

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

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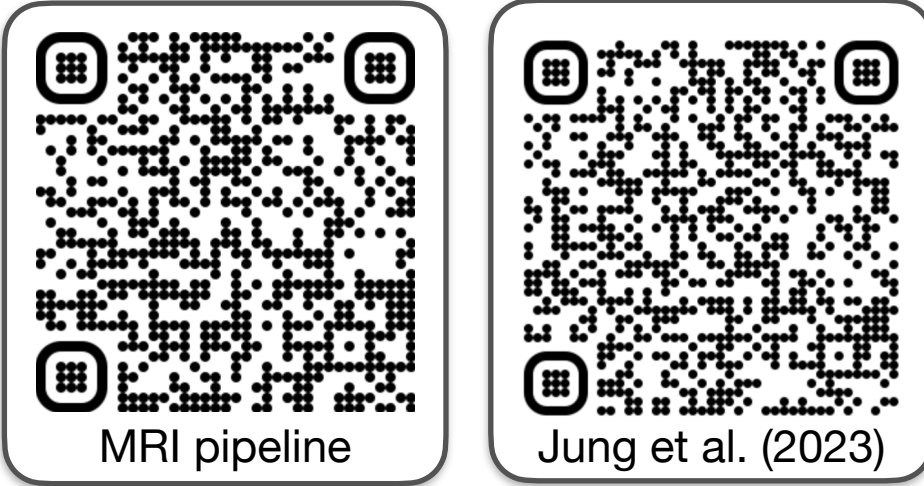


Introduction

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.

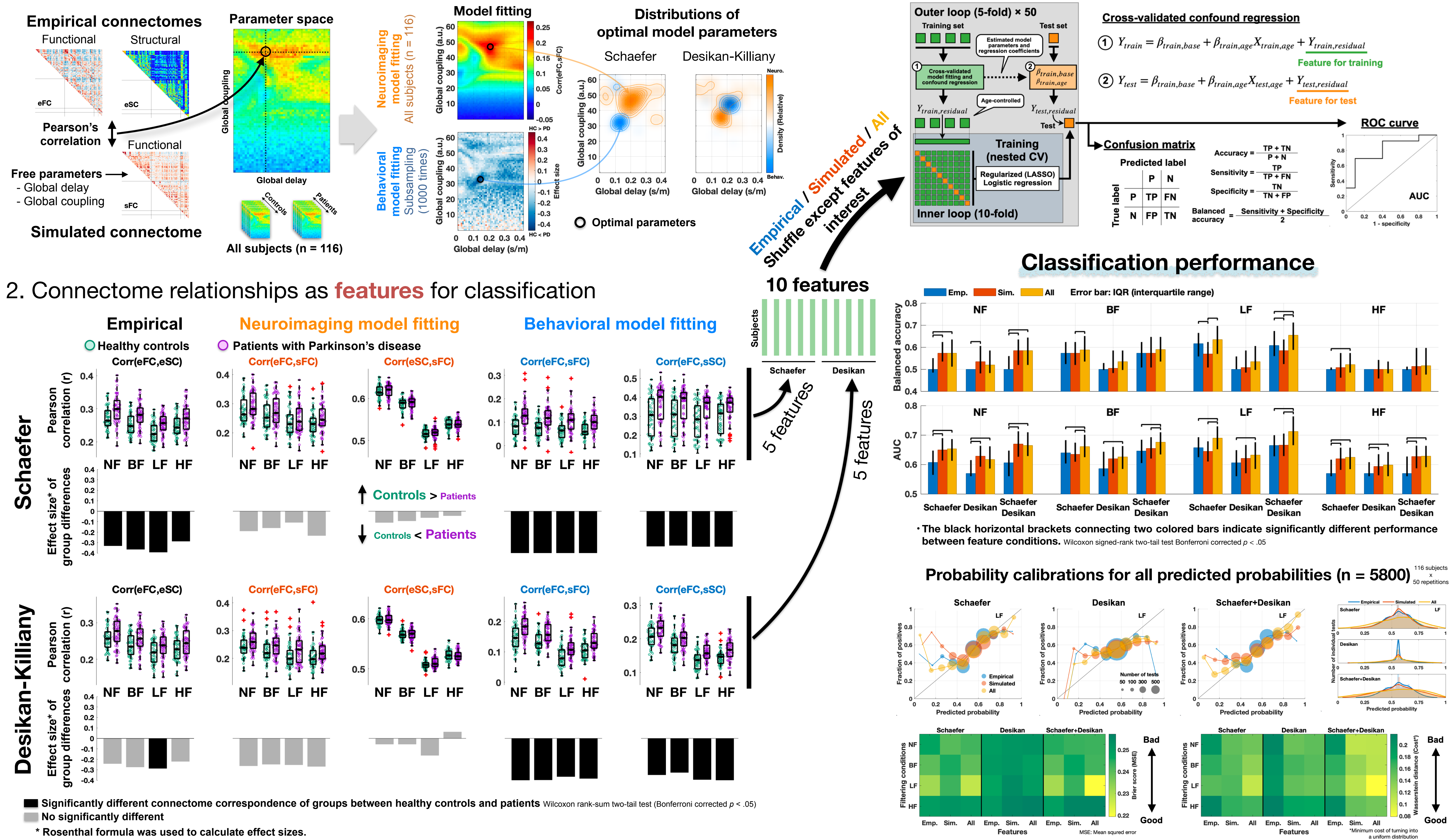
Methods: Whole-brain dynamical modeling and classification using machine learning

- ❖ **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
- ❖ **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
3. **Training** using a cross-validated confound regression



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.

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) - 49111487. 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, Roebroek 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.