Whole-brain dynamical modeling for classification of Parkinson's disease

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Introduction

1. Simulated whole-brain connectomes demonstrate an enhanced inter-individual variability depending on data processing and modeling approach.
2. We thus hypothesized that **MRI data processing** can impact the application of whole-brain models to subject classification and affect their performance.
3. We also introduced **a novel validation approach** for whole-brain dynamical models to enhance the classification performance.
4. To this end, we investigate how empirical and simulated whole-brain connectome-derived features can be utilized to classify patients with Parkinson's disease against healthy controls in light of varying data processing and model validation.

Methods: Whole-brain dynamical modeling and classification using machine learning

❖**Participants: 51** (30 males) **healthy controls** and **65** (45 males) **patients** with Parkinson's disease

- MRI acquisition: T1-weighted image, resting-state fMRI (rsfMRI), and diffusion-weighted images (DWI) with 64 directions
- MRI processing: Extracting blood oxygenation level-dependent (BOLD) signals from rsfMRI and reconstructing whole-brain tractography with 10M streamlines using DWI

MRI pipeline

Jung et al. (2023)

❖**Whole-brain model:** Convolution-based two-population model (Jansen-Rit type[1,2]) for electrical signals + Balloon-Windkessel model[3,4] for BOLD signals

❖**Experimental conditions:** Four temporal filters (NF, BF, LF, and HF) for empirical and simulated BOLD signals + Two parcellation schemes (Schaefer 100 Parcels and Desikan-Killiany)

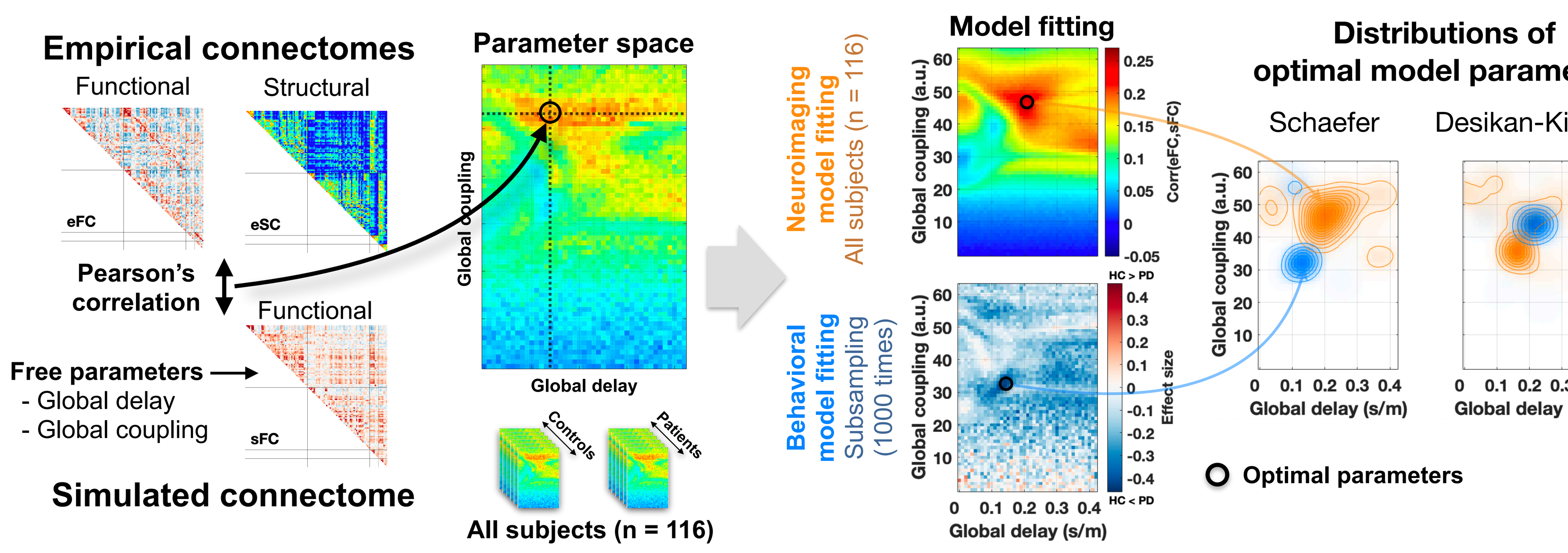
- **NF:** no filtering, **BF:** broad frequency band [0.01,0.1] Hz, **LF:** low frequency band [0.01,0.05] Hz, **HF:** high frequency band [0.05,0.1] Hz

✓ Neuroimaging model fitting: Search for the optimal model parameters corresponding to **the maximal similarity** between empirical and simulated connectomes
✓ Behavioral model fitting (a novel approach): Search for the optimal model parameters corresponding to **the maximal difference** between groups of controls and patients

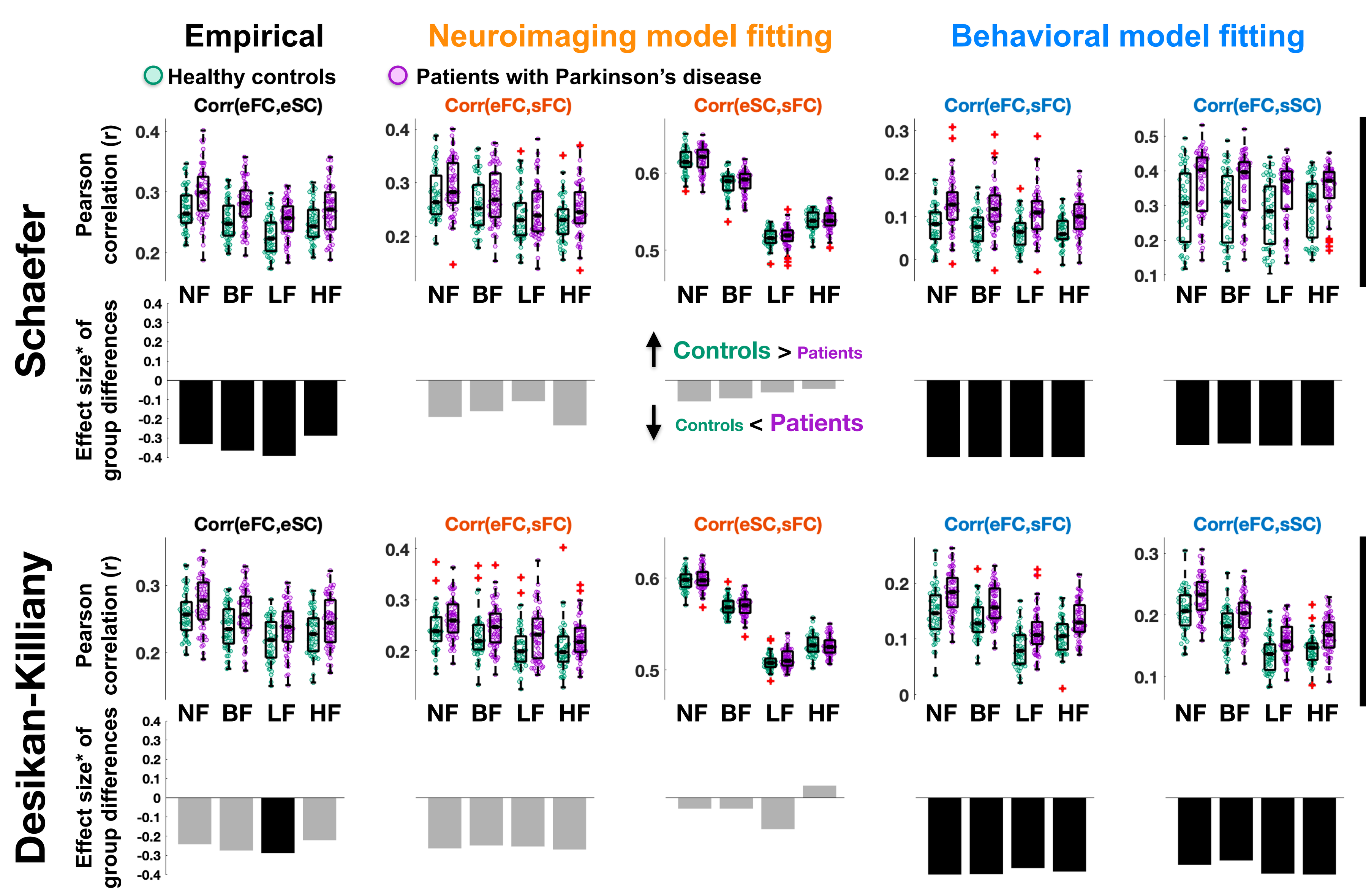
❖**Machine learning:** A **regularized** (**LASSO**: the least absolute shrinkage and selection operator) **logistic regression** using a **cross-validated model fitting and confound regression**[5]

Results: Data processing and model fitting for effective classification of Parkinson's disease

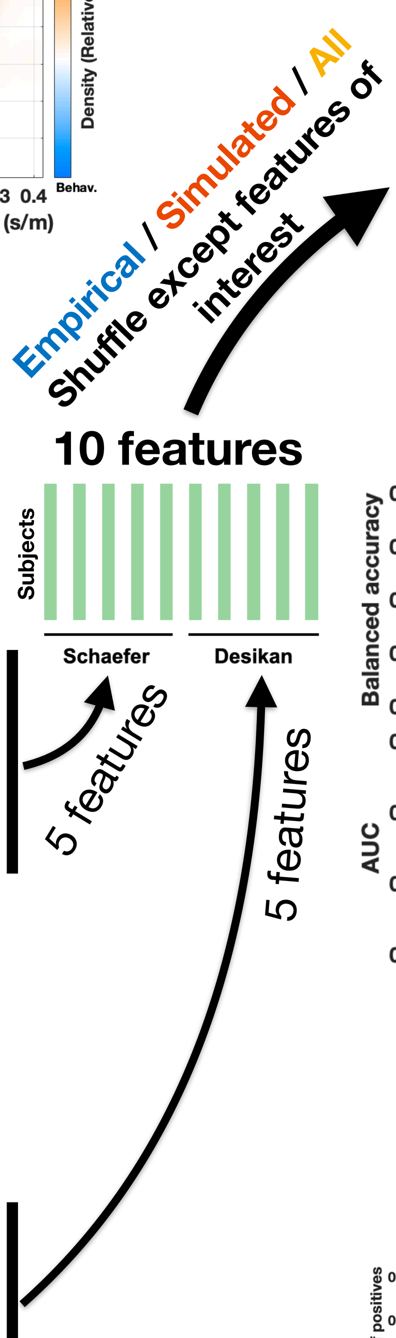
1. Empirical and simulated connectomes for model fitting



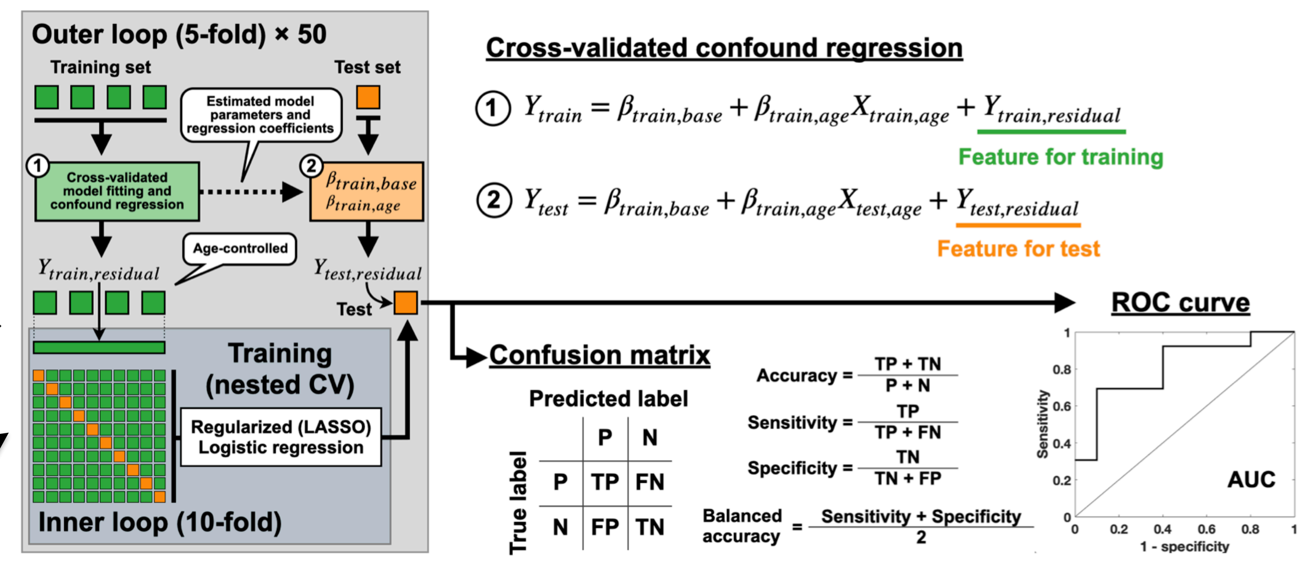
2. Connectome relationships as features for classification



Significantly different connectome correspondence of groups between healthy controls and patients Wilcoxon rank-sum two-tail test (Bonferroni corrected $p < .05$)
No significantly different
* Rosenthal formula was used to calculate effect sizes.



3. Training using a cross-validated confound regression

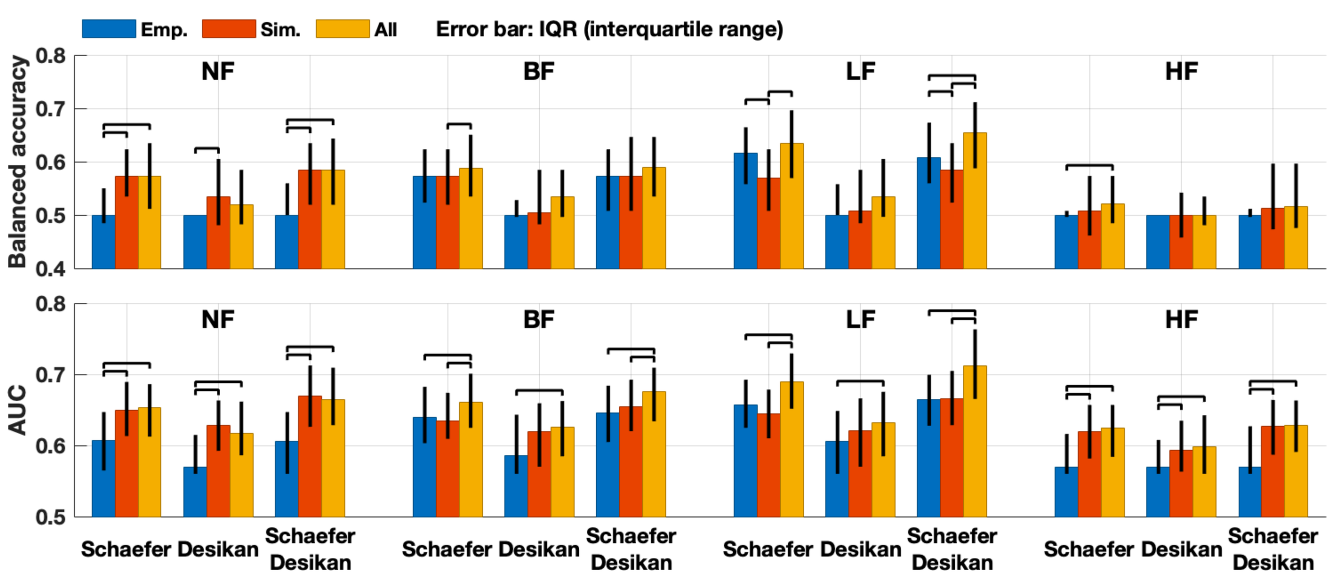


$$① \ Y_{train} = \beta_{train,base} + \beta_{train,age}X_{train,age} + Y_{train,residual}$$

$$② \ Y_{test} = \beta_{train,base} + \beta_{train,age}X_{test,age} + Y_{test,residual}$$

Accuracy $= \frac{TP + TN}{P + N}$, Sensitivity $= \frac{TP}{TP + FN}$, Specificity $= \frac{TN}{TN + FP}$, Balanced accuracy $= \frac{\text{Sensitivity} + \text{Specificity}}{2}$

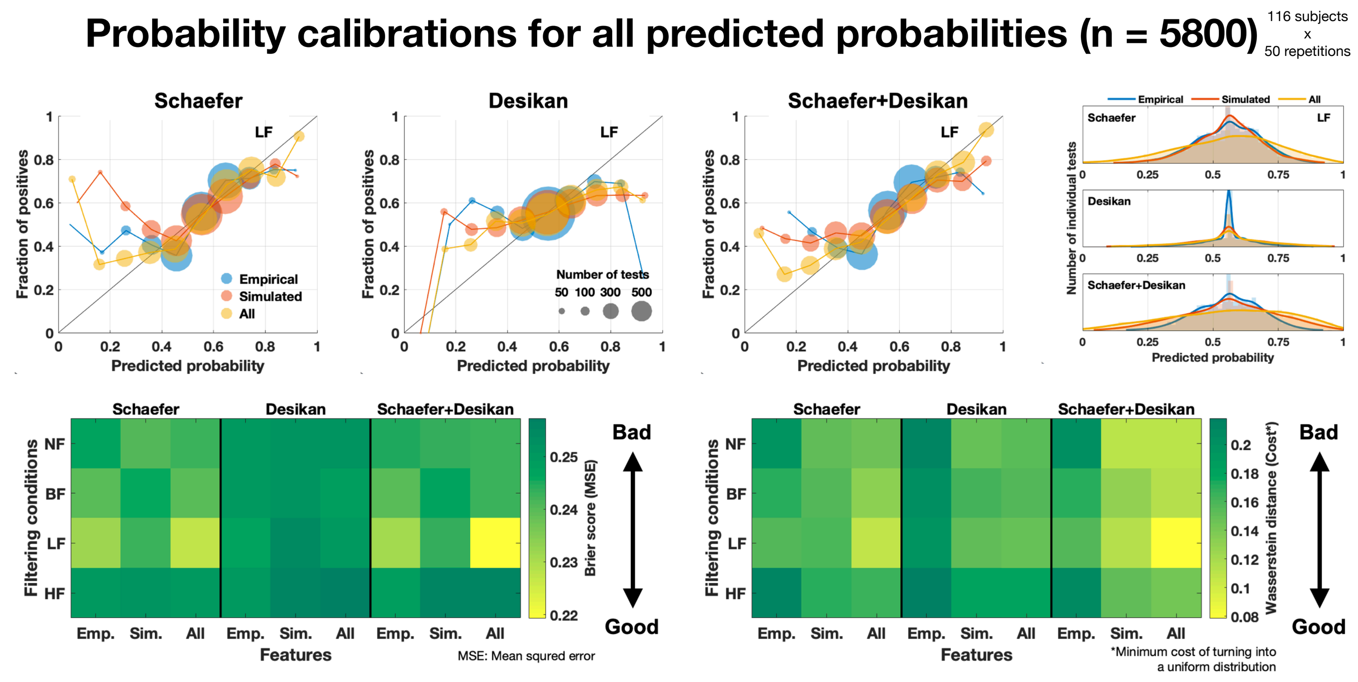
Classification performance



* The black horizontal brackets connecting two colored bars indicate significantly different performance between feature conditions. Wilcoxon signed-rank two-tail test Bonferroni corrected $p < .05$

Probability calibrations for all predicted probabilities (n = 5800)

116 subjects × 50 repetitions



Conclusion

- The novel **behavioral model fitting paradigm** results in an **enhanced differentiation** of disease and control groups and **improved classification** of Parkinsonian patients by machine-learning approaches.
- The **low-frequency [0.01,0.05] Hz** band-pass filtering of BOLD signals can have a beneficial effect on the prediction performance of Parkinson's disease.
- The prediction performance can further be improved when **multiple brain parcellation schemes** were utilized.
- With the current approach, we suggest further **applications of whole-brain dynamical modeling** for cognitive or clinical measures and their interpretations.

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References

1. Jansen BH, Rit VG. Electroencephalogram and visual evoked potential generation in a mathematical model of coupled cortical columns. Biol Cybern. 1995;73(4):357-366.
2. Lopes da Silva FH, Hoeks A, Smits H, Zetterberg LH. Model of brain rhythmic activity. The alpha-rhythm of the thalamus. Kybernetik. 1974;15(1):27-37.
3. Friston KJ, Harrison L, Penny W. Dynamic causal modelling. NeuroImage. 2003;19(4):1273-1302.
4. Havlicek M, Roebroeck A, Friston K, Gardumi A, Ivanov D, Uludag K. Physiologically informed dynamic causal modeling of fMRI data. NeuroImage. 2015;122:355-372.
5. More S, Eickhoff SB, Caspers J, Patil KR. Confound Removal and Normalization in Practice: A Neuroimaging Based Sex Prediction Case Study. 2021; Cham.