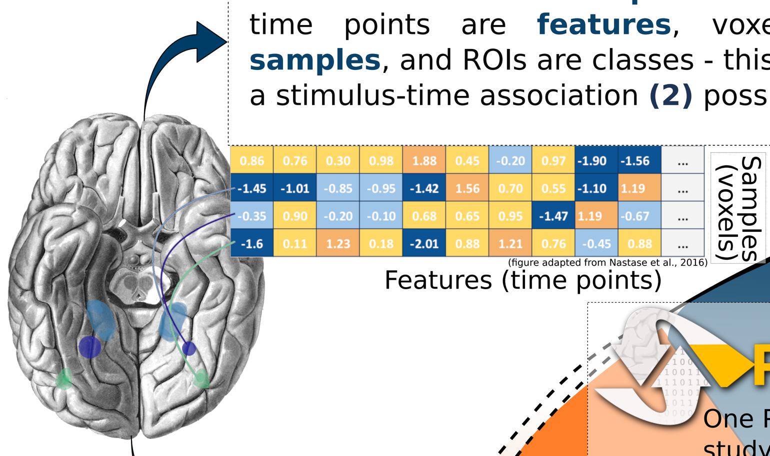
Functional ROI localization in a rich stimuli dataset requires **non-GLM style** approach

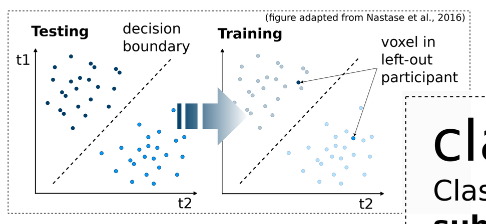
Turn it sideways: a new approach to determine the specificity of functional ROIs

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 unambiguously, and are not tuned to highest sensitivitiy and specificity. 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 analyses 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 could classify voxel more accurately, helps to provide empirical, maximally discriminative contrasts for new data, and demonstrates more diverse functionality especially under more complex stimulation in ROIs derived from simplistic designs.



The fMRI dataset is **transposed** such that time points are **features**, voxels are **samples**, and ROIs are classes - this makes a stimulus-time association **(2)** possible.

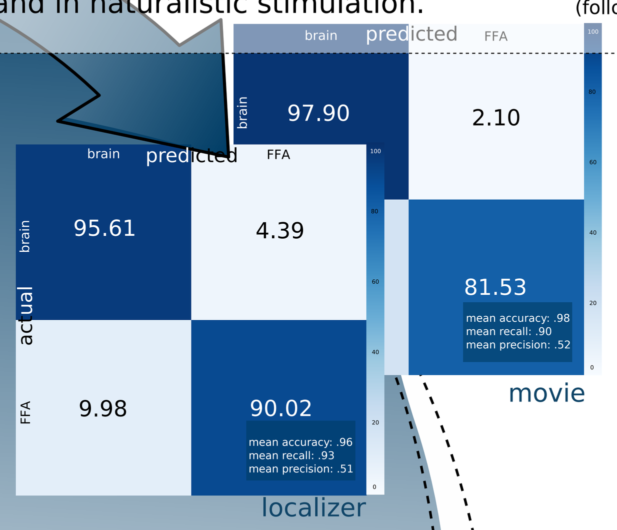


The Dataset is left **'as is'**.

PyMVPA
One PyMVPA Dataset per study (localizer/movie)

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)

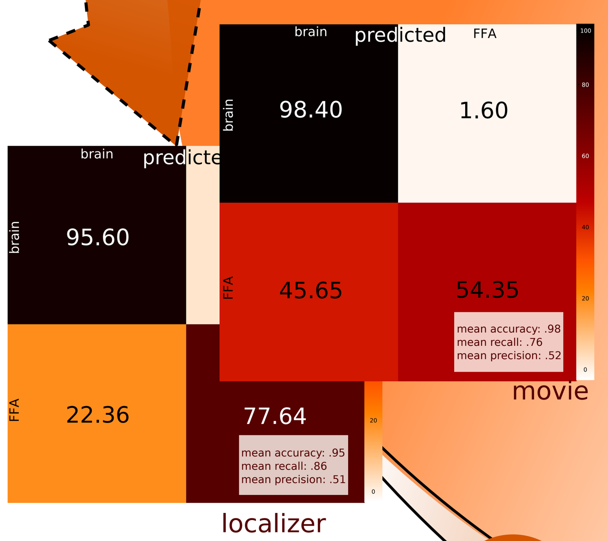


	localizer	movie
model-free	0.93	0.90
model-based	0.86	0.76

mean Recall (average True Positive Rate per category)

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.



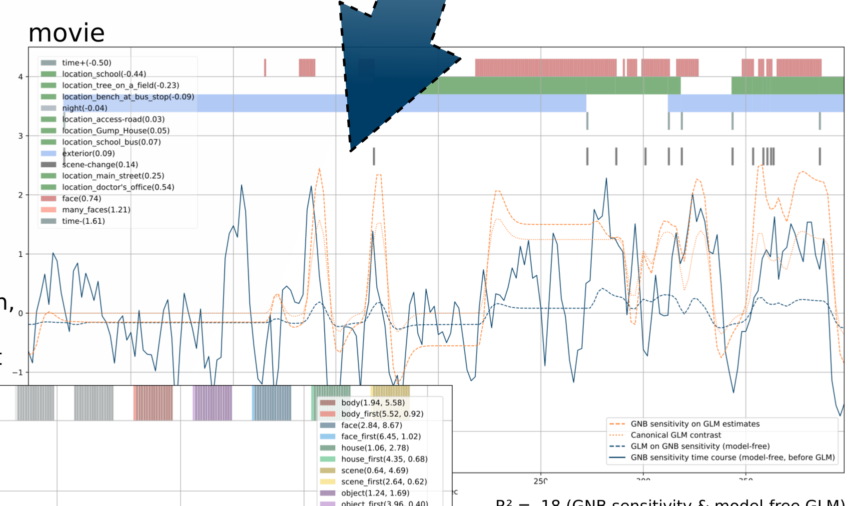
2 GLM

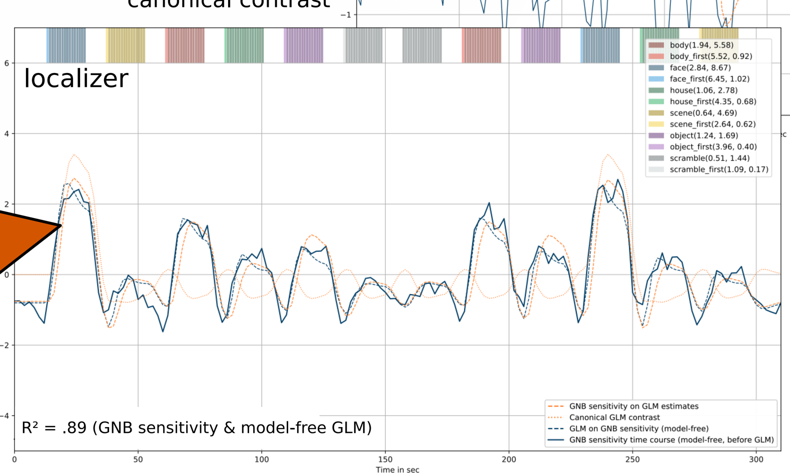
The resulting averaged **time course of sensitivities** is modeled with the available **experimental design** (localizer) or **annotations** (movie).

2 classification

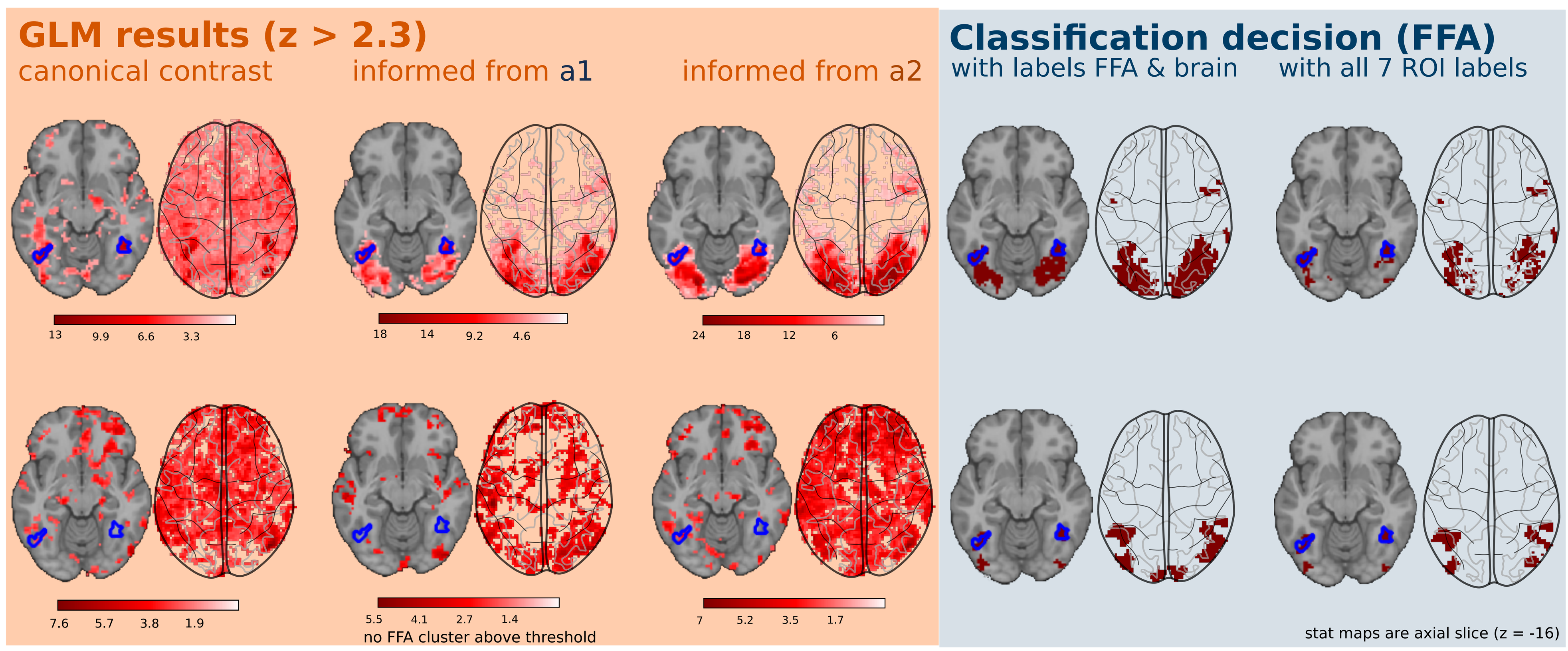
To assess how much location information is preserved after imposing a model onto the time-series data, a classification with a leave-one-out crossvalidation is performed on the results of the GLM. The classification performance (recall) drops; this effect is stronger for naturalistic stimulation.

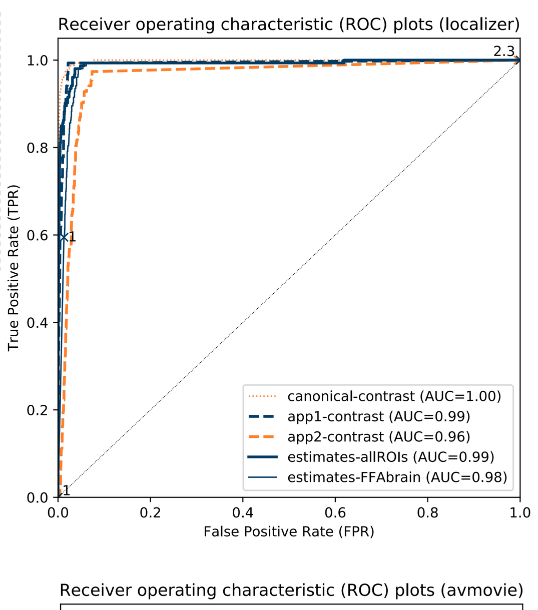
Normed time courses of sensitivity profiles from each approach, GLM fit (1) and canonical contrast

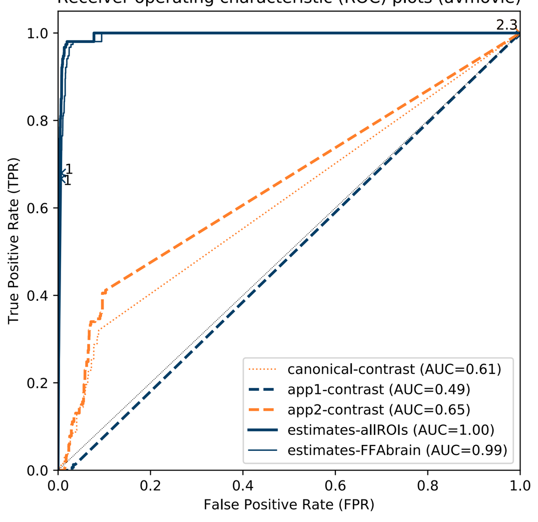




To assess the quality of GLM & classification results, we plot results from three different contrasts exceeding a threshold of z > 2.3, and the classifiers decision per voxel (stat maps & glass brain plots). **Canonical contrasts**: Faces vs other categories (see Sengupta et al., 2016; localizer), dummy contrast from face-containing frames (movie). **Informed contrasts** are derived from GLM results on sensitivies (approach 1) or sensitivies of univariate GLM results (approach 2). Results from one example subject.
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).

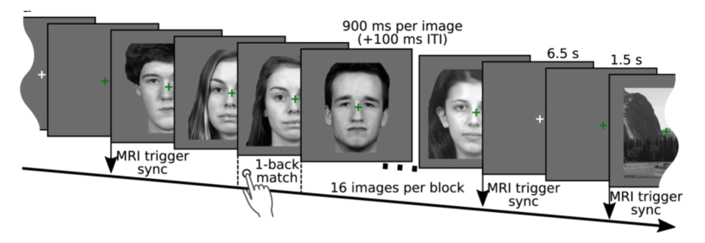






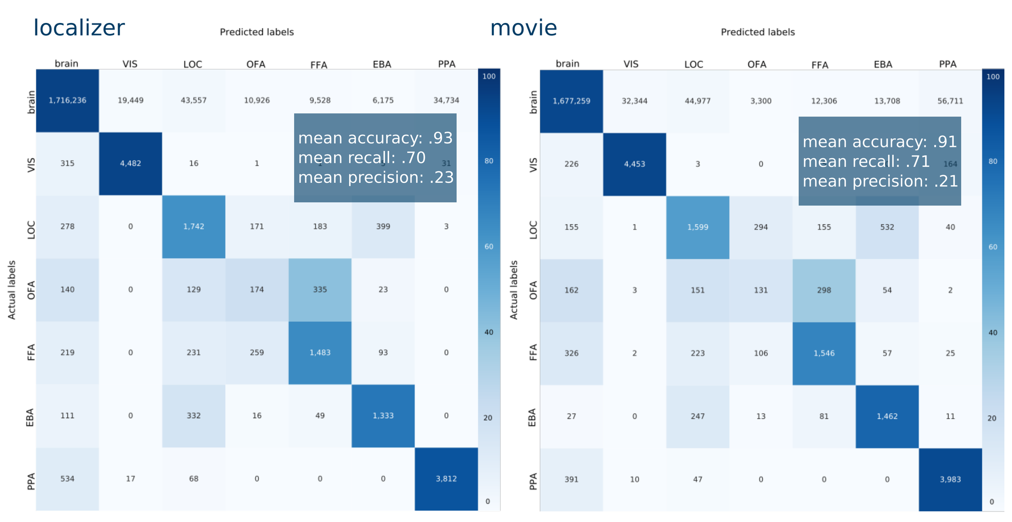
Data

fMRI data from **N = 15** subjects (m_{age}=29.4, 6F) from a standard **localizer** paradigm (face, body, house, scene, object, scrambled image) 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.

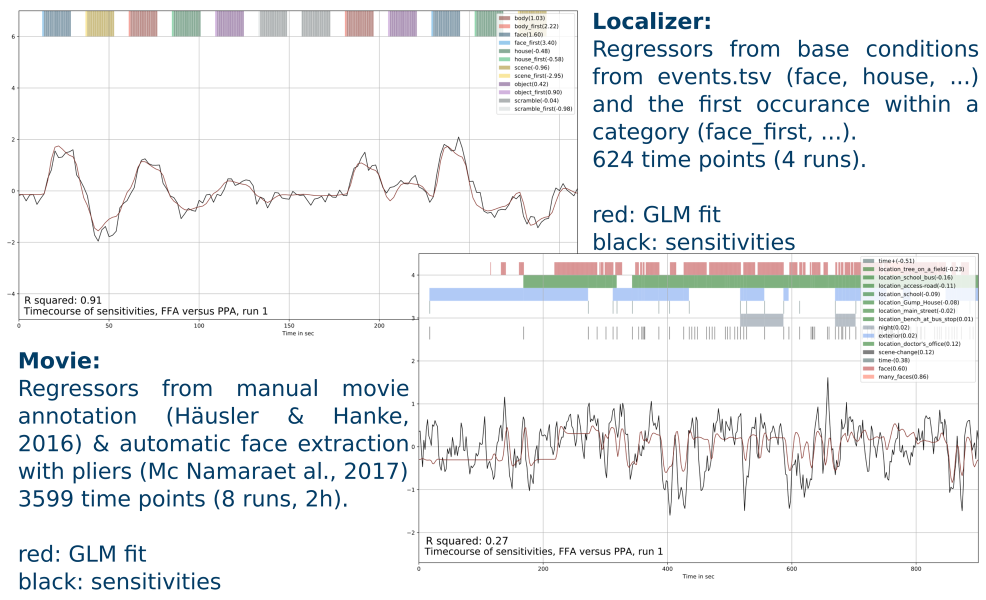
classification analysis on all 6 higher visual areas



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 depicts 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 (Mc Namaraet 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**:

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

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

Dartmouth

HEINRICH HEINE UNIVERSITÄT DÜSSELDORF

[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

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