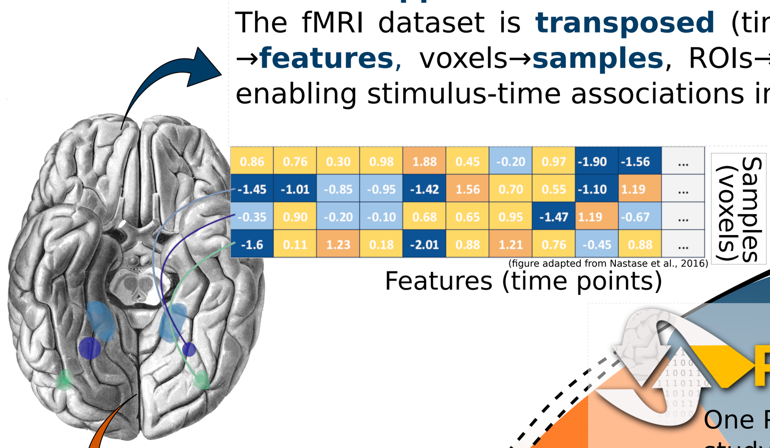
# **Functional ROI** localization in a rich stimuli dataset requires **non-GLM style** approach

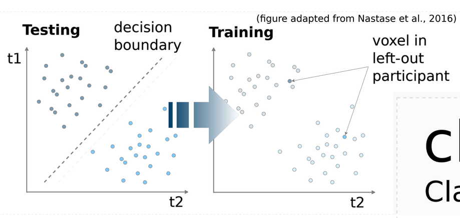
## **Turn it sideways:** a new approach to determine the specificity of functional ROIs

Adina S. Wagner[1], Samuel A. Nastase[3], Michael Hanke[1,2], Yaroslav O. Halchenko[4]

Paradigms for localizing functional regions of interest (ROIs) typically contrast responses to different categories of controlled stimuli (e.g. faces or houses). Their lack of complexity would make naturalistic designs such as movie watching a more ecologically valid option, though. Typical GLM contrasts are constructed using prior functional assumptions from simplistic designs, which may fail to characterize the ROIs in question completely and unambiguosly. Using 1) a fMRI localizer experiment (Sengupta et al., 2016), and 2) fMRI data obtained during 2h of movie watching (Hanke et al., 2016) of N = 15 subjects, we demonstrate that for naturalistic stimulation, the typical univariate analysis approach leads to a loss of location information for the distinction between the fusiform face area (FFA) and the rest of the brain. A multivariate, classification-based alternative classifies voxel more accurately, could provide empirical, maximally discriminative contrasts for new data, and demonstrates more diverse functional signatures in ROIs derived from simplistic designs especially under more complex stimulation .

**The new approach:**
The fMRI dataset is **transposed** (timepoints →**features**, voxels→**samples**, ROIs→**labels**), enabling stimulus-time associations in **(2)**.




**PyMVPA**
One PyMVPA Dataset per study (localizer/movie)

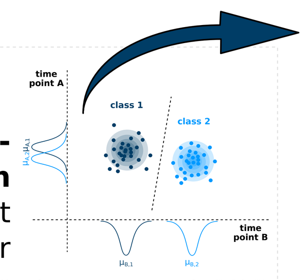
**The standard univariate approach:**
The Dataset is left **'as is'**.

### 1 GLM

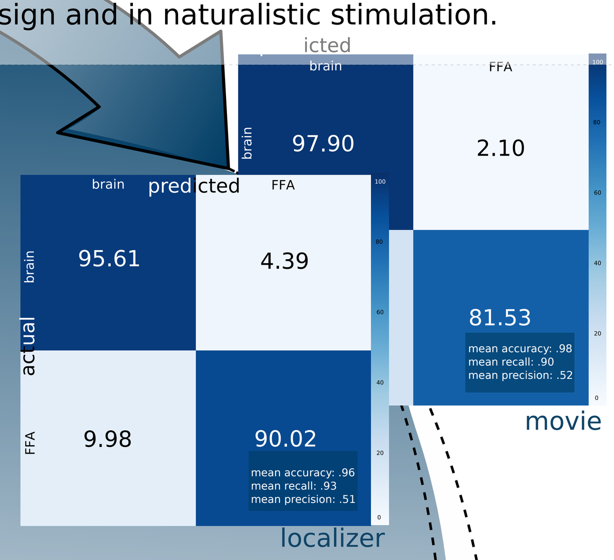
Standard univariate modeling approach: The **activation time course** is modeled with EVs based on the **experimental design** (localizer data) or **annotations** (movie) using canonical contrasts.

### 1 classification

Classification of voxel into ROIs in a **leave-one-subj-out crossvalidation** with **linear Gaussian Naive Bayes** (GNB) classifier leads to almost identical classification performance in the localizer design and in naturalistic stimulation.



(following Nastase et al., 2016)

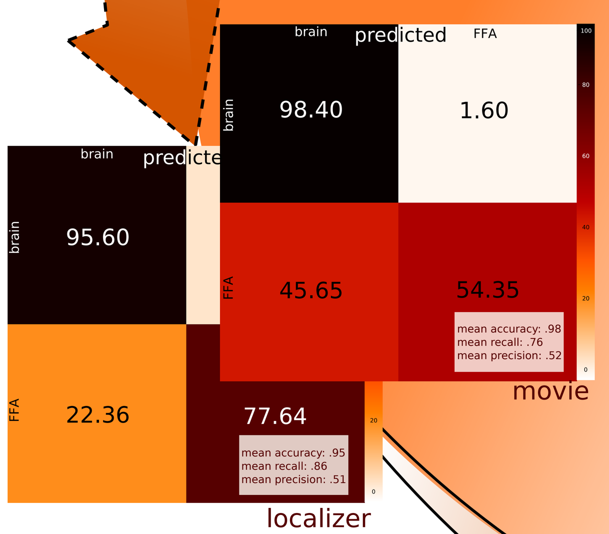



| | localizer | movie |
|---|---|---|
| model-free | 0.93 | 0.90 |
| model-based | 0.86 | 0.76 |

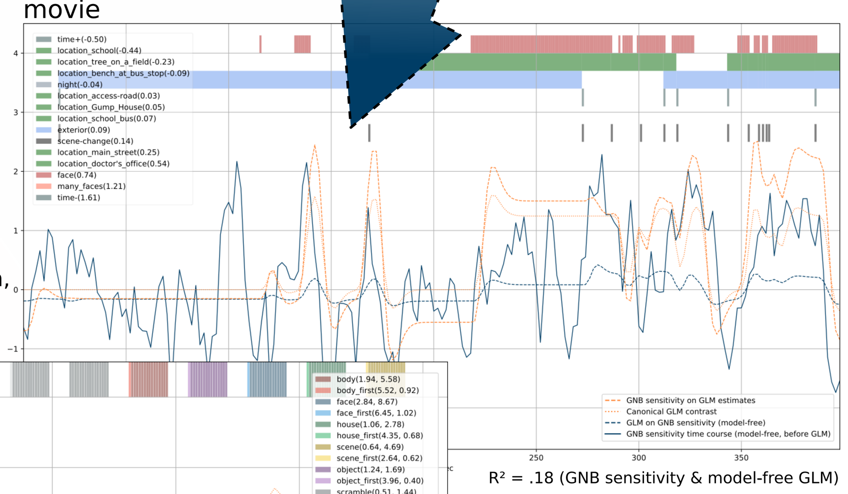
mean Recall (average True Positive Rate per category)

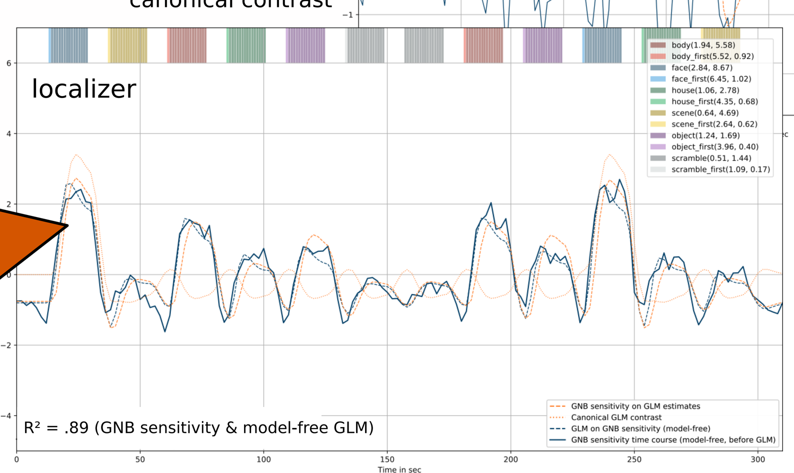
### GLM 2

The resulting averaged **time course of sensitivities** is modeled with the available **experimental design** (localizer) or **annotations** (movie).




**Normed** time courses of sensitivity profiles from each approach, GLM fit (1) and canonical contrast

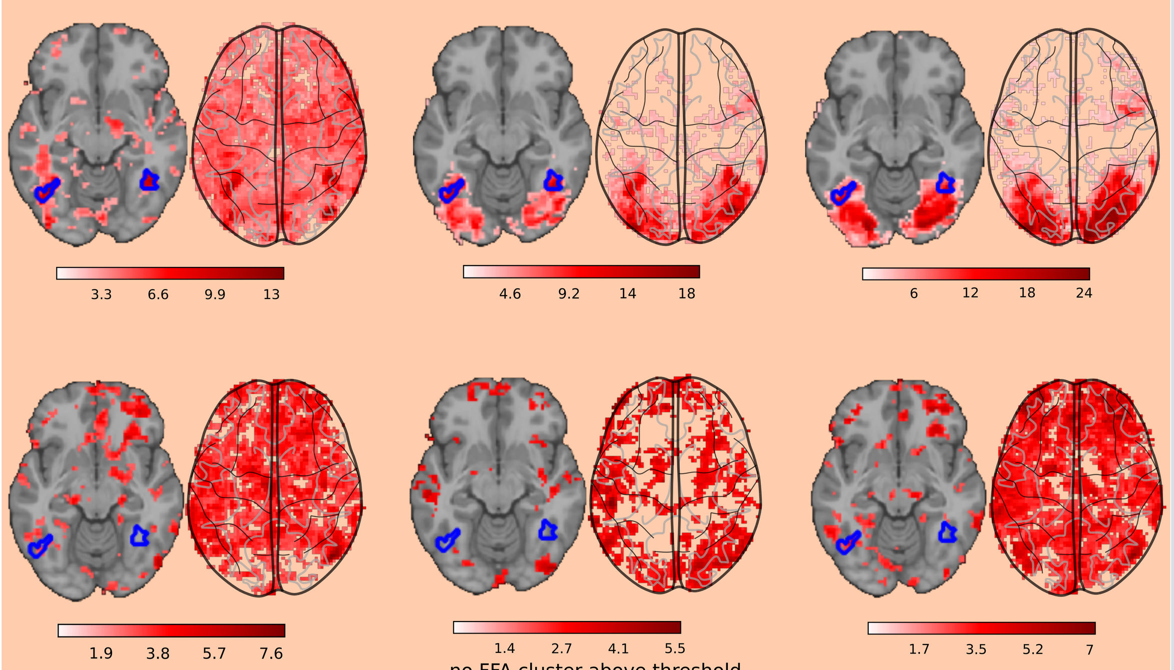


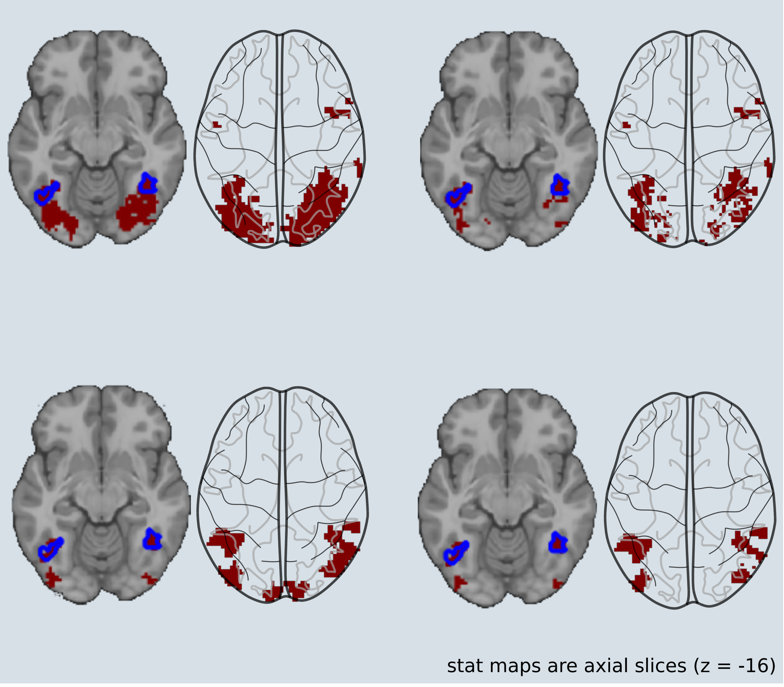



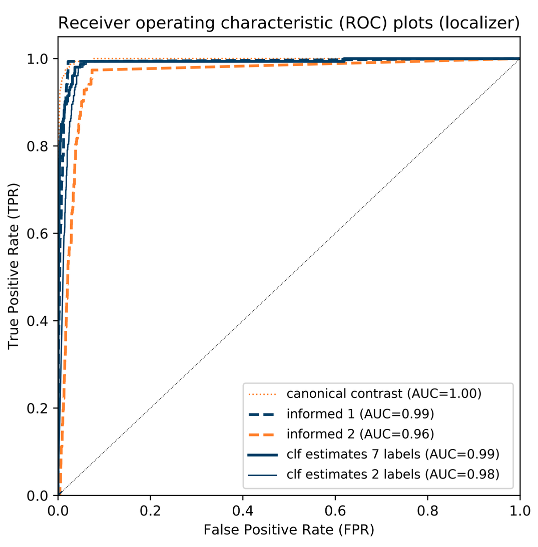

### classification 2

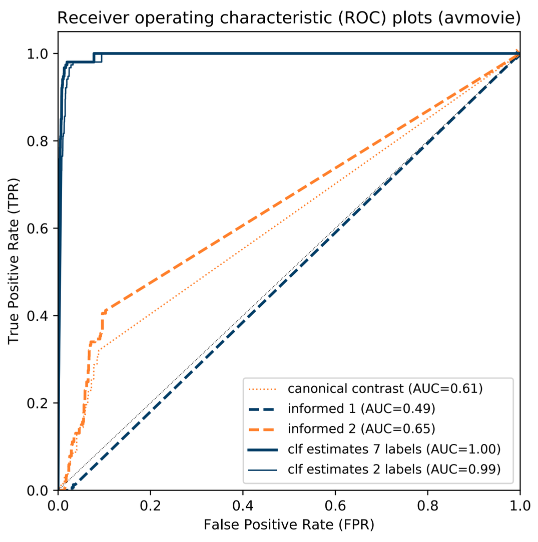
To assess how much location information is preserved after imposing a model onto the time-series data, a classification with a leave-one-out crossvalidation is performed on the results of the GLM. The classification performance (recall) drops; this effect is stronger for naturalistic stimulation.

For a quality check of GLM & classification results, we plot results from three different contrasts exceeding a threshold of z > 2.3, and the classifiers decision per voxel (stat maps & glass brain plots). **Canonical contrasts**: Faces vs other categories (see Sengupta et al., 2016; localizer), dummy contrast from face-containing frames (movie). **Informed contrasts** are derived from GLM results on sensitivies (approach 1) or sensitivities of univariate GLM results (approach 2). **Receiver operating characteristic** (ROC) curves plot True Positive Rate against False Positive Rate, showing that for naturalistic designs, classification based results are better than GLM results, even if GLM contrasts are maximally informative (& overfitted). Results from one example subject.



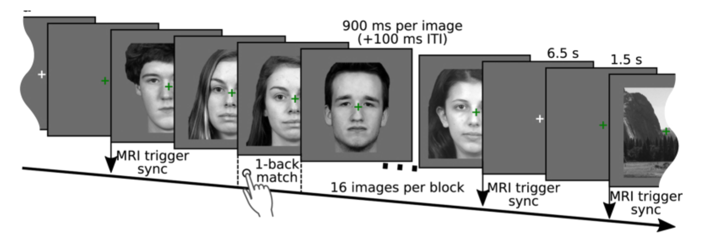



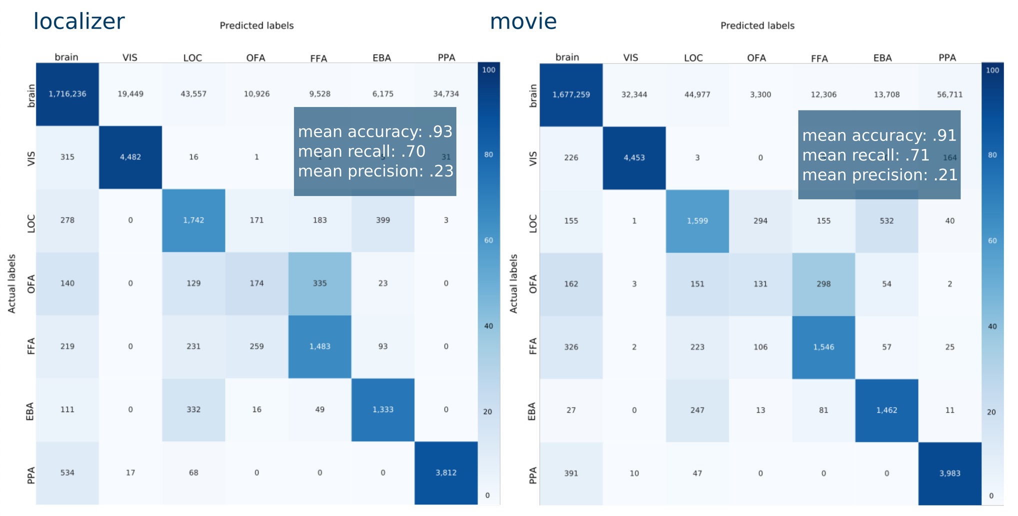

## Data

fMRI data from **N = 15** subjects ($m_{age}$=29.4, 6F) from a standard **localizer** paradigm (face, body, house, scene, object, scrambled image block design) and **movie watching** (~2h), and subject specific ROI masks for 6 higher visual areas (FFA, PPA, EBA, LOC, OFA, early visual cortex) (studyforrest.org).




- 3T, TR = 2.0s, 3.0mm isotropic voxels (resliced to 2.5mm).
- Identical preprocessing: motion correction, whole-brain masking, spatial smoothing (Gaussian kernel, 4mm FWHM), low-pass filtering (0.1Hz) & warped into study-specific group template.

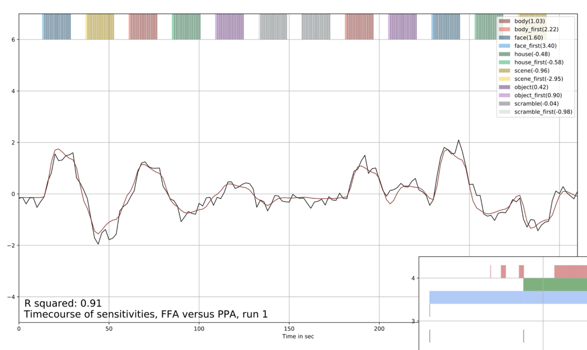
### classification analysis on all six higher visual areas




### Sensitivity derivation

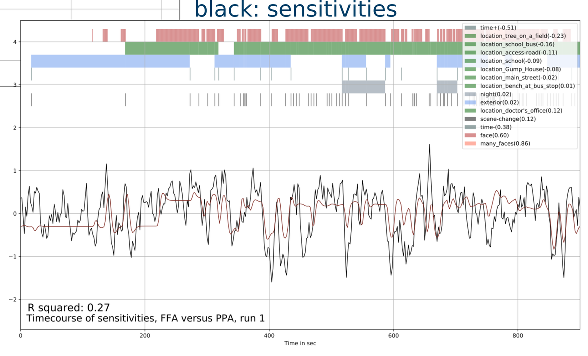
During classification, the time-course of sensitivities - the decision hyperplane parameters - are derived for all pairwise combinations of ROIs (e.g. FFA vs PPA, or FFA vs non-FFA). The resulting time-course may depict the maximally discriminative contrast between the two ROIs functional signatures.

### Time-stimulus associations shed light on functional distinctions between ROIs



**Localizer:**
Regressors from base conditions from events.tsv (face, house, ...) and the first occurance within a category (face_first, ...).
624 time points (4 runs).

red: GLM fit
black: sensitivities



**Movie:**
Regressors from manual movie annotation (Häusler & Hanke, 2016) & automatic face extraction with pliers (McNamara et al., 2017)
3599 time points (8 runs, 2h).

red: GLM fit
black: sensitivities

## Conclusions

### Informed vs canonical contrasts

Simple, canonical contrasts to locate functional ROIs work for simple experimental designs, but fail to capture functional differences in data obtained from complex stimulation. An "informed" contrast from functional information may improve localization in a different (independent) dataset, but shows even in this supoptimal demonstration low detection power. The classification-based approach may be a promising alternative with high cross-subject specificity. At the same time, the results show more complex functional signatures in ROIs under complex stimulation (see also Th408). The method presented here could hence also serve as a diagnostic tool to evaluate the quality or functionality of ROIs further.

### Caveats & Limitations

***ROIs for the analysis were created from the localizer data (Sengupta et al., 2016)! "Double-dipping" for informed contrasts!*** Descriptive analyses presented here serve as a method proposal, and yet need validation on independent data.

### Future directions

- Further annotation from automated tools: Easier interpretable, available, and comparable than manual labels.
- Application of contrasts derived from a given dataset to another dataset to investigate generalizability of derived contrasts.
- Application of the method to simulated and independent data as general proof of concept & baseline.

**Note:**
Due to unbalanced class frequencies (brain > visual ROIs), classification performance is evaluated using **recall** and **precision**:

$$recall = \frac{true\ positives}{true\ positives + false\ negatives}$$

$$precision = \frac{true\ positives}{true\ positives + false\ positives}$$

[1] Institute of Neuroscience and Medicine, Brain & Behaviour INM-7, Research Centre Jülich, Germany
[2] Institute of Systems Neuroscience, Medical Faculty, Heinrich Heine University Düsseldorf, Germany
[3] Princeton Neuroscience Institute, Princeton University, NJ, USA
[4] Dartmouth College, NH, USA

corresponding author:
adina.wagner@fz-juelich.de

This analysis was brought to you by open source software

## References

Hanke, M., et al. (2016). Scientific Data 3: 160092.
Nastase, S. A., et al. (2016). Poster at SfN, Washington, DC.
Sengupta, A. et al. (2016). Scientific Data 3: 160093.
Häusler, C. O. & Hanke, M. (2016). F1000 Research, 5:2273
McNamara, Q. et al.(2017). Proc 23rd ACM SIGKDD Int Conf KD & DM, 1567–74. ACM.
Hanke, M. et al. (2009). PyMVPA. Neuroinformatics 7 (1): 37–53.