Inferring olfactory space from glomerular response data

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Overview

Goal: olfactory space

We construct *olfactory space*.

- To each olfactory stimulus, we assign a point $x \in \mathbb{R}^d$, so that stimuli that elicit similar neuronal responses correspond to nearby points in olfactory space.

Input: glomerular response

The input to our algorithm is a matrix r_{ia} of the response of glomerulus i to olfactory stimulus a. We analyzed data from:

- Wachowiak lab: mice, ORN calcium imaging.
- Ma et al.: mouse, ORN calcium imaging.
- Hallem and Carlson: fly, ORN spike counts.

Model for glomerular response

- Each odorant corresponds to a point $x \in \mathbb{R}^d$.
- Each glomerulus corresponds to a vector $w \in \mathbb{R}^d$.

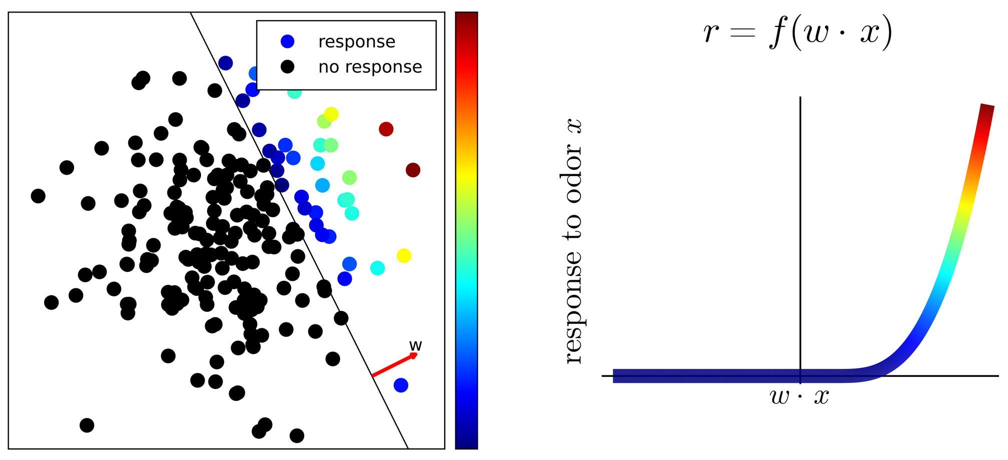

Fig. 1: Illustration of the response model. Each point corresponds to an odorant. A glomerulus with associated vector w responds to an odorant corresponding to point x if $w \cdot x$ is sufficiently large, and responds more strongly the larger $w \cdot x$ is.

Glomerular response

The response r_{ia} of glomerulus i to odorant a is given by

$$r_{ia} = f_i(w_i \cdot x_a),$$

where f_i is an *unknown* monotone function that is different for different glomeruli.

Method overview

Goal

Given the response matrix r_{ia}, fit the model: find the olfactory stimulus points x_a (olfactory space), the glomerulus vectors w_i, and the monotone functions f_i.

Hard step

Given the response matrix r_{ia}, construct a matrix p_{ia} that approximates $w_i \cdot x_a$.

- **Challenge:** We have $r_{ia} \approx f_i(p_{ia})$, but the monotone function f_i is *unknown* and different for each glomerulus.
- **Solution:** For each glomerulus i, the relative rankings of r_{ia} give a percentile rank for each olfactory stimulus; these percentile ranks do not depend on f_i. We let p_{ia} be the value of a standard normal random variable with that percentile rank.

- **Challenge:** *sparsity*. If $r_{ia} = 0$, we do not know the percentile rank of that odorant.
- **Solution:** Treat these as missing p_{ia} values, and estimate them using *compressed sensing*.

Easy step

From the matrix p_{ia}, get the vectors w_i and points x_a so that $p_{ia} \approx w_i \cdot x_a$ via principal component analysis.

Changing odorant concentration captured by first component of olfactory space

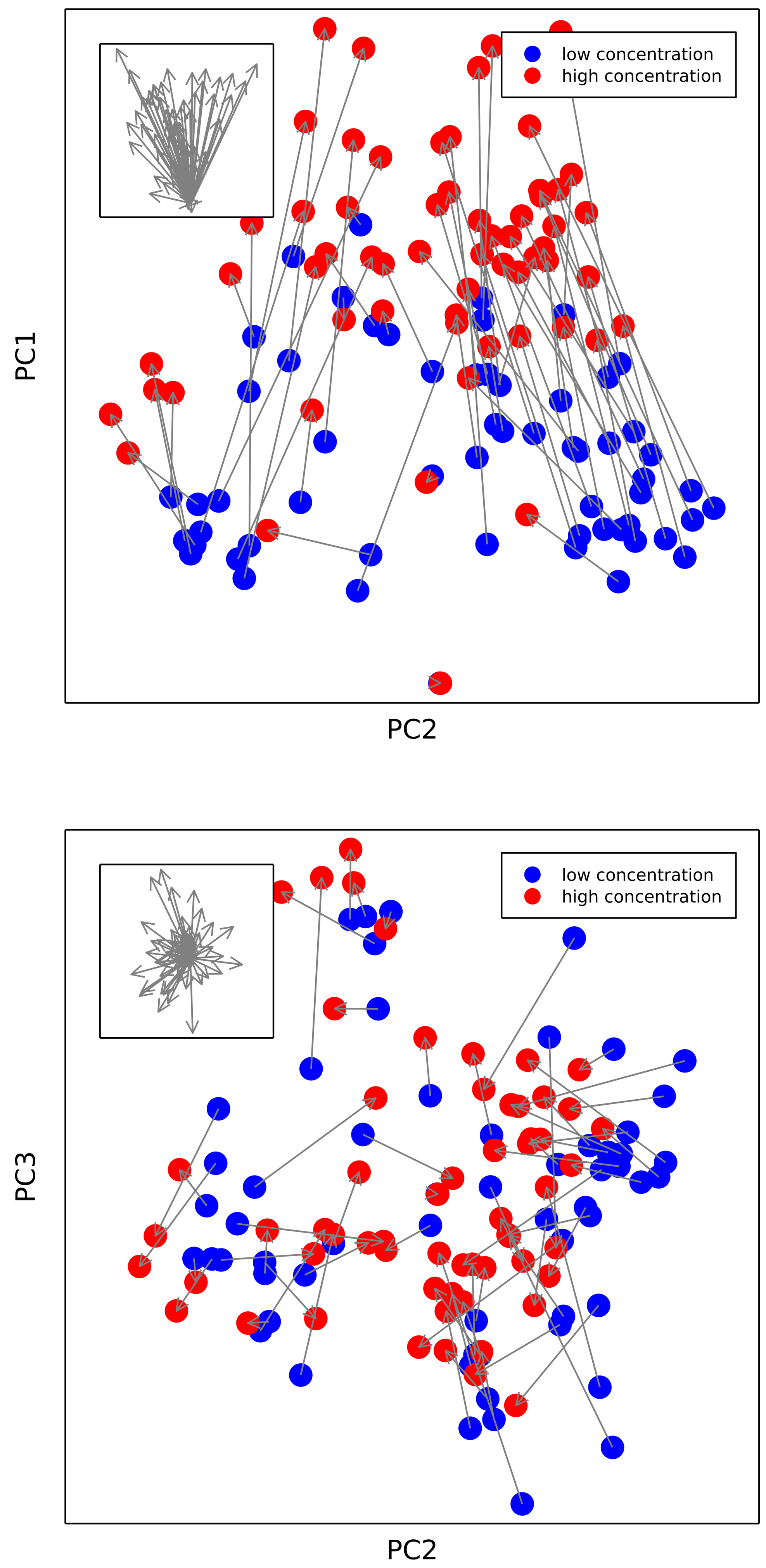

Fig. 2: Each odorant was presented at both low and high concentration. Combining the response data, we constructed olfactory space with stimuli at both concentrations. For each odorant, an arrow joins the low and high concentration stimuli; the insets show those same arrows based at the origin. Two projections are shown. A clear correlation between concentration and the first component is evident, but there is no substantial correlation between concentration and the second and third components.

Odorant classes cluster in olfactory space

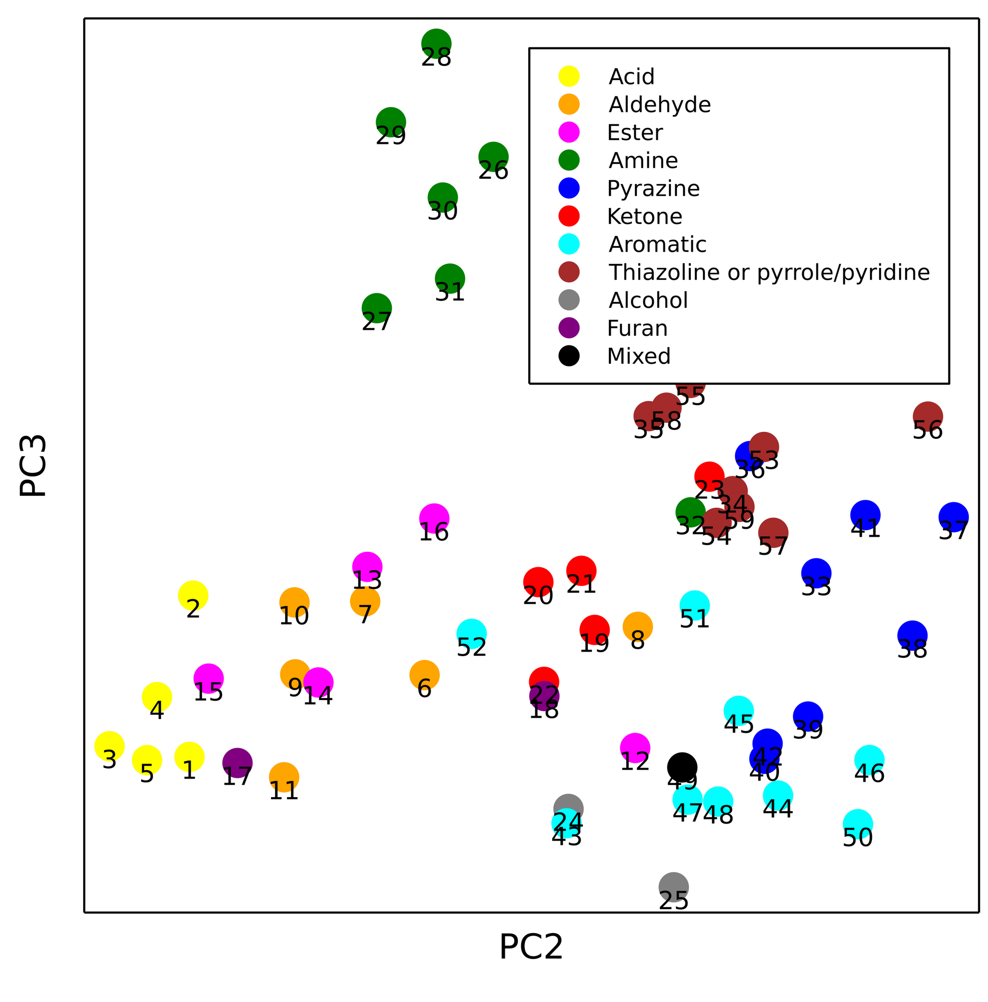

Fig. 3: Using just the high concentration response data and coloring the odorants by chemical class, we observe rough clustering. Note that the algorithm does *not* use the chemical properties of the odorants.

Olfactory space is consistent between individuals

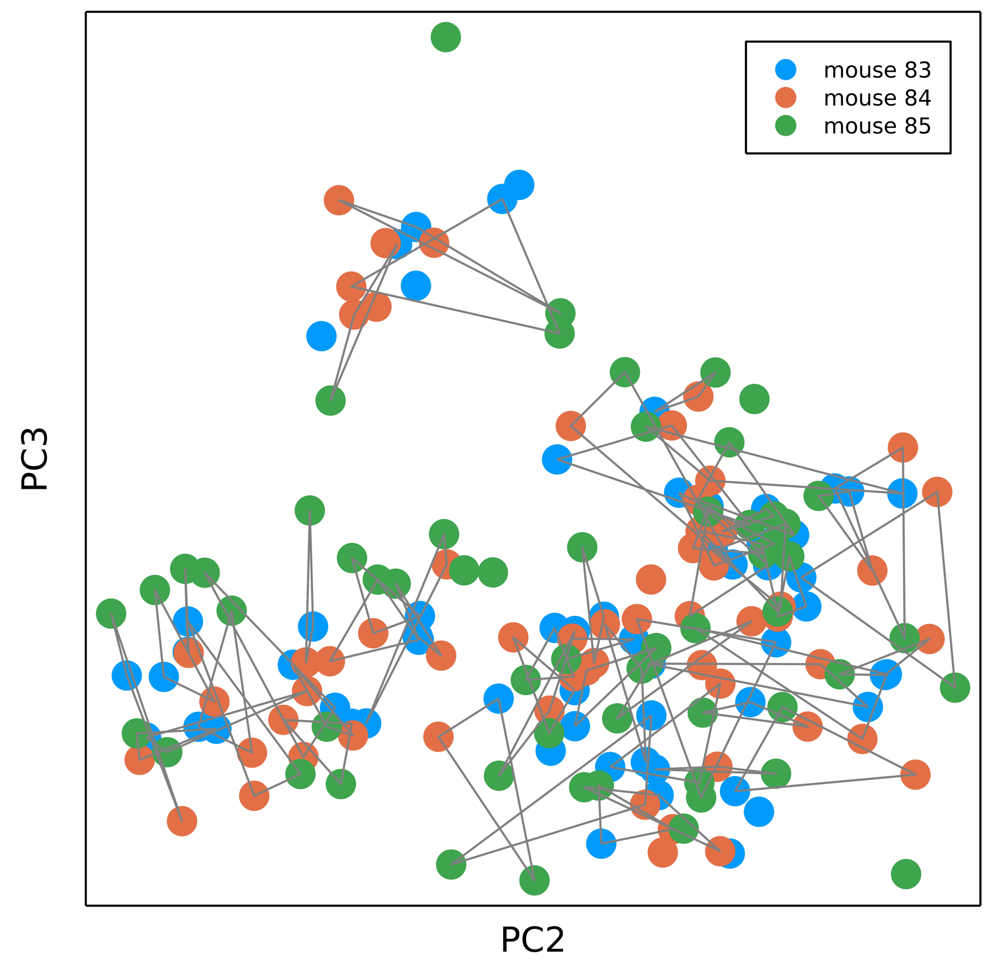

Fig. 4: Glomerular response data was collected from three mice. We construct olfactory space for each mouse, then overlay the three olfactory spaces. Triangles join an odorant's location in each of the three mice's olfactory spaces. For most odorants, the location of the odorant point is consistent between the three mice. Some odorants are outliers. A possible explanation is that, even though the same region of the olfactory bulb was imaged, slightly different sets of glomeruli were captured for each mouse.

Model dimension and prediction accuracy

1. Exclude one odorant from the data.
2. Fit the model.
3. (a) Predict the response of *one mouse* to the excluded odorant using the model and the response of *the other two mice*, *or*
   (b) Predict the response of *one glomerulus* to the excluded odorant using the model and the response of *the other glomeruli*.

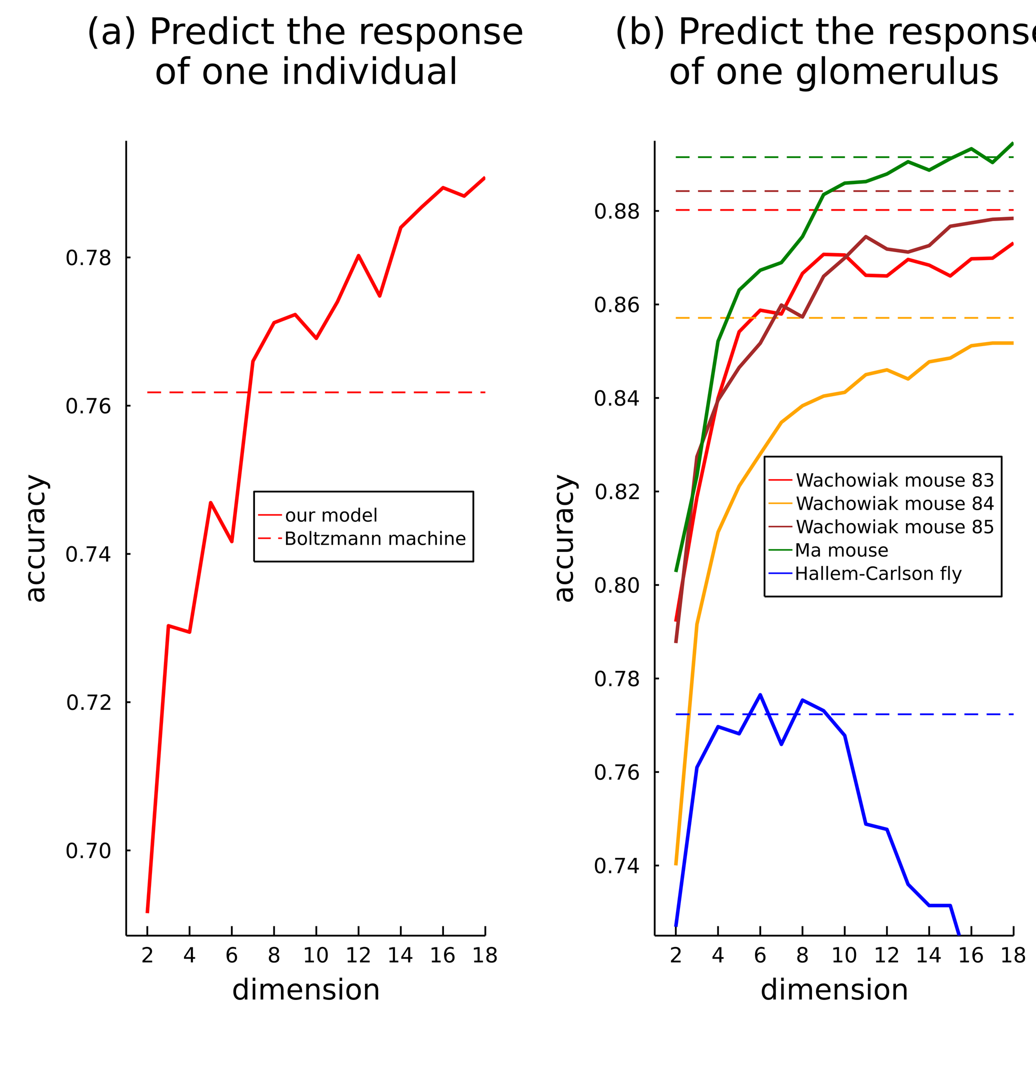

Fig. 5: The accuracy of predicting on/off glomerular response, using our model in each dimension d (thick line) vs. a Boltzmann machine (dashed line).

Conclusions

- We infer the stimulus space despite noise and sparsity.
- Our model performs as well as a Boltzmann machine, but our model also reveals additional structure:
- The space captures the effect of changing odorant concentration, chemical classes roughly cluster, and the space is consistent between individuals.