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

Kyesam Jung[1,2], Esther Florin[3], Kaustubh R. Patil[1,2], Julian Caspers[4], Christian Rubbert[4], Simon B. Eickhoff[1,2], Oleksandr V. Popovych[1,2]

E-mail: k.jung@fz-juelich.de

[1]Institute of Neuroscience and Medicine, Brain and Behaviour (INM-7), Research Centre Jülich, 52425, Germany
[2]Institute for Systems Neuroscience, Medical Faculty, Heinrich-Heine University Düsseldorf, 40225, Germany
[3]Institute of Clinical Neuroscience and Medical Psychology, Medical Faculty, Heinrich-Heine University Düsseldorf, 40225, Germany
[4]Department of Diagnostic and Interventional Radiology, Medical Faculty, Heinrich-Heine University Dusseldorf, 40225, Germany

JÜLICH Forschungszentrum

hhu Heinrich Heine Universität Düsseldorf

medRSD Medical Research School Düsseldorf

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

More details → bioRχiv

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

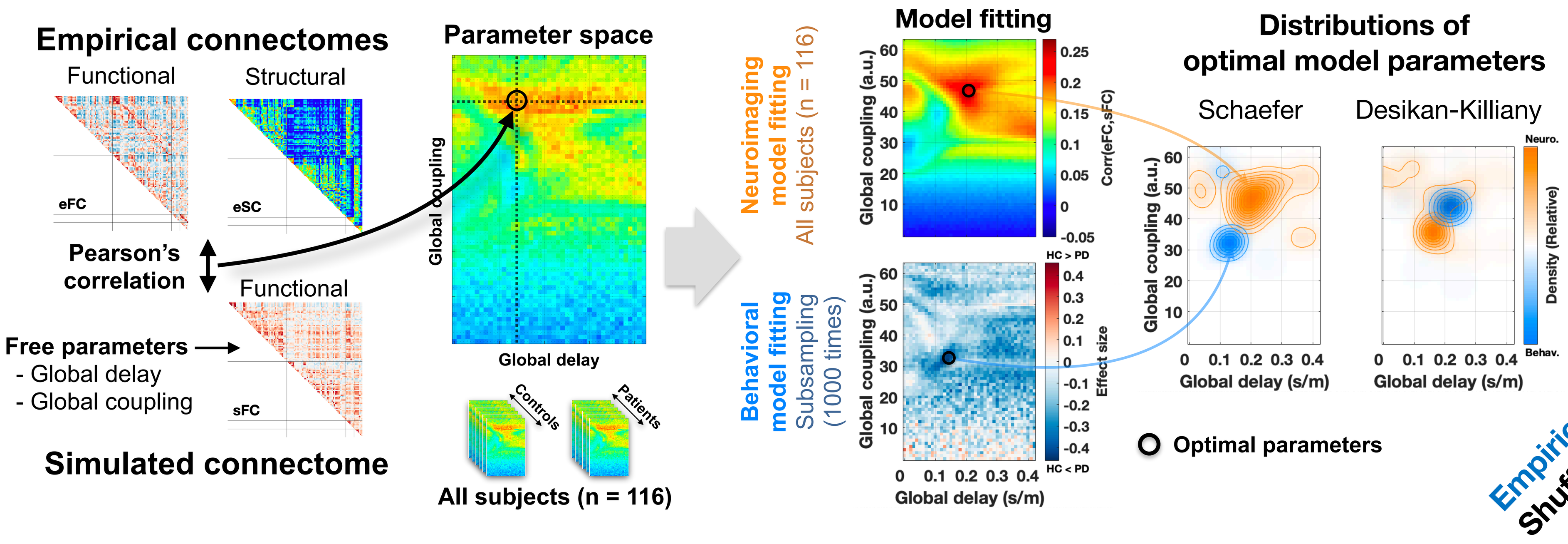
❖**Experimental conditions:** **Four temporal filters (NF, BF, LF, and HF)** for empirical and simulated BOLD signals + **Two parcellation schemes (Schaefer 100 Parcels** and **Desikan-Killiany**)
- **NF:** no filtering, **BF:** broad frequency band [0.01,0.1] Hz, **LF:** low frequency band [0.01,0.05] 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

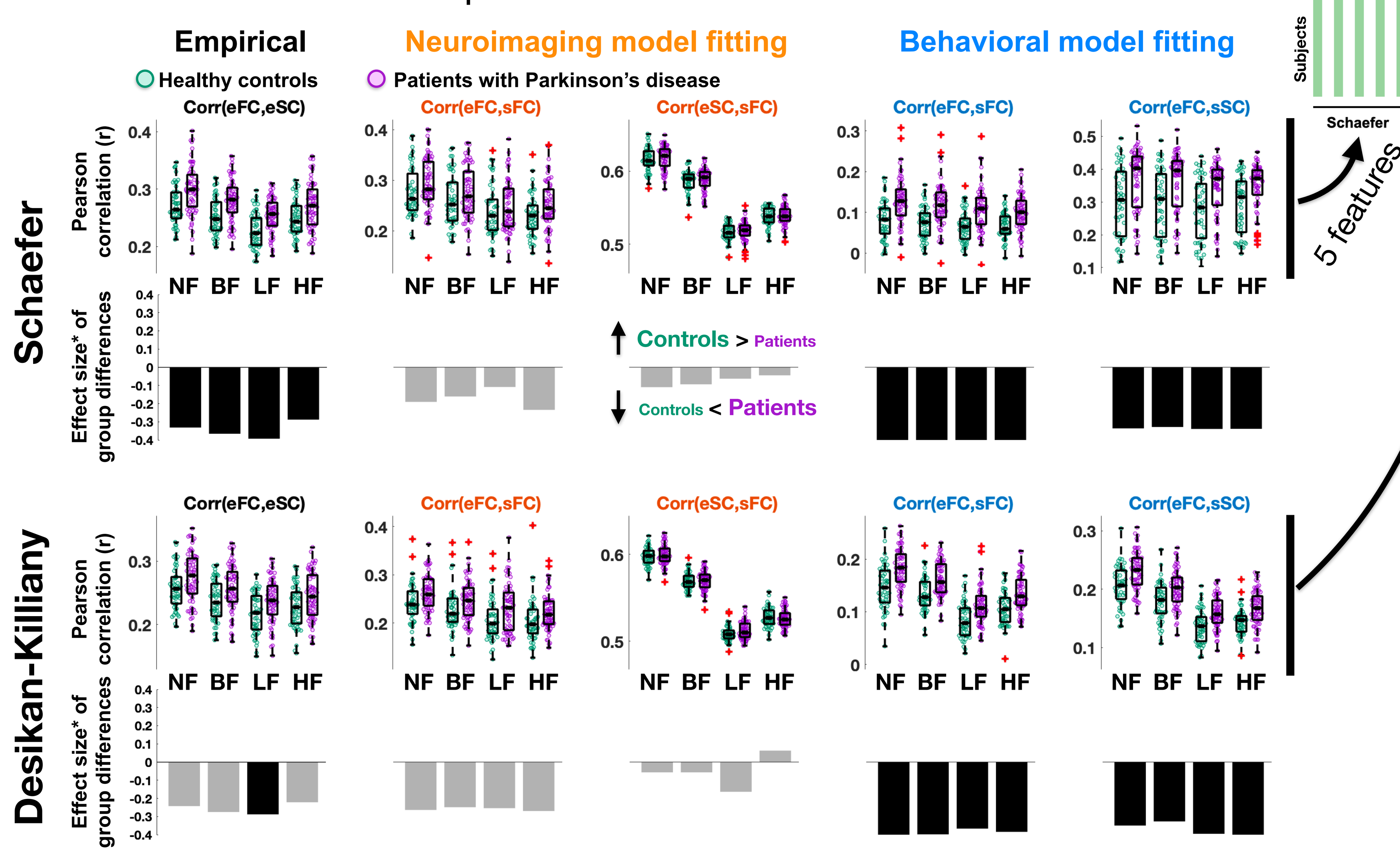
❖**Machine learning:** A **regularized** (**LASSO**: the least absolute shrinkage and selection operator) **logistic regression** using a **cross-validated model fitting and confound regression**[5]

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

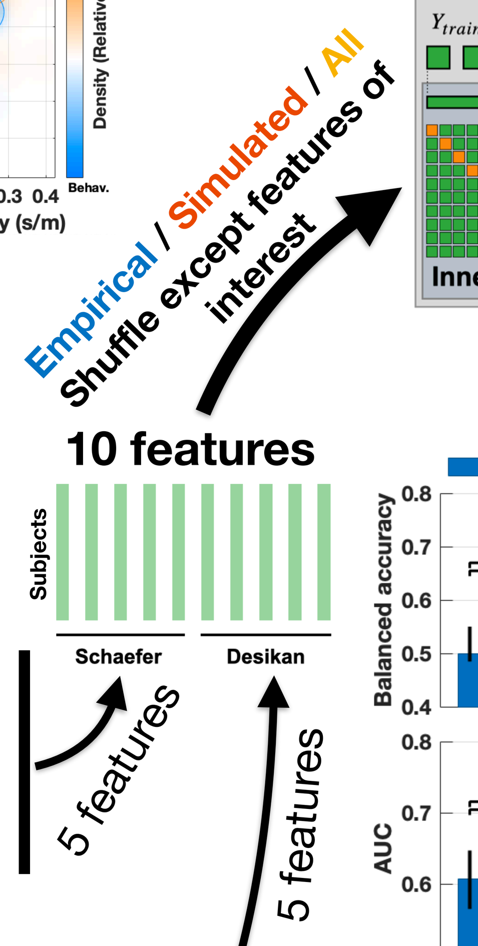
1. Empirical and simulated connectomes for model fitting



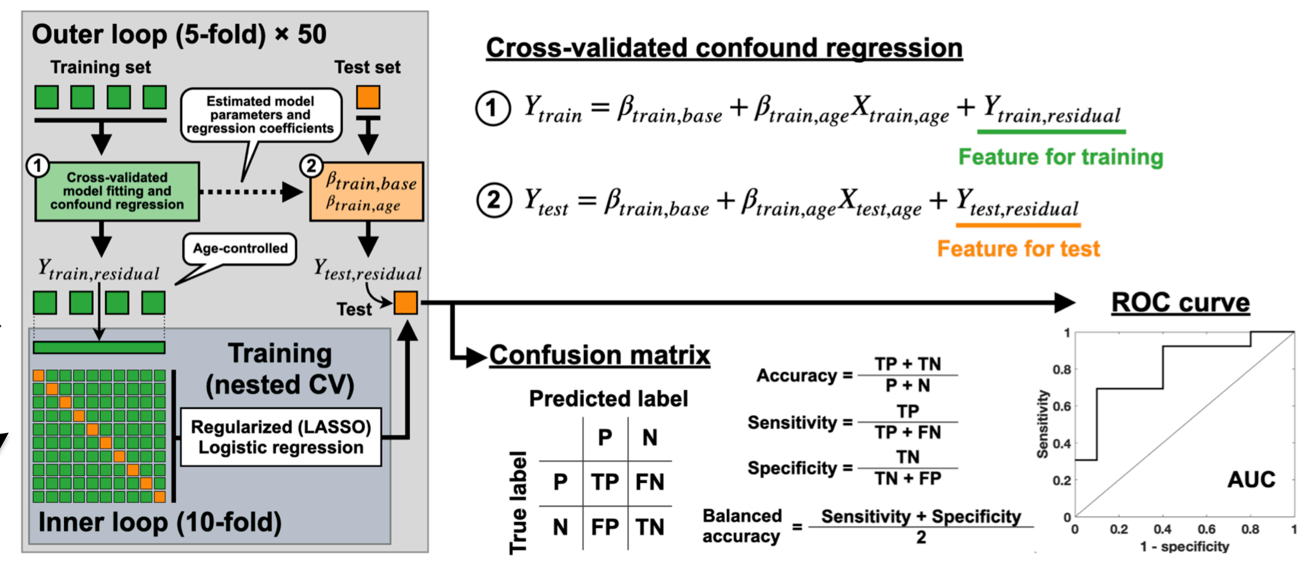
2. Connectome relationships as features for classification



■ 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.



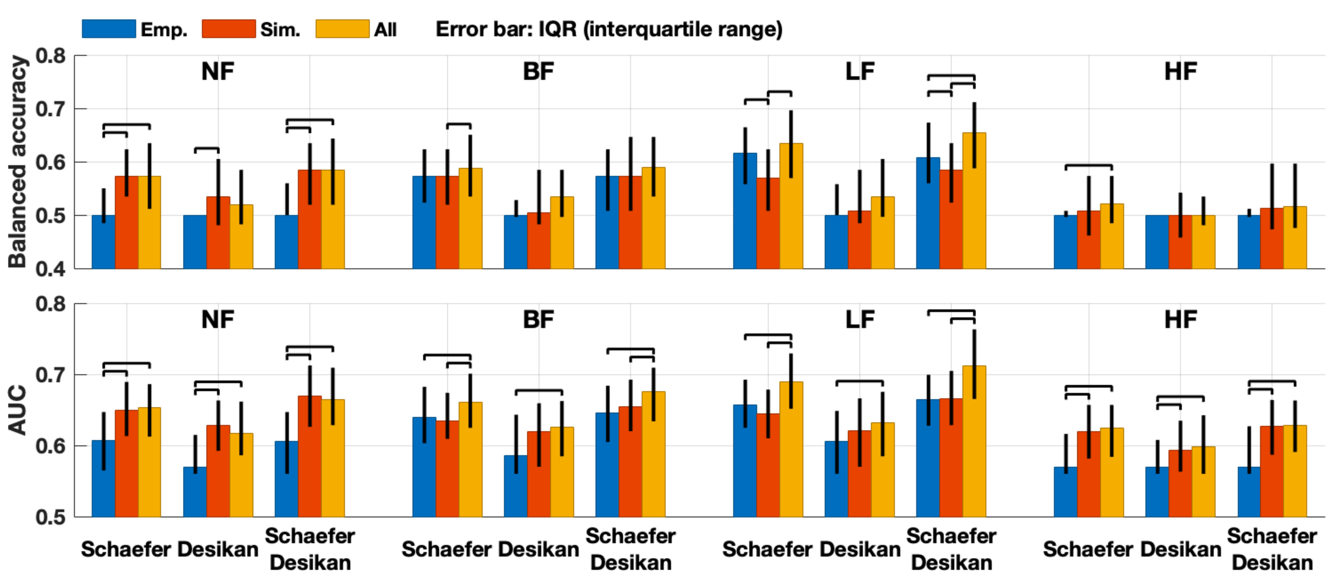
3. Training using a cross-validated confound regression



1. $Y_{train} = \beta_{train,base} + \beta_{train,age} X_{train,age} + Y_{train,residual}$ (Feature for training)
2. $Y_{test} = \beta_{train,base} + \beta_{train,age} X_{test,age} + Y_{test,residual}$ (Feature for test)

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

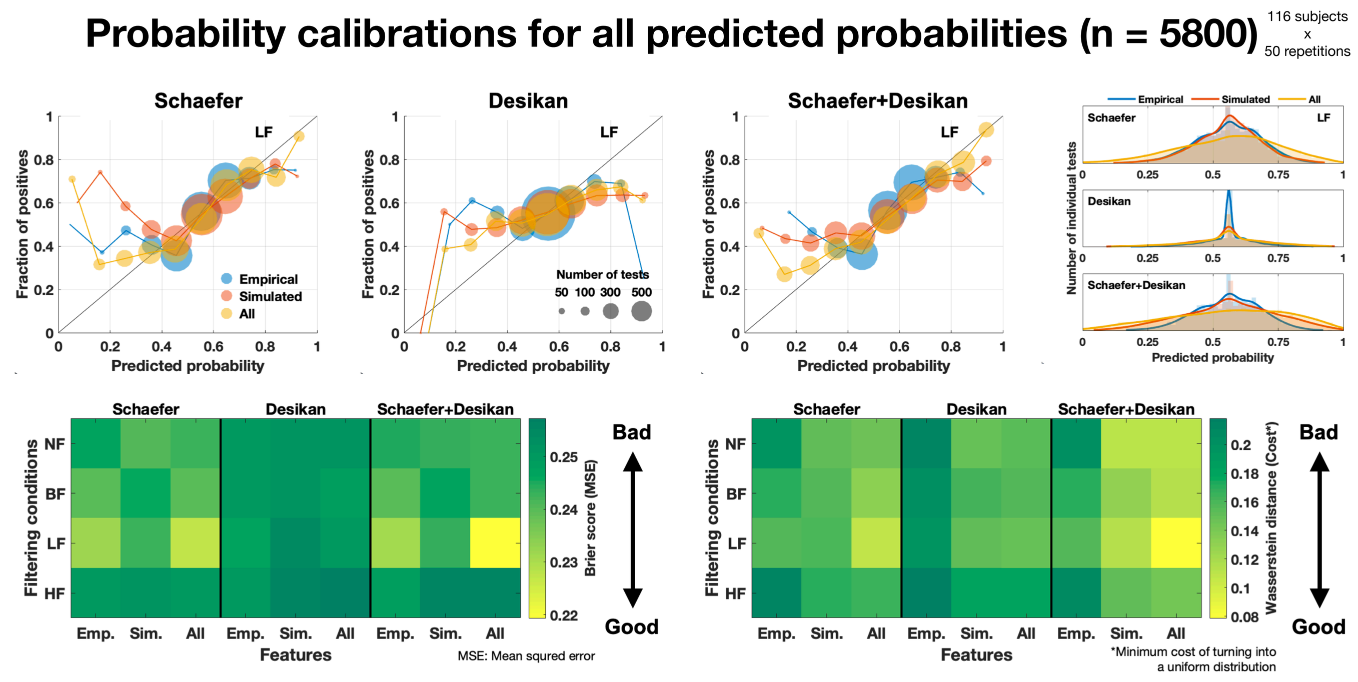
Classification performance



* 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.
- The results further suggest an **application of the results of whole-brain simulations** for cognitive or clinical investigation of inter-individual differences and disease diagnosis.

Acknowledgements and funding

The authors greatly acknowledge the contribution of **Dr. Christian Mathys**, **Dr. Martin Südmeyer**, and **Dr. Christian Hartmann** for the assessment of the Parkinson's disease data. The authors are also grateful to **Shraddha Jain** for the MRI data quality check. The authors gratefully acknowledge the computing time granted through **JARA on the supercomputer JURECA at Forschungszentrum Jülich**.

This work was supported by the Portfolio Theme Supercomputing and Modeling for the Human Brain by the Helmholtz association (https://www.helmholtz.de/en), the Human Brain Project, and the European Union's Horizon 2020 Research and Innovation Programme (https://cordis.europa.eu) under **Grant Agreements 785907 (HBP SGA2)**, **945539 (HBP SGA3)**, and **826421 (VirtualBrainCloud)**. Open access publication was funded by **the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - 491111487**. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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.