Hidden sources of variability modulate populations of sensory neurons

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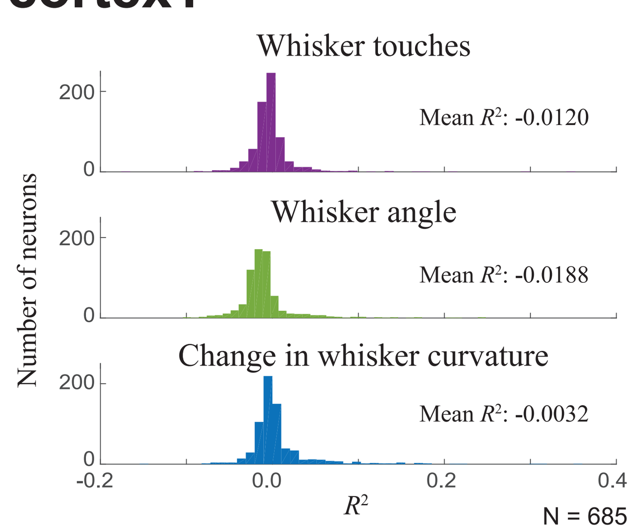
Introduction

The activity of sensory cortical neurons is not only driven by external stimuli, but is also shaped by other sources of input to the cortex. Unlike external stimuli, these other sources of input are challenging to experimentally control or even observe, and as a result contribute to variability of sensory neuron responses in most experimental contexts. However, such sources of variability are likely not "noise", and may play an integral role in sensory cortex function. Here, we introduce the rectified latent variable model (RLVM) in order to identify these sources of variability, and demonstrate its use with simulated and experimental data. This method thus sets the foundation for understanding the role of such variables in sensory cortical function.

What factors drive neural activity in barrel cortex?

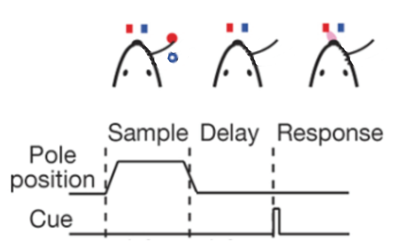


Neural activity is not well-predicted by stimlus

How can we characterize the factors that drive activity?

Experimental Details

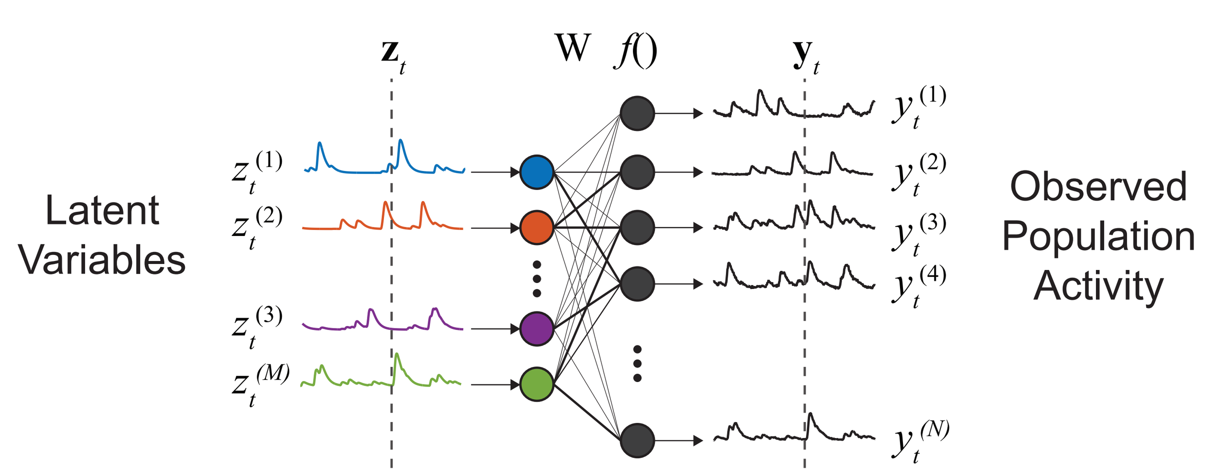
The data used are from a publicly available dataset from the **Svoboda Lab** [1]. Briefly, mice performed a pole localization task with a single spared whisker (see right; figure adapted from [2]). During each trial, the activity of neurons in layer 2/3 of barrel cortex expressing the GCaMP6s calcium indicator was recorded using 2-photon imaging. All recorded neurons were located in the single barrel corresponding to the spared whisker.



Stimulus Model Fitting Details

We fit regularized linear regression models using one of the three stimulus parameters as the predictor for single neuron activity. Time lags were included in the model to account for the long timescales of fluorescence decay. Plotted values are averages over 5 cross-validation folds.

The Rectified Latent Variable Model (RLVM)



$$\mathbf{y}_t = f(W\mathbf{z}_t + \mathbf{b})$$

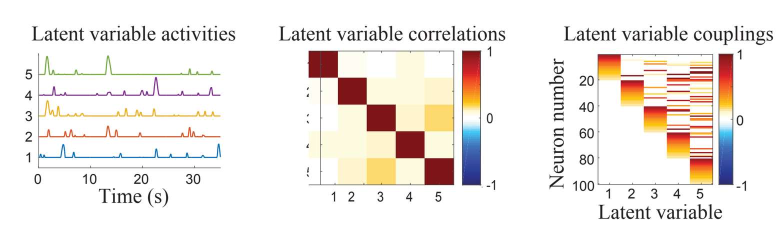
Model Constraints: $\mathbf{z}_t$ is non-negative (rectified)

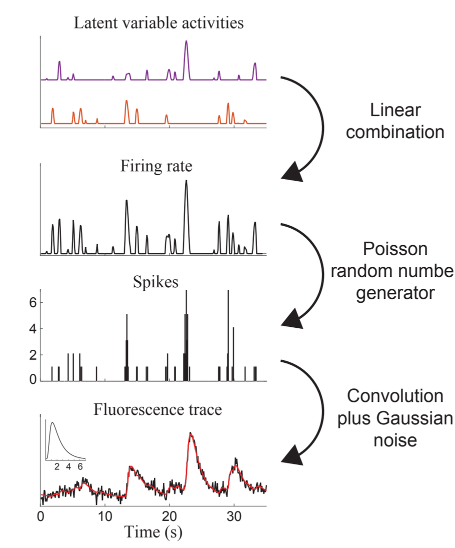
Motivation for rectification

- Neural processes, whether excitatory or inhibitory, must be realized using the action potentials or firing rates of neurons, neither of which can take on negative values
- Can capture sparse latent variables
- Solves rotatioinal degeneracy problem characteristic of linear models: for an orthogonal matrix U, $W^*\mathbf{z}_t = (WU^T)^*(U\mathbf{z}_t)$

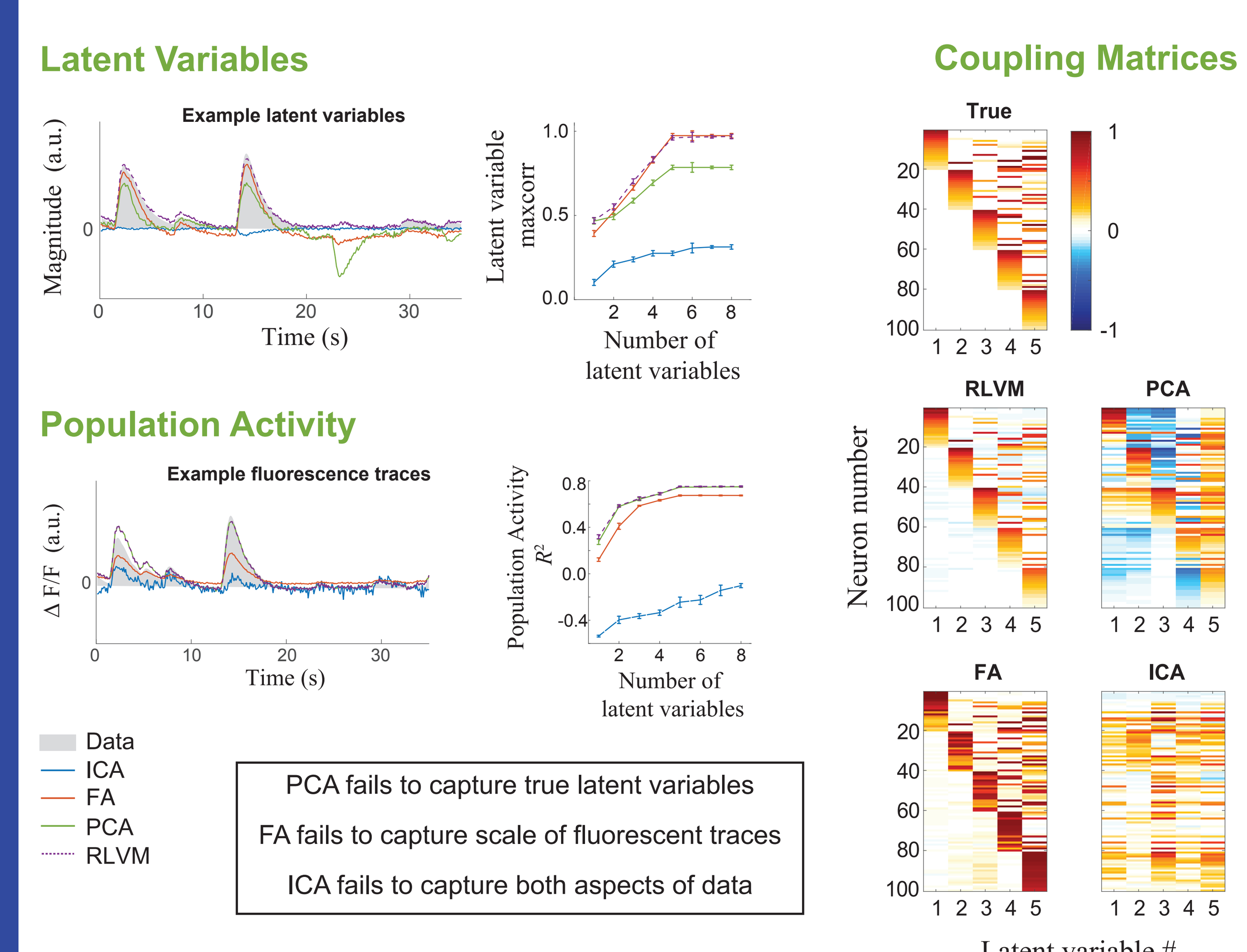
Model Validation with Simulated Data

Data was simulated according the the RLVM structure. 5 correlated, non-negative latent variables were created from the absolute values of smoothed Gaussian noise. The firing rates for 100 individual neurons were then produced from the linear combination of those latent variables using a coupling matrix. Firing rates were passed into a Poisson random number generator to create spikes. The data was further processed by convolving with a kernel and adding Gaussian noise to approximate 2-photon data.





RLVM captures rectified latent variables in simulated dataset



PCA fails to capture true latent variables

FA fails to capture scale of fluorescent traces

ICA fails to capture both aspects of data

Measures of model performance

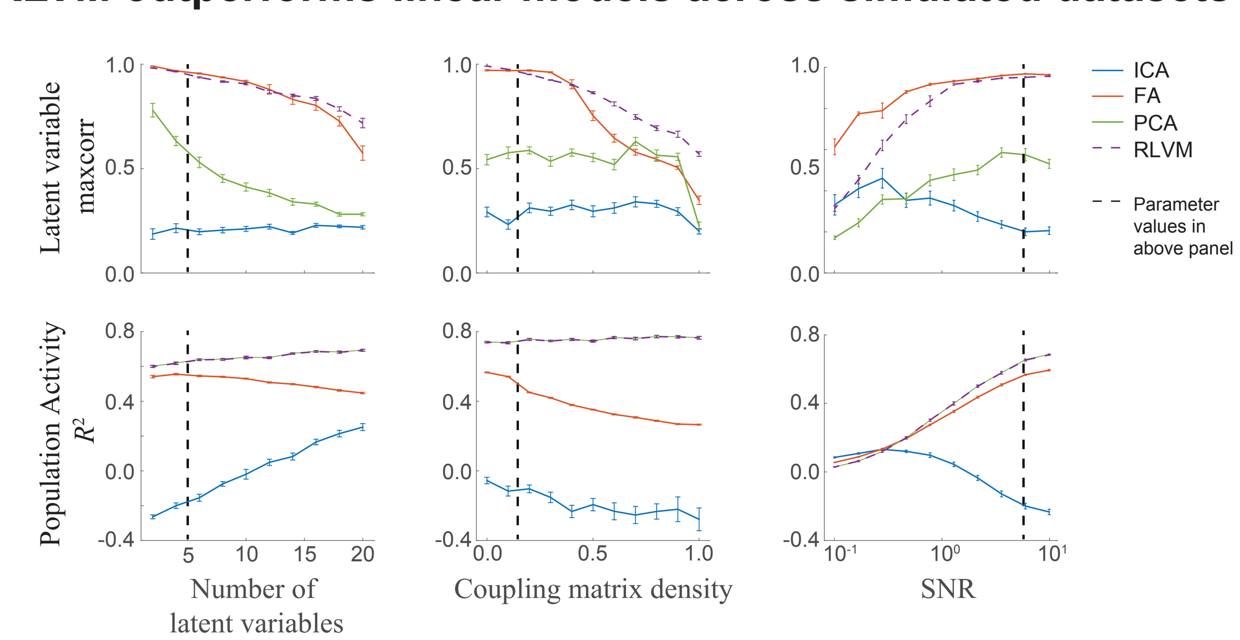
Latent variables:

$$\text{maxcorr} = \frac{1}{M}\sum_{i=1}^{M} \max_{j\in\{1,\dots,N\}} [corr(\mathbf{z}_i, \hat{\mathbf{z}}_j)]$$

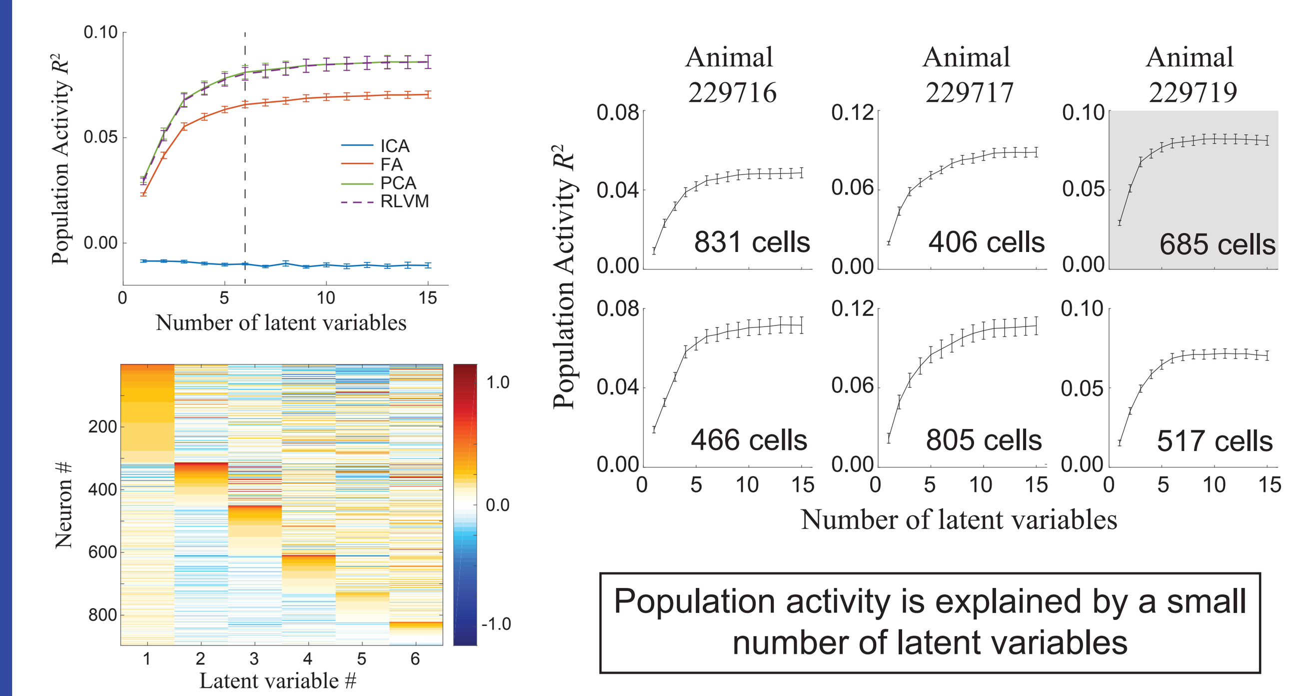
Population activity:

$$R^2 = \frac{1}{N}\sum_{i=1}^{N}\left[1 - \frac{\sum_t (y_t^i - \hat{y}_t^i)^2}{\sum_t (y_t^i - \bar{y}^i)^2}\right]$$

RLVM outperforms linear models across simulated datasets

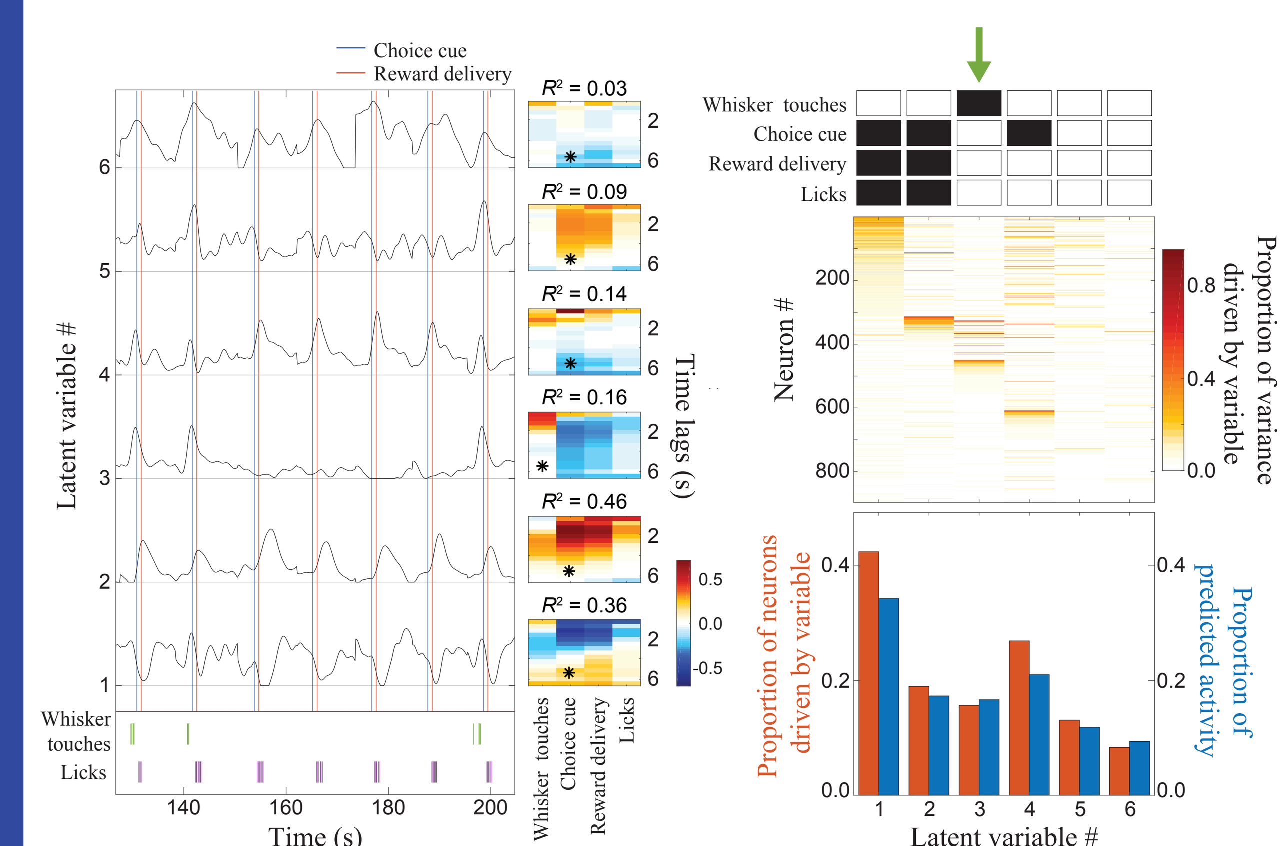


Latent variable models applied to activity in barrel cortex



Population activity is explained by a small number of latent variables

Neurons in barrel cortex are not just driven by whisker movement

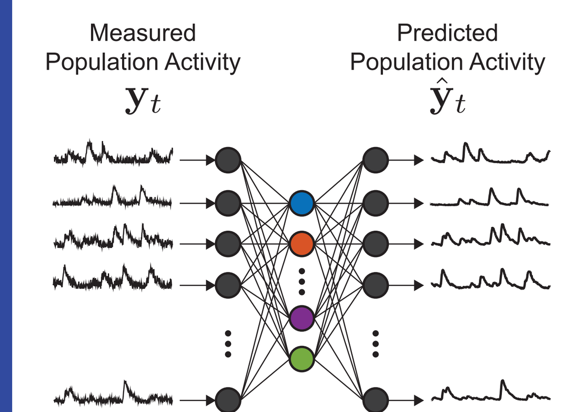


RLVM latent variables show a strong relationship to measured trial variables

Large proportion of population activity is driven by non-tactile sources

RLVM Fitting Details

Latent variables $\mathbf{z}_t$ and model weights W are fit using an autoencoder neural network [3]. To enforce non-negativity of the latent variables, the activation functions *g*() for the middle layer are rectified linear, so that *g*(x) = max(0, x). For modeling 2-photon data, the activation functions f() in the output layer are linear and the cost function is the mean square error between the measured and predicted population activity, which implicitly assumes a Gaussian noise model. Model parameters are optimized using an L-BFGS method. 5-fold cross-validation is used for reporting model performance with both simulated and experimental data.



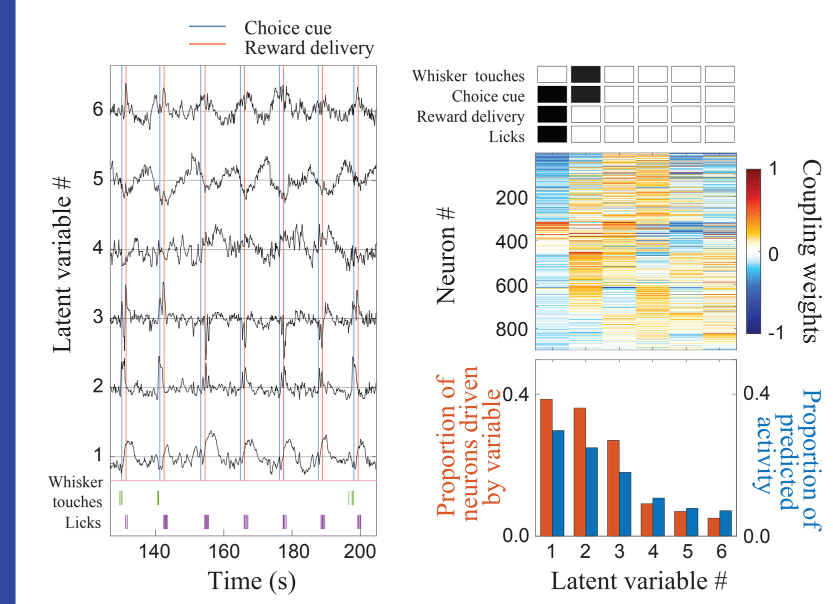
Model Predictions:

$$\begin{aligned}\hat{\mathbf{y}}_t &= f(W_2\mathbf{z}_t + \mathbf{b}_2)\\ &= f(W_2 g(W_1\mathbf{y}_t + \mathbf{b}_1) + \mathbf{b}_2)\end{aligned}$$

Optimization Cost Function:

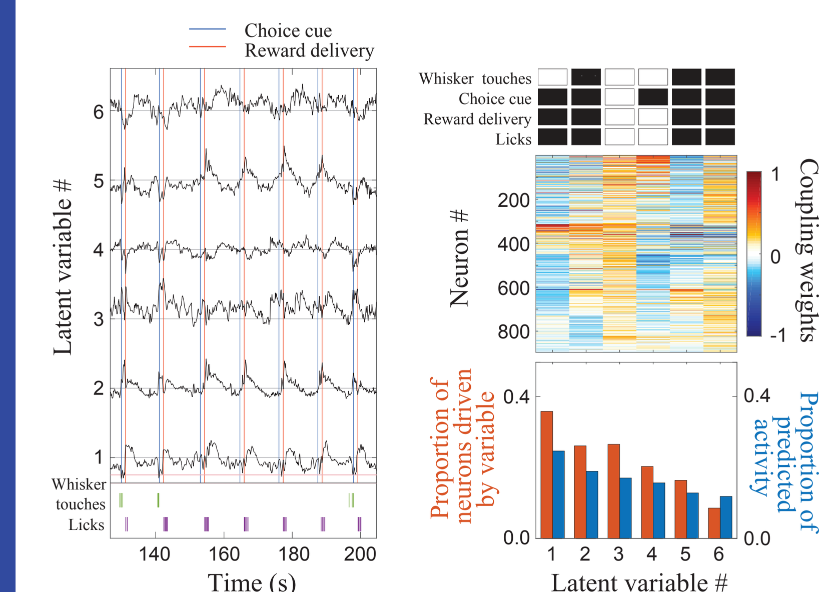
$$\begin{aligned}\hat{\theta} &= \underset{\theta}{\text{argmin}} \sum_t \|\mathbf{y}_t - \hat{\mathbf{y}}_t\|_2^2\\ &= \underset{\theta}{\text{argmin}} \sum_t \|\mathbf{y}_t - (W_2 g(W_1\mathbf{y}_t + \mathbf{b}_1) + \mathbf{b}_2)\|_2^2\end{aligned}$$

Latent variables from linear models mix trial variables



PCA Latent Variables

- First latent variable mixes two subpopulations separated by RLVM
- PCA latent variables cannot capture sparse inputs to cortex like whisker touches
- FA yields similar results (data not shown)



"Linear" RLVM Latent Variables

- First latent variable mixes two subpopulations like PCA
- Implies mixing is not solely due to constraint on PCA latent variables to be uncorrelated
- Demonstrates the importance of rectification for recovering interpretable latent variables

Conclusions

1. Population activity in barrel cortex is driven by more than just sensory inputs. Latent variable models offer an approach to characterize these additional factors.
2. Rectification of latent variables is necessary to recover non-negative latent variables in simulations and leads to important distinctions in the descriptions of population activity in both simulated and experimental data
3. Rectified latent variables separate effects of different trial variables, whereas linear models mix these effects

References

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Acknowledgements

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