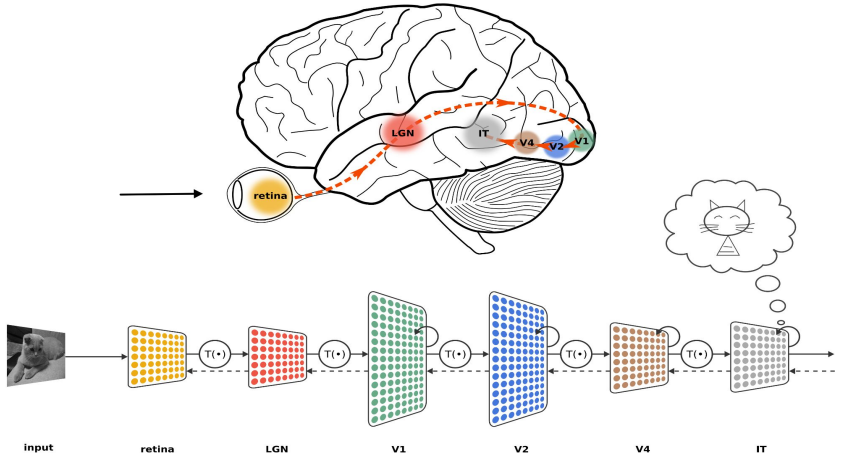
Does engagement matter: Do mice see the world differently when they don't care?

By: Ryan, Franck, Ankit, Jan, Helene, Manusmriti

Team: AwareWolfs (formerly the *Careful Wolfs*)

neuromatch academy

Does engagement matter?



Kubilius, Jonas (2017): Ventral visual stream. figshare. Figure.
https://doi.org/10.6084/m9.figshare.106794.v3

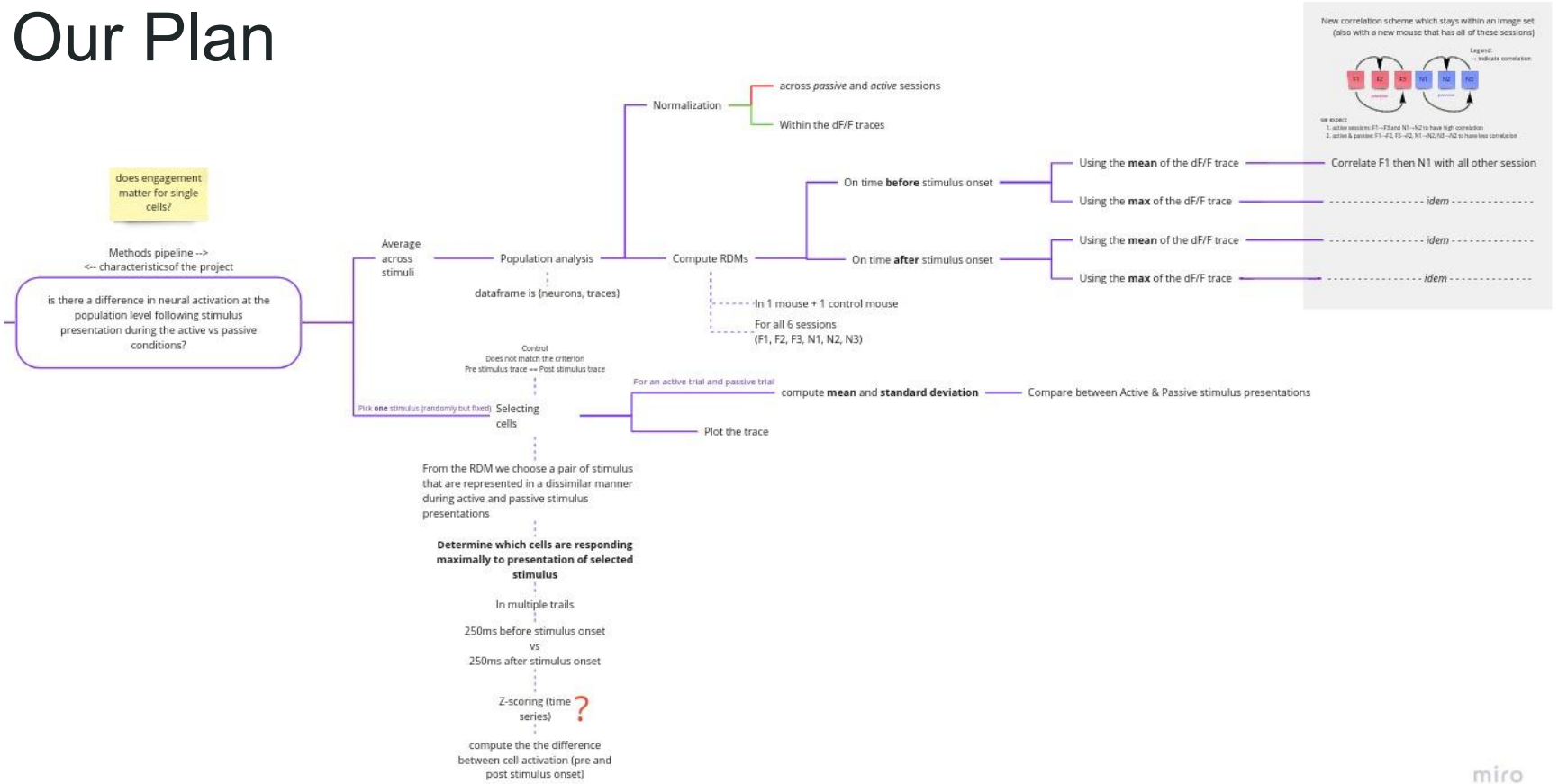
Traditionally V1/VISp is considered a simple feature detector

Stimulus representation in A1 adapts to engagement in go/no-go task
(Bagur et al 2018)

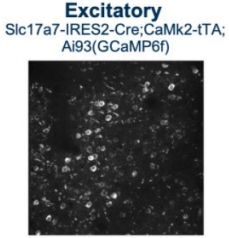
Does stimulus representation in V1 also differ depending on **engagement** (active) and **disengagement** (passive)?

Investigation on cell & population level

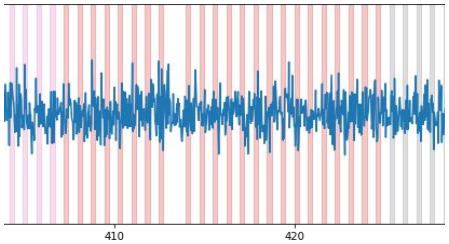
Our Plan


does engagement matter for single cells?
Methods pipeline --> <-- characteristicsof the project
is there a difference in neural activation at the population level following stimulus presentation during the active vs passive conditions?
Average across stimuli
Population analysis
dataframe is (neurons, traces)
Normalization
across passive and active sessions
Within the dF/F traces
Compute RDMs
In 1 mouse + 1 control mouse
For all 6 sessions (F1, F2, F3, N1, N2, N3)
On time before stimulus onset
On time after stimulus onset
Using the mean of the dF/F trace
Using the max of the dF/F trace
Correlate F1 then N1 with all other session
idem
Control
Does not match the criterion
Pre stimulus trace == Post stimulus trace
Pick one stimulus (randomly but fixed)
Selecting cells
For an active trial and passive trial
compute mean and standard deviation
Compare between Active & Passive stimulus presentations
Plot the trace
From the RDM we choose a pair of stimulus that are represented in a dissimilar manner during active and passive stimulus presentations
Determine which cells are responding maximally to presentation of selected stimulus
In multiple trails
250ms before stimulus onset
vs
250ms after stimulus onset
Z-scoring (time series)
compute the the difference between cell activation (pre and post stimulus onset)
New correlation scheme which stays within an image set (also with a new mouse that has all of these sessions)
Legend:
indicate correlation
F1 F2 F3 N1 N2 N3
passive
we expect:
1. active sessions: F1→F3 and N1→N2 to have high correlation
2. active & passive: F1→F2, F3→F2, N1→N2, N3→N2 to have less correlation
miro

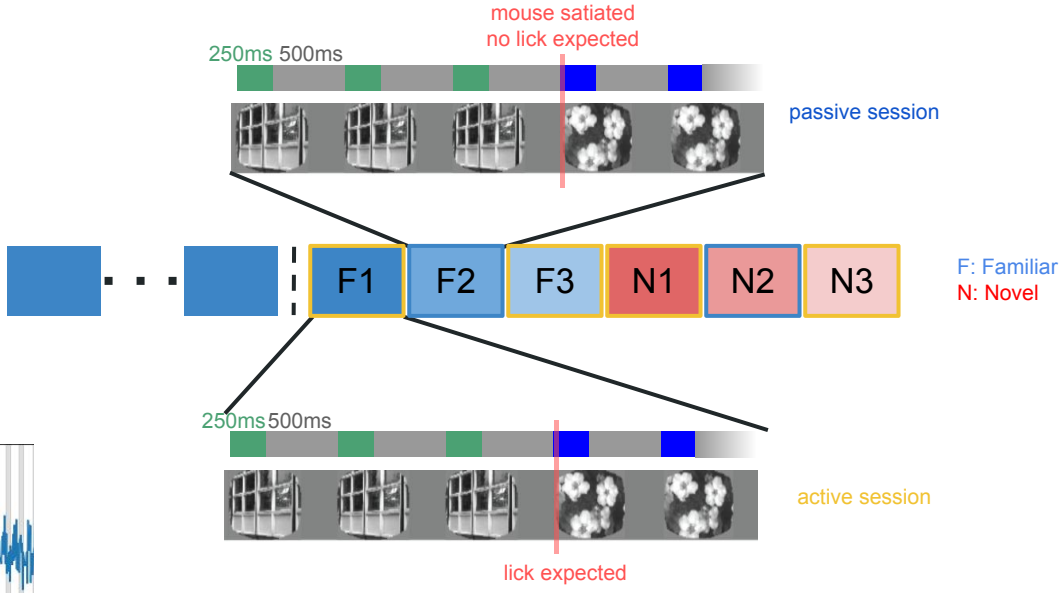
The Allen Institute 2P Visual Behavior Dataset



2-photon imaging



dff traces (fluorescence)



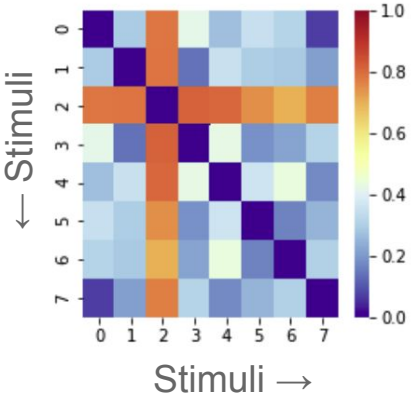
Does engagement matter: Do mice see the world differently when they don't care?

AwareWolfs

Population Analysis

Let's look into the representation of each stimulus in **active** and **passive** sessions

→ Representational dissimilarity matrices (RDM)



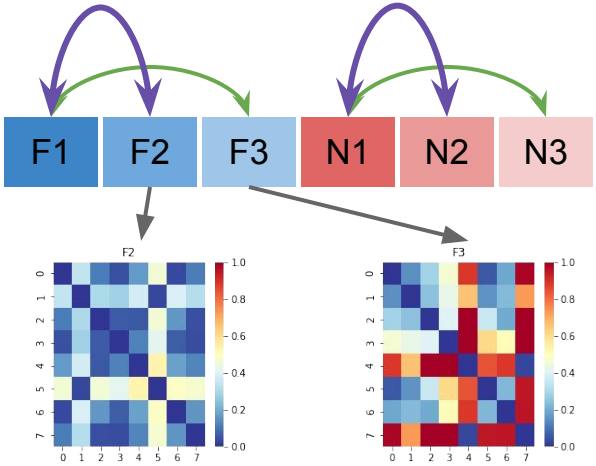
How dissimilar are these pairs of stimuli?

Time Series and sessions:

→ 250ms **before** and **after** stimulus onset

→ All 6 sessions: **familiars** (3) and **novels** (3)

→ **Mean** & **max** of trace for all presentations of one stimulus

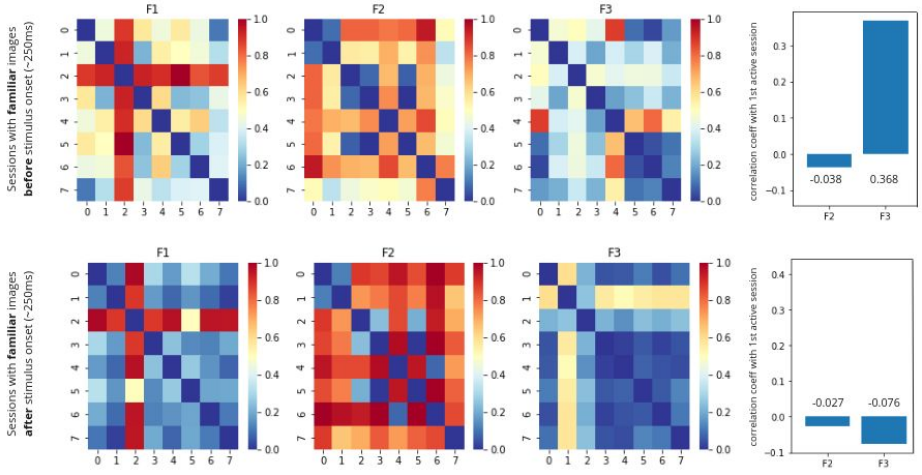


Correlate RDMs & expectations

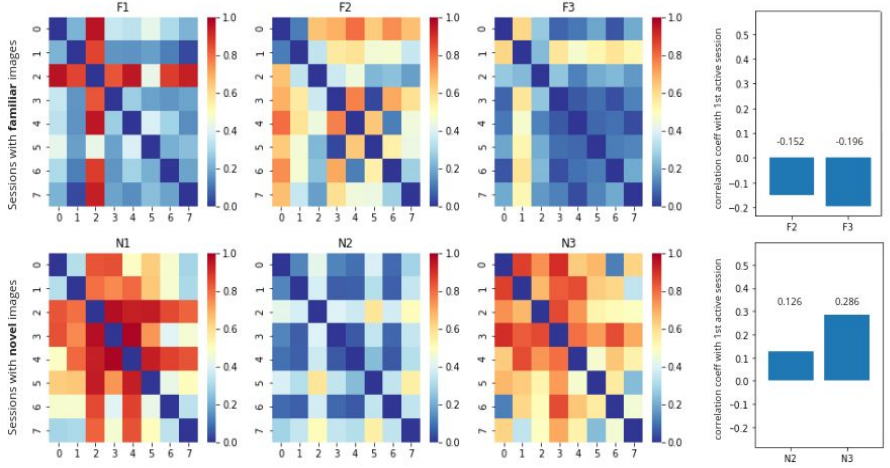
→ F1→F2 and N1→N2 | Low correlation

→ F1→F3 and N1→N3 | High correlation

A few results



Using mean of DFF fluorescence trace



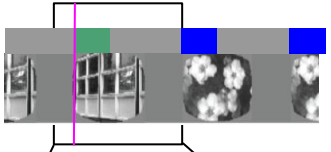
Using max of DFF fluorescence trace

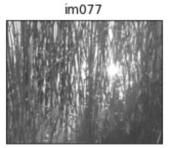
➡ Generally, the correlations remain consistent

Future directions :

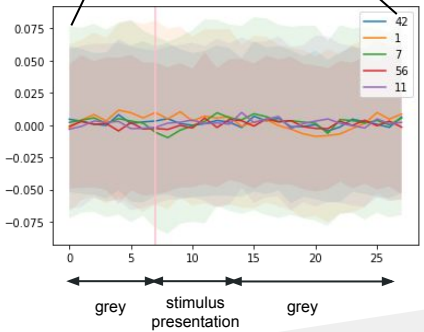
- Filter active cells
- Keep only cells common to sessions
- Take into account cell activity before versus after stimulus onset

Single-Cell Analysis

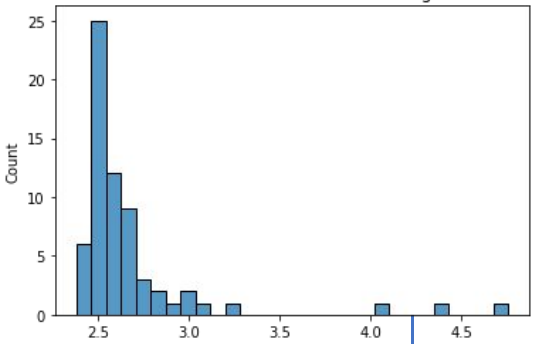




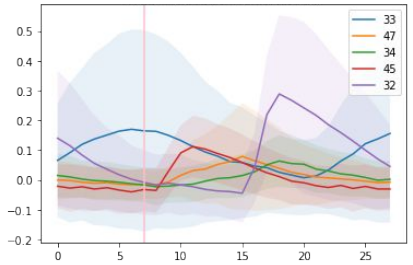
5 least reactive cell dff traces



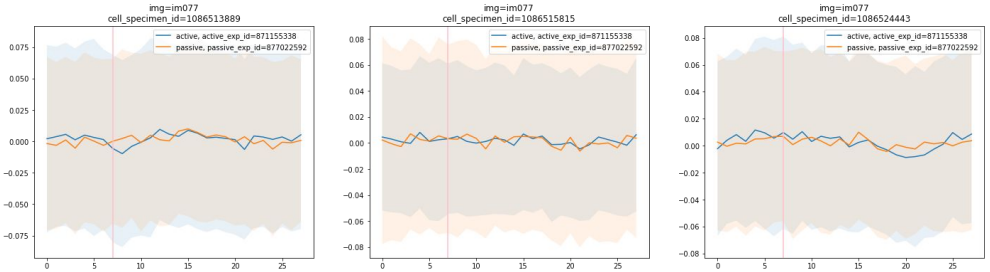
Cells count of maximum zscore (baseline before onset) averaged over stimulus presentation



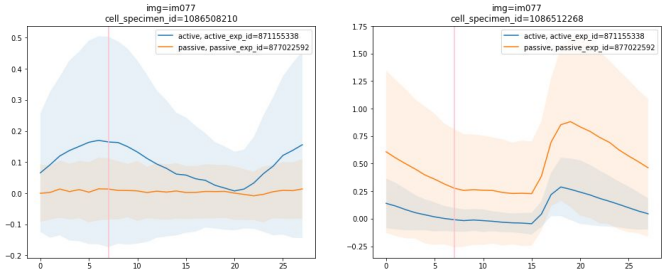
5 most reactive cell dff traces



Lowest z-score (least reactive)



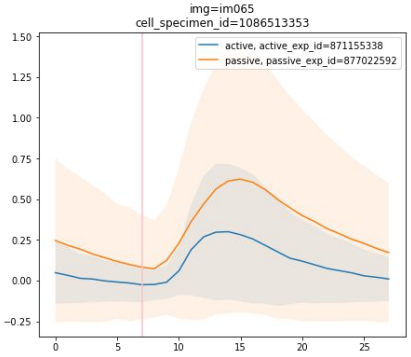
Highest z-score (most reactive)

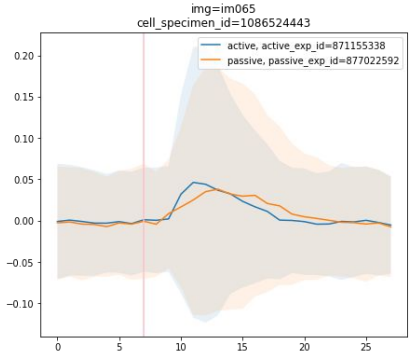


Does engagement matter: Do mice see the world differently when they don't care?

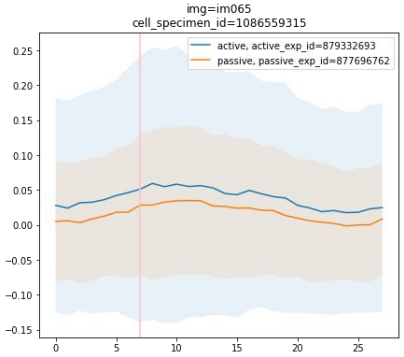
AwareWolfs

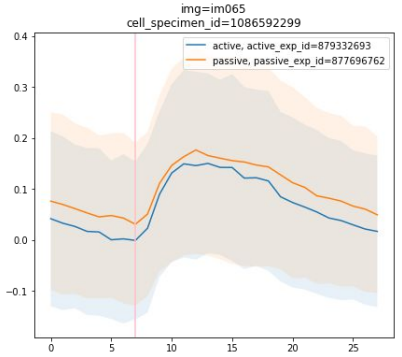
Experiment (fast degrading reporter line)

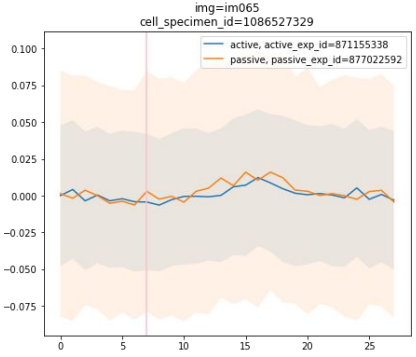


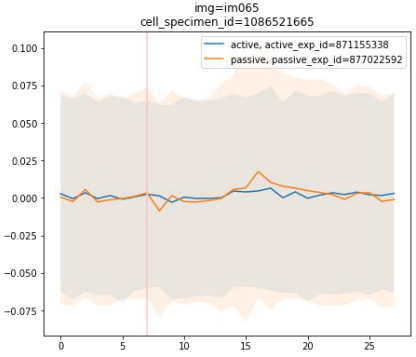


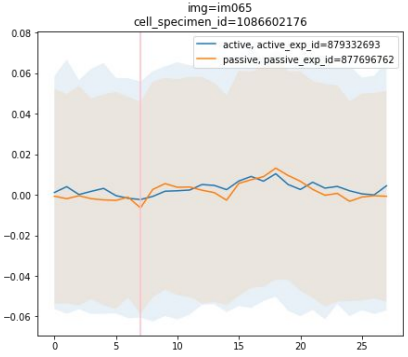
Experiment (slow degrading reporter line)

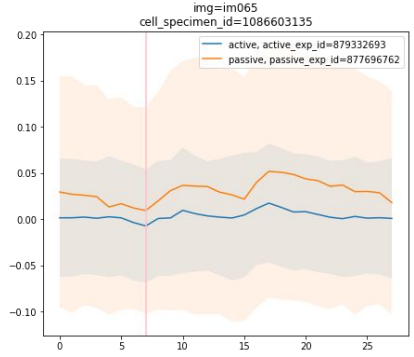












Control (fast degrading reporter line)

Control (slow degrading reporter line)

Conclusions

- ➔ On **single cell** level our methods yield no clear results.
- ➔ **Population level** dissimilarity (RDM) hints at the difference between active and passive session, but with control (pre-stimuli) this difference appears *independent of the stimuli.*

Discussion

- ➔ Despite the above findings there is some variability from general observation. This can be potentially mitigated by using more **behavioral features** (e.g., pupil dilation, running speed).
- ➔ **Single cell analysis —** in the passive condition cell responses *seem to increase* in many cases (though not consistently observed).

The Awarewolfs thank their stars!

Dr. Juliane Jaepel

Our kind mentor

Nishant Jana

Leading the pack

Dr. Agustín Sanchez

Our dataset magician!

Neuromatch Academy

for helping us learn together

References

Bagur, S., Averseng, M., Elgueda, D., David, S., Fritz, J., Yin, P., Shamma, S., Boubenec, Y., & Ostojic, S. (2018). Go/No-Go task engagement enhances population representation of target stimuli in primary auditory cortex. Nature Communications, 9(1). https://doi.org/10.1038/s41467-018-04839-9

Kondo, M., & Matsuzaki, M. (2021). Neuronal representations of reward-predicting cues and outcome history with movement in the frontal cortex. Cell Reports, 34(5), 108704. https://doi.org/10.1016/j.celrep.2021.108704

Kriegeskorte, N. (2008). Representational similarity analysis – connecting the branches of systems neuroscience. Frontiers in Systems Neuroscience. https://doi.org/10.3389/neuro.06.004.2008

Montijn, J. S., Goltstein, P. M., & Pennartz, C. M. (2015). Mouse V1 population correlates of visual detection rely on heterogeneity within neuronal response patterns. ELife, 4, e10163. https://doi.org/10.7554/eLife.10163

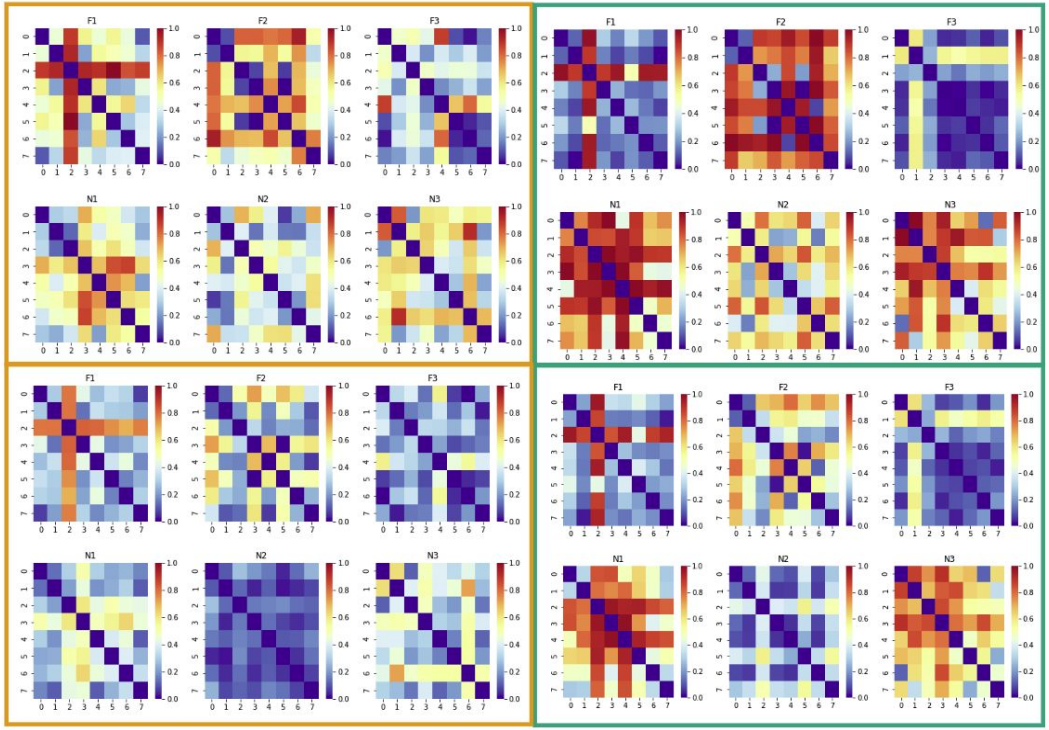
Our fabulous dataset can be found at https://allensdk.readthedocs.io/en/latest/visual_behavior_optical_physiology.html

Before stimulus onset

After stimulus onset

mean DF/F trace

maximum DF/F trace

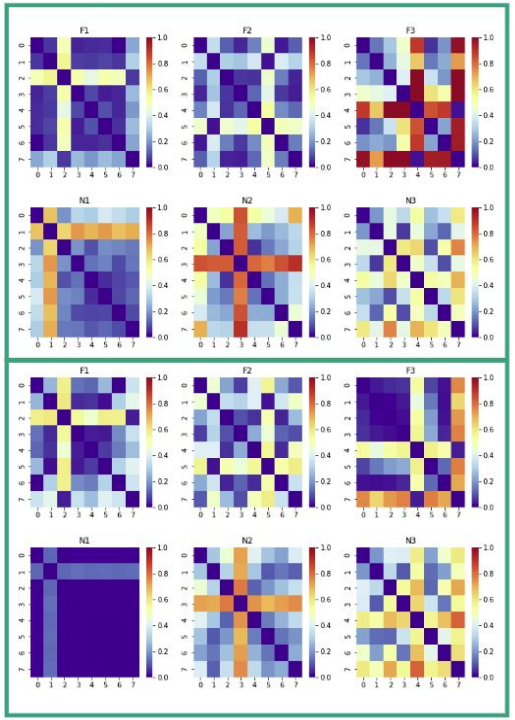


MOUSE 1

After stimulus onset

mean DF/F trace

maximum DF/F trace



MOUSE 2

The Journey

- many ideas, we choose one
- population or individual cells ⇒ why not both?
- population:
  - hey, t-SNE and PCA might be an option
  - use RDMs
- individual cells:
  - mean traces? but how?
  - use z-scoring
  - how to select them?
- later realized there are estimated spiking events
  - but we stayed with dff traces