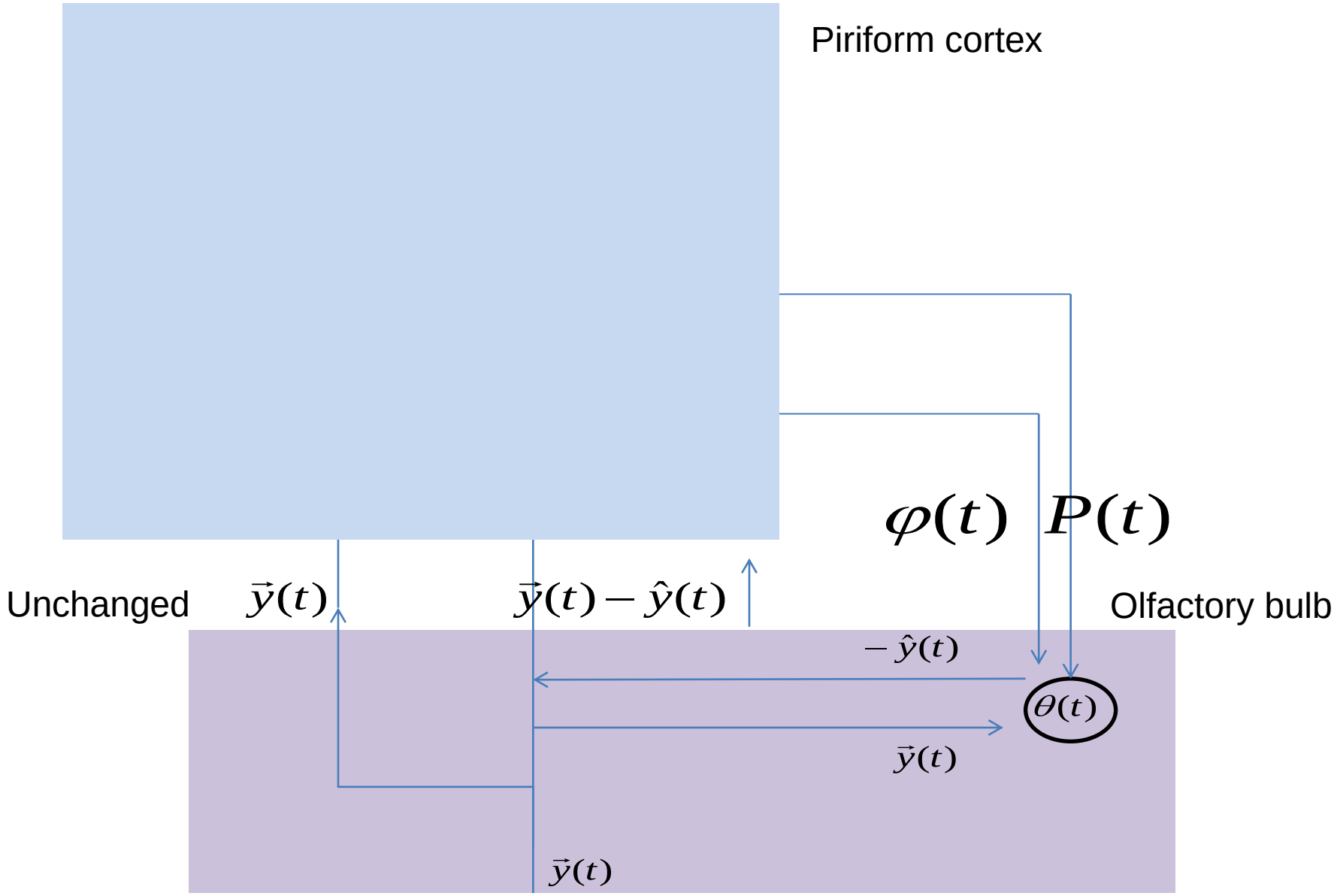


Model predicts feedback signals with different dynamics



$$\theta(T) = \theta(T-1) + P(T)\varphi(T) * (\vec{y}(T) - \hat{y}(T))$$

iCPA requires a feedback independent and a feedback dependent channel



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Experimental questions about piriform cortex feedback

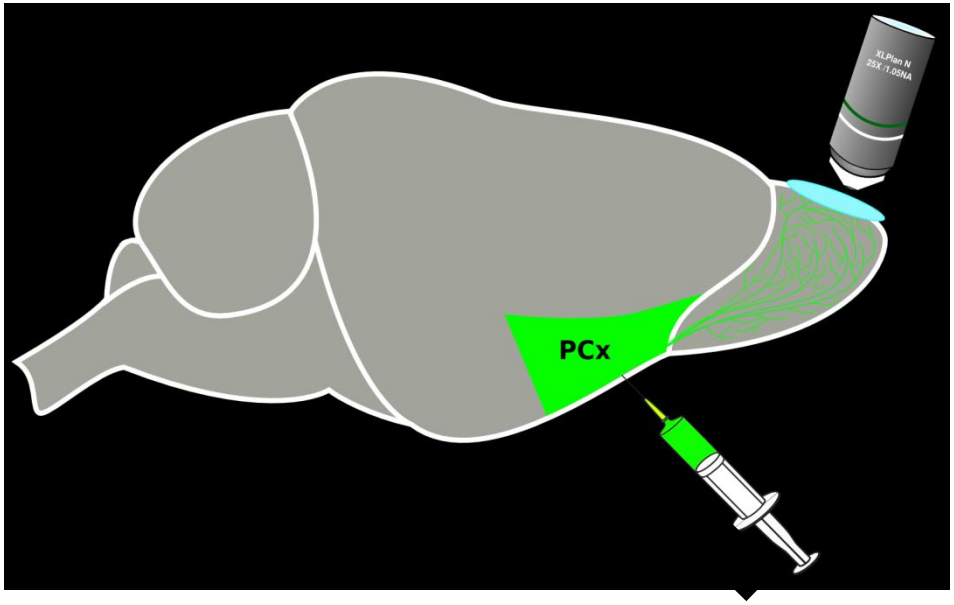
1) What type of signals does the piriform cortex send to the bulb?
2) How does the suppression of cortical feedback affect the output of the bulb?

Hong Goo Chae

Otazu*, Chae*, Davis, and Albeanu, *Neuron*, 2015

* Equal contribution

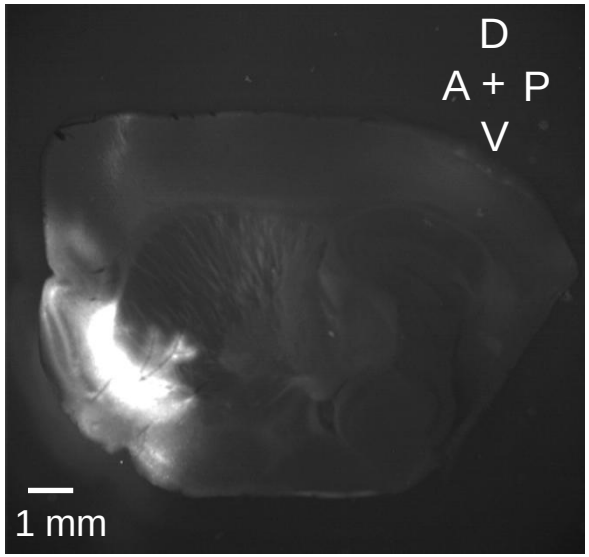
2P Calcium imaging of cortical feedback axons in the olfactory bulb of awake head-fixed mice

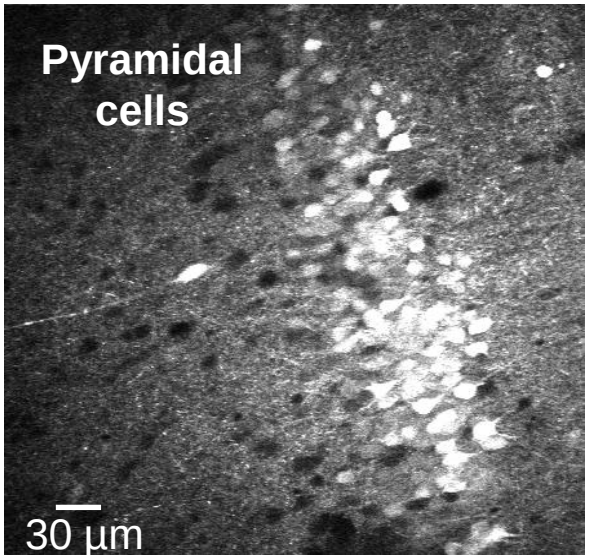


Axonal imaging: Petreanu et al, 2012, Glickfeld et al, 2013

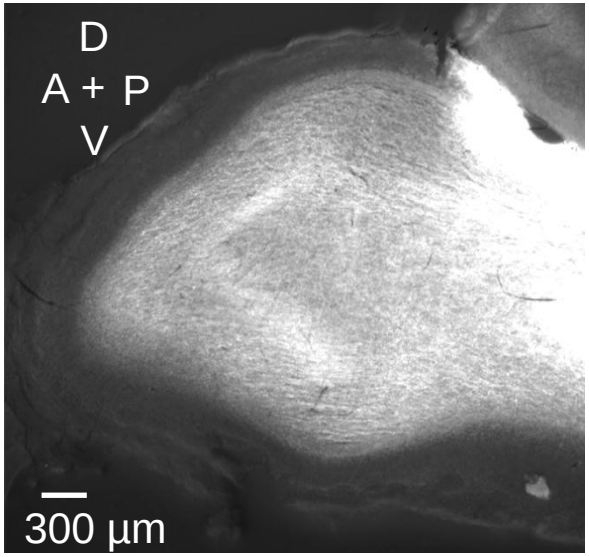
GCaMP5 expression in cortico-bulbar feedback axons

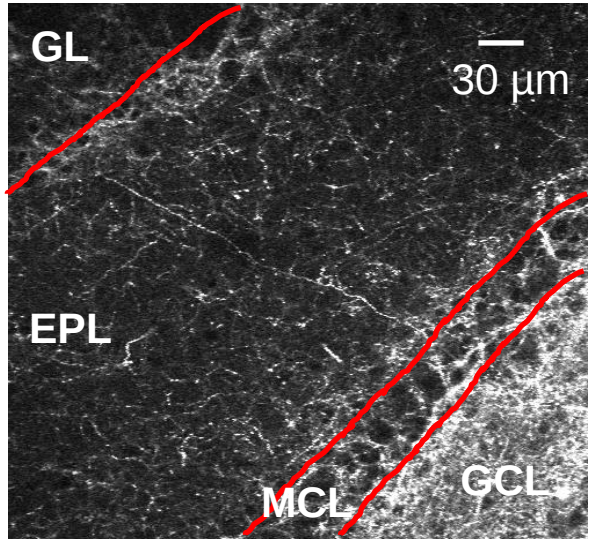
Piriform Cortex



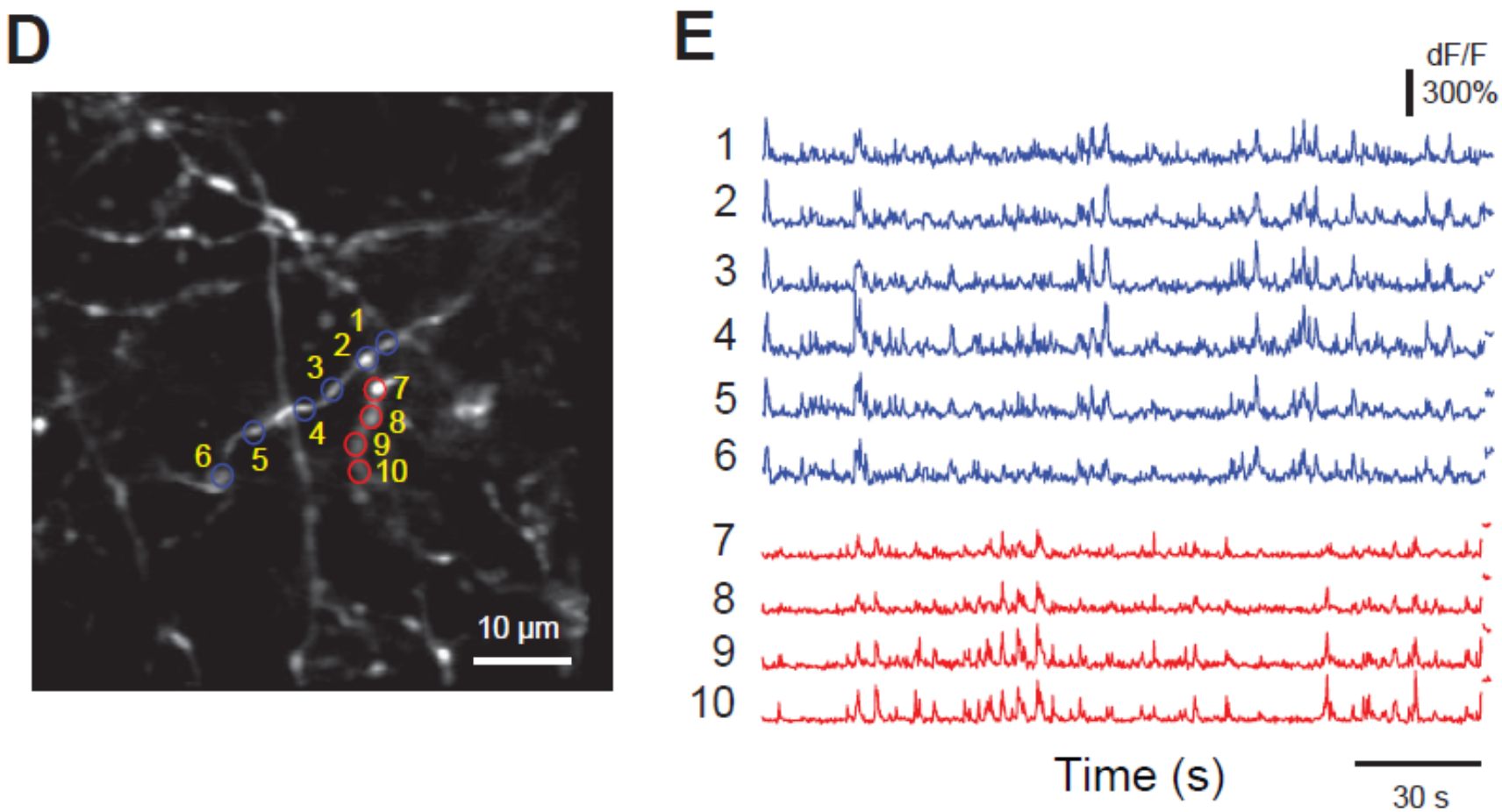


Cortical feedback fibers in the bulb



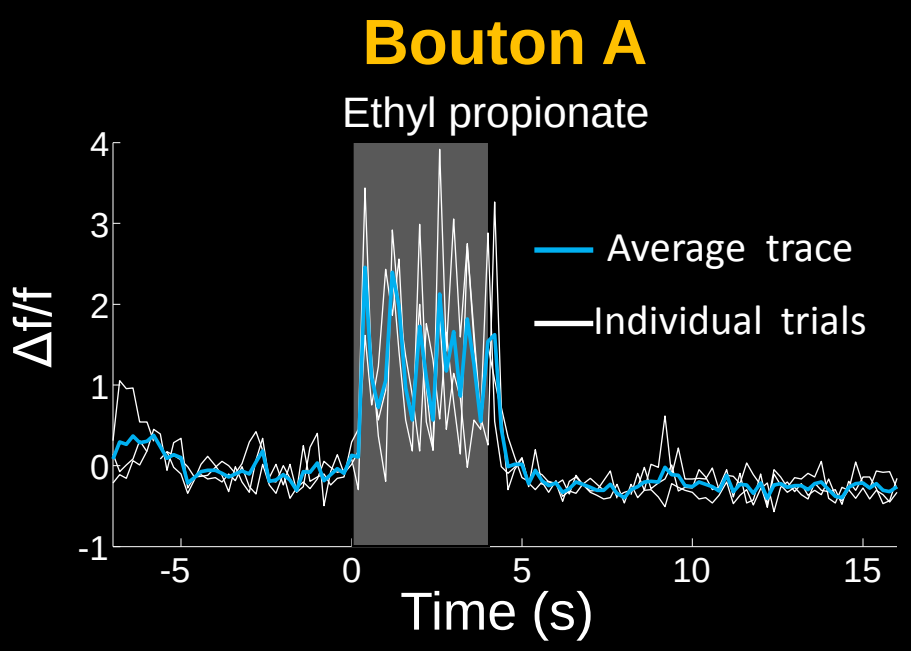


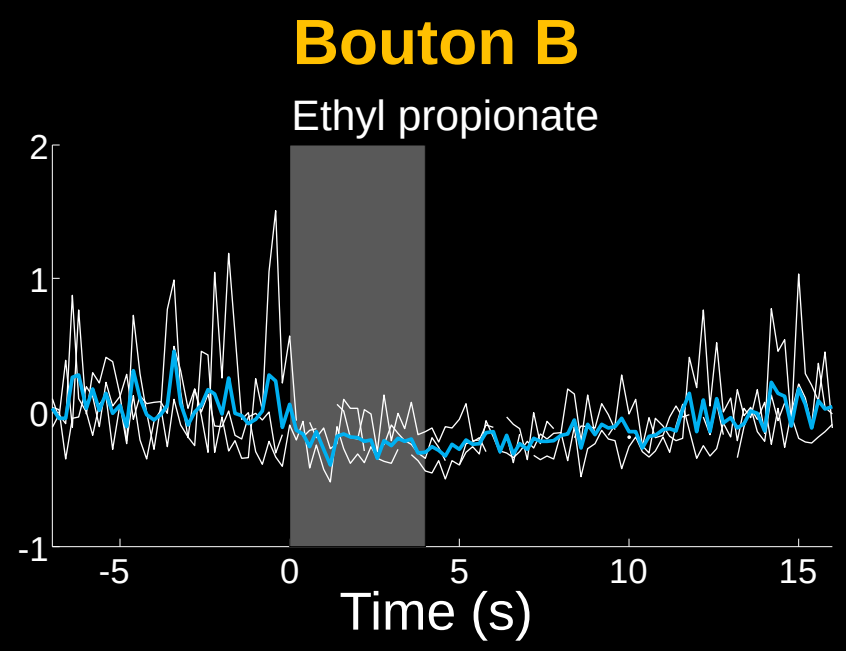
Rich spontaneous activity in cortical feedback boutons

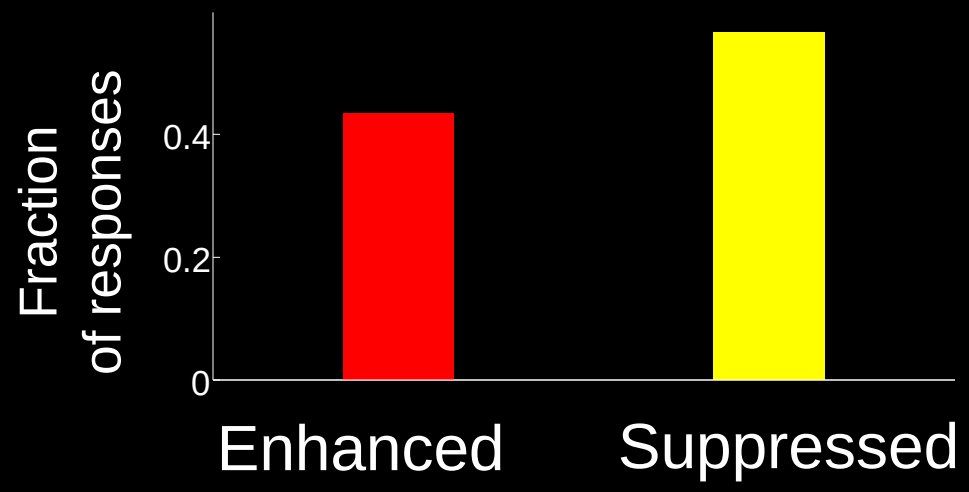


- 5,221 boutons, 4 mice
- **57%** boutons show spontaneous activity
- **Brief (<1 s)** and **locally diverse** events

Odors can enhance or suppress cortical feedback

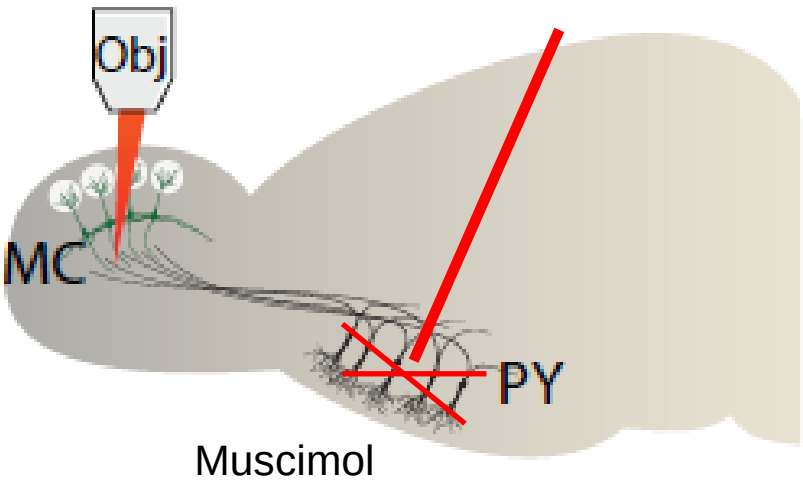


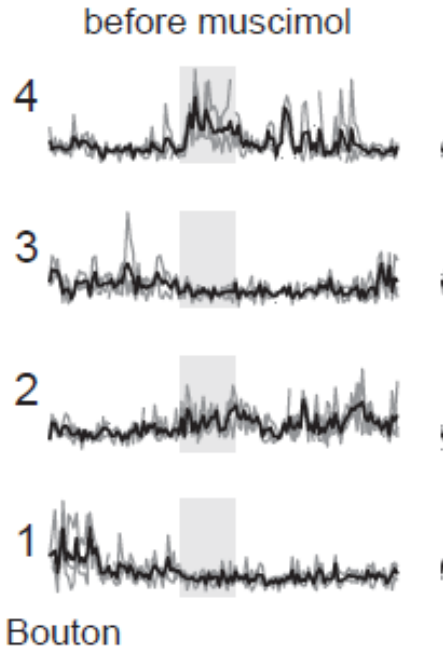


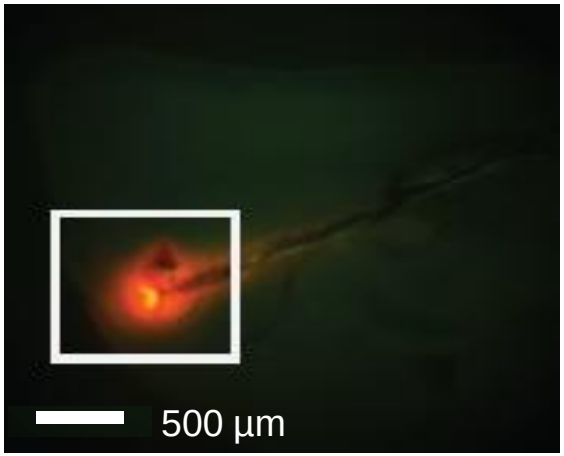


3,776 responses
4 mice

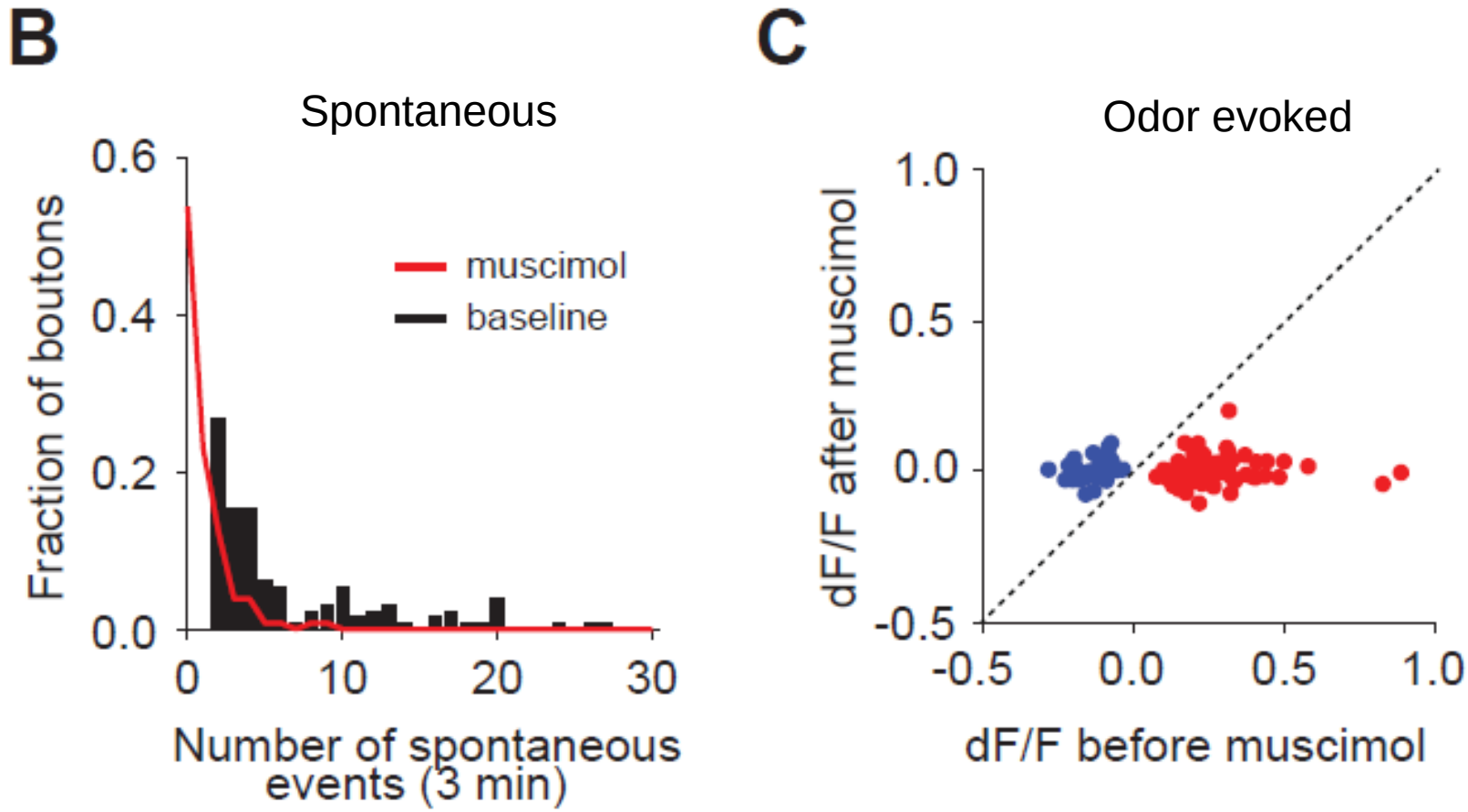
Cortical feedback axons are silenced by piriform cortical inactivation



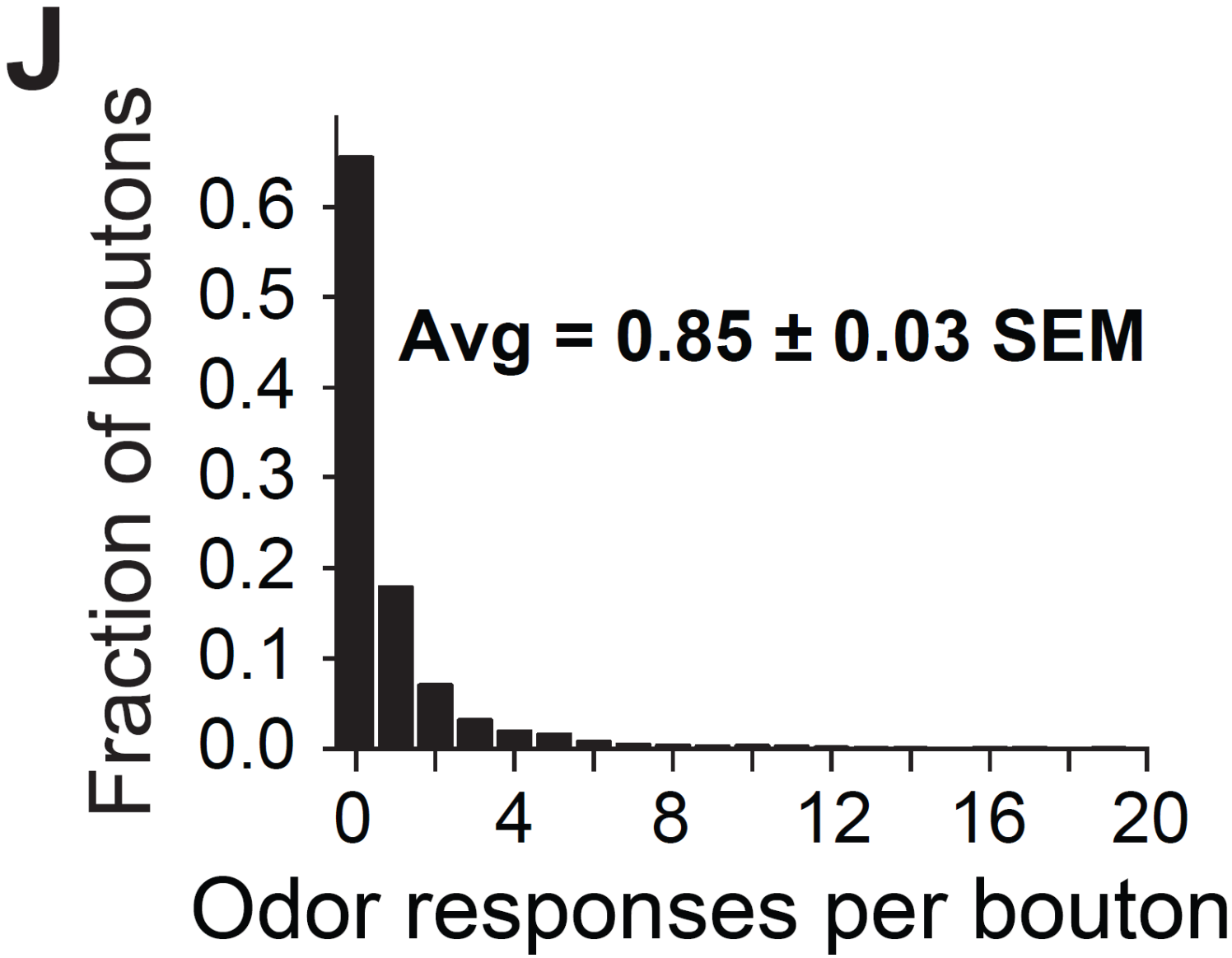




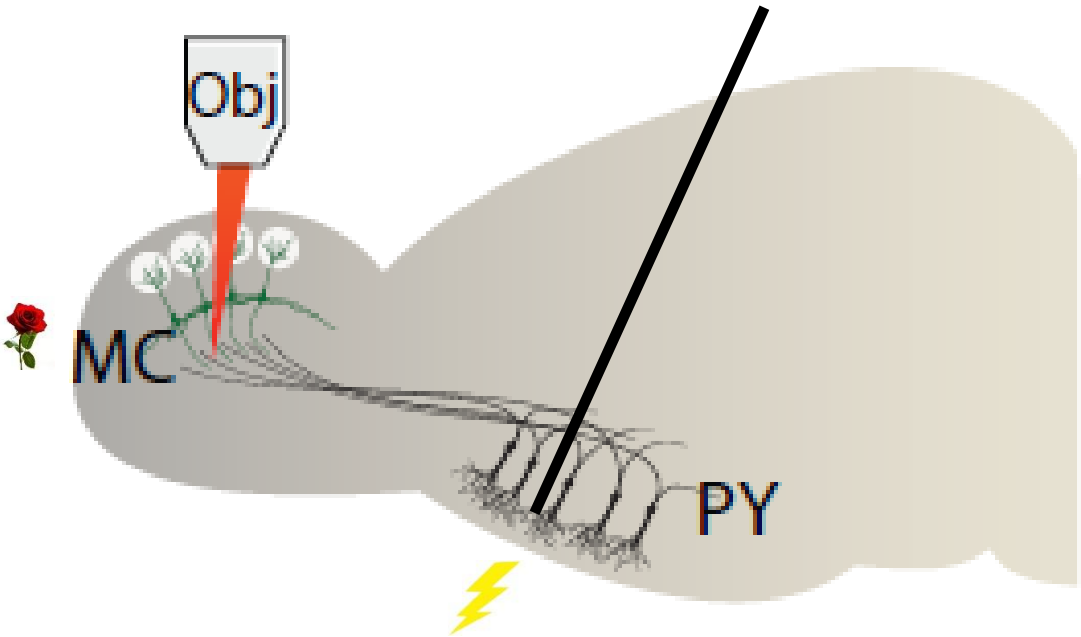
Cortical feedback axons are silenced by piriform cortical inactivation

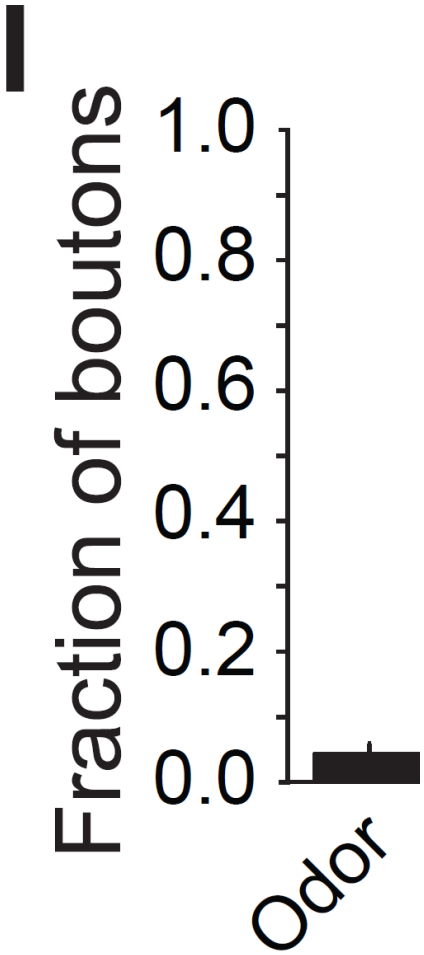


Cortical feedback axons respond to only a few odors



Cortical feedback responses are sparse

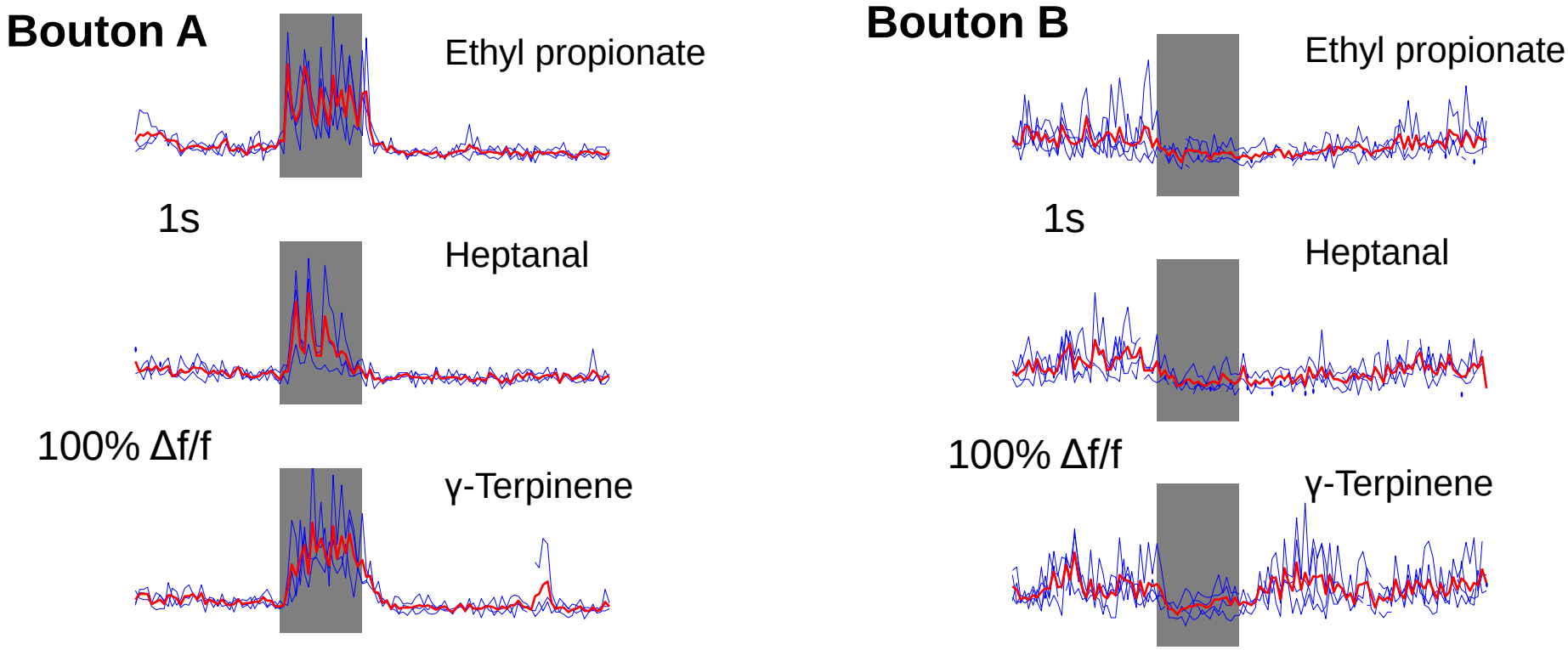




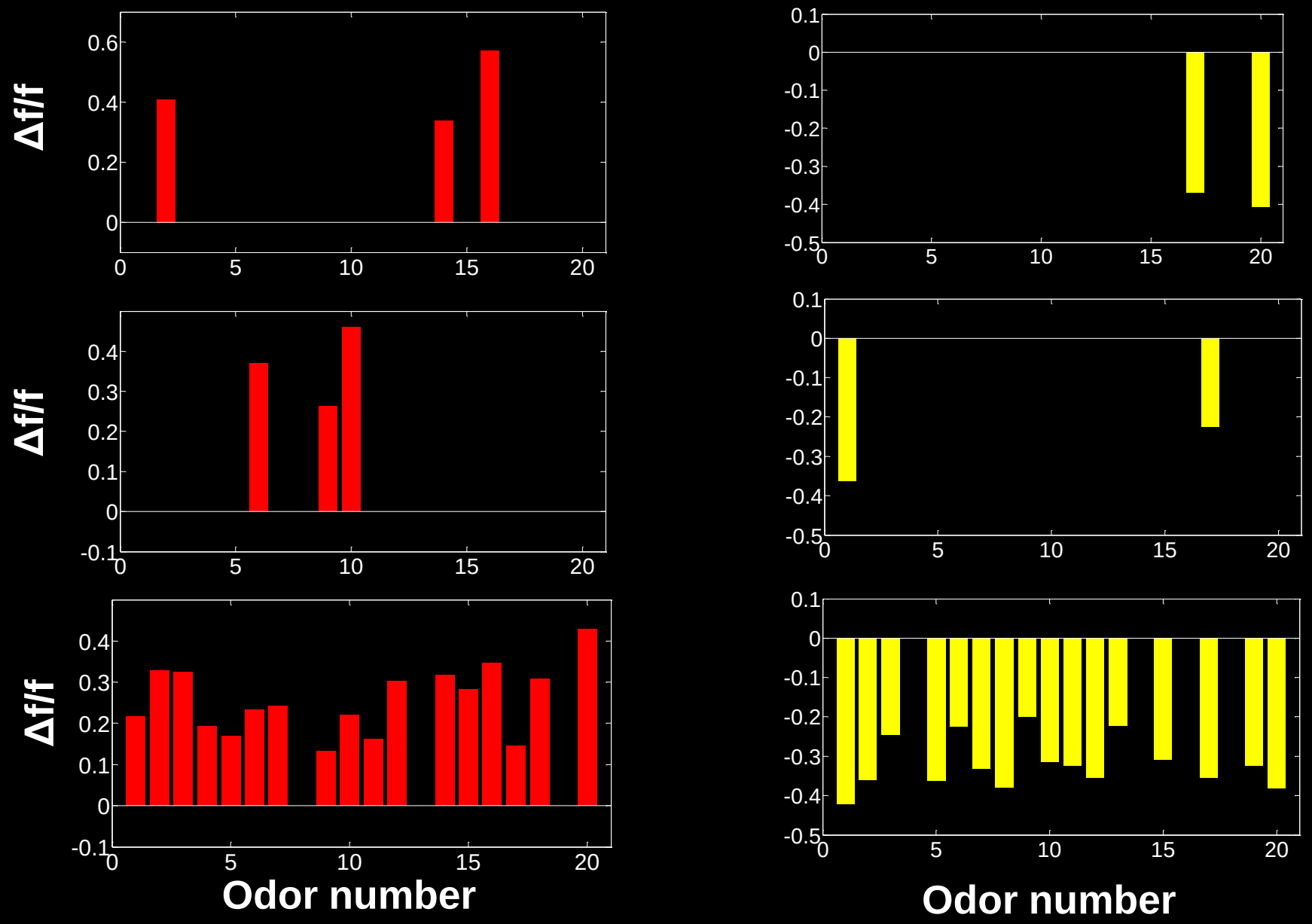
Amplitude:30 µA,
Frequency:100 Hz,
Pulse widht: 100 µs
Duration: 0.4 s

Cortical feedback boutons are sparse and odor selective

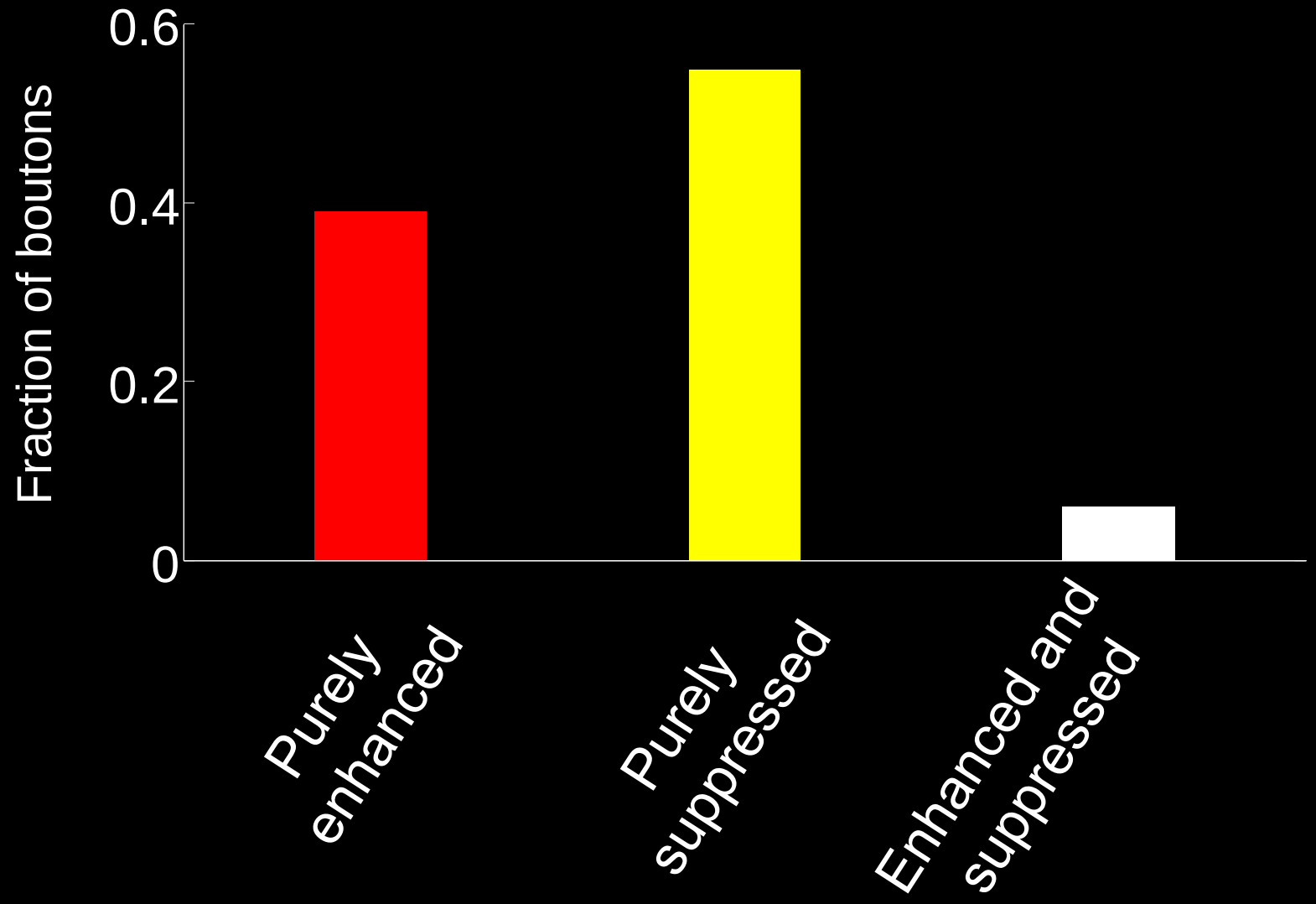
Boutons show either enhancement or suppression across odors



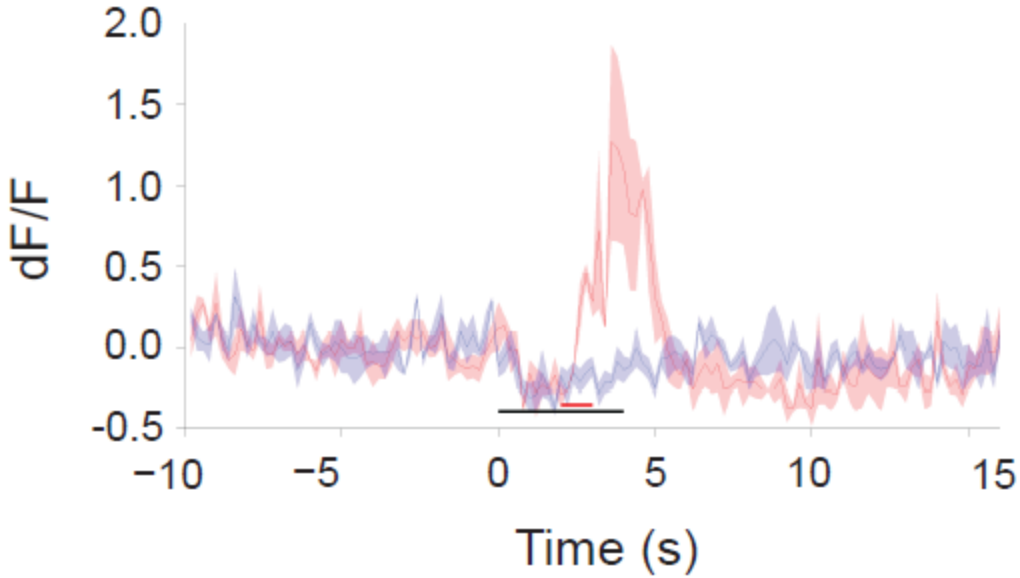
Boutons show either enhancement or suppression across odors

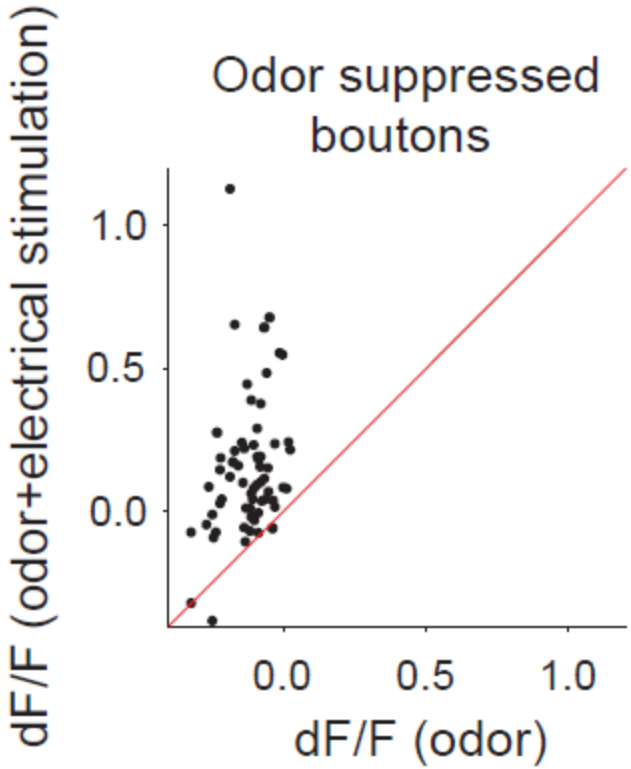


Very few boutons show both enhanced and suppressed responses

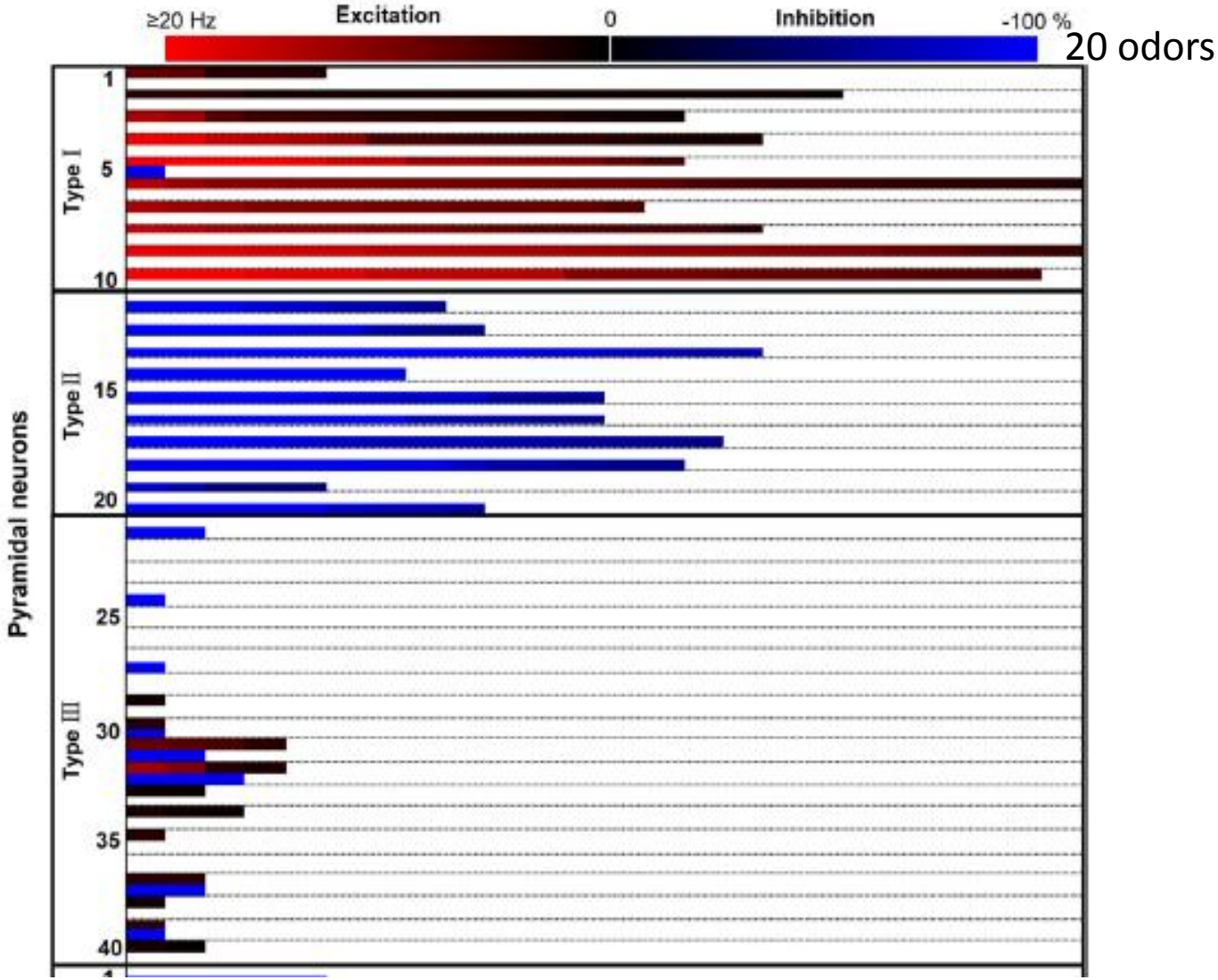


Odor evoked suppression can be overcome by electrical stimulation



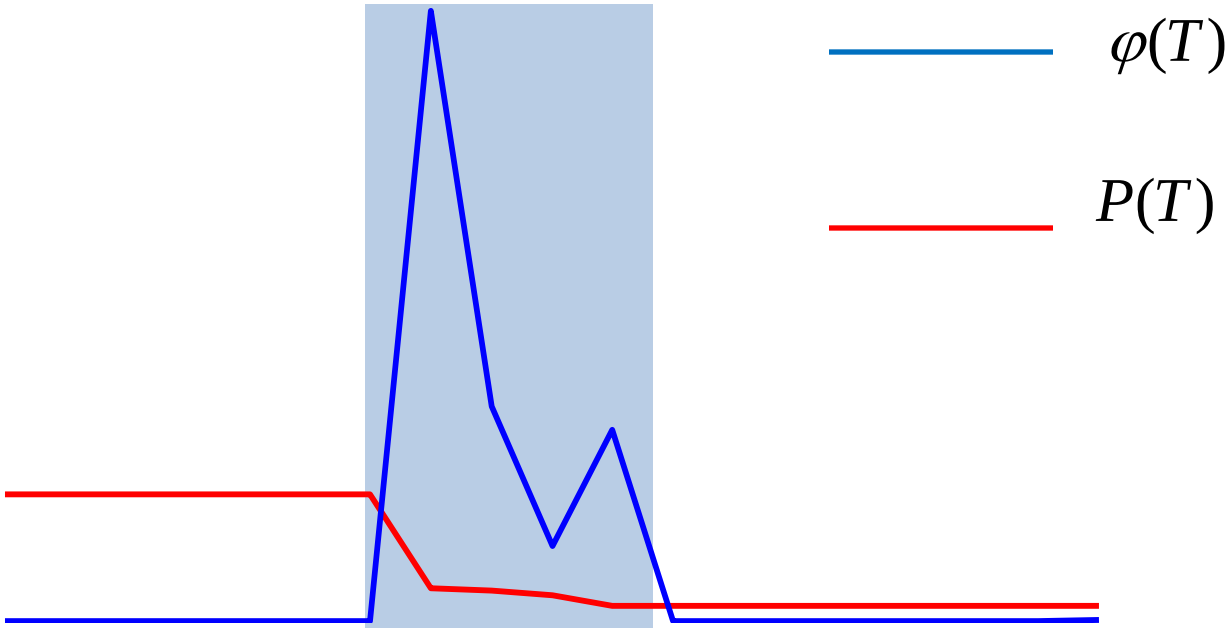


Locally recorded piriform cortical neurons showed purely enhanced and purely suppressed cells



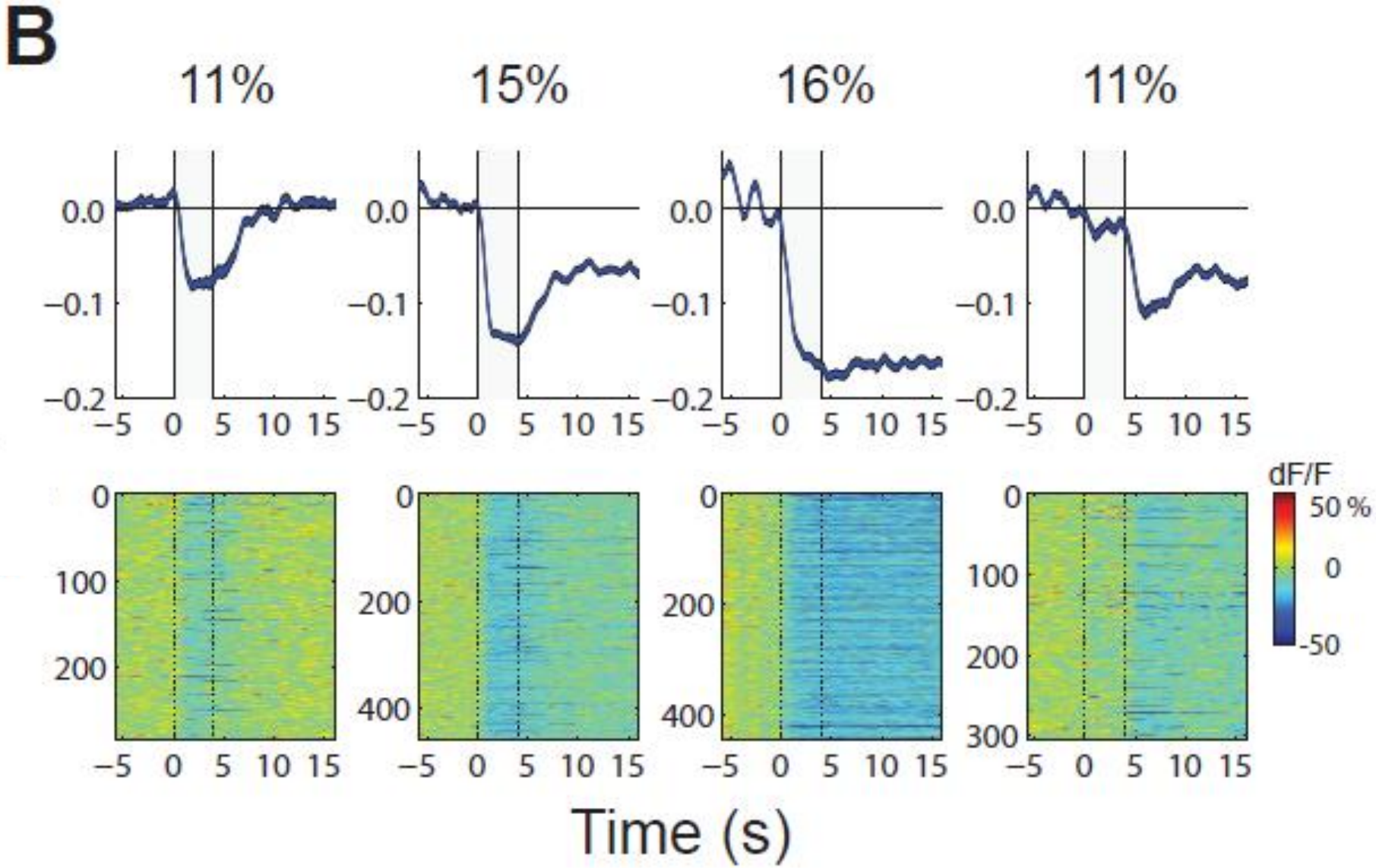
Zhan and Luo, 2010

Model predicts that feedback signals have different dynamics

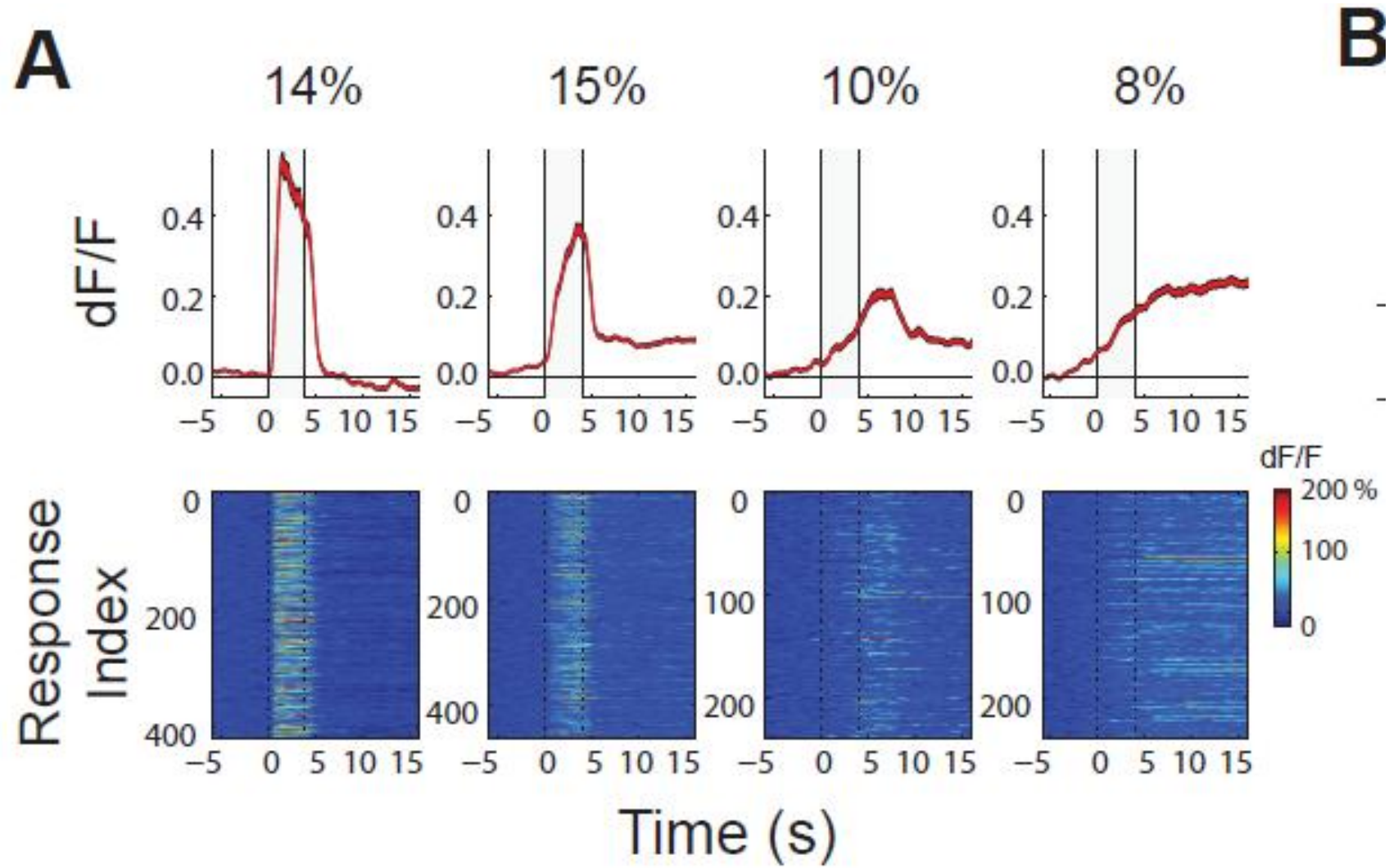


$$\theta(T) = \theta(T-1) + P(T)\varphi(T) * (\vec{y}(T) - \hat{y}(T))$$

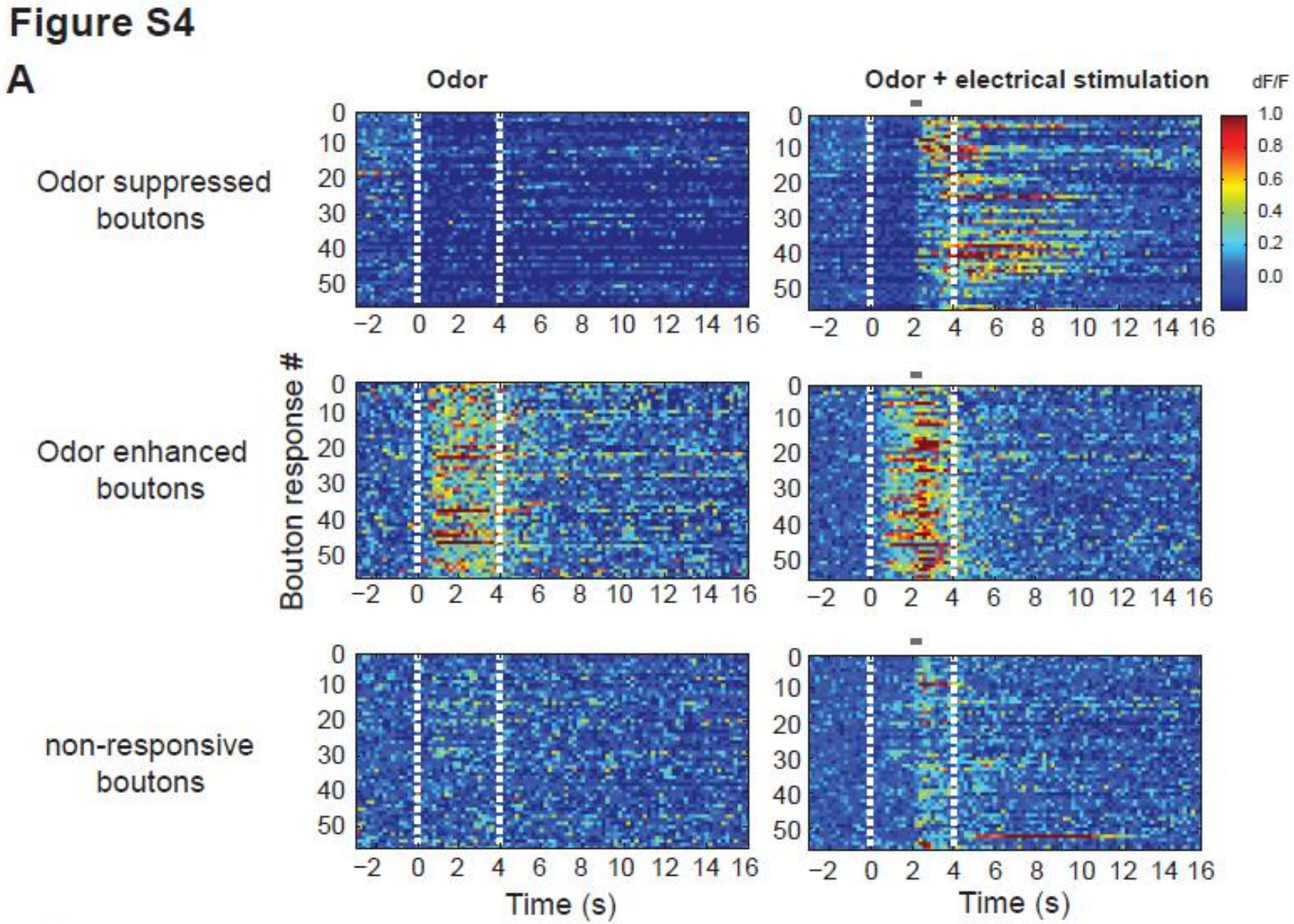
Most suppressed responses outlast odor presentation



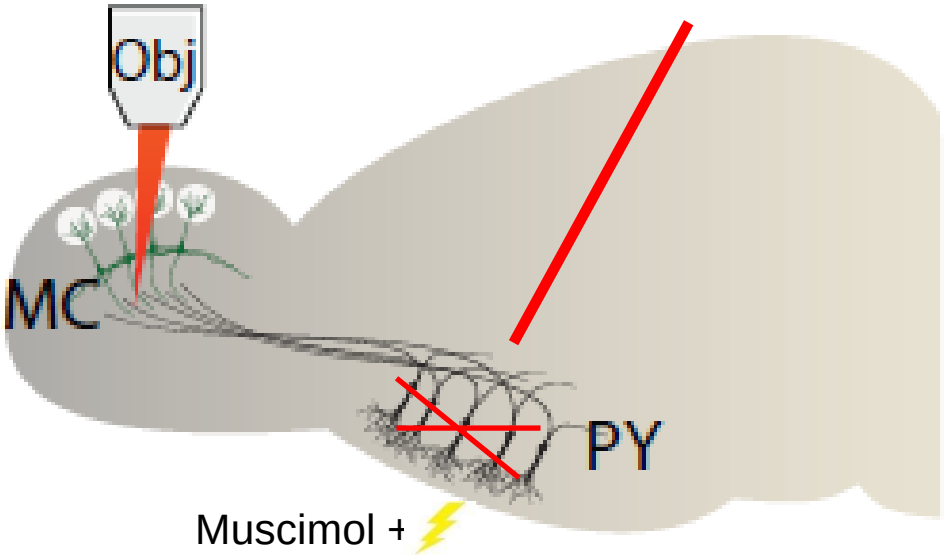
Enhanced responses have less long lasting responses



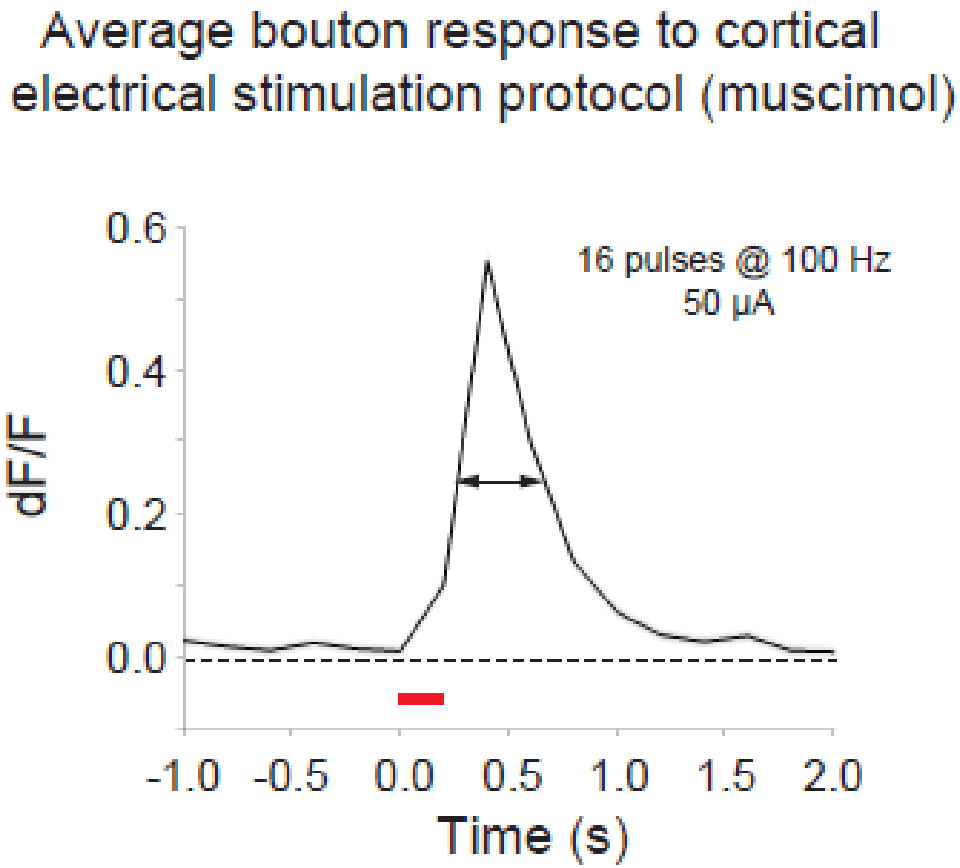
Piriform electrical stimulation triggers long lasting enhancement in suppressed response boutons



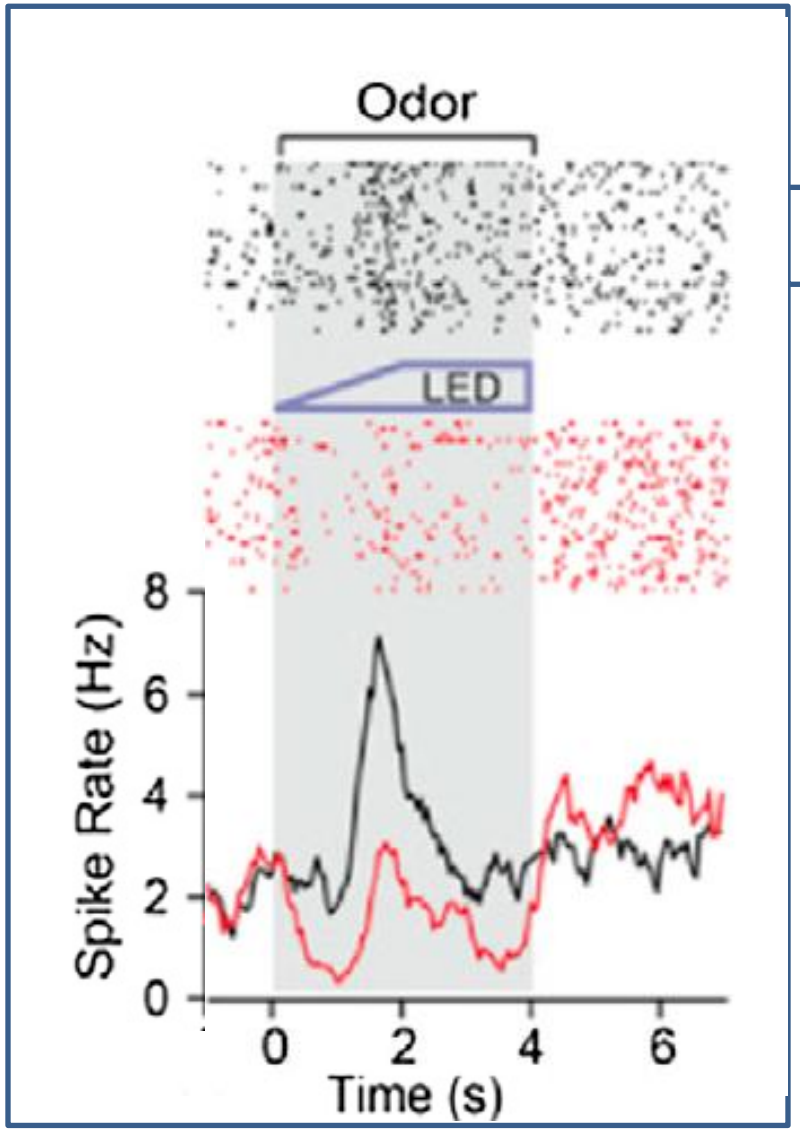
Determination of temporal dynamics in axonal boutons



Feedback bouton calcium dynamicst is fast

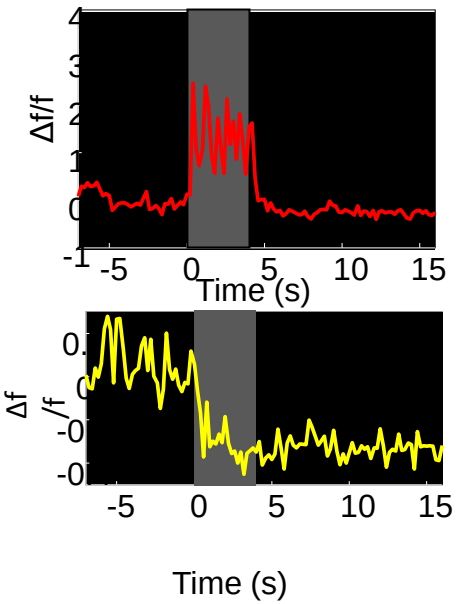


Optogenetic activation of cortical feedback suppresses olfactory bulb output



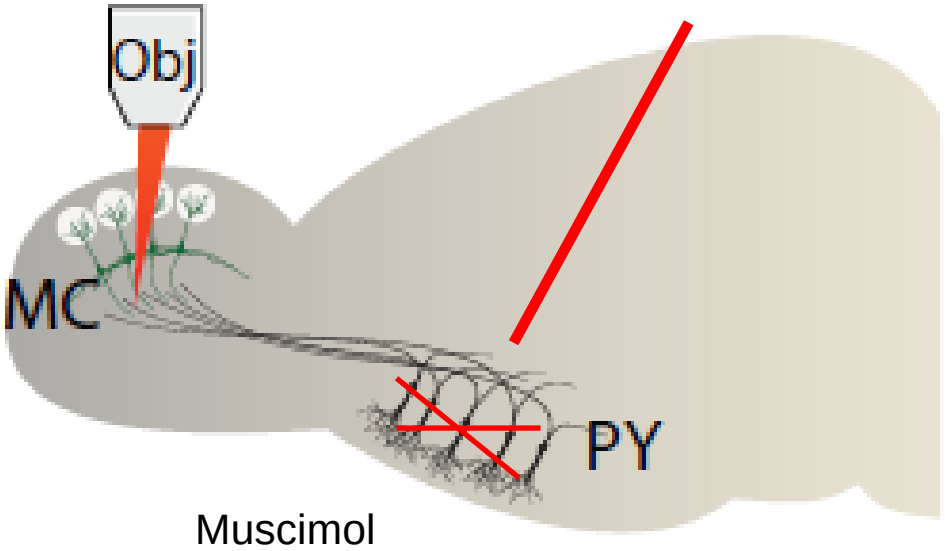
Without feedback activation

With feedback activation



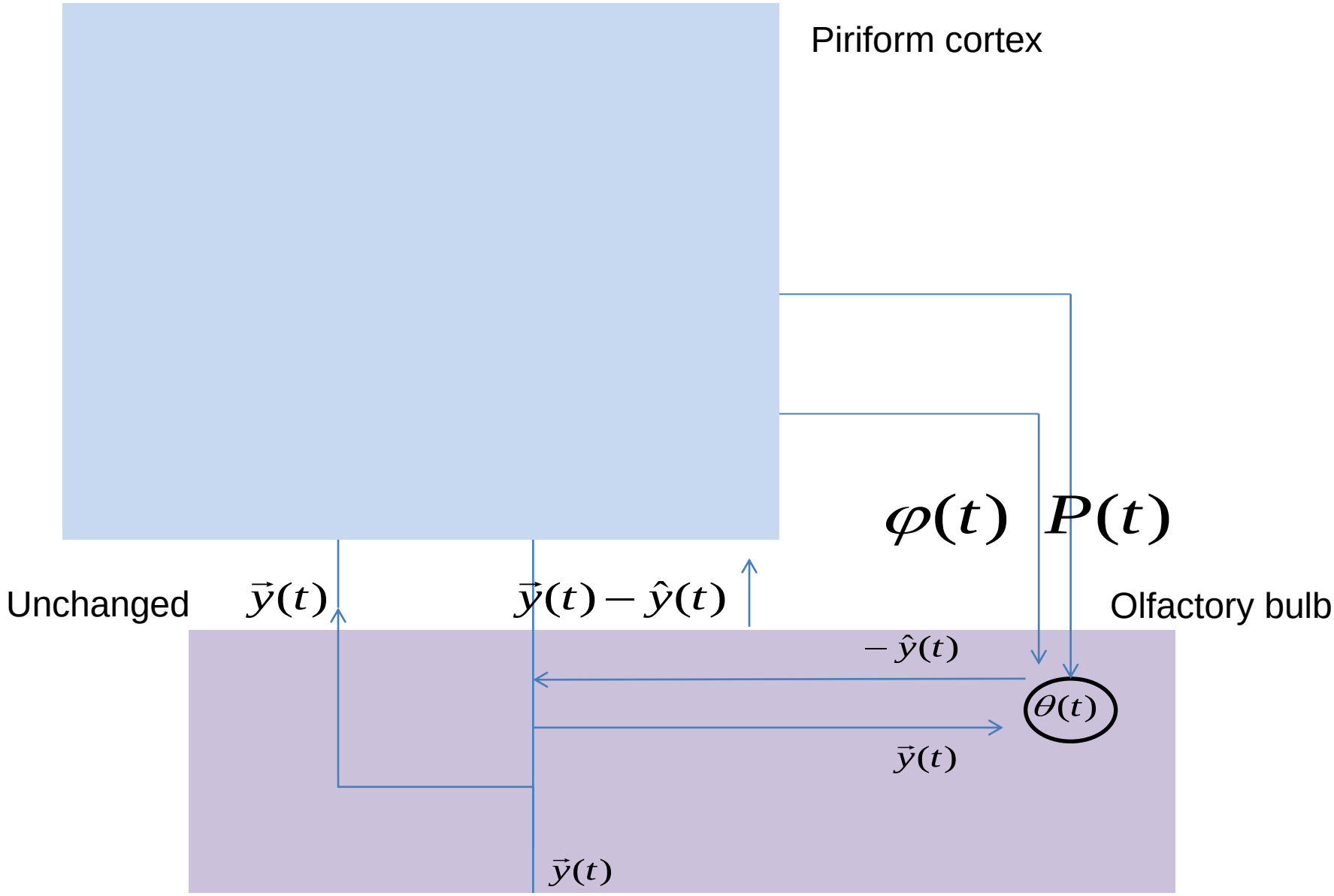
Boyd et al., 2012 , Markopoulos et al., 2012

Pharmacological inactivation of piriform cortex

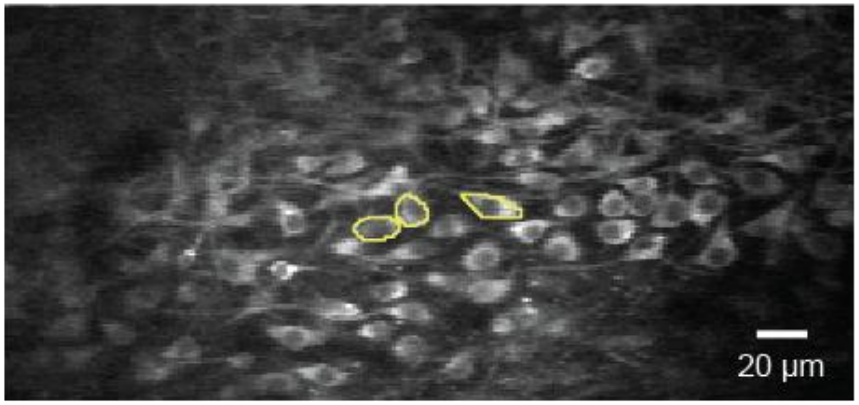


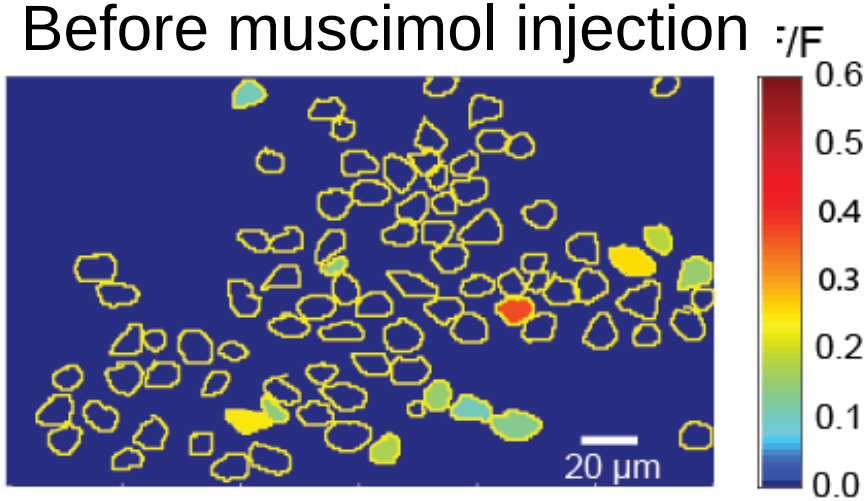
How does cortical feedback modulate the output of the bulb?

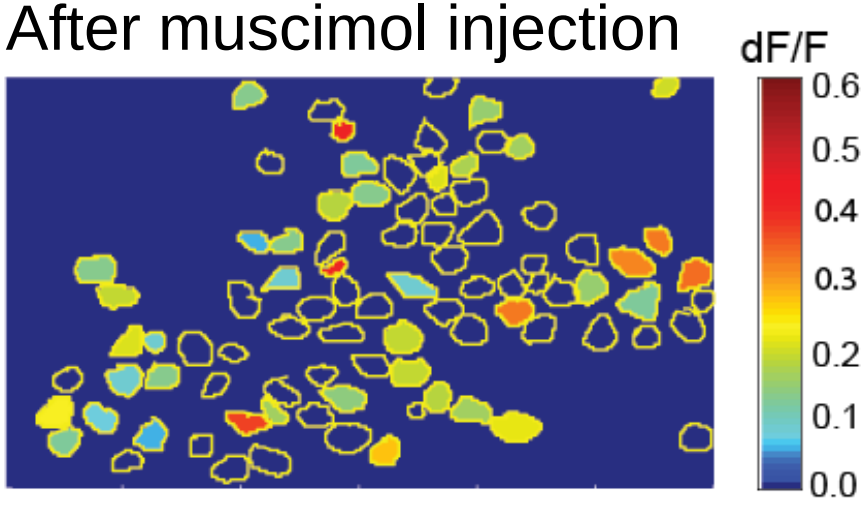
iCPA requires a feedback independent and a feedback dependent channel



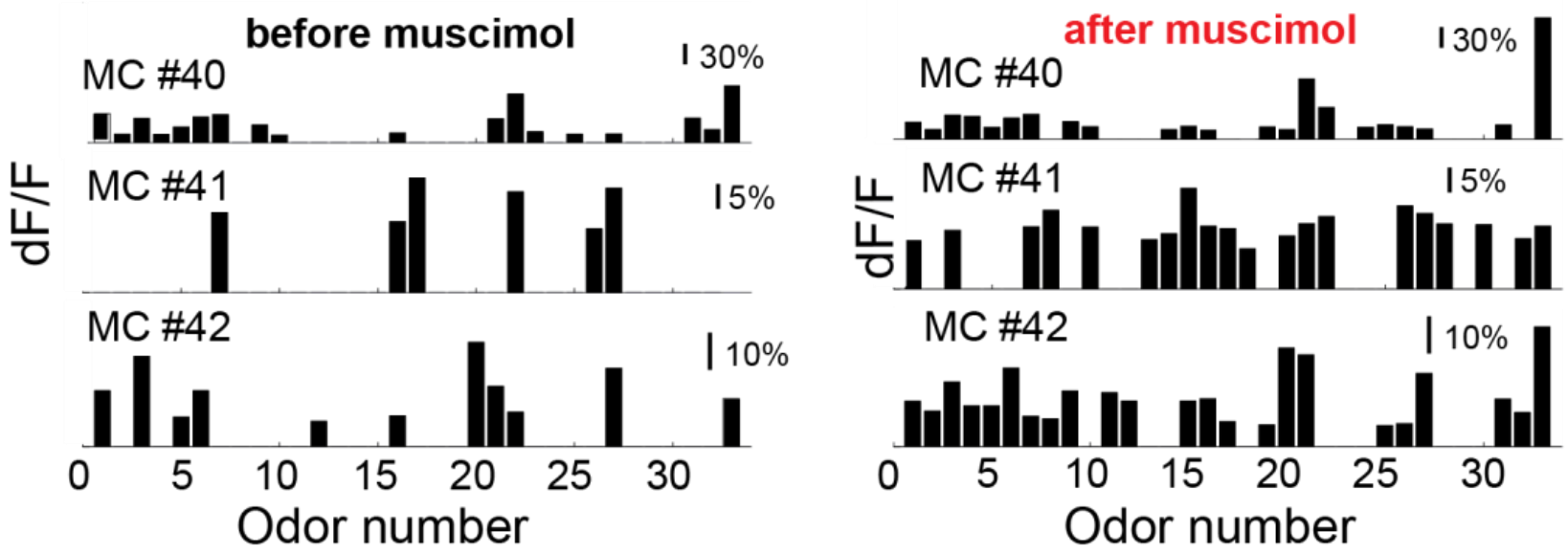
Piriform inactivation enhances the number of responsive mitral cells



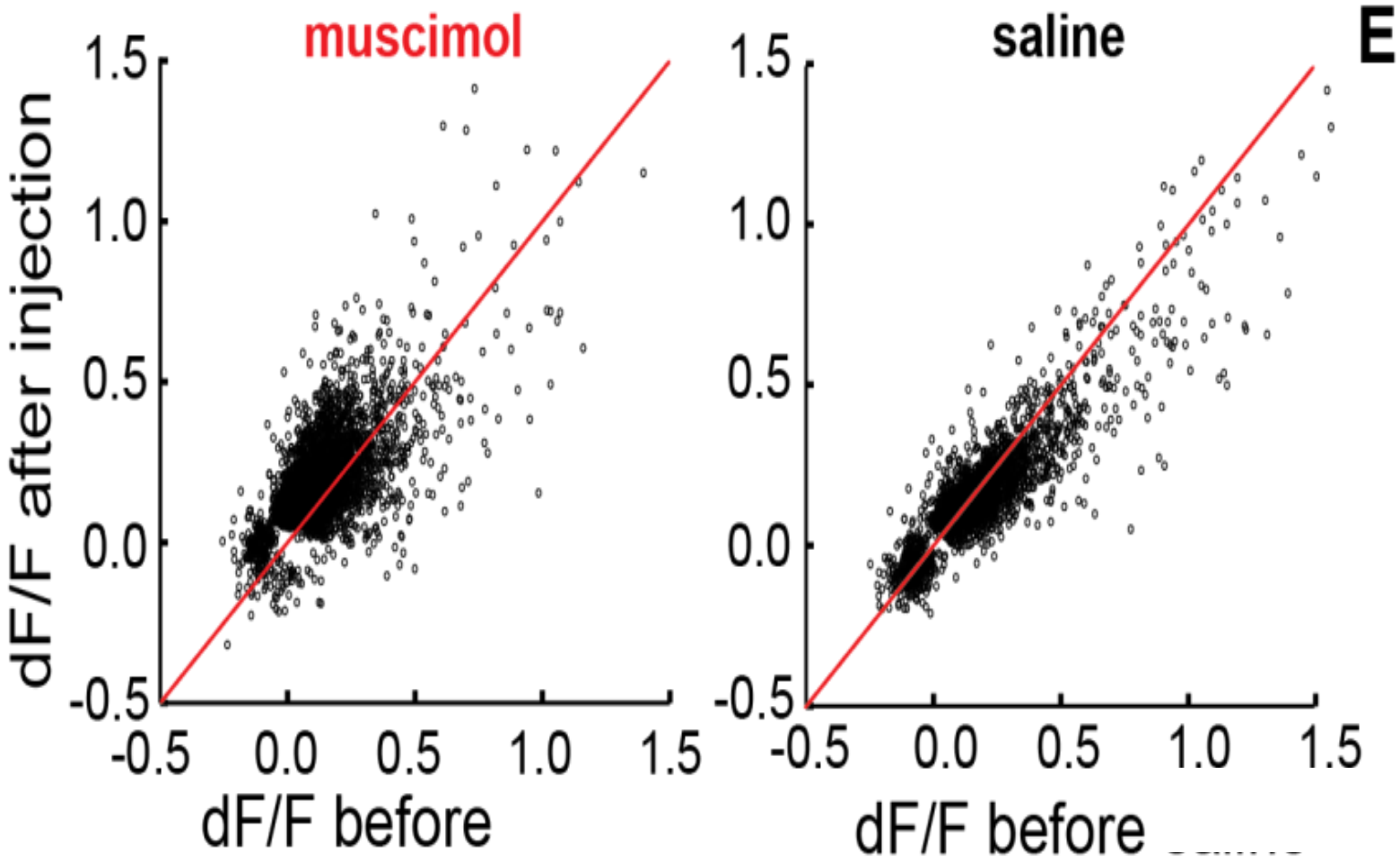




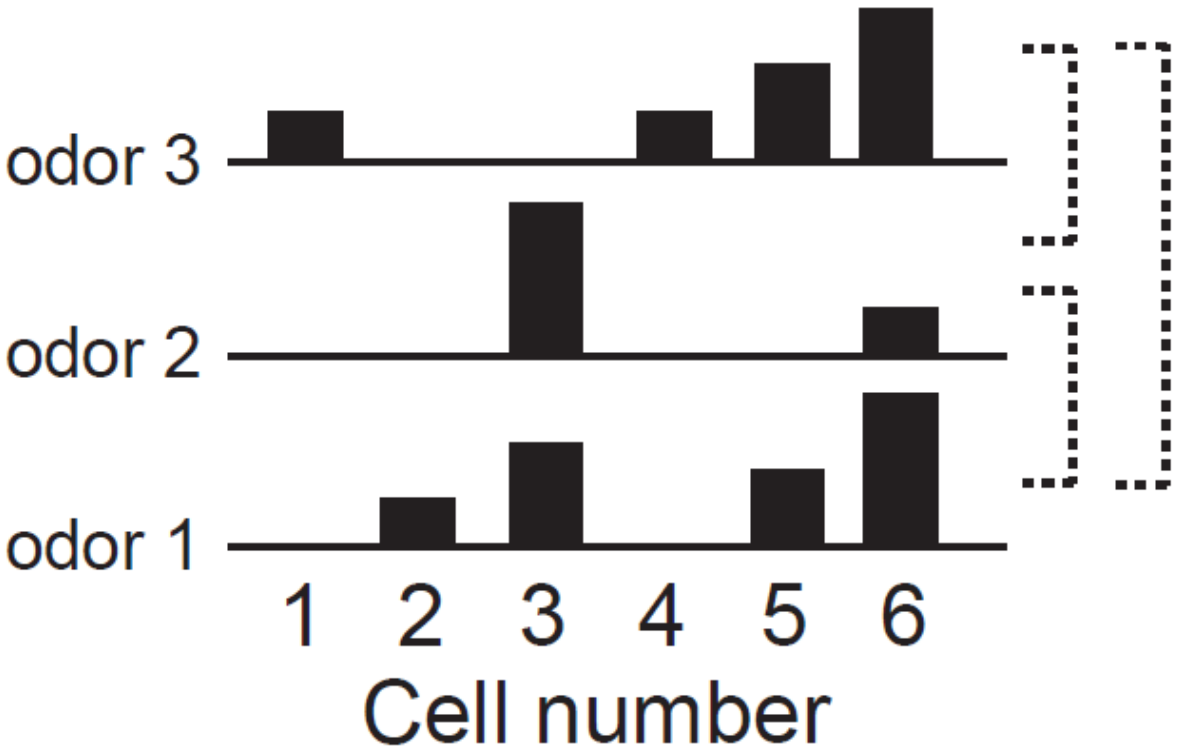
Piriform cortex inactivation enhances the responses of individual mitral cells



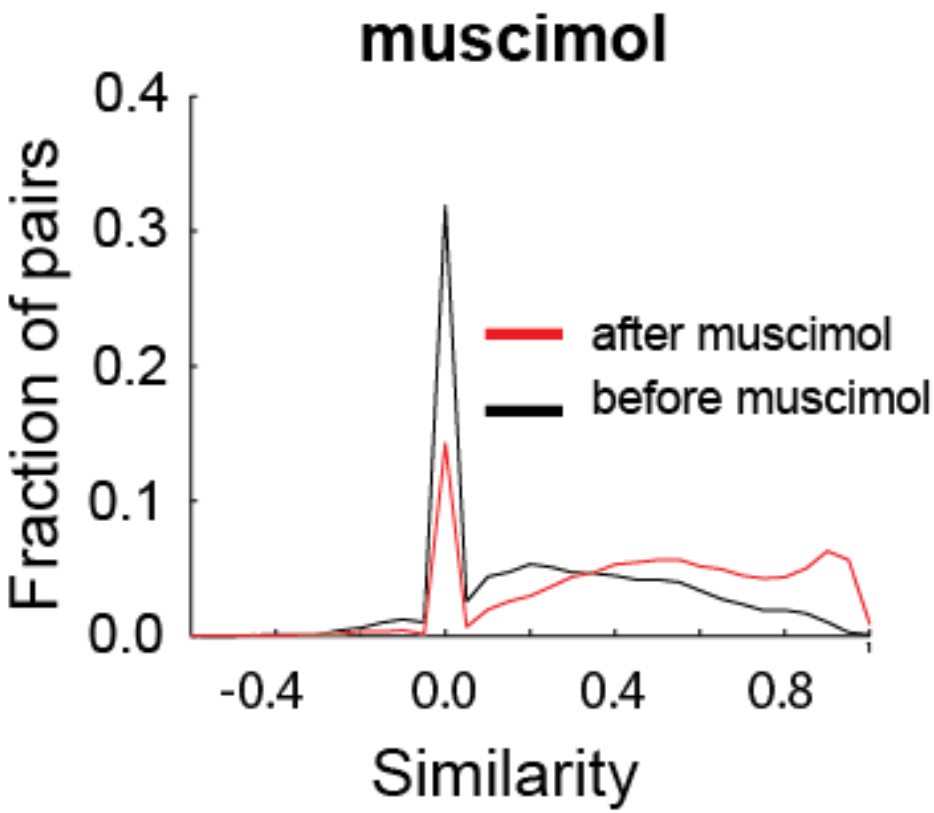
Piriform cortex inactivation enhances the responses of individual mitral cells

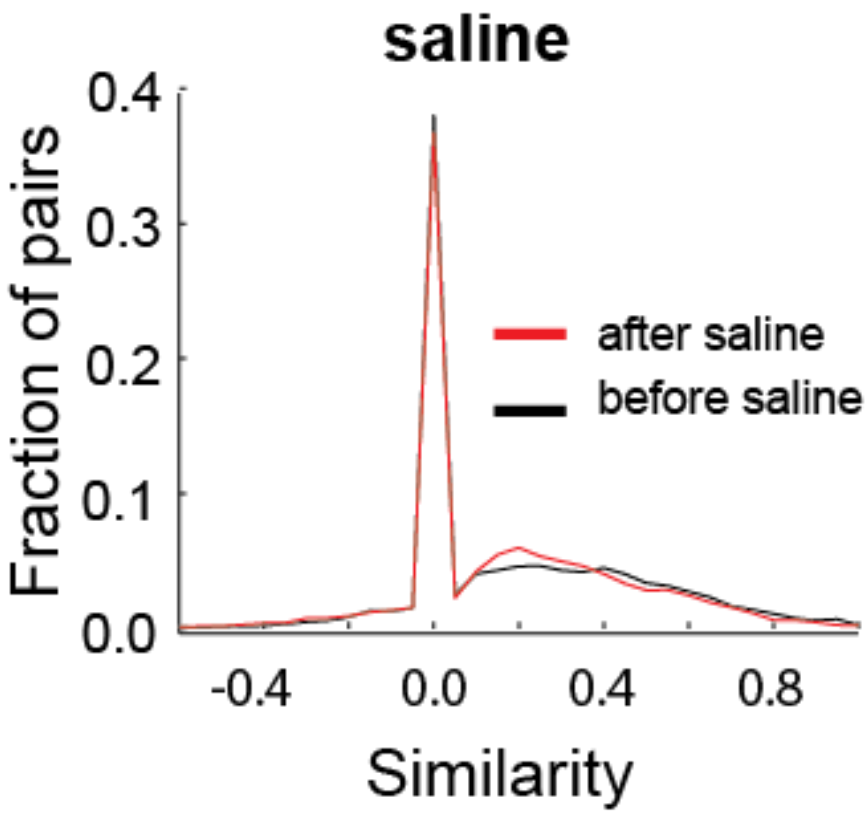


Does cortical feedback enhance odor discriminability?

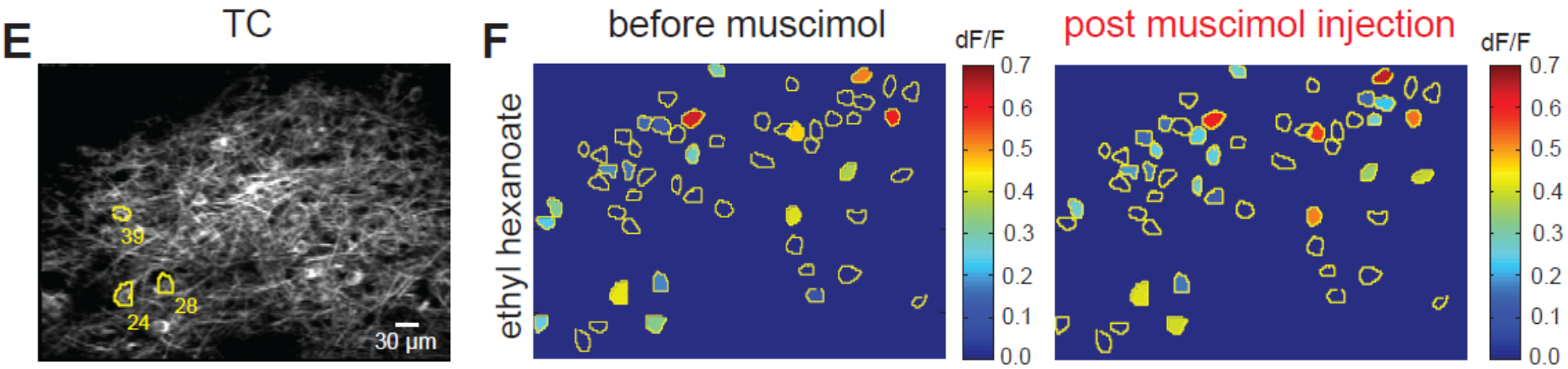


Cortical feedback enhances odor discriminability

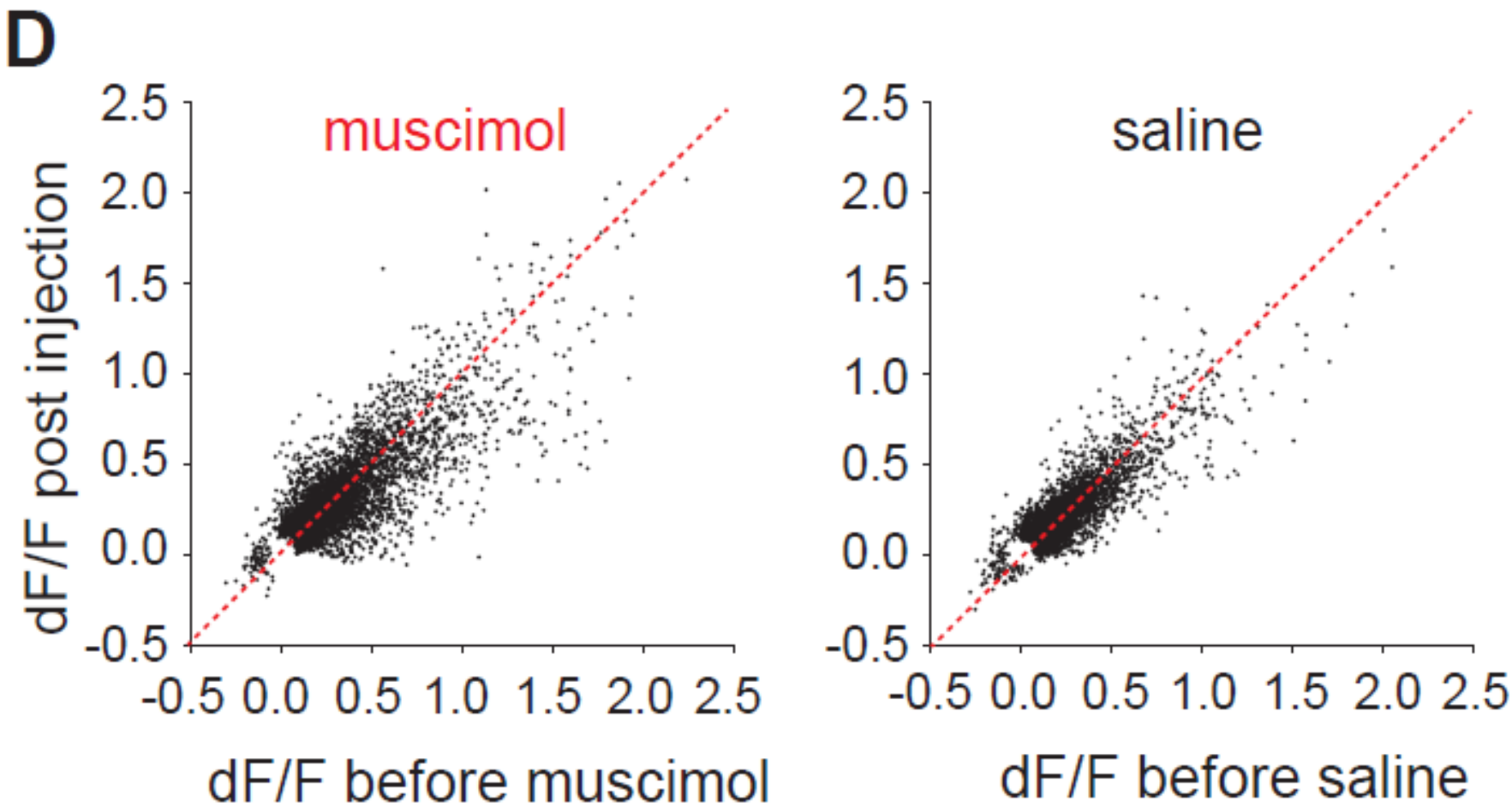




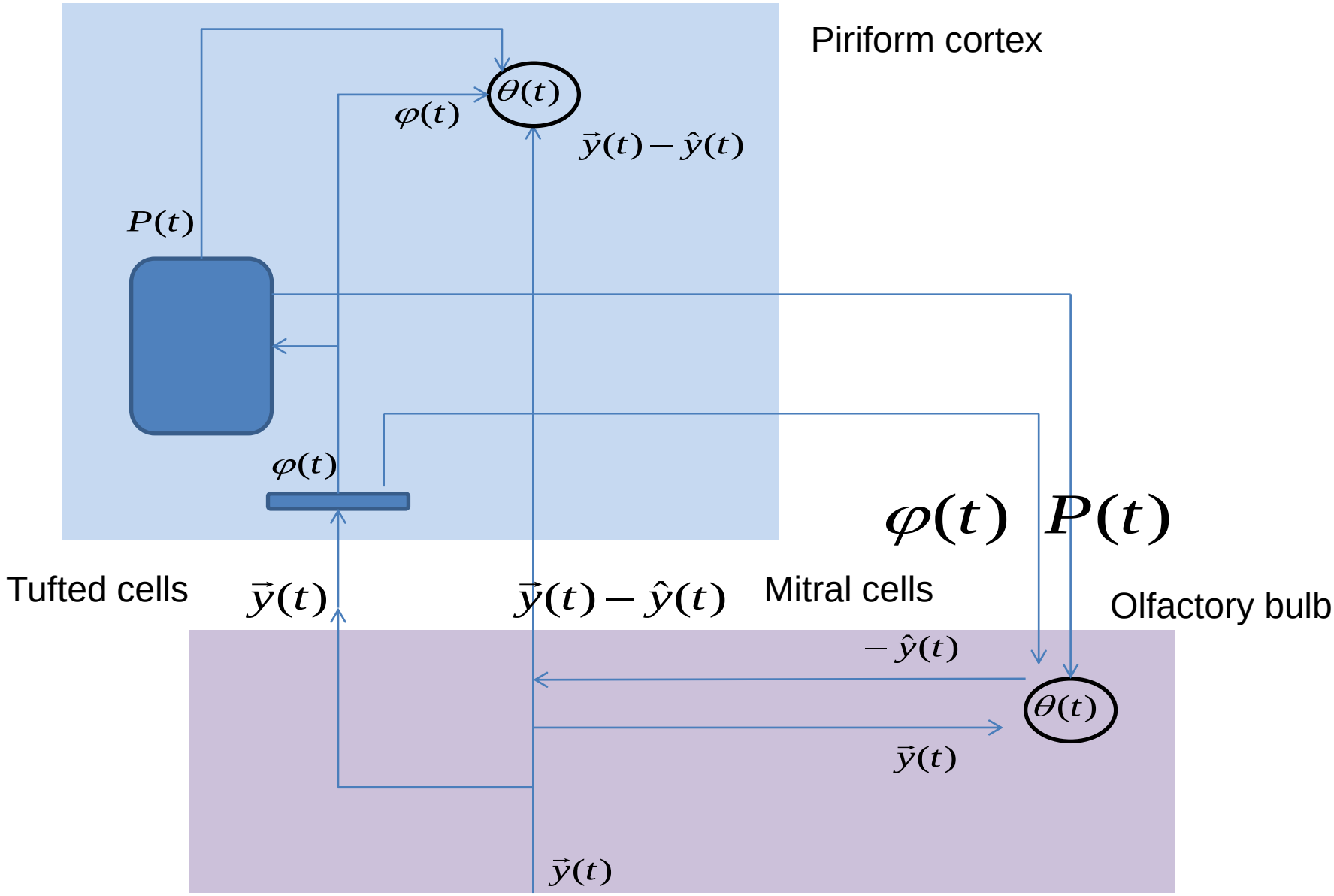
Piriform cortex inactivation does not affect the responses of tufted cells



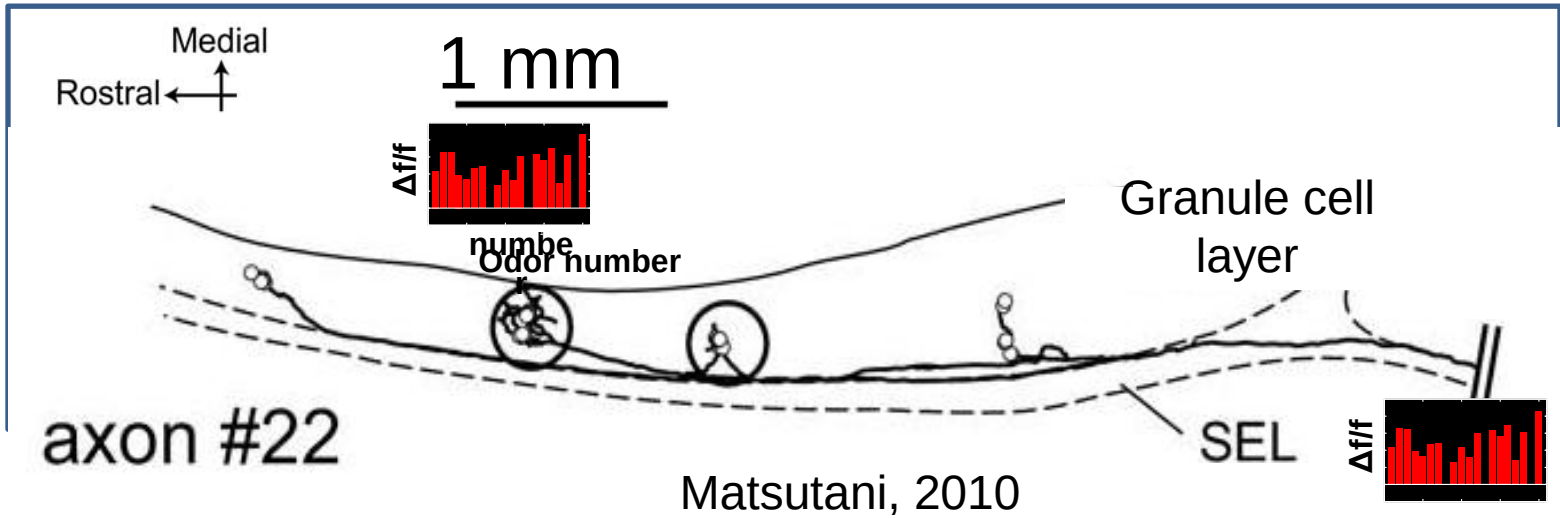
Piriform cortex inactivation does not affect the responses of individual tufted cells



iCPA requires a feedback independent and a feedback dependent channel



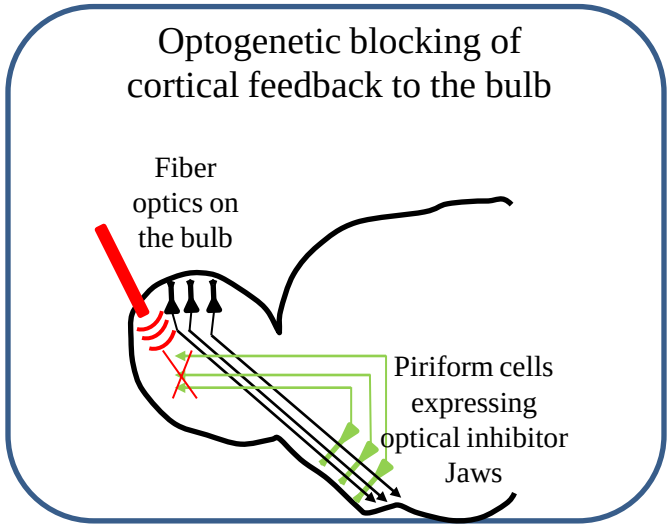
Open questions



Matsutani, 2010

1) What is the functional connectivity between feedback axons and their target areas?

2) What is the role of cortical feedback during olfactory behavior?



Thanks!

Albeanu Lab

Francesca Anselmi
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Matt Koh
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Computational model

Christian Leibold (LMU, Munich)

Paul Masset (WSBS)

The matrix $\Phi^T\Phi$ is positive definite

$$x^T\left(\Phi^T\Phi\right)x > 0$$ For all vectors x

The single elements of $\Phi^T\Phi_{i,j}$ *are:* $$\left(\Phi^T\Phi\right)_{i,j} = \sum_{t=1}^{T}\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(\vec{y}(t)\cdot\vec{B}_j\right)\left(\vec{B}_i\cdot\vec{B}_j\right)$$

$$x^T\left(\Phi^T\Phi\right)x = \sum_{t=1}^{T}\sum_{i=1}^{N}\sum_{j=1}^{N} x_i x_j\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(\vec{y}(t)\cdot\vec{B}_j\right)\left(\vec{B}_i\cdot\vec{B}_j\right)$$

$$= \sum_{t=1}^{T}\sum_{i=1}^{N}(x_i)^2\left(\vec{y}(t)\cdot\vec{B}_i\right)^2 + \sum_{t=1}^{T}\sum_{i=1}^{N}\sum_{j=1,\, j\neq i}^{N} 2\frac{x_i}{\sqrt{2}}\frac{x_j}{\sqrt{2}}\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(\vec{y}(t)\cdot\vec{B}_j\right)\sum_{k=1}^{M} B_{m,i}B_{m,j}$$

$$+\sum_{t=1}^{T}\sum_{k=1}^{M}\sum_{i=1}^{N}\frac{(x_i)^2}{2}\left(\vec{y}(t)\cdot\vec{B}_i\right)^2\left(B_{m,i}\right)^2 - \sum_{t=1}^{T}\sum_{k=1}^{M}\sum_{i=1}^{N}\frac{(x_i)^2}{2}\left(\vec{y}(t)\cdot\vec{B}_i\right)^2\left(B_{m,i}\right)^2$$

- All the eigenvalues of $\Phi^T\Phi$ are positive
- No zero eigenvalues, therefore, $\Phi^T\Phi$ is invertible

The matrix $\Phi^T\Phi$ is positive definite

$$x^T\left(\Phi^T\Phi\right)x = \sum_{t=1}^{T}\sum_{i=1}^{N}\left(x_i\right)^2\left(\vec{y}(t)\cdot\vec{B}_i\right)^2 + \sum_{t=1}^{T}\sum_{i=1}^{N}\sum_{j=1,\,j\neq i}^{N} 2\frac{x_i}{\sqrt{2}}\frac{x_j}{\sqrt{2}}\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(\vec{y}(t)\cdot\vec{B}_j\right)\sum_{m=1}^{M}B_{m,i}B_{m,j}$$

$$+\sum_{t=1}^{T}\sum_{m=1}^{M}\sum_{i=1}^{N}\frac{\left(x_i\right)^2}{2}\left(\vec{y}(t)\cdot\vec{B}_i\right)^2\left(B_{m,i}\right)^2 - \sum_{t=1}^{T}\sum_{m=1}^{M}\sum_{i=1}^{N}\frac{\left(x_i\right)^2}{2}\left(\vec{y}(t)\cdot\vec{B}_i\right)^2\left(B_{m,i}\right)^2$$

$$=\sum_{t=1}^{T}\sum_{m=1}^{M}\left(\sum_{i=1}^{N}\frac{\left(x_i\right)}{\sqrt{2}}\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(B_{m,i}\right)\right)^2 + \sum_{t=1}^{T}\sum_{i=1}^{N}\left(x_i\right)^2\left(\vec{y}(t)\cdot\vec{B}_i\right)^2\left(1-\sum_{m=1}^{M}\frac{1}{2}\left(B_{m,i}\right)^2\right)$$

$$=\sum_{t=1}^{T}\sum_{m=1}^{M}\left(\sum_{i=1}^{N}\frac{\left(x_i\right)}{\sqrt{2}}\left(\vec{y}(t)\cdot\vec{B}_i\right)\left(B_{m,i}\right)\right)^2 + \sum_{t=1}^{T}\sum_{i=1}^{N}\left(x_i\right)^2\left(\vec{y}(t)\cdot\vec{B}_i\right)^2\left(\frac{1}{2}\right) > 0$$

- All the eigenvalues of $\Phi^T\Phi$ are positive
- No zero eigenvalues, therefore, $\Phi^T\Phi$ is invertible