Activity of Stimulus Responsive Neurons in attentional set-shifting task

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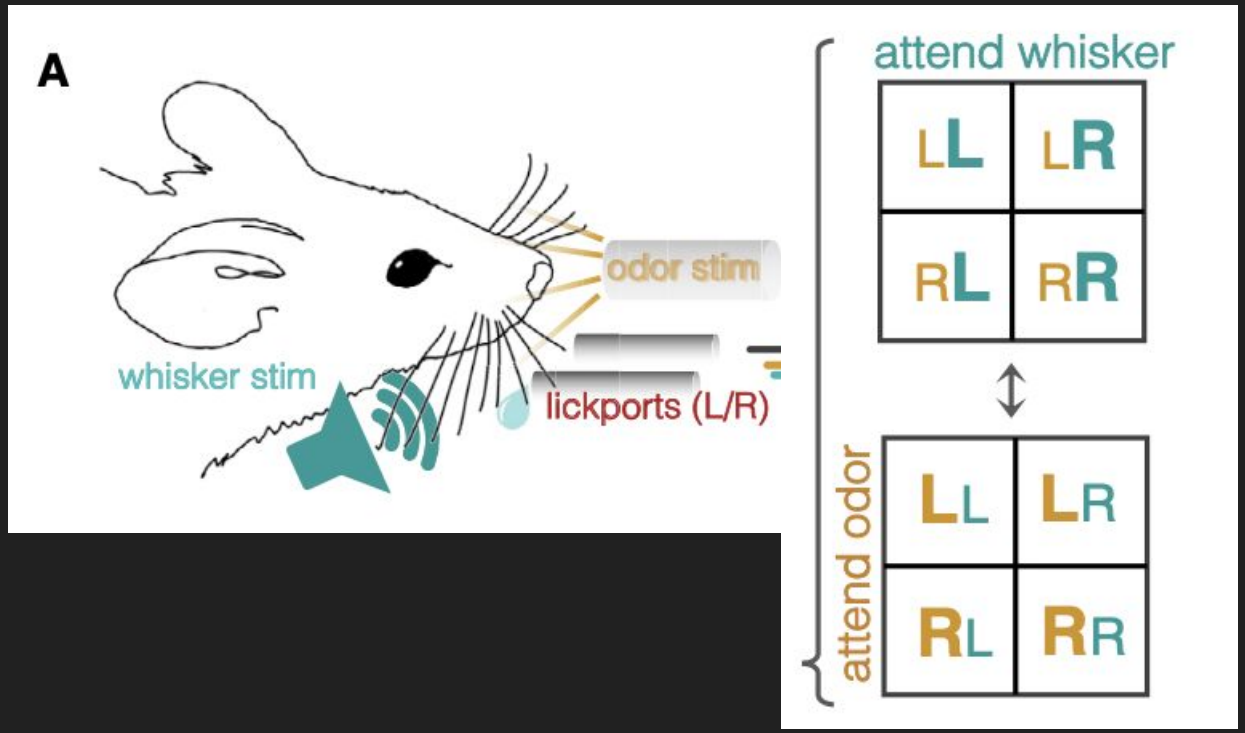
Why do we care about attentional set-shifting?

- Cognitive flexibility: ability to adapt to changing environments
- Attentional set-shifting: measurement of cognitive flexibility
- Previous research has shown that patients with schizophrenia and bipolar disorder have deficits in attentional set-shifting ability (McKirdy et al. 2009).

What is attentional set-shifting?

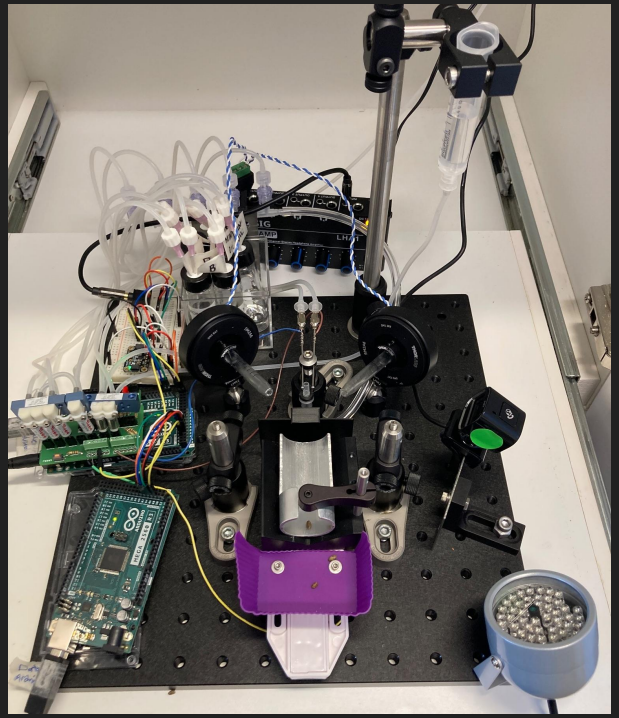


Bold: correct answer

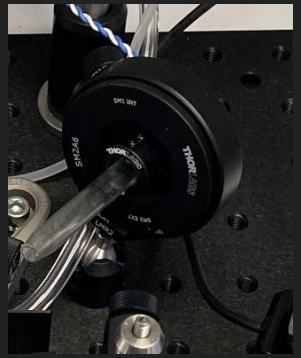
Blue: Whisker stimulus

Yellow: Odor stimulus

How to train mouse to master this task?



Whisker Stimulus
(Speaker Vibration)



Odor Stimulus

Reward
(Watersprouts)

Research Question:

How does activity level of stimulus responsive neurons change throughout a trial and across trials during attentional set-shifting task?

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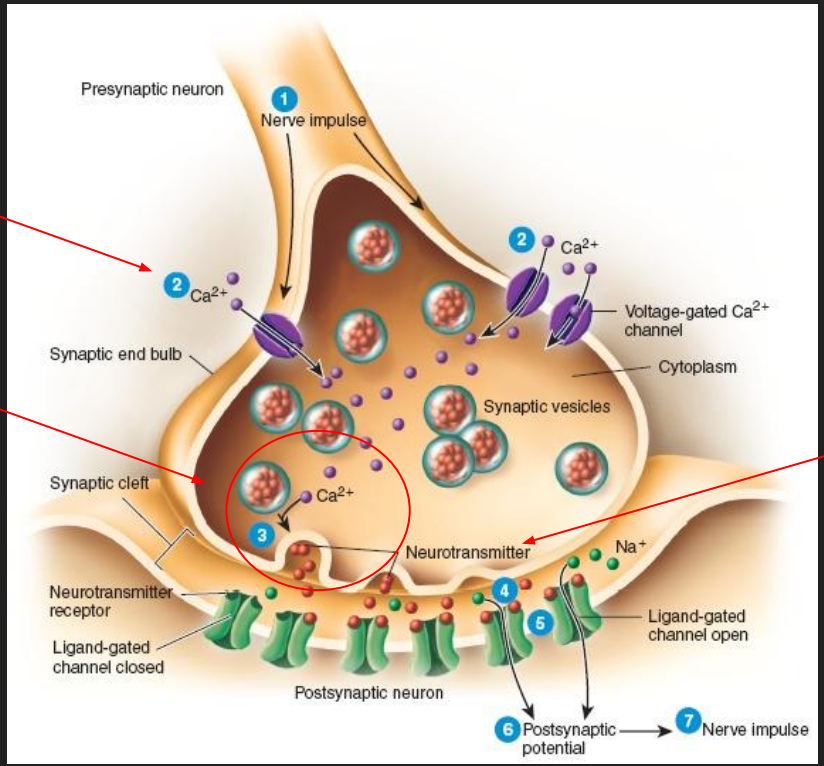
1. activity level: Calcium Imaging

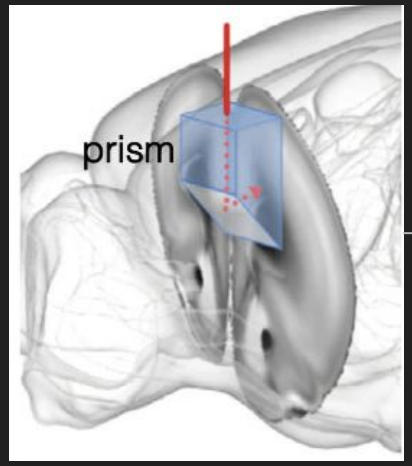
1. Calcium imaging captures neuron activity in mPFC

Ca2+ binds to Calmodulin to release vesicles

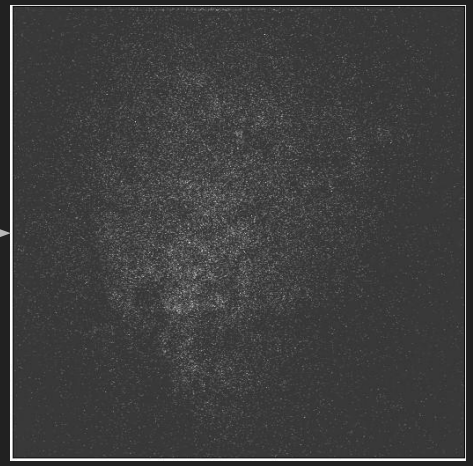
Excess Ca2+ binds to GCaMP, indicating vesicular release



1. Calcium imaging captures neuron activity in mPFC

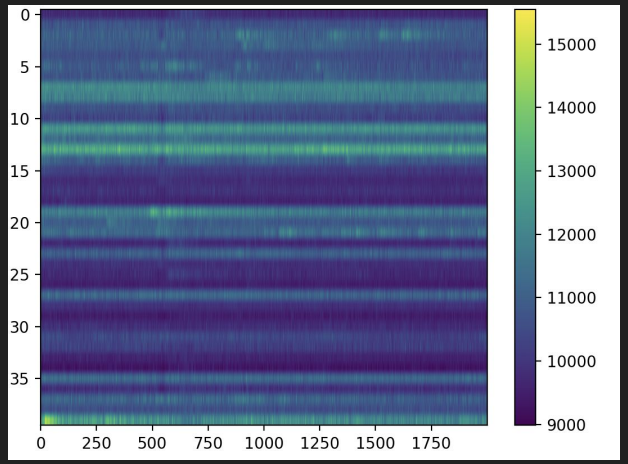


Prism put in mPFC region in brain

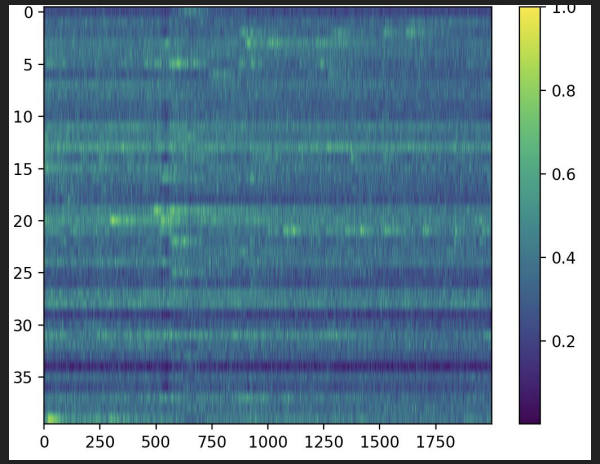


Raw imaging movie of neuronal activity

1. Suite2P: identify regions of interest



Suite2P output
fluorescence traces



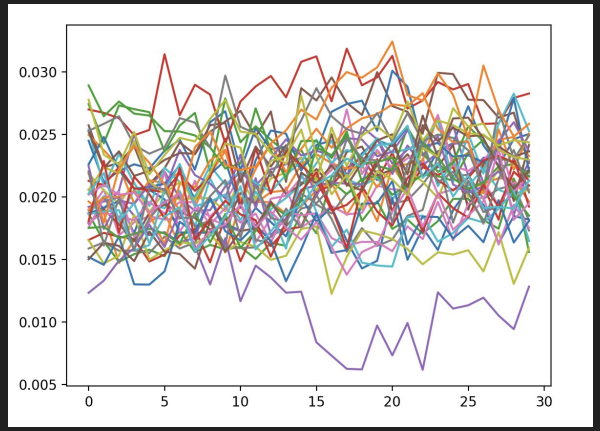
Normalized
fluorescence traces

Research Question:

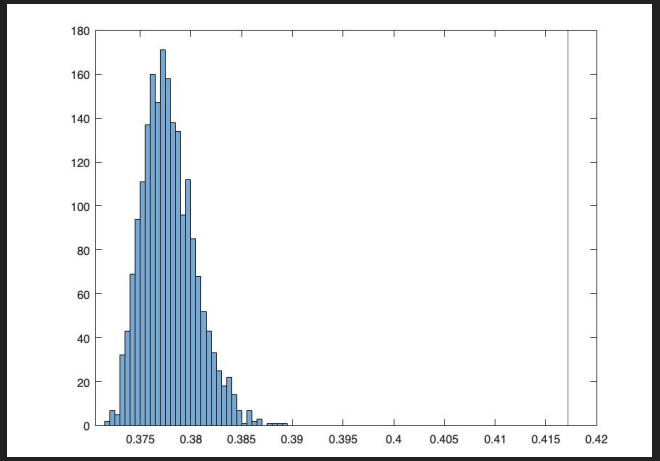
How does activity level of stimulus responsive neurons change throughout a trial and across trials during attentional set-shifting task?

1. activity level: Calcium Imaging
2. stimulus responsive neurons: shuffle test

2. Trial-shuffle method tests the significance of change in neural activity in response to stimulus



Trial averaged fluorescence traces 1s window centered around stimulus onset



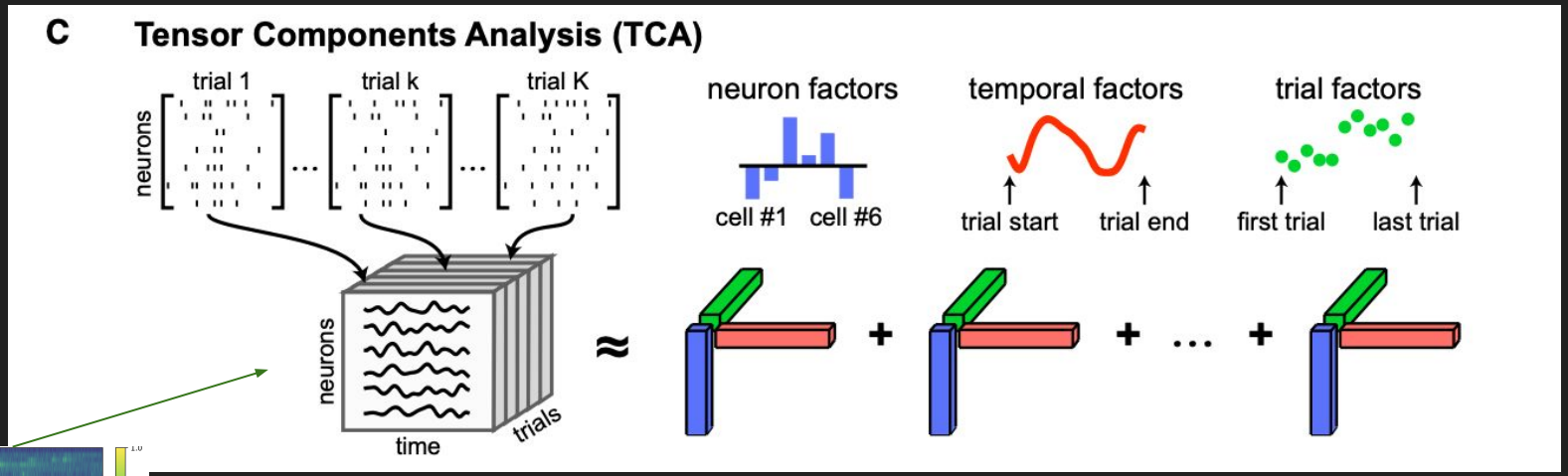
circularly shift each trial → 1000 times → distribution of maximum fluorescence traces

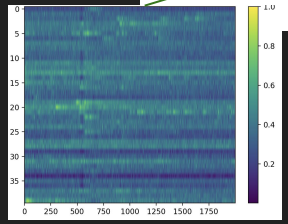
Research Question:

How does activity level of stimulus responsive neurons change throughout a trial and across trials during attentional set-shifting task?

1. activity level: Calcium Imaging
2. stimulus responsive neurons: shuffle test
3. throughout a trial across trial: Tensor Component Analysis

3. Tensor Component Analysis unravels neuronal, temporal, and trial factors





Normalized fluorescence traces

(Williams et al., 2018)

3. Tensor Component Analysis unravels neuronal, temporal, and trial factors

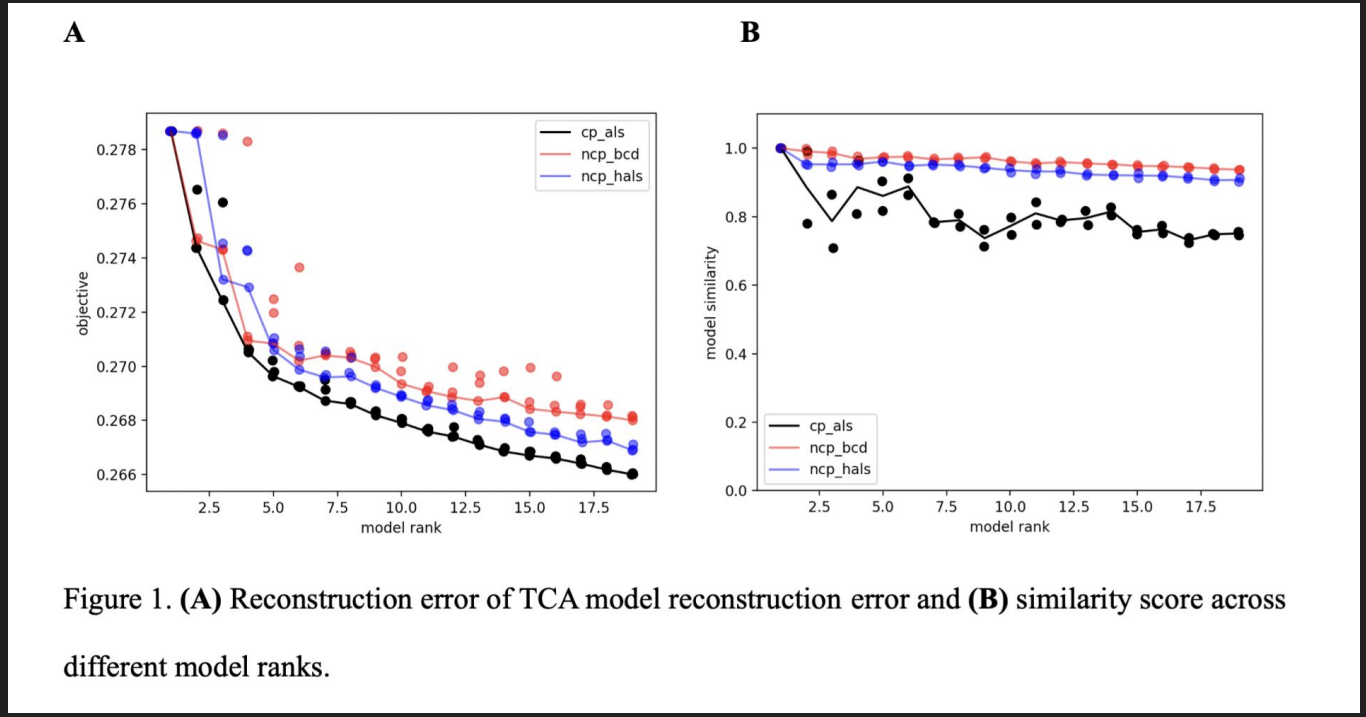
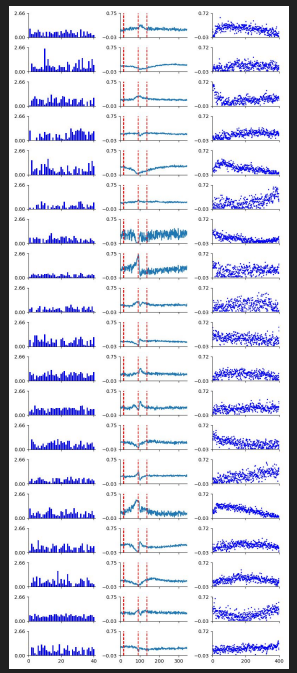


Figure 1. **(A)** Reconstruction error of TCA model reconstruction error and **(B)** similarity score across different model ranks.

3. Tensor Component Analysis unravels neuronal, temporal, and trial factors



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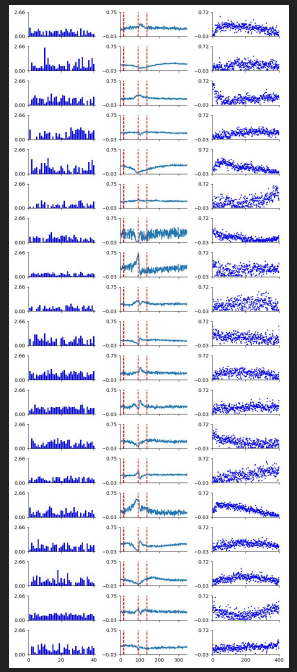
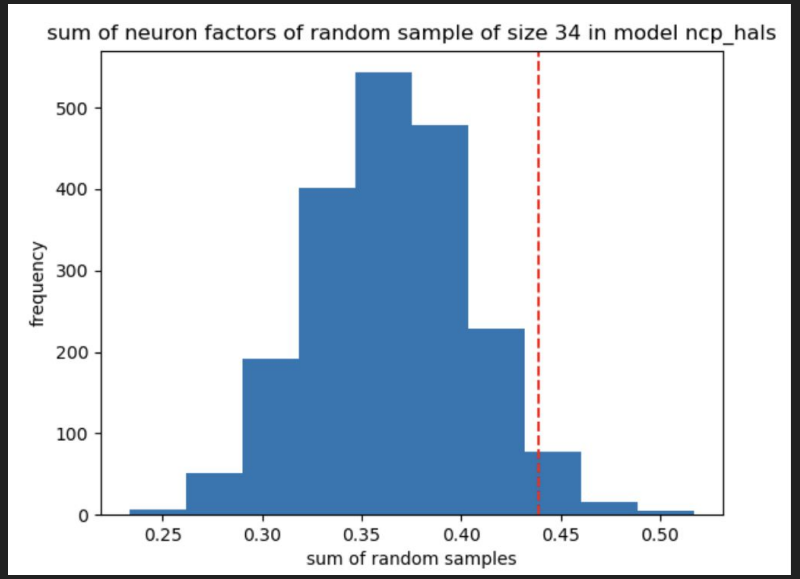
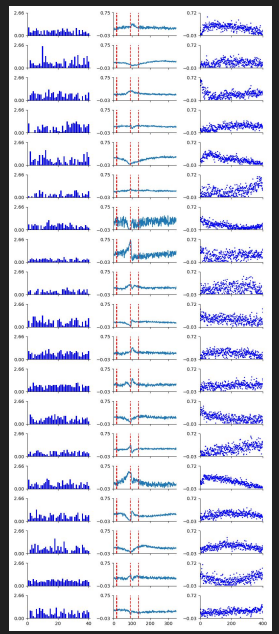


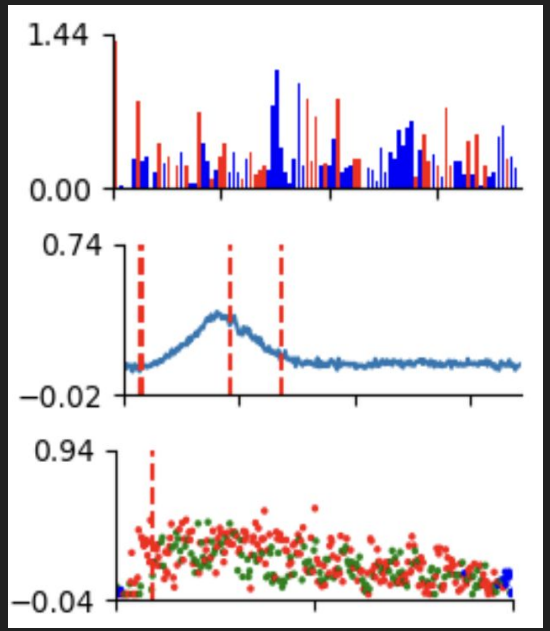


3. Tensor Component Analysis unravels neuronal, temporal, and trial factors

All 20 Components



Component for Stimulus (Whisker and Odor)



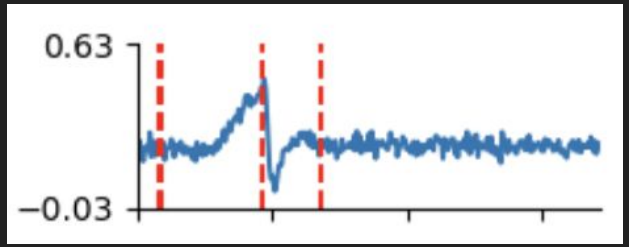
Neuronal factor: contribution of each neuron

Temporal Factor: change in neuronal activity within a trial

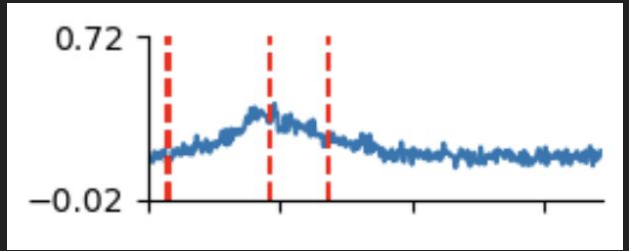
Trial Factor: change in neuronal activity across trials

3. Tensor Component Analysis unravels neuronal, temporal, and trial factors

Component for
Whisker Stimulus



Component for
Odor Stimulus



Conclusion

1. Stimulus responsive neurons have increased activity during stimulus presentation period but not in reward period and inter trial interval

2. Differential response towards left and right stimulus may indicate a good learning outcome, while no difference in response to left and right stimulus may indicate disengagement or inability to master the task

Future Directions

1. Investigate genetically defined neurons' activity within a trial and across trials, such as Parvalbumin (PV) interneurons and Vasoactive intestinal peptide (VIP) interneurons.

2. Investigate reward responsive neurons activity within and across trials, and their activity during stimulus period.

Acknowledgements

McKirdy, J., Sussmann, J. E., Hall, J., Lawrie, S. M., Johnstone, E. C., & McIntosh, A. M. (2009). Set shifting and reversal learning in patients with bipolar disorder or schizophrenia. Psychological medicine, 39(8), 1289–1293. https://doi.org/10.1017/S0033291708004935

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Williams, A. H., Kim, T. H., Wang, F., Vyas, S., Ryu, S. I., Shenoy, K. V., Schnitzer, M., Kolda, T. G., & Ganguli, S. (2018). Unsupervised Discovery of Demixed, Low-Dimensional Neural Dynamics across Multiple Timescales through Tensor Component Analysis. Neuron, 98(6), 1099–1115.e8. https://doi.org/10.1016/j.neuron.2018.05.015