

Olfactory inference using correlated priors with sister cells

Sina Tootoonian
Schaefer Lab

Neuroscience Interest Group
2025/05/28

Section 1

Overview

- Olfactory bulb, sister cells

Outline

- Olfactory bulb, sister cells
- Top-down understanding of neural circuits

Outline

- Olfactory bulb, sister cells
- Top-down understanding of neural circuits
- Olfactory inference

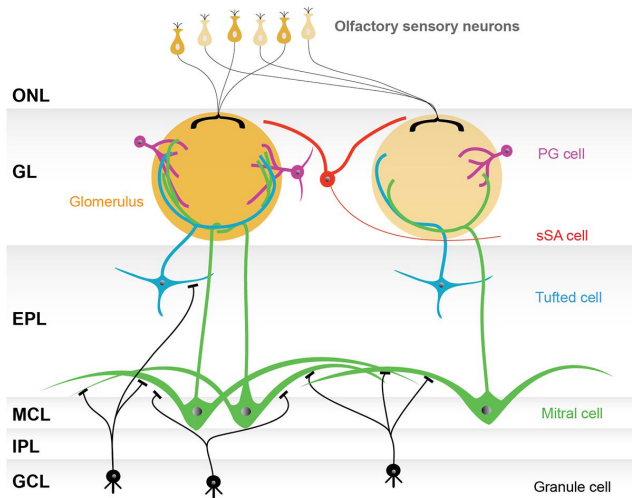
- Olfactory bulb, sister cells
- Top-down understanding of neural circuits
- Olfactory inference
- Circuits for inference

Outline

- Olfactory bulb, sister cells
- Top-down understanding of neural circuits
- Olfactory inference
- Circuits for inference
- Incorporating sister cells

- Olfactory bulb, sister cells
- Top-down understanding of neural circuits
- Olfactory inference
- Circuits for inference
- Incorporating sister cells
- Preprint at <http://arxiv.org/abs/2505.14579>

The olfactory bulb



Nagayama et al. 2014

Two approaches to understanding neural circuits

- Bottom-up

Two approaches to understanding neural circuits

- Bottom-up
- Top-down

Two approaches to understanding neural circuits

- Bottom-up
- Top-down
 - Marr's levels:

Two approaches to understanding neural circuits

- Bottom-up
- Top-down
 - Marr's levels:
 - 1 What is the computation?

Two approaches to understanding neural circuits

- Bottom-up
- Top-down
 - Marr's levels:
 - 1 What is the computation?
 - 2 What is the algorithm?

Two approaches to understanding neural circuits

- Bottom-up
- Top-down
 - Marr's levels:
 - 1 What is the computation?
 - 2 What is the algorithm?
 - 3 What is the implementation?

The computation: Olfactory inference

- The environment contains odours **x** animals care about.

The computation: Olfactory inference

- The environment contains odours \mathbf{x} animals care about.
- These have a *prior* probability $p(\mathbf{x})$.

The computation: Olfactory inference

- The environment contains odours \mathbf{x} animals care about.
- These have a *prior* probability $p(\mathbf{x})$.
- Odours produce receptor responses \mathbf{r} according to $p(\mathbf{r}|\mathbf{x})$.

The computation: Olfactory inference

- The environment contains odours \mathbf{x} animals care about.
- These have a *prior* probability $p(\mathbf{x})$.
- Odours produce receptor responses \mathbf{r} according to $p(\mathbf{r}|\mathbf{x})$.
- Combining these gives a *posterior* probability $p(\mathbf{x}|\mathbf{r})$

The computation: Olfactory inference

- The environment contains odours \mathbf{x} animals care about.
- These have a *prior* probability $p(\mathbf{x})$.
- Odours produce receptor responses \mathbf{r} according to $p(\mathbf{r}|\mathbf{x})$.
- Combining these gives a *posterior* probability $p(\mathbf{x}|\mathbf{r})$
- Computation: Find the odour with highest posterior probability

$$\hat{\mathbf{x}} = \max_{\mathbf{x}} p(\mathbf{x}|\mathbf{r}).$$

The algorithm: Hill climbing

- Our computation:

$$\hat{\mathbf{x}} = \max_{\mathbf{x}} p(\mathbf{x}|\mathbf{r}) = \max_{\mathbf{x}} \log p(\mathbf{x}|\mathbf{r})$$

The algorithm: Hill climbing

- Our computation:

$$\hat{\mathbf{x}} = \max_{\mathbf{x}} p(\mathbf{x}|\mathbf{r}) = \max_{\mathbf{x}} \log p(\mathbf{x}|\mathbf{r})$$

- Improve a guess $\hat{\mathbf{x}}$ by moving up the probability hill

$$\frac{d\hat{\mathbf{x}}}{dt} \propto \nabla \log p(\hat{\mathbf{x}}|\mathbf{r})$$

The algorithm: Hill climbing

- Our computation:

$$\hat{\mathbf{x}} = \max_{\mathbf{x}} p(\mathbf{x}|\mathbf{r}) = \max_{\mathbf{x}} \log p(\mathbf{x}|\mathbf{r})$$

- Improve a guess $\hat{\mathbf{x}}$ by moving up the probability hill

$$\frac{d\hat{\mathbf{x}}}{dt} \propto \nabla \log p(\hat{\mathbf{x}}|\mathbf{r})$$

- Use Bayes' rule to relate the posterior to the prior and likelihood:

$$\log p(\mathbf{x}|\mathbf{r}) = \log p(\mathbf{x}) + \log p(\mathbf{r}|\mathbf{x}).$$

The algorithm: Hill climbing

- Our computation:

$$\hat{\mathbf{x}} = \max_{\mathbf{x}} p(\mathbf{x}|\mathbf{r}) = \max_{\mathbf{x}} \log p(\mathbf{x}|\mathbf{r})$$

- Improve a guess $\hat{\mathbf{x}}$ by moving up the probability hill

$$\frac{d\hat{\mathbf{x}}}{dt} \propto \nabla \log p(\hat{\mathbf{x}}|\mathbf{r})$$

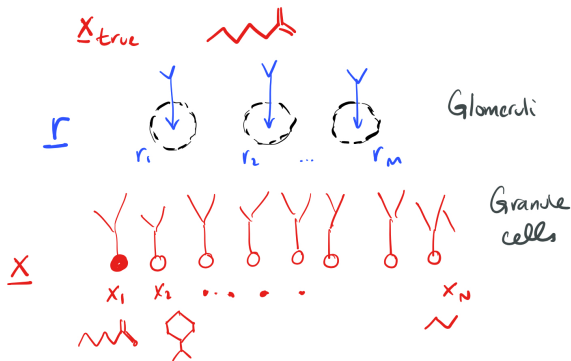
- Use Bayes' rule to relate the posterior to the prior and likelihood:

$$\log p(\mathbf{x}|\mathbf{r}) = \log p(\mathbf{x}) + \log p(\mathbf{r}|\mathbf{x}).$$

- Two contributions to the dynamics

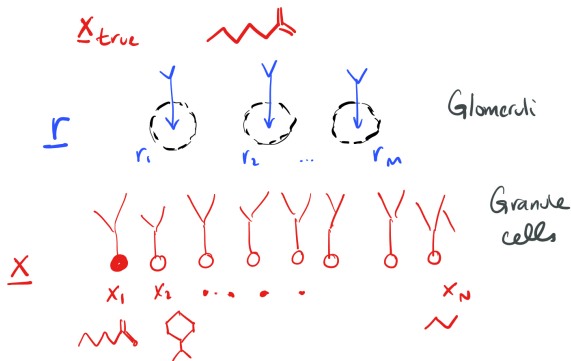
$$\frac{d\hat{\mathbf{x}}}{dt} \propto \nabla \log p(\hat{\mathbf{x}}) + \nabla \log p(\mathbf{r}|\hat{\mathbf{x}}).$$

Implementation: Representations



- Receptors r : glomeruli.

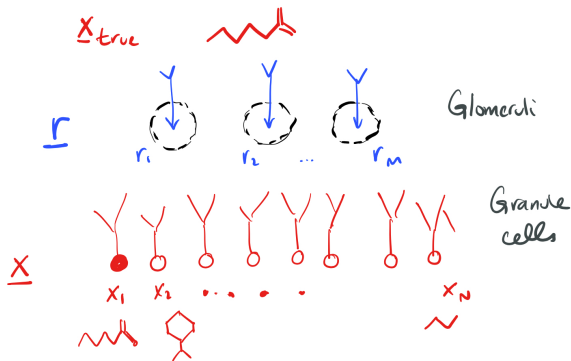
Implementation: Representations



- Receptors \mathbf{r} : glomeruli.
- Odours = Vectors of molecular concentrations:

$$\mathbf{x} = \{x_1, x_2, \dots, x_N\}.$$

Implementation: Representations



- Receptors \mathbf{r} : glomeruli.
- Odours = Vectors of molecular concentrations:

$$\mathbf{x} = \{x_1, x_2, \dots, x_N\}.$$

- Assign one molecular species to one granule cell.

Specifying a prior

- How to specify $p(\mathbf{x}) = p(x_1, x_2, \dots, x_N)$?

Specifying a prior

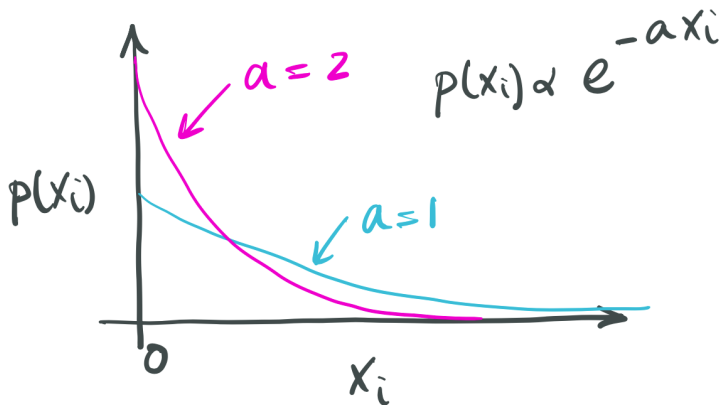
- How to specify $p(\mathbf{x}) = p(x_1, x_2, \dots, x_N)$?
- Natural odours are *sparse*: most likely concentration is zero.

Specifying a prior

- How to specify $p(\mathbf{x}) = p(x_1, x_2, \dots, x_N)$?
- Natural odours are *sparse*: most likely concentration is zero.
- Suggests e.g.

$$p(x_i) \propto e^{-ax_i}.$$

Specifying a prior



Specifying a prior

- How to get $p(x_1, \dots, x_N)$ from $p(x_i)$?

Specifying a prior

- How to get $p(x_1, \dots, x_N)$ from $p(x_i)$?
- Assume independence!

$$p(x_1, \dots, x_N) = p(x_1)p(x_2) \dots$$

Specifying a prior

- How to get $p(x_1, \dots, x_N)$ from $p(x_i)$?
- Assume independence!

$$p(x_1, \dots, x_N) = p(x_1)p(x_2) \dots$$

- Plays nicely with dynamics

$$\frac{dx_i}{dt} \propto \frac{\partial \log p(\mathbf{x})}{\partial x_i} + \dots = -a + \dots$$

Correlated priors

- Independence is nice, but natural odour components are correlated.

Correlated priors

- Independence is nice, but natural odour components are correlated.
- Using that information would improve inference.

Correlated priors

- Independence is nice, but natural odour components are correlated.
- Using that information would improve inference.
- Easy to incorporate into the prior, e.g.

$$p(\mathbf{x}) \propto e^{-C_{ij}x_i x_j}.$$

- Independence is nice, but natural odour components are correlated.
- Using that information would improve inference.
- Easy to incorporate into the prior, e.g.

$$p(\mathbf{x}) \propto e^{-C_{ij}x_i x_j}.$$

- Introduces interactions into the dynamics

$$\frac{dx_i}{dt} \propto \frac{\partial \log p(\mathbf{x})}{\partial x_i} + \dots = -a - C_{ij}x_j + \dots$$

Evidence from receptor activations

- Assume receptors are linearly excited by odours:

$$r_i = \sum_j A_{ij} x_j + \text{noise}.$$

Evidence from receptor activations

- Assume receptors are linearly excited by odours:

$$r_i = \sum_j A_{ij} x_j + \text{noise}.$$

- A_{ij} is the **affinity** of receptor i for molecule j .

Evidence from receptor activations

- Assume receptors are linearly excited by odours:

$$r_i = \sum_j A_{ij} x_j + \text{noise}.$$

- A_{ij} is the **affinity** of receptor i for molecule j .
- Then error when guessing odour \mathbf{x} caused the response r_i , is

$$(r_i - \sum_j A_{ij} x_j)^2$$

Evidence from receptor activations

- Assume receptors are linearly excited by odours:

$$r_i = \sum_j A_{ij} x_j + \text{noise}.$$

- A_{ij} is the **affinity** of receptor i for molecule j .
- Then error when guessing odour \mathbf{x} caused the response r_i , is

$$(r_i - \sum_j A_{ij} x_j)^2$$

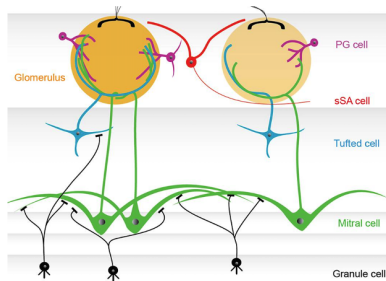
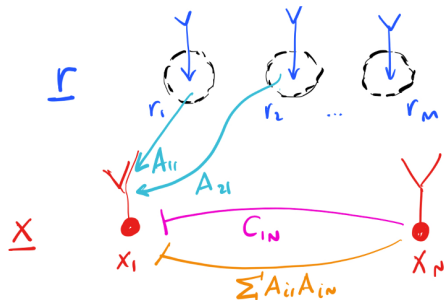
- We sum the evidence from all the receptors

$$\log p(\mathbf{r}|\mathbf{x}) = - \sum_i (r_i - \sum_j A_{ij} x_j)^2.$$

Inference circuit, v. 1

- We have all the pieces we need to specify the dynamics:

$$\frac{dx_i}{dt} \propto \underbrace{-a - \sum_j C_{ij} x_j}_{\partial \text{prior} / \partial x_i} + \underbrace{\sum_k A_{ki} r_k - \sum_j \left[\sum_k A_{ki} A_{kj} \right] x_j}_{\partial \text{evidence} / \partial x_i}.$$

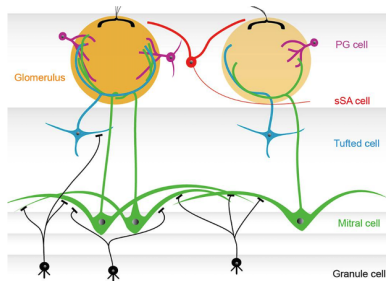
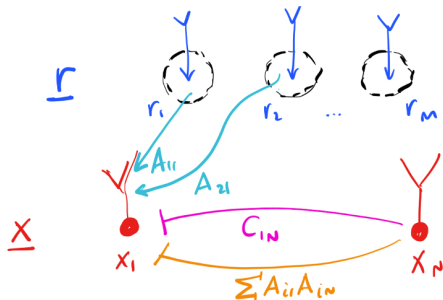


Inference circuit, v. 1

- We have all the pieces we need to specify the dynamics:

$$\frac{dx_i}{dt} \propto \underbrace{-a - \sum_j C_{ij} x_j}_{\partial \text{prior} / \partial x_i} + \underbrace{\sum_k A_{ki} r_k - \sum_j \left[\sum_k A_{ki} A_{kj} \right] x_j}_{\partial \text{evidence} / \partial x_i}.$$

- But it doesn't look like the bulb. . .



- Drop the cross term in the prior

$$\frac{dx_i}{dt} = -a + \sum_j \cancel{C_{ij}} x_j + \sum_k A_{ki} (r_k - \sum_j A_{kj} x_j)$$

- Drop the cross term in the prior

$$\frac{dx_i}{dt} = -a + \sum_j \cancel{C_{ij}} x_j + \sum_k A_{ki} (r_k - \sum_j A_{kj} x_j)$$

- Add a population of 'mitral cells' to encode glomerular residuals:

$$\frac{dm_k}{dt} = -m_k + r_k - \sum_j A_{kj} x_j.$$

- Drop the cross term in the prior

$$\frac{dx_i}{dt} = -a + \sum_j \cancel{C_{ij}} x_j + \sum_k A_{ki} (r_k - \sum_j A_{kj} x_j)$$

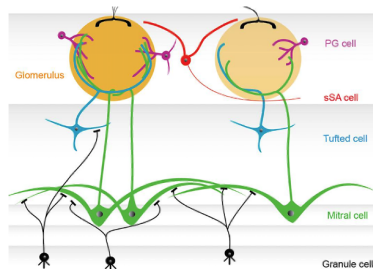
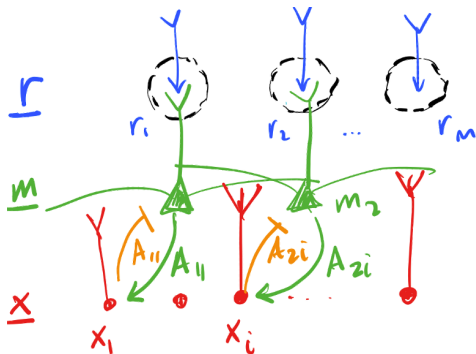
- Add a population of 'mitral cells' to encode glomerular residuals:

$$\frac{dm_k}{dt} = -m_k + r_k - \sum_j A_{kj} x_j.$$

- Granule cells now only interact with mitral cells:

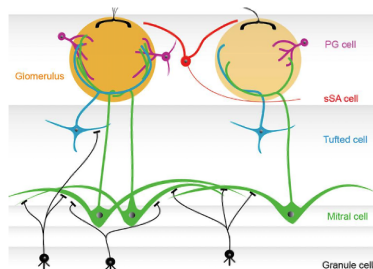
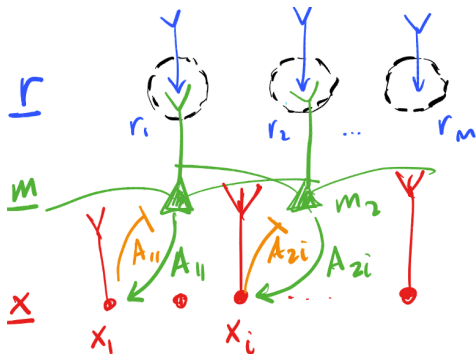
$$\frac{dx_j}{dt} = -a + \sum_k A_{kj} m_k.$$

Mission accomplished?



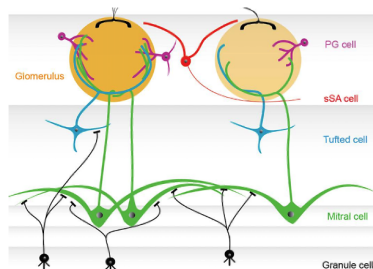
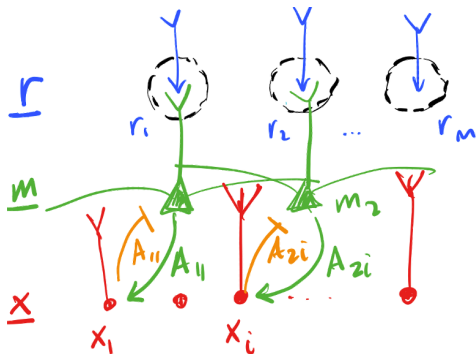
- Looks like the bulb!

Mission accomplished?



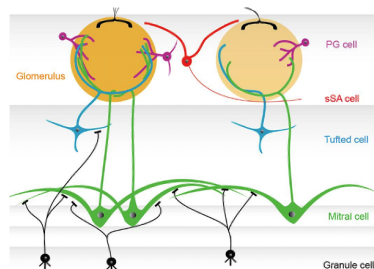
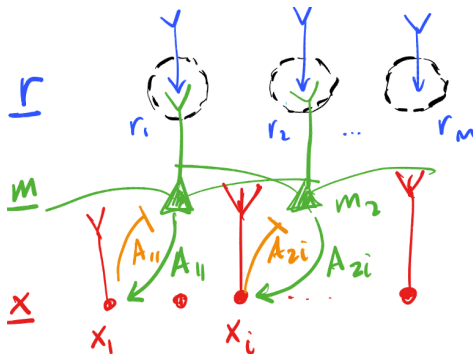
- Looks like the bulb!
- MC-to-GC weights A_{ij} store affinities.

Mission accomplished?



- Looks like the bulb!
- MC-to-GC weights A_{ij} store affinities.
- But: using an independent prior

Mission accomplished?

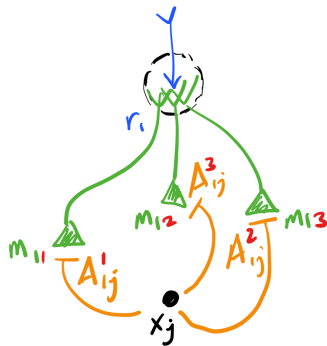
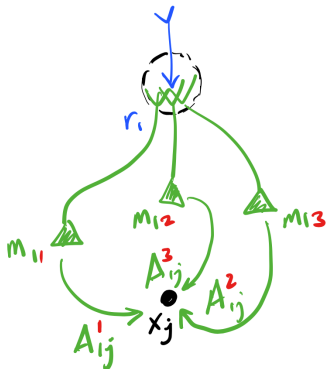


- Looks like the bulb!
- MC-to-GC weights A_{ij} store affinities.
- But: using an independent prior
- No sister cells...

To include sister cells, just add 's' to the dynamics

$$\frac{dm_{i\mathbf{s}}}{dt} = -m_{i\mathbf{s}} + r_i - \sum_j A_{ij}^{\mathbf{s}} x_j.$$

$$\frac{dx_j}{dt} = -a + \sum_{i,\mathbf{s}} A_{ij}^{\mathbf{s}} m_{i\mathbf{s}}.$$



The objective of the dynamics

- We *derived* the old dynamics to maximize the posterior.

$$L(\mathbf{x}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_i (r_i - A_{ij}x_j)^2}_{\text{log evidence}}.$$

The objective of the dynamics

- We *derived* the old dynamics to maximize the posterior.

$$L(\mathbf{x}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_i (r_i - A_{ij}x_j)^2}_{\text{log evidence}}.$$

- We derived the sister dynamics heuristically - no guarantee that they maximize anything.

The objective of the dynamics

- We *derived* the old dynamics to maximize the posterior.

$$L(\mathbf{x}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_i (r_i - A_{ij}x_j)^2}_{\text{log evidence}}.$$

- We derived the sister dynamics heuristically - no guarantee that they maximize anything.
- But in fact, they maximize

$$L(\mathbf{x}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_{i,s} (r_i - A_{ij}^s x_j)^2}_{\text{log evidence?}}.$$

The objective of the dynamics

- We *derived* the old dynamics to maximize the posterior.

$$L(\mathbf{x}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_i (r_i - A_{ij}x_j)^2}_{\text{log evidence}}.$$

- We derived the sister dynamics heuristically - no guarantee that they maximize anything.
- But in fact, they maximize

$$L(\mathbf{x}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_{i,s} (r_i - A_{ij}^s x_j)^2}_{\text{log evidence?}}.$$

- How to interpret this?

Interpreting the new objective

- The original objective maximized a log posterior:

$$\log p(\mathbf{x}|\mathbf{r}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_i (r_i - A_{ij}x_j)^2}_{\text{log evidence}}.$$

Intrepreting the new objective

- The original objective maximized a log posterior:

$$\log p(\mathbf{x}|\mathbf{r}) = - \underbrace{\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_i (r_i - A_{ij}x_j)^2}_{\text{log evidence}}.$$

- To interpret the new objective...

$$L(\mathbf{x}) = - \sum_j ax_j - \sum_{i,s} (r_i - A_{ij}^s x_j)^2.$$

Intrepreting the new objective

- The original objective maximized a log posterior:

$$\log p(\mathbf{x}|\mathbf{r}) = \underbrace{-\sum_j ax_j}_{\text{log prior}} - \underbrace{\sum_i (r_i - A_{ij}x_j)^2}_{\text{log evidence}}.$$

- To interpret the new objective...

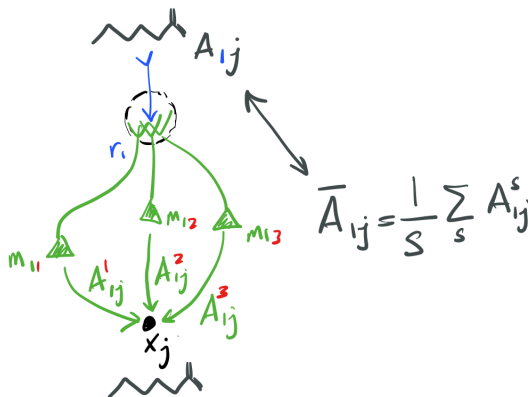
$$L(\mathbf{x}) = -\sum_j ax_j - \sum_{i,s} (r_i - A_{ij}^s x_j)^2.$$

- ... we express it in the same form as the old

$$L(\mathbf{x}) = \underbrace{-\sum_j ax_j - \sum_{j,k} C_{jk} x_j x_k}_{\text{log prior}} - \underbrace{\sum_i S_i (r_i - \sum_j \overline{A}_{ij} x_j)^2}_{\text{log evidence}}.$$

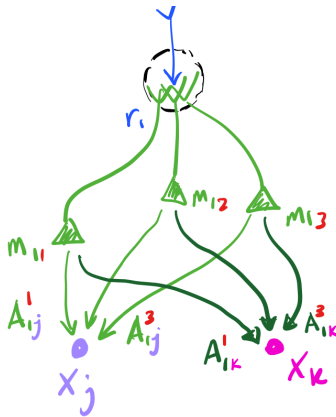
Mean connectivity encodes affinity

$$L(\mathbf{x}) = - \sum_j a x_j - \sum_{j,k} C_{jk} x_j x_k - \sum_i S_i (r_i - \sum_j \overline{A_{ij}} x_j)^2.$$



Covariance of connectivity encodes correlated priors

$$L(\mathbf{x}) = - \sum_j a x_j - \sum_{j,k} C_{jk} x_j x_k - \sum_i S_i (r_i - \sum_j \overline{A_{ij}} x_j)^2.$$



$$C'_{jk} = \text{cov}_s(A_{ij}^s, A_{ik}^s)$$

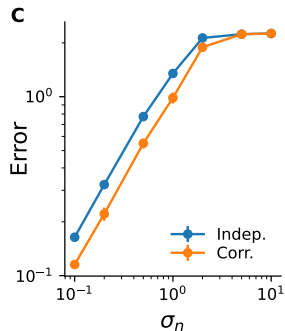
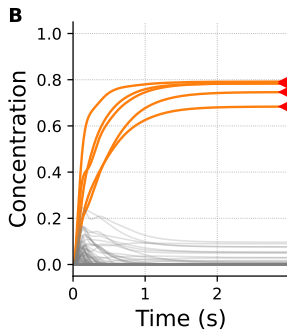
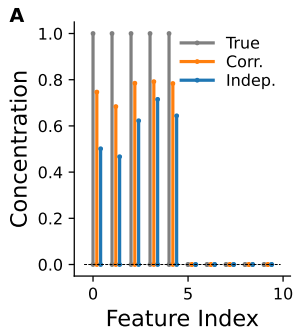
$$C_{jk} = \sum_i S_i C'_{jk}$$

How many odours can we encode correlations for?

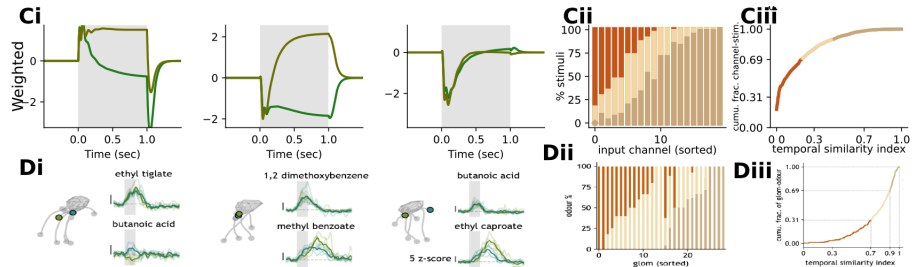
Connectivity solutions exist whenever

$$n \leq \underbrace{S}_{\text{total \# sisters}} - \underbrace{M}_{\text{\# glomeruli}} .$$

Simulations: Using correlated priors helps



Simulations: Comparison to experimental data



Data from Zhang et al. 2025

Conclusions

- Natural odour components are correlated.

Conclusions

- Natural odour components are correlated.
- Optimal inference should use correlated priors.

Conclusions

- Natural odour components are correlated.
- Optimal inference should use correlated priors.
- Naive implementation requires GCs to talk to each other (they don't).

Conclusions

- Natural odour components are correlated.
- Optimal inference should use correlated priors.
- Naive implementation requires GCs to talk to each other (they don't).
- Sisters cells can encode correlated priors in their connectivity.

Conclusions

- Natural odour components are correlated.
- Optimal inference should use correlated priors.
- Naive implementation requires GCs to talk to each other (they don't).
- Sisters cells can encode correlated priors in their connectivity.
- Details: <https://arxiv.org/abs/2505.14579>

Section 2

Thank you Schaefer Lab,
esp. Yuxin and Carles,
and you for your attention!