REDEFINING AUTISM SUBTYPES VIA MULTISCALE BRAIN NETWORK TOPOLOGY: PERSISTENT HOMOLOGY AND COMPLEX NETWORK ANALYSIS OF FMRI CONNECTIVITY

Caroline L. Alves[1,*] and Michael Moeckel[1,†]

[1] *Laboratory for Hybrid Modeling, Aschaffenburg University of Applied Sciences, Aschaffenburg, Germany*

We investigate whether multiscale topological properties of brain networks can differentiate autism subtypes defined under the DSM-IV, namely Asperger Syndrome (AS), from classical Autism Spectrum Disorder (ASD) and typically developing controls (TD) using Autism Brain Imaging Data Exchange (ABIDE) data. Functional networks were derived from resting-state fMRI BOLD time series across 122 predefined brain regions of interest (ROI), using Spearman correlations to define edge weights. The regions were selected based on the Bootstrap Analysis of Stable Clusters (BASC) atlas, chosen for their superior performance in distinguishing ASD phenotypes using deep learning approaches, as reported in prior work. This study extends our previous analysis by including four diagnostic groups—AS (N = 80), ASD (N = 282), and TD (N = 518)—and shifting the analytical focus from voxel-wise patterns to a mesoscale, region-based network approach. We computed 26 complex network metrics reflecting topological integration, segregation, modularity, and centrality. To capture higher-order topological signatures, we applied persistent homology to Vietoris–Rips complexes computed across multiple distance thresholds. From the resulting persistence diagrams, we extracted fractal dimension (via the scaling behavior of simplex growth) and persistence entropy (quantifying the lifespan diversity of homological features). Additionally, Betti curves and simplicial profiles were computed up to dimension 4, providing insight into the distribution of cycles and cavities across diagnostic groups. The AS group exhibited significantly elevated fractal dimension and persistence entropy, revealing more hierarchical and variable network architectures. These findings correlate with the AS phenotype, marked by high verbal reasoning and localized social deficits, and point to greater multiscale integration. AS also exhibited pronounced hemispheric asymmetry, notably reduced right-hemisphere efficiency, a pattern linked to deficits in spatial and social cognition. Together, these findings illustrate how persistent homology and complex network theory can uncover latent mesoscale structures in brain function that align with clinical heterogeneity, supporting the classification of AS as a distinct group alongside ASD due to its unique neurobiological characteristics.

[1] A. Abraham et al., Frontiers in Neuroinformatics **8**, 14 (2014).
[2] C. L. Alves et al., Scientific Reports **13**(1), 8072 (2023).
[3] C. L. Alves et al., J. Phys.: Complexity **3**(2), 025001 (2022).
[4] C. L. Alves et al., PLOS ONE **17**(12), e0277257 (2022).
[5] C. L. Alves et al., J. Neural Engineering (2023).
[6] S. Das et al., PLOS ONE **18**(3), e0276419 (2023).
[7] G. Carlsson, Nat. Rev. Phys. **2**(12), 697–708 (2020).
[8] A. B. El-Yaagoubi et al., Frontiers in Neuroinformatics **18**, 1387400 (2024).
[9] G. Datseris et al., Chaos **33**(10) (2023).
[10] B. Benigni et al., Network Neuroscience **5**(3), 831–850 (2021).

* Caroline.LourencoAlves@th-ab.de
† Michael.Moeckel@th-ab.de

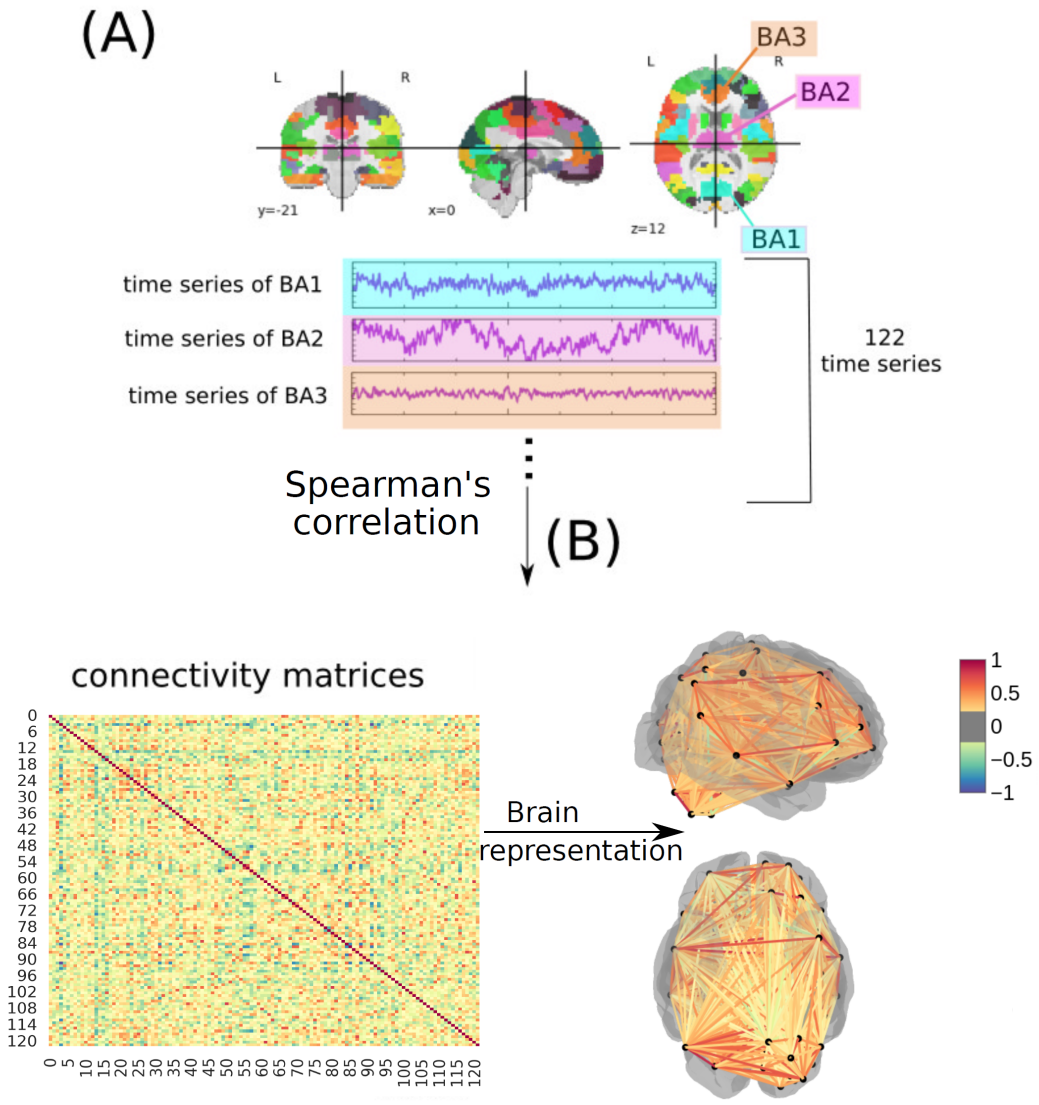

FIG. 1. Approach for generating connectivity matrices as described in [2]. (A) A time series is extracted from 122 ROIs in the fMRI data using the BASC BOLD atlas (highlighted in blue, purple, and orange). These time series are then correlated (B) to generate the connectivity matrices, where each row and column corresponds to one of the brain areas for a patient with AS, ASD, or TD (the figure illustrates an example for a subject with AS). The highlighted matrices represent the brain, as shown in a three-dimensional scheme.