Predictive Modeling of Significance Thresholding in Activation Likelihood Estimation Meta-Analysis

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Introduction

- **Activation Likelihood Estimation** employs **cluster- (cFWE)** and **voxel-level family-wise error (vFWE) correction**
  - approximate a **null distribution of spatial convergence**, through monte-carlo simulation procedure [1,2]
    - **Random coordinates**, but using **experiment characteristics from original dataset**
  - At least **5000 - 10000 iterations required to converge**, which takes **many hours**
    - **95%** of ALE **computation time** spent on monte-carlo simulation

Hypotheses:

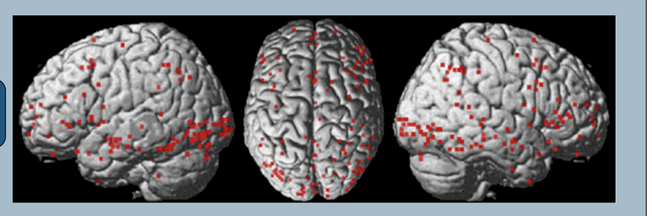
- Null-distribution of **spatial convergence** is fully **determined by dataset characteristics**
- Time intensive **monte-carlo simulation** can be **replaced by machine learning prediction**

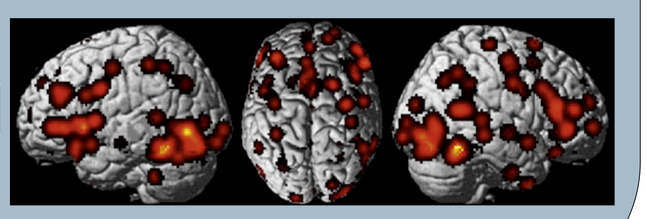
Methods

Quick ALE recap

Literature → Foci → ALE

	A	B	C	D	E	F	G
1	**Paper**	**Subjects**	**x**	**y**	**z**	**MNI/TAL**	**visual/auditory**
2	A et al., 1999	14	42	40	-1	TAL	visual
3	A et al., 1999	14	36	23	33	TAL	visual
4	A et al., 1999	14	34	6	34	TAL	visual
5	A et al., 1999	14	41	36	22	TAL	visual
6	A et al., 1999	14	33	17	2	TAL	visual
7	A et al., 1999	14	36	8	-3	TAL	visual
8							
9	B et al., 2000	14	45	-75	-10	MNI	auditory
10	B et al., 2000	14	22	-60	-10	MNI	auditory





ML workflow

Training Data:

- Simulated **68100 datasets** with **10 to 150 experiments**
  - parameter distributions similar to what is found in **BrainMap's functional database** [3]
  - Extreme datasets with high subjects/foci/both
- **True labels**: vFWE & cFWE tresholds using monte-carlo simulations with **15000 iterations.**

Feature engineering:

- **23 features** based on parameters of the dataset:
  - Number of Experiments
  - Number of Subjects
  - Number of Foci
- **Summary statistics**:
  - Total
  - Mean/median
  - SD/Skewness/Kurtosis
  - Ratios
- Created by trial-and-error & optimization after establishing a baseline

Performance and Validation:

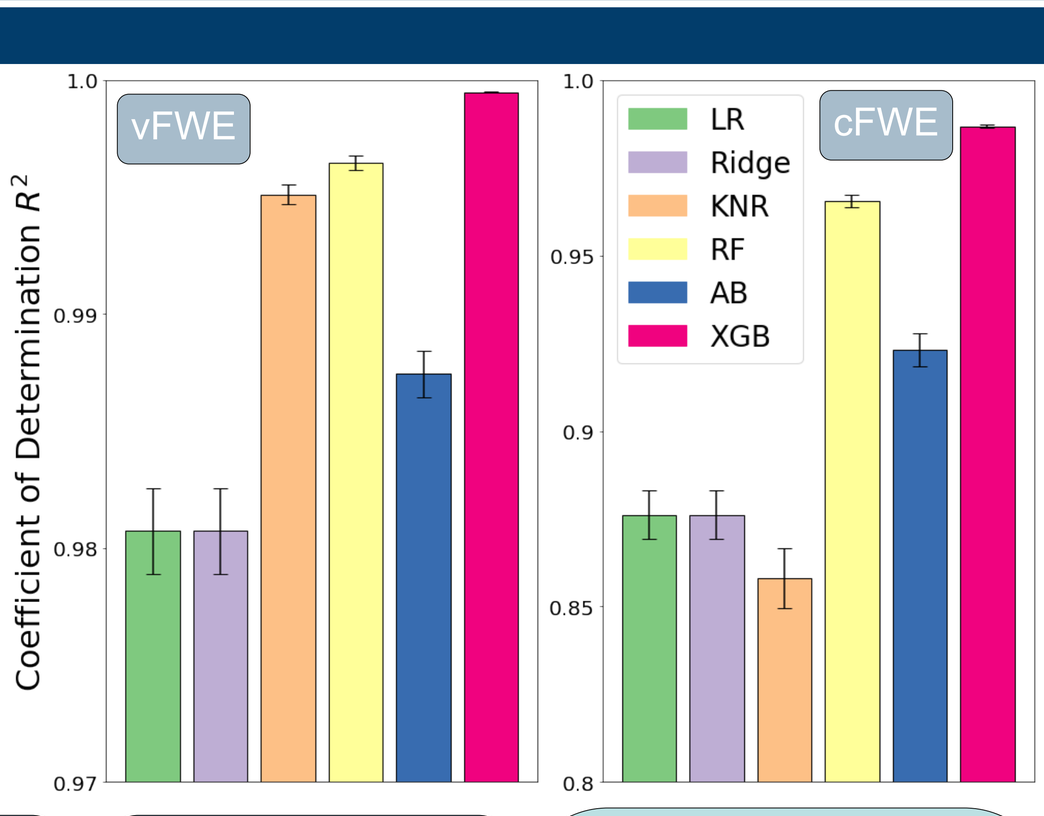
- Model selection:
  - **10-fold CV** on **simulated** data.
  - Linear Regression, Ridge Regresssion, K-nearest Neighbour, Random Forest, AdaBoost, XGBoost [4]
- External Validation:
  - **21 real-life ALE contrasts**
  - broad range of **domains** and dataset **sizes**.

Results

1. Cutoff convergence for monte-carlo simulation.

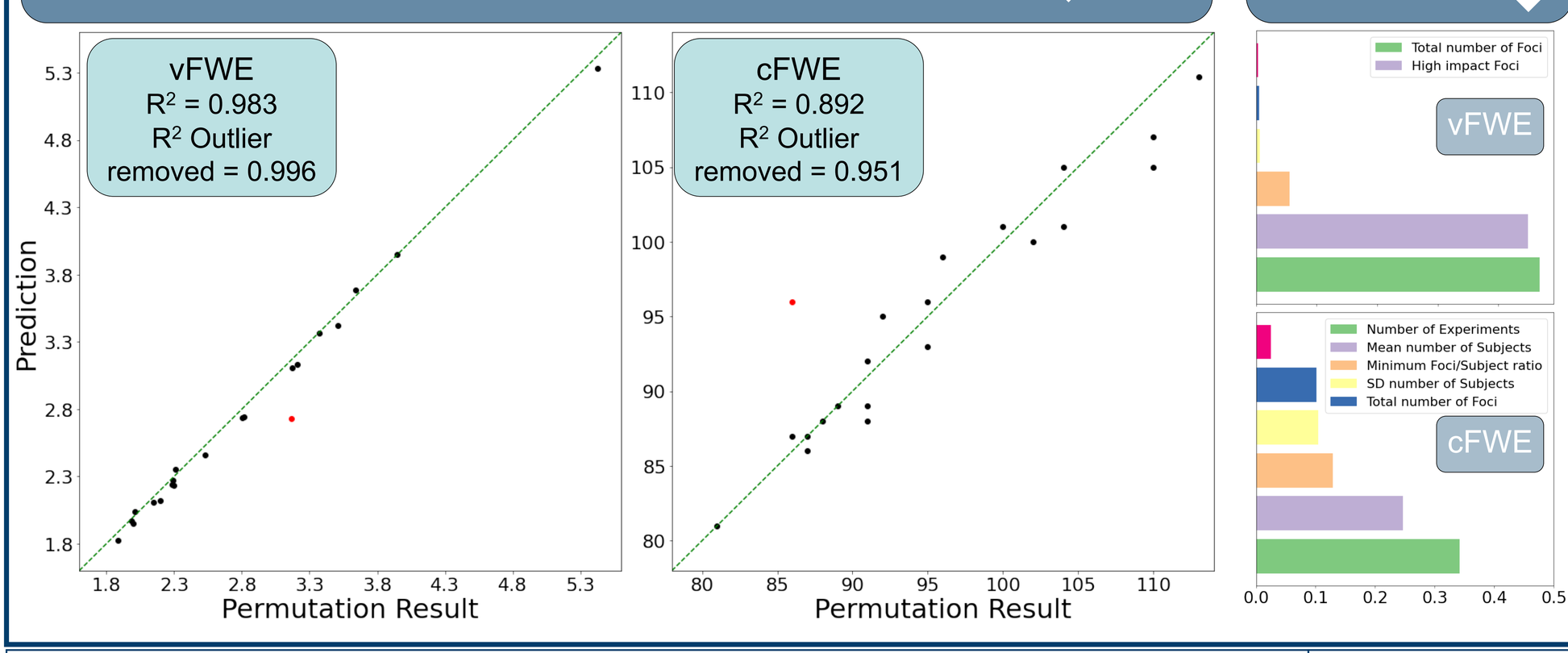
- Reduced replicability
- Negatively impacts machine learning

2. Model selection based on simulated data using a **10-fold CV** scheme.



3. Prediction performance of the **XGBoost** regression for **unseen naturalistic datasets.**

- Red dot => outlier dataset; parameters out of range of training data
- Parameter check necessary before prediction is trusted



4. Feature importance for XGBoost models

Conclusion:

- Our model predicts significance thresholds in ALE meta-analyses with **very high accuracy**
- We advocate our efficient prediction approach as a **replacement for the time-consuming permutation testing procedure** in future ALE analyses.
- This will **save hours of computation time and energy consumption**

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Acknowledgments:

This study was supported by the Deutsche Forschungsgemeinschaft (DFG, EI 816/11-1 & International Research Training Group 2150, 269953372/GRK2150), the National Institute of Mental Health (R01-MH074457), the National Institute of Aging: (P30-AG066546), and the Jülich-Aachen Research Alliance (JARA) granting computation time on the supercomputer JURECA (Jülich Supercomputing Centre, 2018) at Forschungszentrum Jülich.