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## Introduction

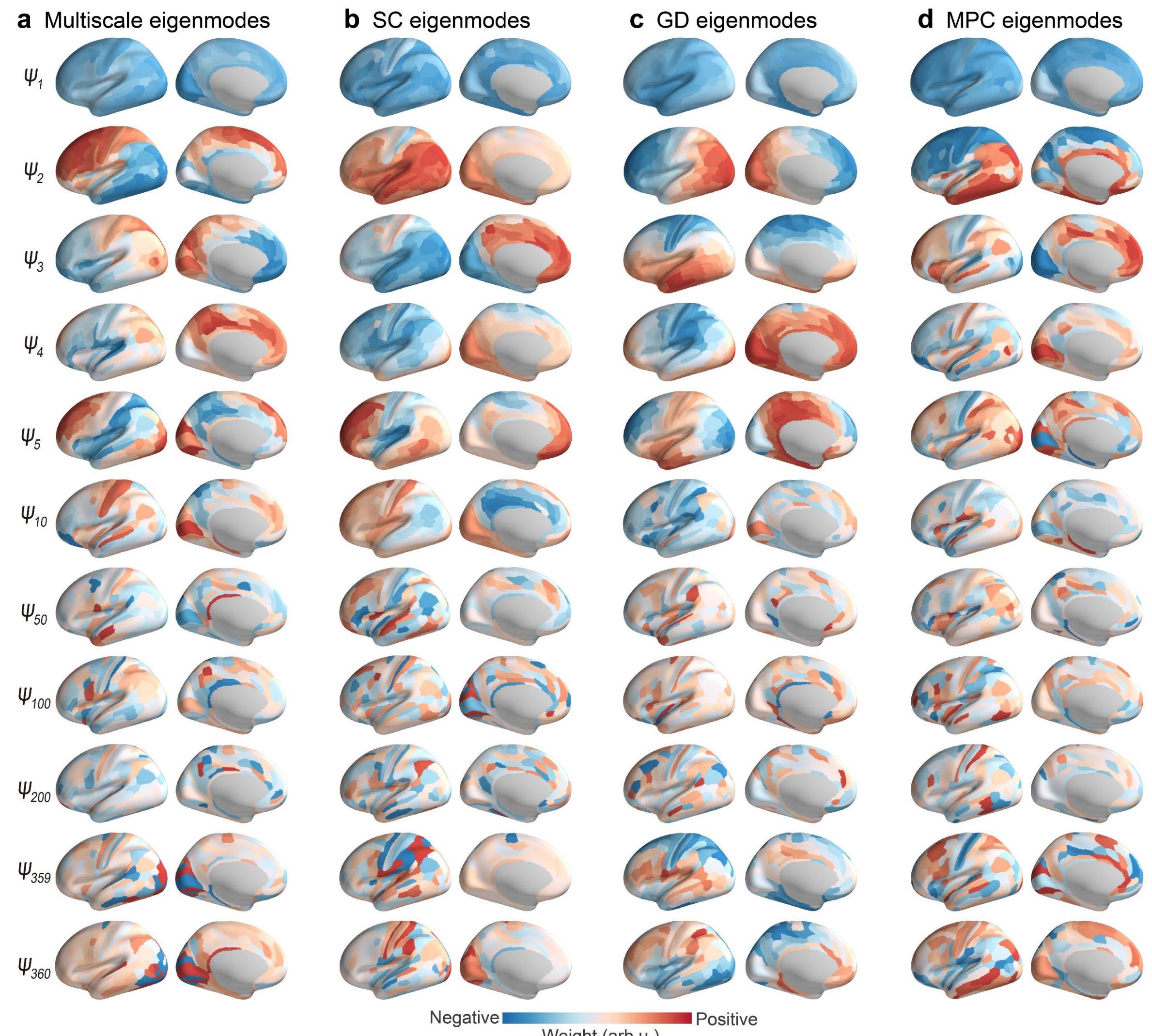
- The human brain is an intricate network organized across multiple spatial scales [1,2]. Understanding the relationship between structure and function in human at different scales remains a long-term goal of neuroscience.
- Multiscale structural organization arises from complex biological mechanisms and provides the anatomical foundation for functional interactions [3,4].
- However, the extent to which multiscale structural connectome constrains functional activity remains largely uncharted.
- Here, we deciphered the relationship between multiscale structural connectome and cortical activity using graph signal processing.

## Methods

- Dataset:** 100 unrelated healthy adults ( $N = 100$ ; 54 females; 22-36 years) from the Human Connectome Project (HCP).
- Atlas:** The HCP multimodal parcellation (HCP-MMP) atlas.
- Construction of multiscale structural connectome (MSC):** The MSC was constructed by integrating three complimentary features [3,4]: geodesic distance (GD), microstructural profile covariance (MPC), and tract strength (TS).
- Modal decomposition of brain activity:** Spontaneous and task-evoked cortical activity derived from functional MRI was decomposed into a weighted linear combination of orthogonal MSC eigenmodes [5].
- Quantifying multiscale structure-function decoupling (MSFD):** The MSFD was quantified as the logarithmic ratio between the L<sub>2</sub>-norm of high-frequency to low-frequency components over time points [6,7].

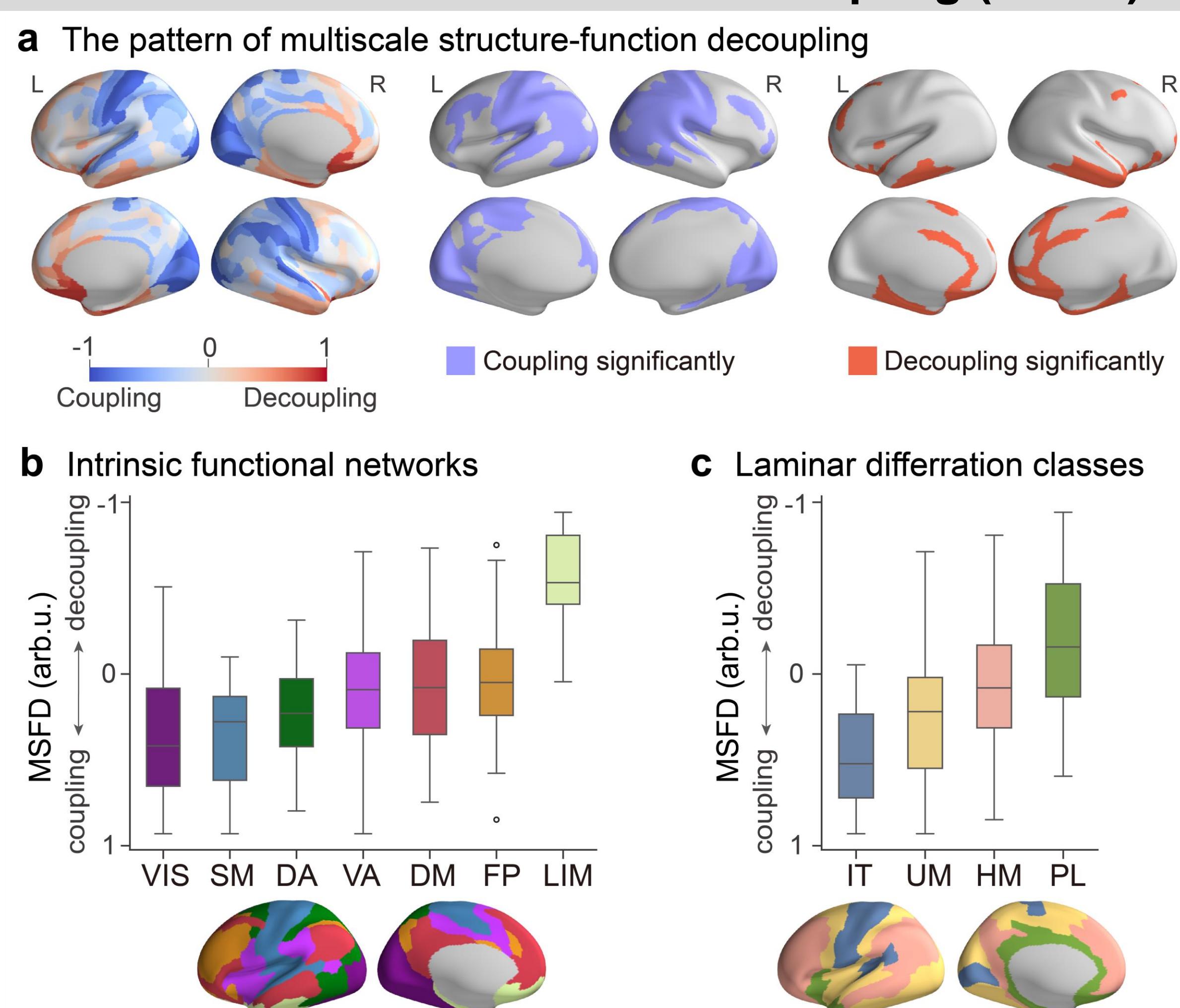
## Results

### Multiscale structural connectome eigenmodes



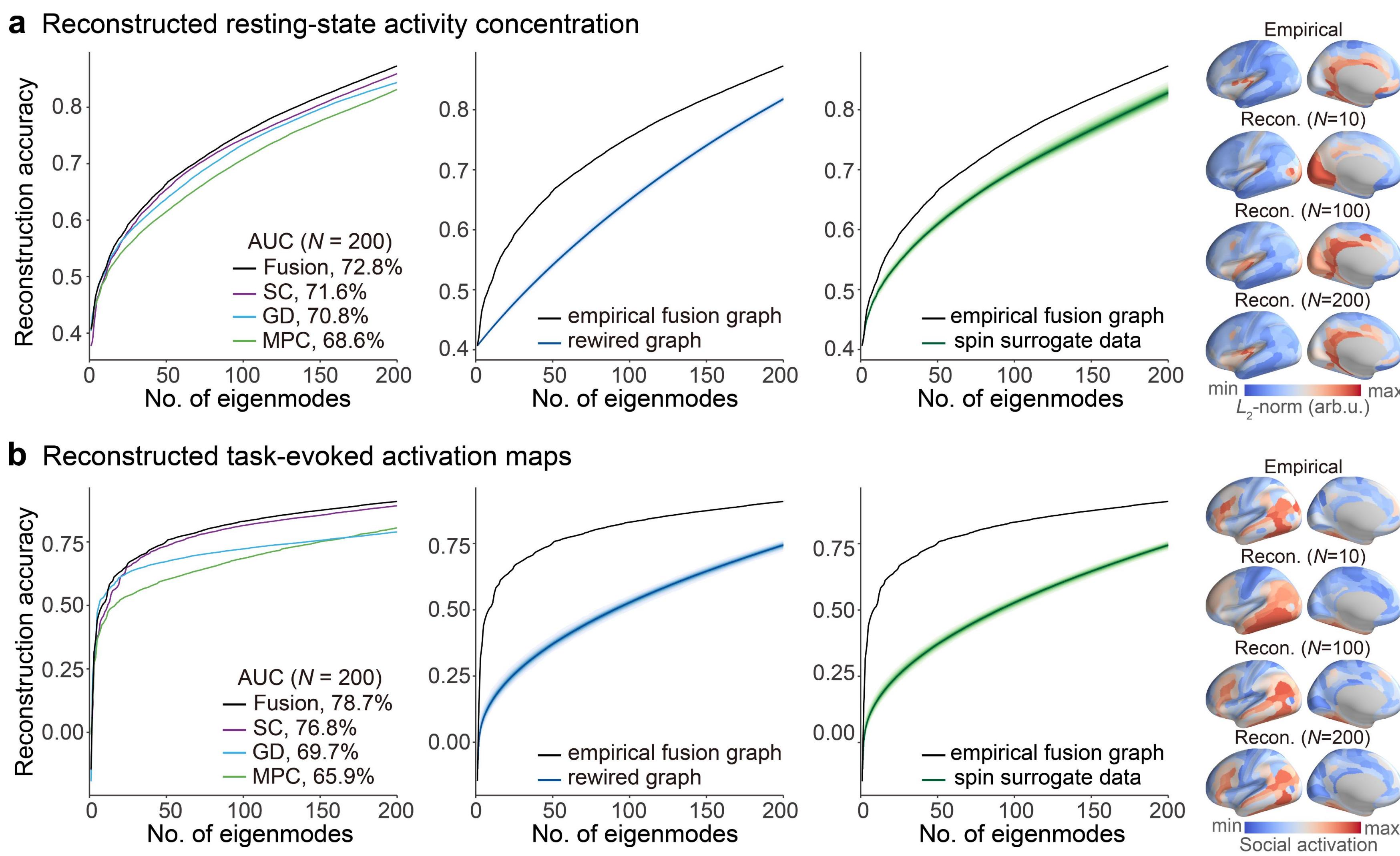
**Fig. 1 Eigenmode basis sets.** Negative-zero-positive values are coloured as blue-white-red.

### Multiscale structure-function decoupling (MSFD)



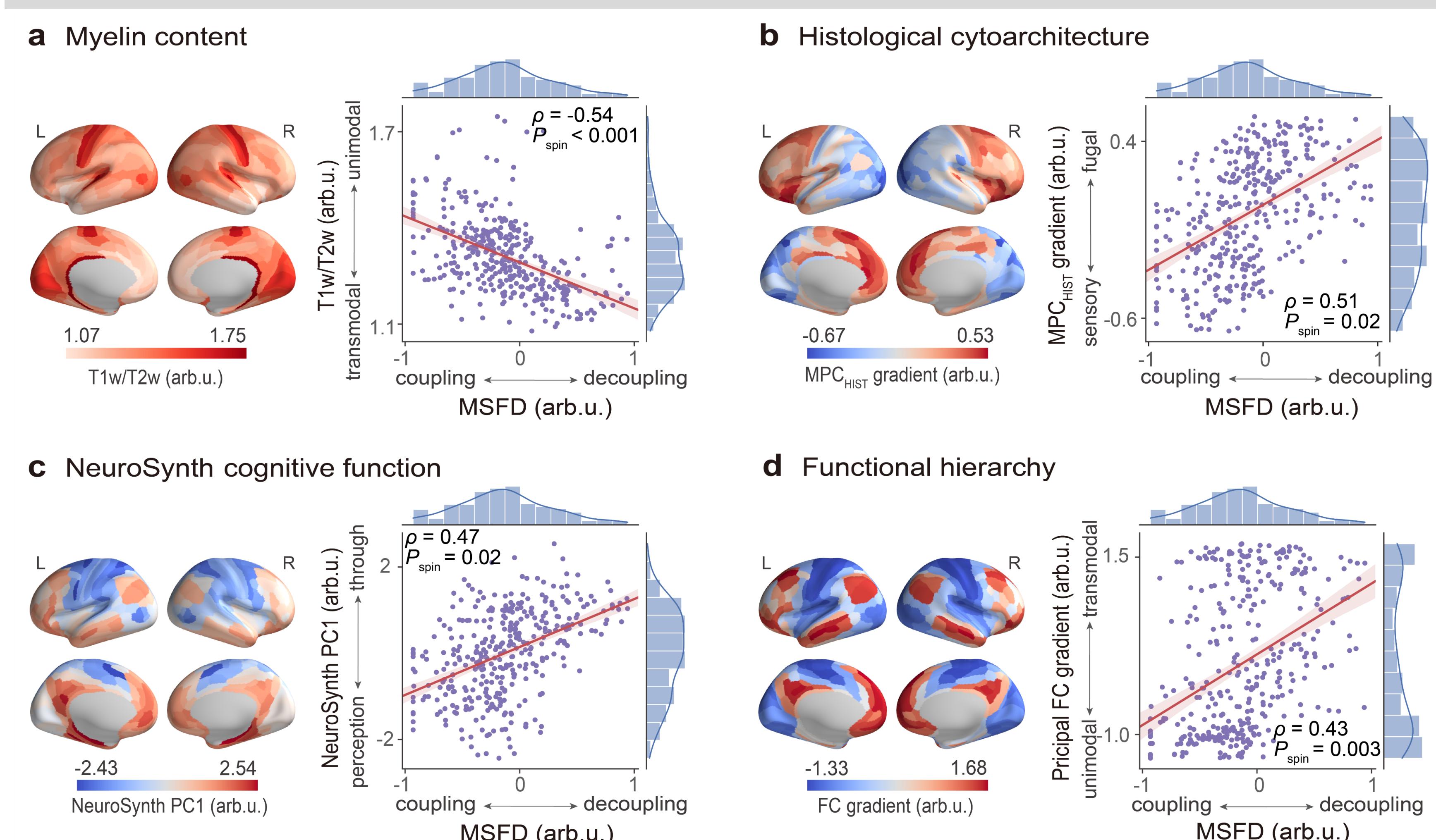
**Fig. 3 The spatial pattern of the MSFD.** (a) The statistically significant areas were grouped into coupling and decoupling patterns. The MSFD values within each of intrinsic functional networks (b) and laminar differentiation classes (c) are presented as box plots.

### Multiscale structural connectome eigenmodes constrain brain activity



**Fig. 2 (a)** Reconstruction accuracy of resting-state activity concentration achieved by four distinct eigenmodes. **(b)** Mean reconstruction accuracy of 47 HCP task-evoked activation maps.

### The MSFD follows microstructure and macroscale hierarchies



**Fig. 4 Relation to microscale and macroscale hierarchies.** Regional MSFD correlated with the myelin content (a), the principal histological cytoarchitecture gradient (b), the first principal component of NeuroSynth meta-analytic decodings (c), and the principal functional connectivity gradient (d).

## Conclusion

- Multiscale connectome eigenmodes provide a more compact representation of spontaneous and task-evoked cortical activity, outperforming eigenmodes derived from any single connectome.
- Multiscale structure-function relationship was gradually decoupled from the sensorimotor to transmodal cortices, reflecting microstructure and macroscale functional hierarchies.
- These findings highlight that the multiscale cortical wiring diagram serves as a powerful anatomical scaffold in shaping macroscale intrinsic human brain function.

## References

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