

Addressing High Dimensionality in Functional Connectivity Analysis



A Network Stacking Approach for Neuroscientific Predictive Modeling

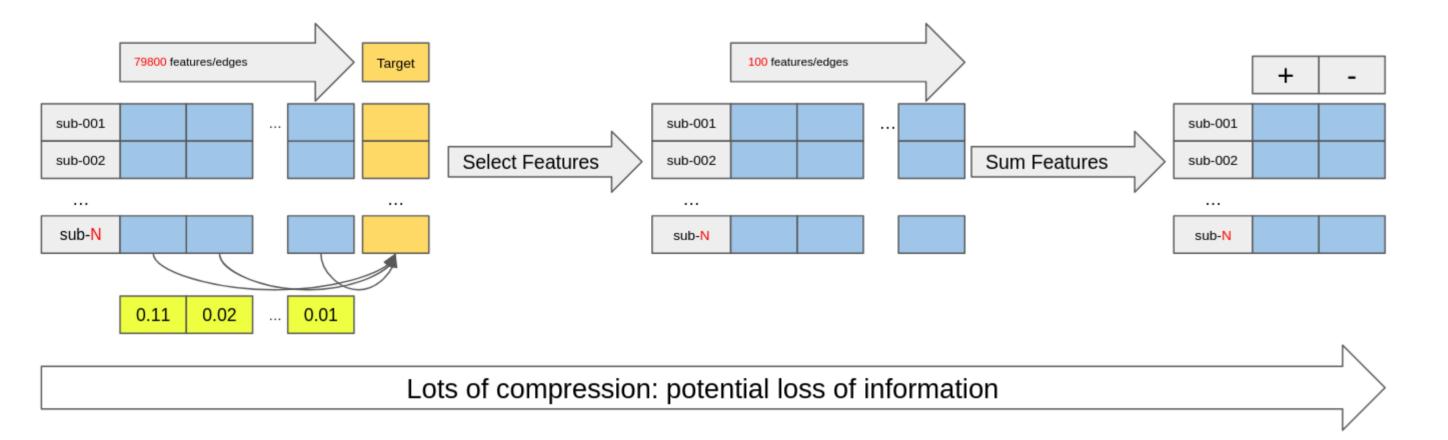
Leonard Sasse^{1,2,3}, Sami Hamdan^{1,2}, Federico Raimondo^{1,2}, Simon B. Eickhoff^{1,2}, and Kaustubh R. Patil^{*1,2}



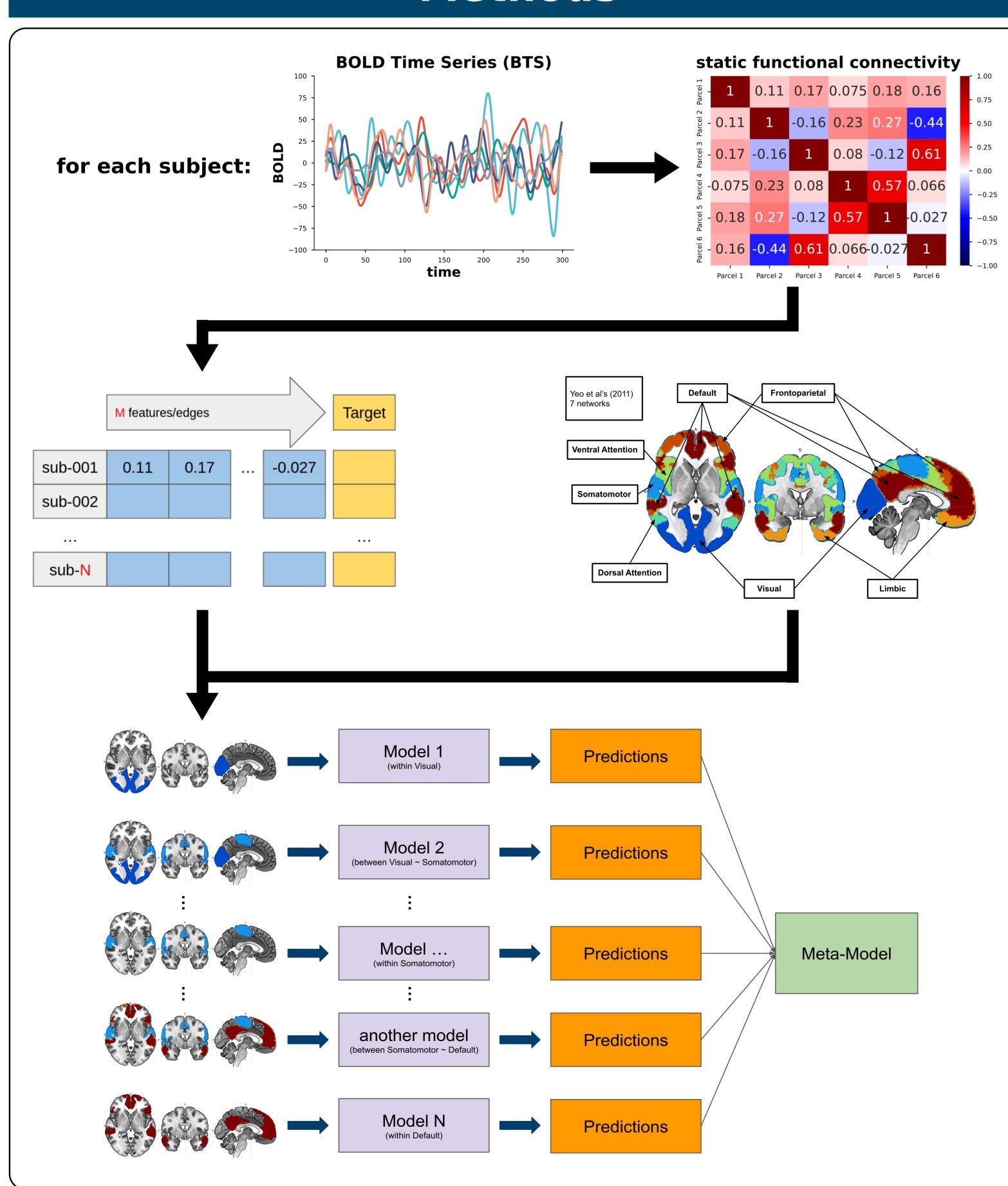
¹Institute of Neuroscience and Medicine, Brain and Behaviour (INM-7), Research Centre Jülich, Jülich, Germany; ²Institute of Systems Neuroscience, Medical Faculty, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany; ³Max Planck School of Cognition, Stephanstrasse 1a, Leipzig, Germany

Introduction

- Functional Connectivity (FC) refers to the statistical dependencies between the activity of distinct brain areas [1].
- FC has shown significant potential as a biomarker in various studies, indicating its future applicability:
- It varies between individuals and remains consistent within an individual, demonstrating its stability [2,3].
- FC is associated with individual cognition and clinically relevant symptoms of mental disorders, highlighting its importance in research and clinical contexts [4,5].
- High-dimensionality poses a challenge for FC as it often leads to overfitting, reducing its ability to generalize effectively, which is exacerbated by the typically limited size of MRI datasets due to expensive data acquisition [6].
- Current approaches trying to deal with this tend to compress the data aggressively, potentially leading to loss of signal of interest. Example: CPM [4]

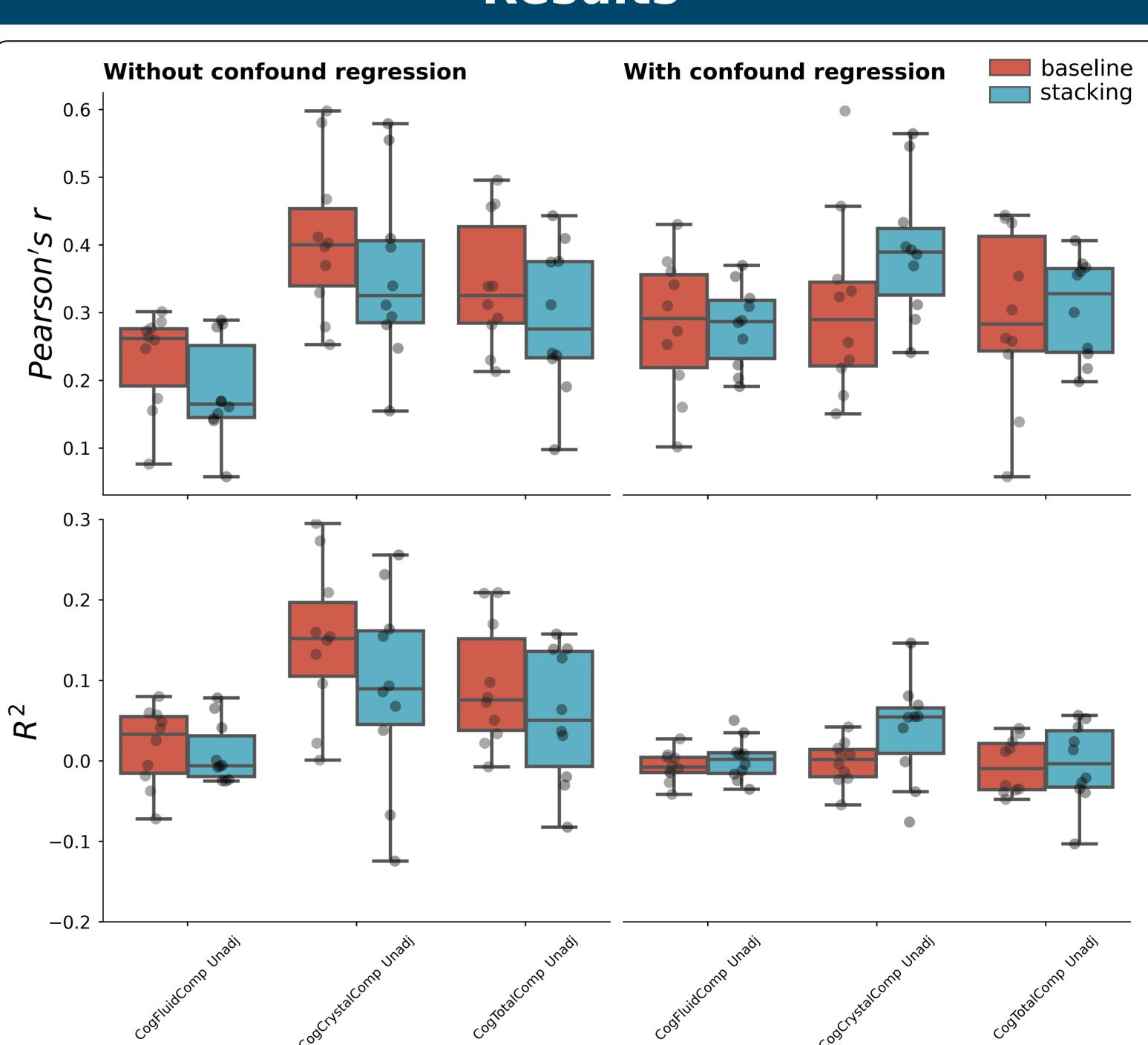


Methods



- Objective: predict 3 cognitive targets in Human Connectome Project (HCP) [7] dataset (N = 968)
- stacking_7: Yeo's 7 [8] networks are stacked by building a model for every set of between-network connections and every set of within-network connections (all models are SVM's with RBF kernel)
- baseline: "connectome-wide" model fitting (i.e. one model is fitted on all features; RBF SVM)
- 10-fold grouped cross-validation for evaluation of out-of-sample performance

Results



Discussion

- No advantage of stacking over baseline "connectome-wide" model fitting when confounds are not removed.
- Advantage of stacking over baseline "connectome-wide" model fitting in the prediction of crystallised intelligence when removing confounds.
- Next steps:
 - attempt stacking in age prediction in an independent dataset
 - attempt more complex combination of model families in stacking

References

- [1] Biswal, B., Yetkin, F. Z., Haughton, V. M. & Hyde, J. S. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magnetic Resonance in Medicine* **34**, 537-541 (1995).
- [2] Finn, E. S. et al. Functional connectome fingerprinting: Identifying individuals using patterns of brain connectivity. *Nature Neuroscience* **18**, 1664–1671 (2015).
- [3] Amico, E. & Goñi, J. The quest for identifiability in human functional connectomes. Scientific Reports 8, 8254 (2018).
- [4] Shen, X. et al. Using connectome-based predictive modeling to predict individual behavior from brain connectivity. *Nature Protocols* **12**, 506–518 (2017).

 [5] He, T. et al. Deep neural networks and kernel regression achieve comparable accuracies for functional connectivity prediction of behavior and demographics.
- Neuroimage **206**, 116276 (2020).

 [6] Wu, J. et al. The challenges and prospects of brain-based prediction of behaviour. Nature Human Behaviour **7**, 1255-1264 (2023).
- [7] Van Essen, D.C. et al. The WU-minn human connectome project: An overview. Neuroimage 80, 62-79 (2013).
- [8] Yeo, B. T. et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 106(2), 1125–1165 (2011).