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
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

\[ \vec{B}_1 \]

\[ \vec{B}_2 \]

\[ \vec{B}_3 \]
The observed signal is a combination of few elements

Dictionary of elements

Elements present

Dictionary of elements

The observed signal is a combination of few elements
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.

\[ \mathbf{y}_1 \mathbf{\rho} \]
\[ \mathbf{y}_2 \mathbf{\rho} \]
\[ \mathbf{y} \mathbf{\rho} \]
\[ \mathbf{B}_1 \mathbf{\rho} \]
\[ \mathbf{B}_2 \mathbf{\rho} \]
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.
2) Minimize the estimation error using the sparsest solution

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
- 1, if element \( i \) is present
- Time-varying component
- 0, if element \( i \) is not present in a scene
Estimation of the time-varying component

\[ B = \begin{bmatrix} B_1 & B_2 & \cdots & B_M \end{bmatrix} \]

In general, \( M \gg n \)
Estimation of the time varying component

\[ \hat{y}(t) = B \Theta \hat{A}(t) \]
Estimation of the time varying component

By calculating the estimated square error:

\[ C = \left( \tilde{y}(t) - \hat{y}(t) \right)^T \left( \tilde{y}(t) - \hat{y}(t) \right) \]

And taking the derivative we obtain:

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

\[ \left( BB^T \right)^{-1} \approx I \quad \text{if glomerular are uncorrelated} \]
Estimation of the time varying component

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

\[ \hat{A}_2(t) = \vec{B}_2 \cdot \vec{y}(t) \]

\[ \hat{A}_3(t) = \vec{B}_3 \cdot \vec{y}(t) \]

\[ \hat{A}_4(t) = \vec{B}_4 \cdot \vec{y}(t) \]

\[ \hat{A}_1(t) = \vec{B}_1 \cdot \vec{y}(t) \]
We can find a sparse solution at each time step

\[ \tilde{y}(1) = B \theta(1) \]
We can find a sparse solution at each time step

\[
\tilde{y}(2) = B \theta(2)
\]
We can find a sparse solution at each time step

\[
\hat{y}(3) \quad B \quad \theta(3)
\]
We can find a sparse solution at each time step

\[ \tilde{y}(4) = B \theta(4) \]
We find a single solution for all time steps.

\( \tilde{y}(1) \) = \( B \) = \( \theta(1) \)
We find a single solution for all time steps

\[ \tilde{y}(1) = \varphi(1) \cdot \theta \]

\[ \tilde{\varphi}_1(1) \quad \tilde{B}_1 \quad \tilde{B}_1\tilde{A}_1 \quad \tilde{y}(1) \]
We find a single solution for all time steps

\[ \tilde{y}(1) = \varphi(1) \]

\[ \tilde{y}(2) = \varphi(2) \]

\[ \tilde{y}(3) = \varphi(3) \]
We find a single solution for all time steps

\[ Y = \Phi \theta \]
We find a single solution for all time steps

\[ Y = \Phi \theta \]

The solution is given by

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

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

\[ (\Phi^T \Phi) \]

to be invertible. Under which conditions is it invertible?

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

$$x^T (\Phi^T \Phi) x > 0$$

For all vectors $x$

The single elements of $\Phi^T \Phi$ are:

$$\left( \Phi^T \Phi \right)_{i,j} = \sum_{t=1}^{T} \left( \bar{y}(t) \cdot \bar{B}_i \right) \left( \bar{y}(t) \cdot \bar{B}_j \right) \left( \bar{B}_i \cdot \bar{B}_j \right)$$

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

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

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

1) Calculate the projections

Corrected Projections Algorithm (CPA)

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

\[ \hat{y}(1) = \hat{\phi}_1(1) + \hat{\phi}_2(1) + \hat{\phi}_3(1) + \hat{\phi}_4(1) \]
Corrected Projections Algorithm (CPA)

2) Use the projections to create an estimate of the observed signal
Corrected Projections Algorithm (CPA)

3) Correct the projections by a factor $\vartheta$
Corrected Projections Algorithm (CPA)

3) Find the $\theta$ that minimize the error between the estimate and the observed signal.

Minimal error is given if the sources present are orthogonal

Model of the olfactory scene

\[ \bar{y}(t) = A_1(t)\bar{B}_1 + A_2(t)\bar{B}_2 \]

Lets assume that \[ \bar{B}_1 \] and \[ \bar{B}_2 \] are orthogonal, that is:

\[ \bar{B}_1 \cdot \bar{B}_2 = 0 \]

CPA creates its estimate using the projections

\[ \hat{y}(t) = \theta_1(\bar{y}(t) \cdot \bar{B}_1)\bar{B}_1 + \theta_2(\bar{y}(t) \cdot \bar{B}_2)\bar{B}_2 + \ldots + \theta_n(\bar{y}(t) \cdot \bar{B}_n)\bar{B}_n \]

\[ \hat{y}(t) = \theta_1 \left( A_1(t)\bar{B}_1 \cdot \bar{B}_1 + A_2(t)\bar{B}_2 \cdot \bar{B}_1 \right)\bar{B}_1 + \theta_2 \left( A_1(t)\bar{B}_1 \cdot \bar{B}_2 + A_2(t)\bar{B}_2 \cdot \bar{B}_2 \right)\bar{B}_2 + \ldots + \theta_n(\bar{y}(t) \cdot \bar{B}_n)\bar{B}_n \]

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

If we choose then \[ \theta_1 = 1, \theta_2 = 1, \] and \[ \theta_k = 0, \text{if} \, k \neq 1, 2 \]

\[ \hat{y}(t) = A_1(t)\bar{B}_1 + A_2(t)\bar{B}_2 = \bar{y}(t) \]

Therefore

\[ \left| \hat{y}(t) - \bar{y}(t) \right|^2 = 0 \]

Then \[ \theta_1 = 1, \theta_2 = 1, \] and \[ \theta_k = 0, \text{if} \, k \neq 1, 2 \] is the solution
Matrices taken from a random ensemble satisfy the restricted isometry property (RIP)

\[ n = O\left(k \times \log\left(\frac{M}{k}\right) \right) \]
The number of receptors determine the complexity of the scene and the maximum size of the dictionary

\[ n = O\left( k \times \log\left( \frac{M}{k} \right) \right) \]

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

Element 5

Time Signal Generated by odor 5

Element 10

Time Signal Generated by odor 10

\[ Y \]

Time

Magnitude

Actual contribution

Estimated parameter

Element number / \( \theta \)
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 noise of twice the amplitude of the signal
CPA identifies sources under challenging conditions

Template matching

Matching pursuit (≈L1 minimization)

PCA (blind separation)

CPA
CPA can use very large dictionaries


400 dimensions
68000 dictionary elements
7 time samples
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Standard CPA computation can be simplified

\[ Y = \Phi \theta \quad \theta = \left( \Phi^T \Phi \right)^{-1} \Phi^T Y \]

(\( \Phi^T \Phi \)) is M by M
Iterative CPA (iCPA) process each observation when it arrives

\[ P(T) = P(T-1) - P(T-1)\varphi^T(T)(I + \varphi(T)P(T-1)\varphi^T(T))^{-1}\varphi(T)P(T-1) \]

\[ \hat{y}(T) = \varphi(T)\hat{\Theta}(T-1) \]

Estimation error

\[ \theta(T) = \theta(T-1) + P(T)\varphi(T)^*(\tilde{y}(T) - \hat{y}(T)) \]

\[ \Delta\theta(T) \]
iCPA have variables of different dimensionality and different dynamics

\[ P(T) = P(T - 1) - P(T - 1) \varphi^T(T)(I + \varphi(T)P(T - 1)\varphi^T(T))^{-1} \varphi(T)P(T - 1) \]

\[ \hat{y}(T) = \varphi(T)\theta(T - 1) \]

\[ \theta(T) = \theta(T - 1) + P(T)\varphi(T)^*(\hat{y}(T) - \hat{y}(T)) \]

Largest dimension variables (order M by M): \( P \)
Second dimension variables (order N by M): \( \varphi \)
Third largest variable (order M by 1): \( \theta \)
Smallest variable (order N by 1): \( \hat{y}(t), \hat{y}(t) \)

2 variables for temporal integration: \( P, \theta \)
Possible iCPA implementation in piriform/olfactory bulb circuit
Model predicts feedback signals with different dynamics

\[ \theta(T) = \theta(T - 1) + P(T)\varphi(T) \ast (\tilde{y}(T) - \hat{y}(T)) \]
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?


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

GCaMP5 expression in cortico-bulbar feedback axons

Piriform Cortex

Cortical feedback fibers in the bulb

Pyramidal cells

1 mm

300 µm

30 µm

30 µm
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

**Bouton A**
- Ethyl propionate
- Graph showing Δf/f over time (s) with average trace and individual trials.

**Bouton B**
- Ethyl propionate
- Graph showing Δf/f over time (s) with average trace and individual trials.

**Fraction of responses**
- Enhanced: 0.4
- Suppressed: 0.5

3,776 responses
4 mice
Cortical feedback axons are silenced by piriform cortical inactivation

Muscimol

before muscimol

Bouton

500 µm
Cortical feedback axons are silenced by piriform cortical inactivation.
Cortical feedback axons respond to only a few odors

\[
\text{Avg} = 0.85 \pm 0.03 \text{ SEM}
\]
Cortical feedback responses are sparse

Amplitude: 30 µA,
Frequency: 100 Hz,
Pulse width: 100 µs
Duration: 0.4 s
Cortical feedback boutons are sparse and odor selective
Boutons show either enhancement or suppression across odors

**Bouton A**

- Ethyl propionate
- Heptanal
- γ-Terpinene

**Bouton B**

- Ethyl propionate
- Heptanal
- γ-Terpinene
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
Model predicts that feedback signals have different dynamics.

\[ \theta(T) = \theta(T - 1) + P(T)\phi(T) \ast (\tilde{y}(T) - \hat{y}(T)) \]
Most suppressed responses outlast odor presentation
Enhanced responses have less long lasting responses.
Piriform electrical stimulation triggers long lasting enhancement in suppressed response boutons

Figure S4

A

Odor suppressed boutons

Odor enhanced boutons

Non-responsive boutons

Odor
Odor + electrical stimulation

Bouton response #

Time (s)
Determination of temporal dynamics in axonal boutons

Muscimol +
Feedback bouton calcium dynamics is fast.
Optogenetic activation of cortical feedback suppresses olfactory bulb output

Boyd et al., 2012, Markopoulos et al., 2012
Pharmacological inactivation of piriform cortex

Muscimol
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.

Before muscimol injection

After muscimol injection
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

![Graph showing the effect of muscimol and saline on odor discriminability.](image)

- **Muscimol**
  - Red line: after muscimol
  - Black line: before muscimol

- **Saline**
  - Red line: after saline
  - Black line: before saline

The graphs illustrate the fraction of pairs as a function of similarity for both muscimol and saline treatments, showing an enhancement in odor discriminability after the application of muscimol compared to saline.
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.
1) What is the functional connectivity between feedback axons and their target areas?

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

Matsutani, 2010
Thanks!

Francesca Anselmi
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Hency Patel
Benjamin Rebouillat
Sourabh Singhal

Computational model

Christian Leibold (LMU, Munich)

Paul Masset (WSBS)
The matrix $\Phi^T \Phi$ is positive definite

$$x^T (\Phi^T \Phi)x > 0$$

For all vectors $x$

The single elements of $\Phi^T \Phi_{i,j}$ are:

$$\left( \Phi^T \Phi \right)_{i,j} = \sum_{t=1}^{T} \left( \mathbf{y}(t) \cdot \mathbf{B}_i \right) \left( \mathbf{y}(t) \cdot \mathbf{B}_j \right) \left( \mathbf{B}_i \cdot \mathbf{B}_j \right)$$

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

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

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

- 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

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

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

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

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

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