the framework of:

Probabilistic Functional Modes

part 2

- Description of PFM framework and its key features
- PFM Network Matrices, comparison to ICA, and interpretability of functional connectivity
- PFMs for big data and prediction of individualistic traits

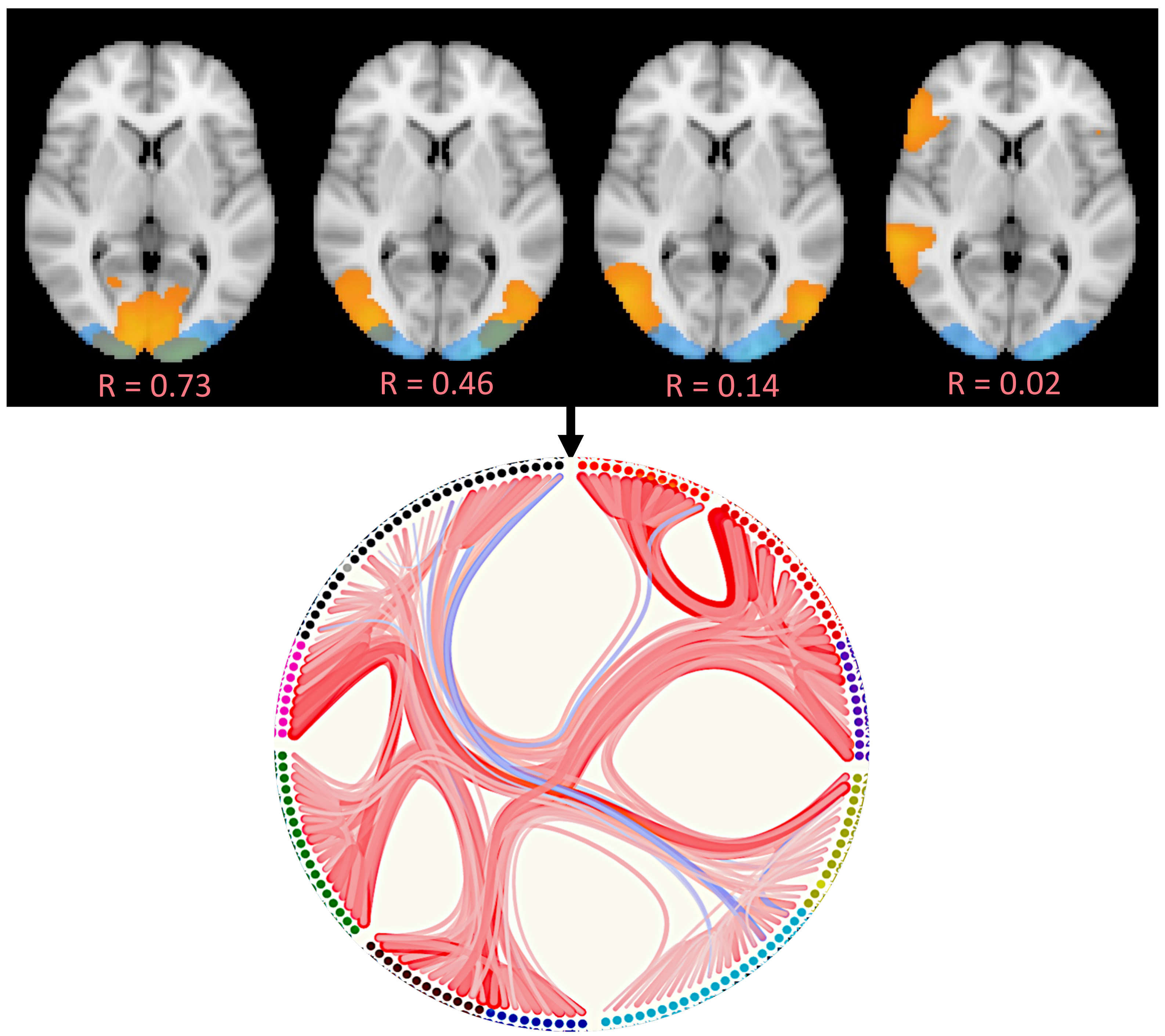
PFM NetMats and comparison to ICA

Network Matrices (NetMats)

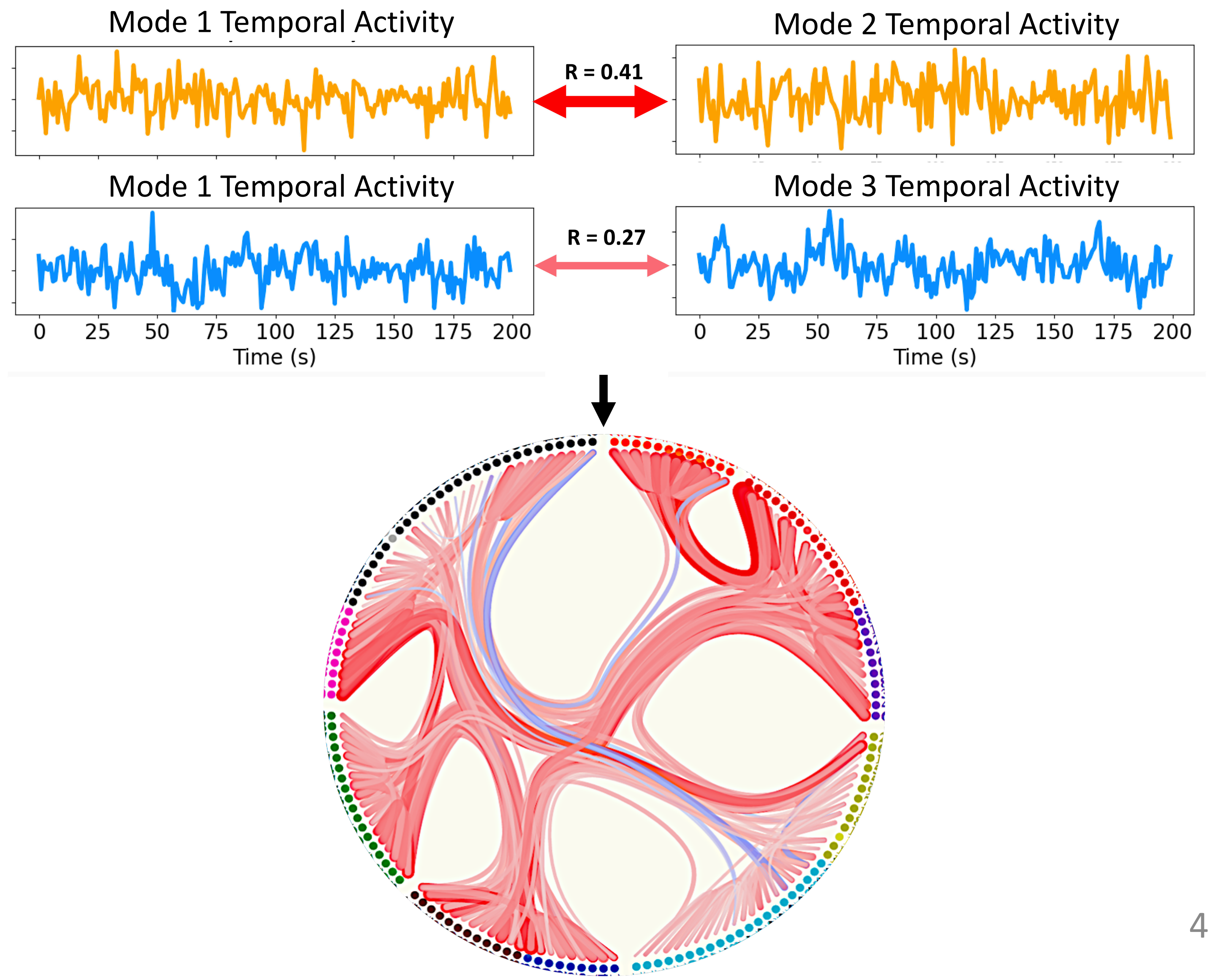
NetMats are used to characterise the relationships of functional modes with each other, and can be categorised into two types:

- Spatial NetMat -> Correlation between spatial layout of modes: an indicator of “**spatial overlap**” between the modes.
- Temporal NetMat -> Correlation between Timecourses of the modes: an indicator of “**functional connectivity**” between the modes.
  - Temporal NetMats are estimated hierarchically in PFMs (details in lecture part 1)

Spatial NetMat

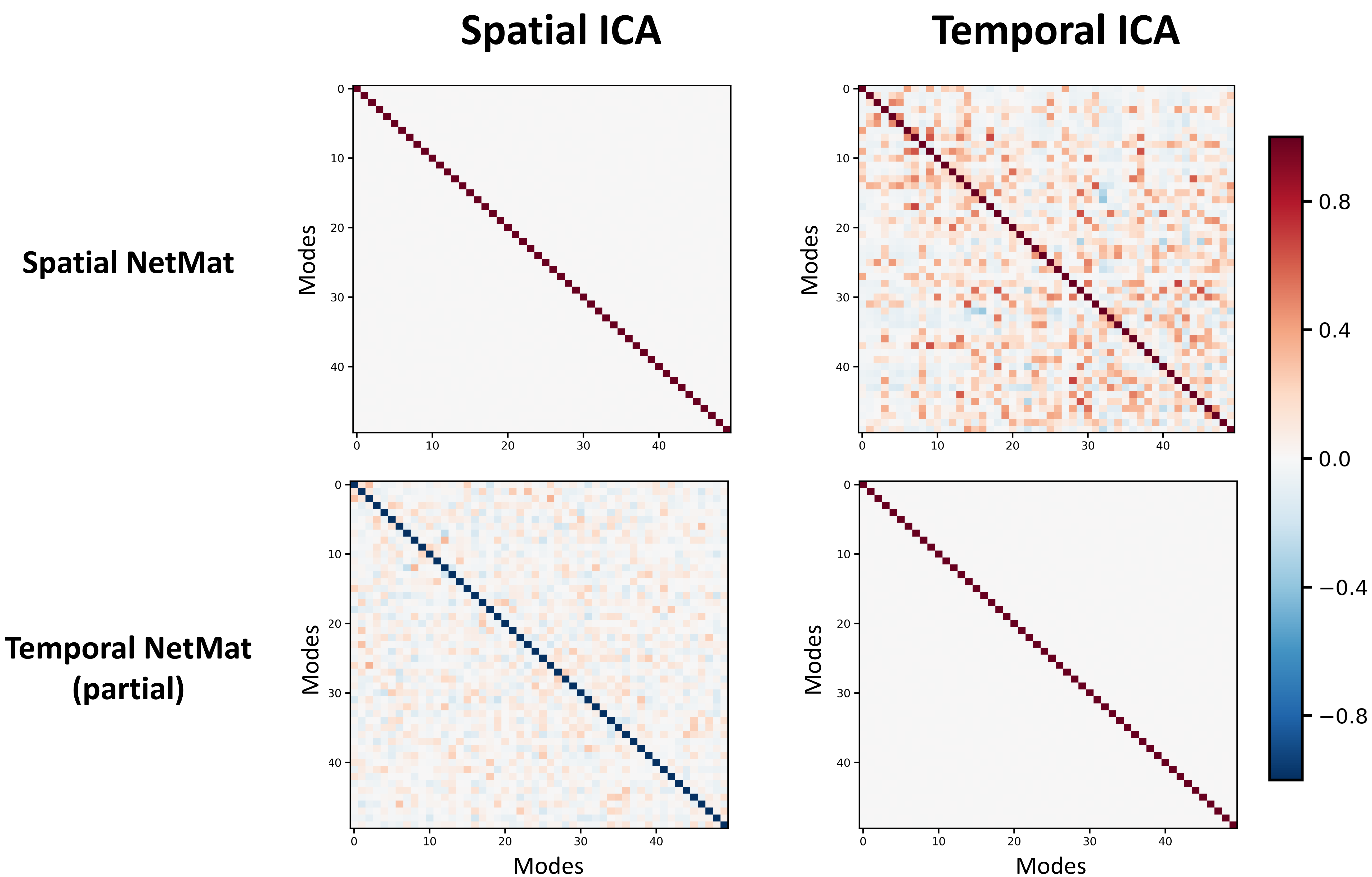


Temporal NetMat



Temporal and Spatial NetMats in ICA

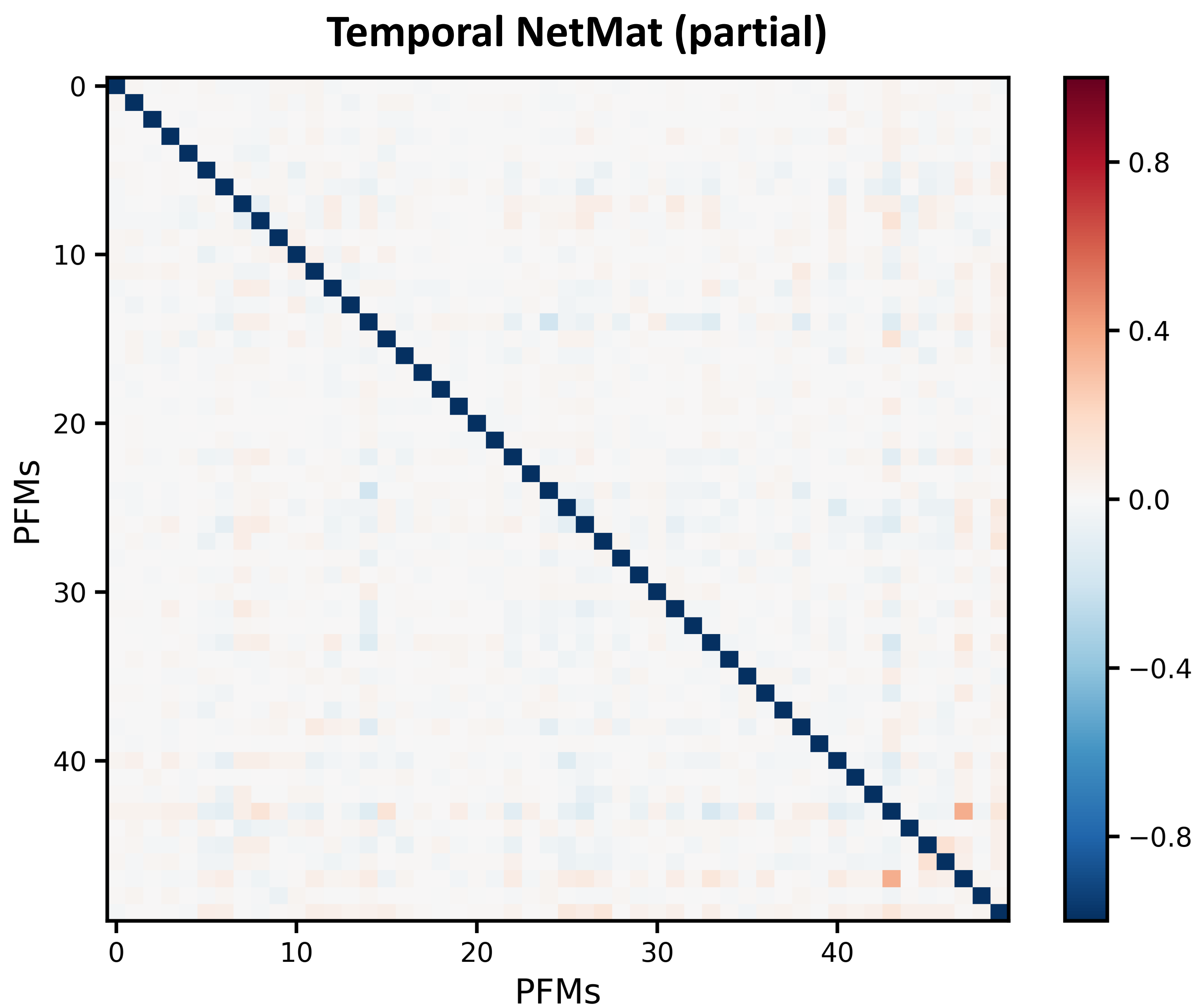
- ICA works around the core idea of ‘mode independence’
  - Spatial ICA -> modes spatially independent -> minimal spatial overlap
  - Temporal ICA -> modes temporally independent -> minimal functional connectivity

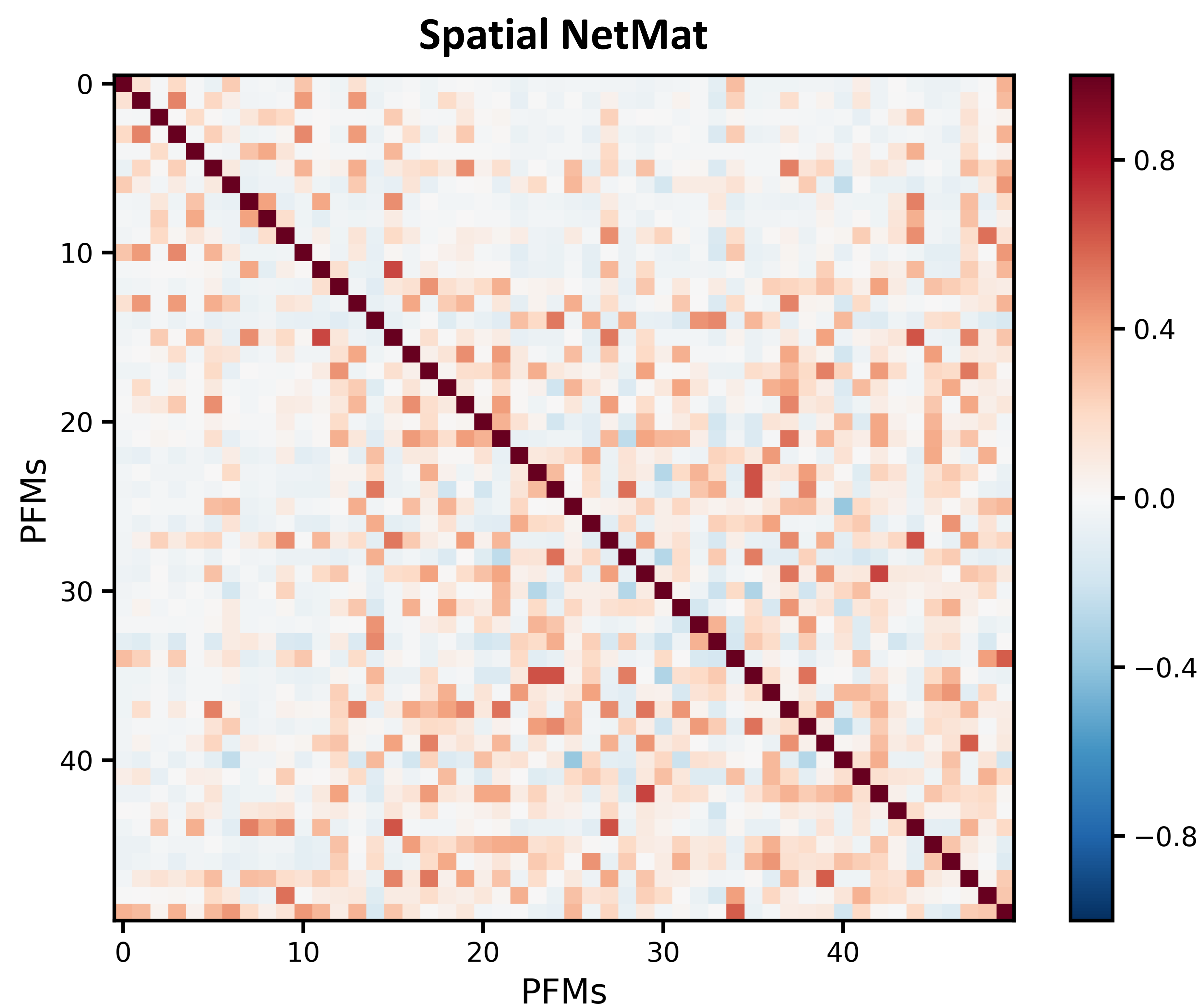


No requirement for mode independence in PFMs -> effect on NetMats

PFMs do not impose mode independence

- Expected to allow finding spatially overlapping and/or temporally correlated modes, as evidence supported by the data.
- They end up somewhere in between spatial and temporal ICA

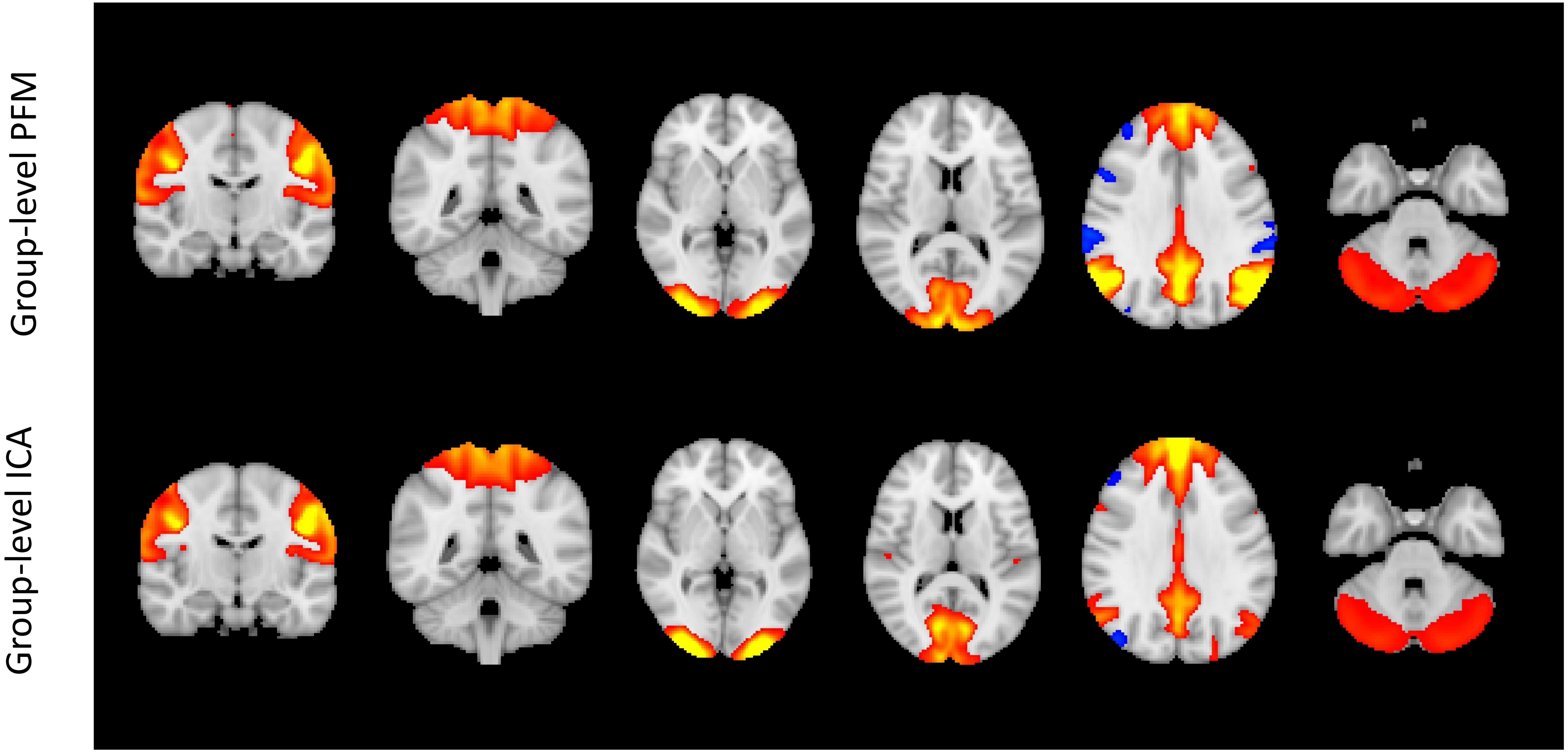




Effect of mode independence on low- vs. high- dimensional decomposition

PFM vs. spatial ICA: low-dimensional decompositions

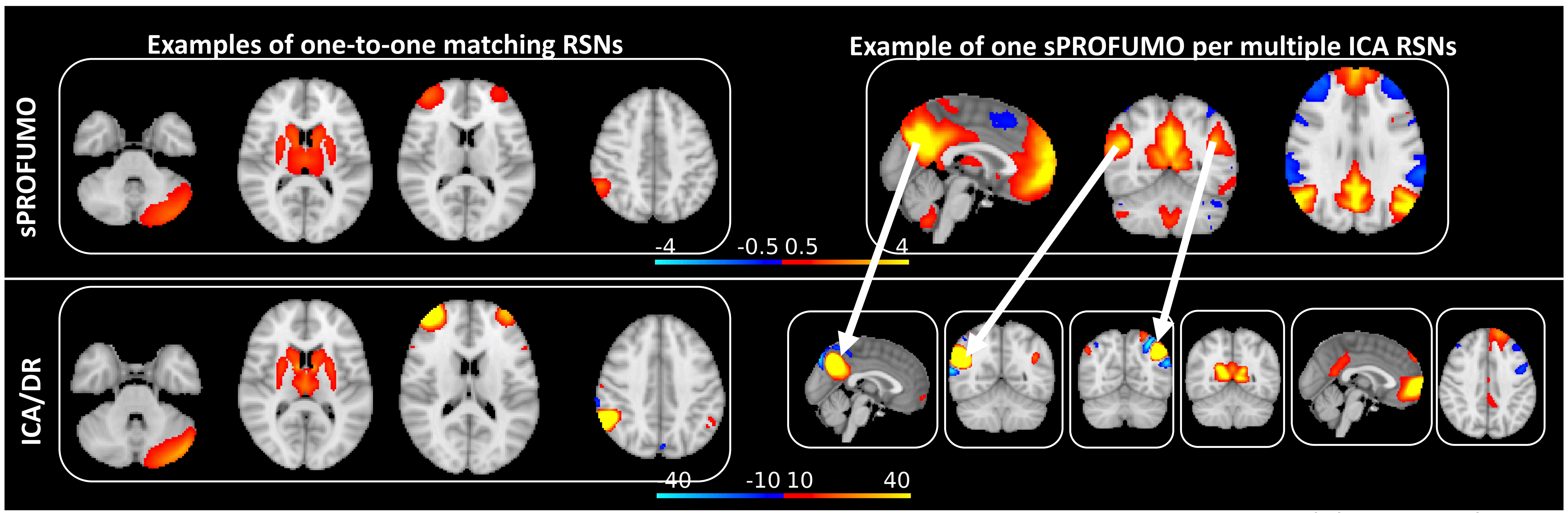
- For low-dimensional decompositions (e.g. 25), there is generally a good spatial correspondence between group-level PFM and ICA maps.



PFM vs. spatial ICA: high-dimensional decompositions

- For high-dimensional decompositions (e.g. 150 shown here), we will have two set of matching
  - Fine-grained modes -> good one-to-one matching
  - Distributed modes -> one PFM corresponding to multiple ICs

(b) Group-level: one-to-one vs. one-to-many matching



Farahibozorg et al., 2021

Interpretability of functional connectivity

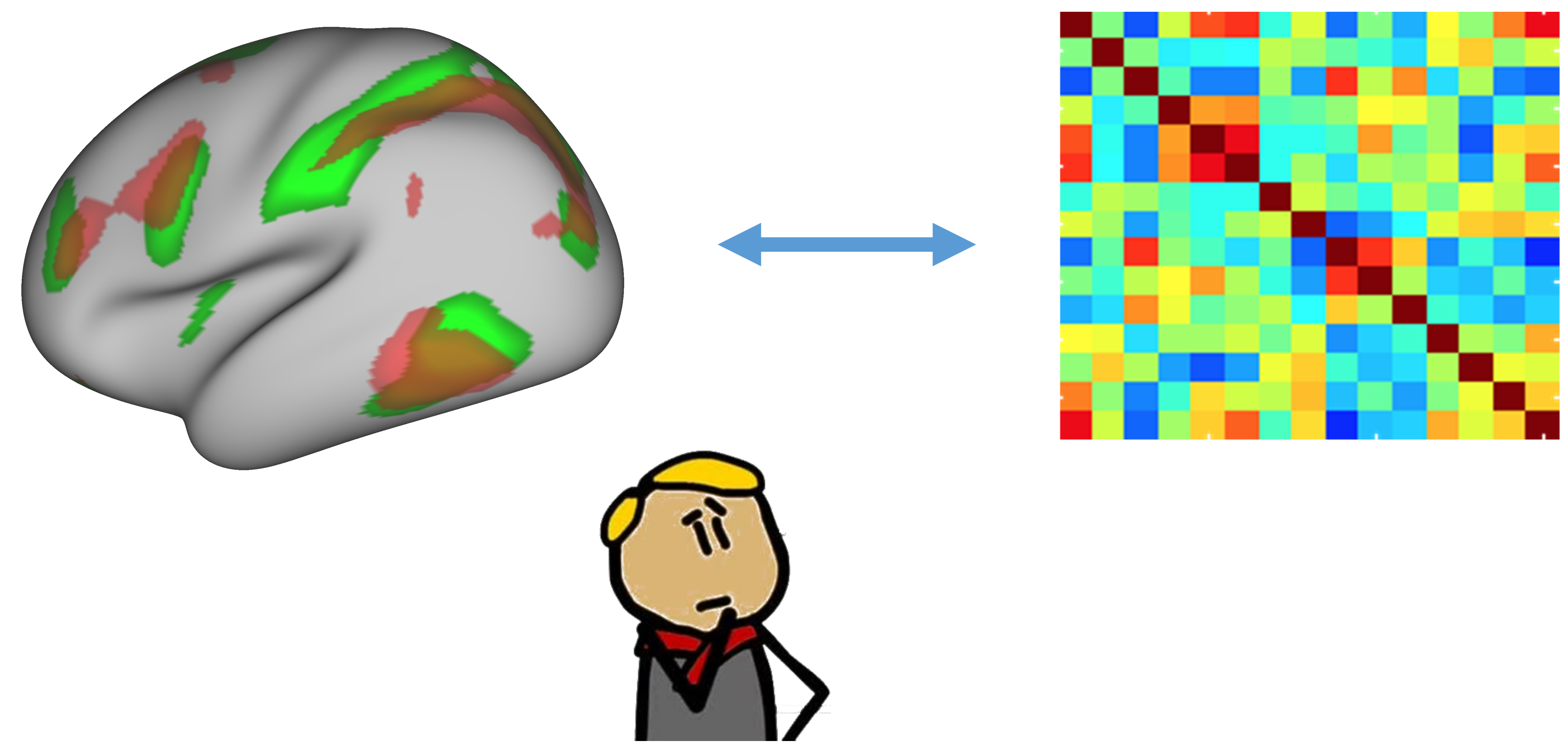
Spatial versus temporal variability in brain

Disentangling cross-subject variability in spatial versus temporal characteristics of the brain function can be very challenging

- Recent evidence shows that if spatial variations are not accurately accounted for, this can bias the estimation of functional connectivity (Bijsterbosch et al., 2018, 2019).
- This will have serious effects on the interpretability of functional mode modelling.
- Here we focus on two sources of spatio-temporal entanglement:

  a. Cross-subject spatial variability (misalignment);

  b. spatial mode overlap.



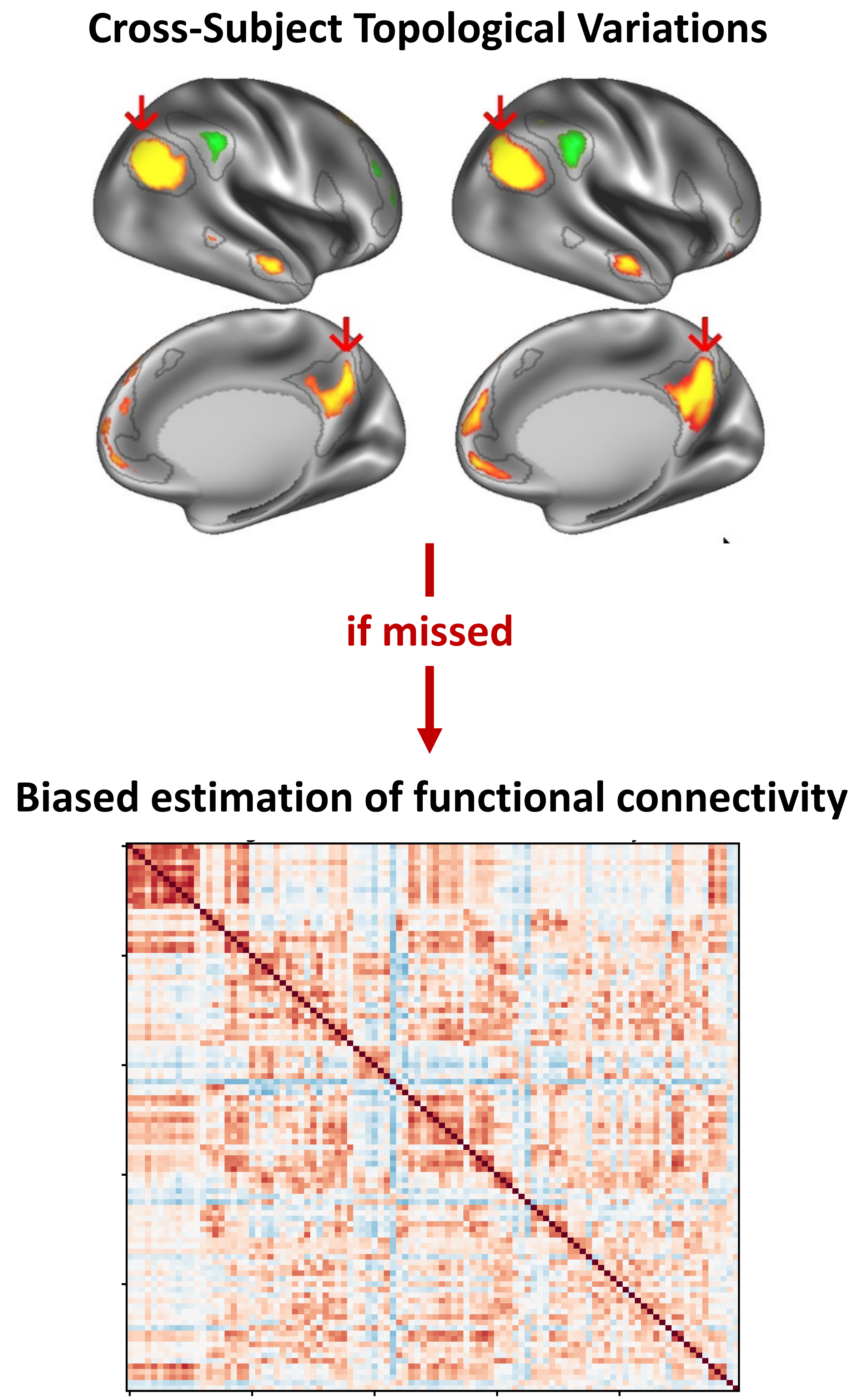
Cross-subject spatial variability (misalignment)

Functional connectivity estimation can be compromised if:

- Cross-subject topological variations are not accurately accounted for,
- A model might mix signals across multiple modes
- And mis-represent spatial variations as functional connectivity

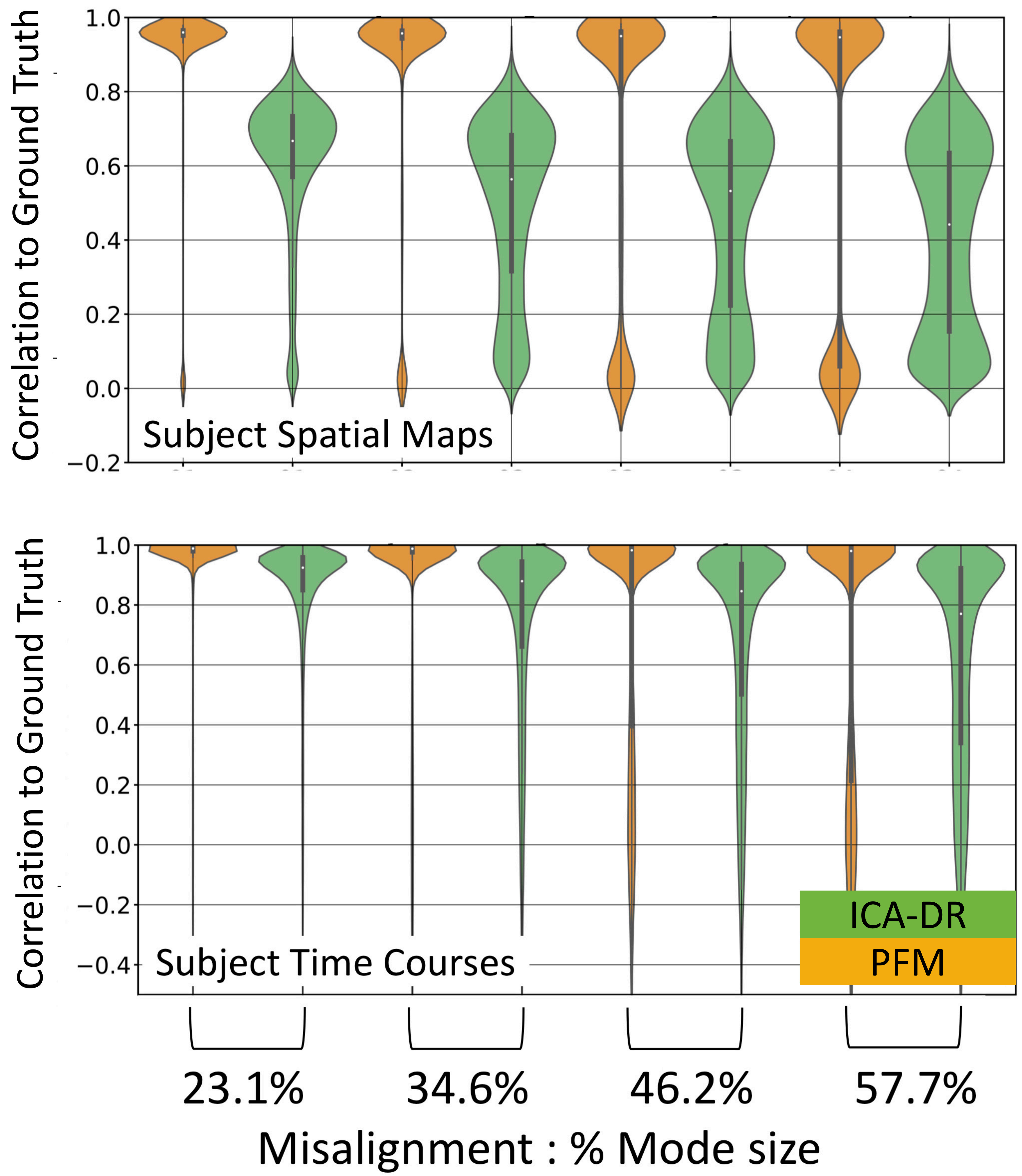
Two PFM features can help circumvent this problem

- Explicit subject modelling
- Bidirectional hierarchy

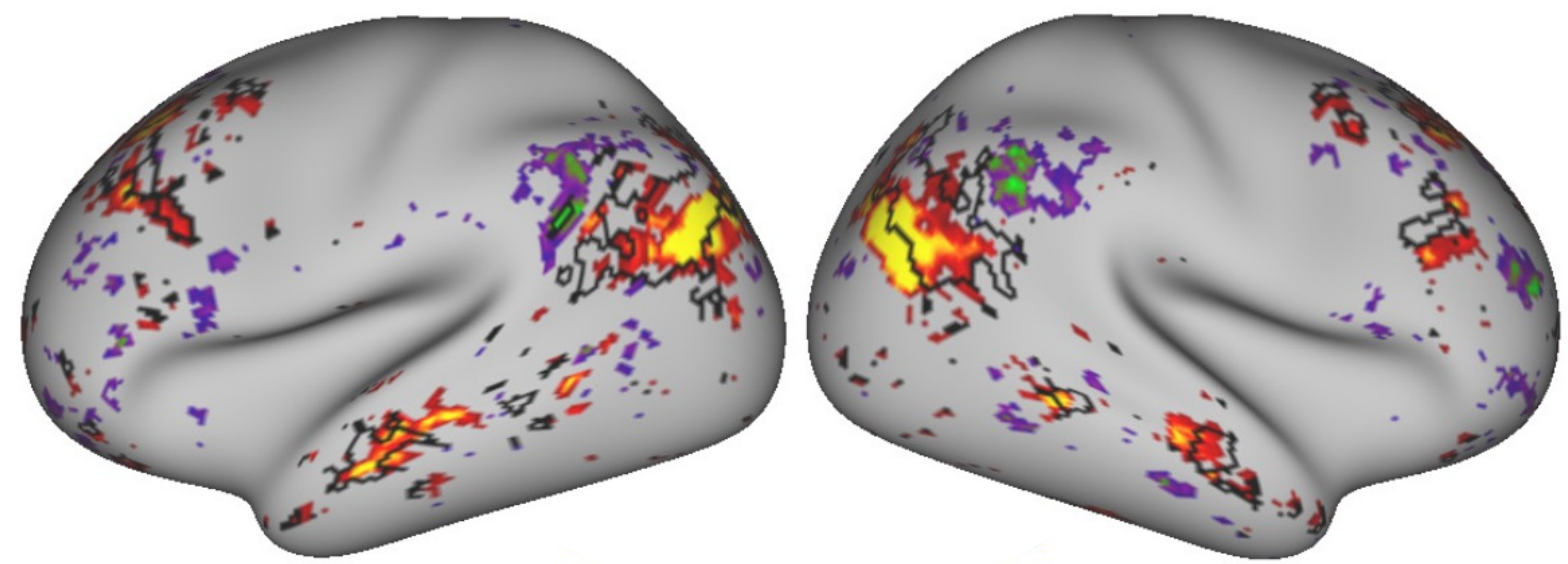


Based on Bijsterbosch et al., 2018

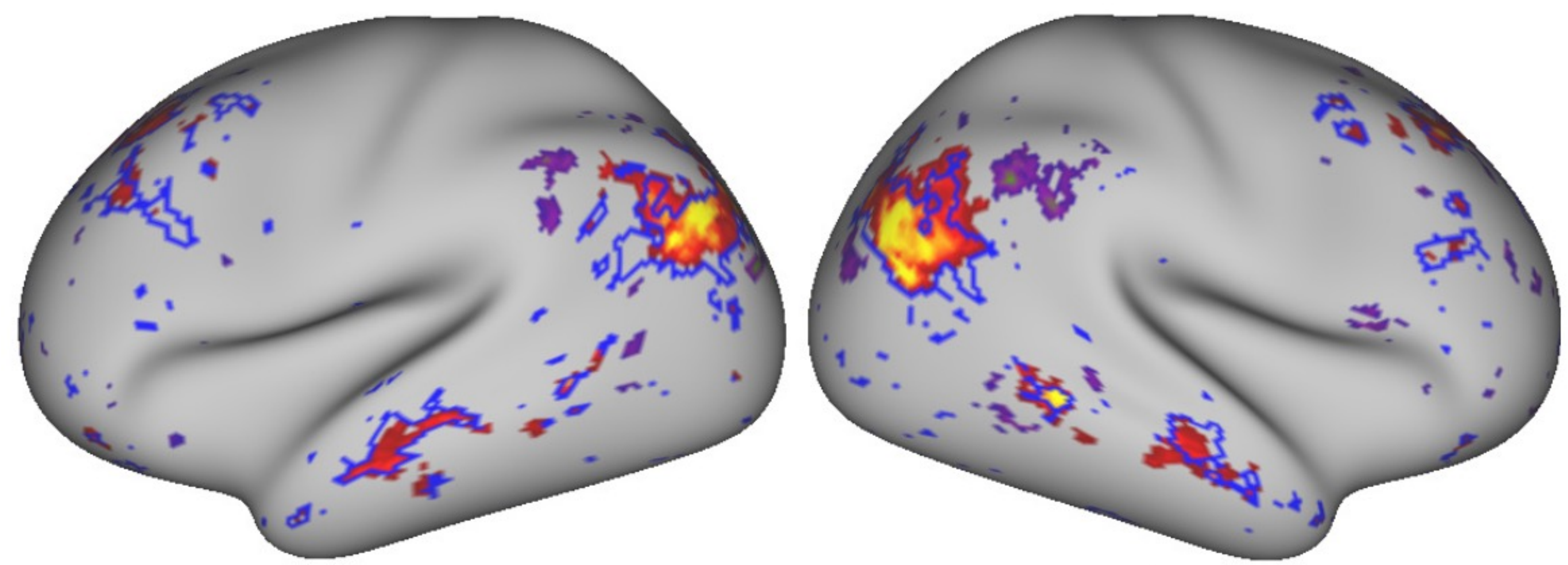
Comparing PFM and Dual Regression for different degrees of misalignment



Example of misalignment:



Ability of ICA-DR to handle this misalignment:



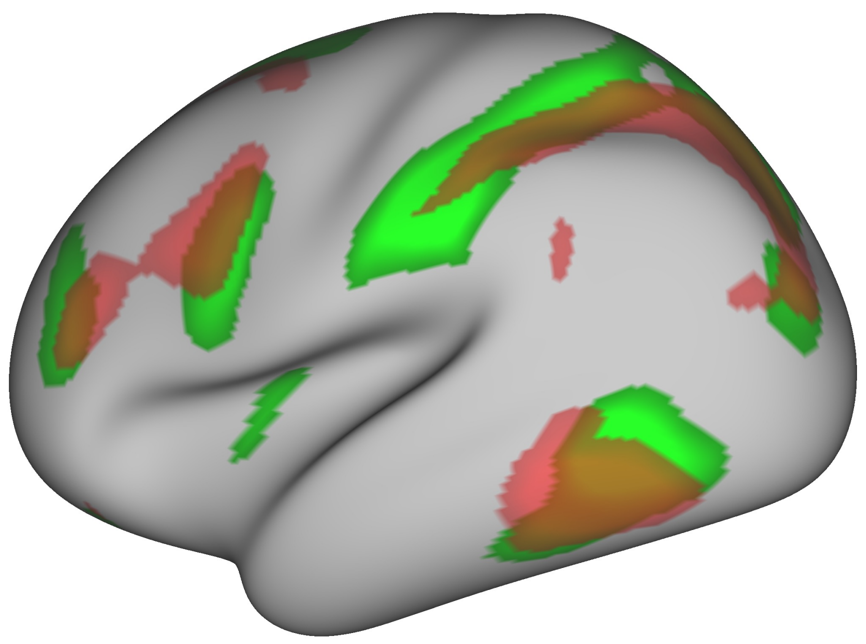
Based on Farahibozorg et al., 2021

Interpretability of functional connectivity: spatial overlap

Functional connectivity estimation can be compromised if:

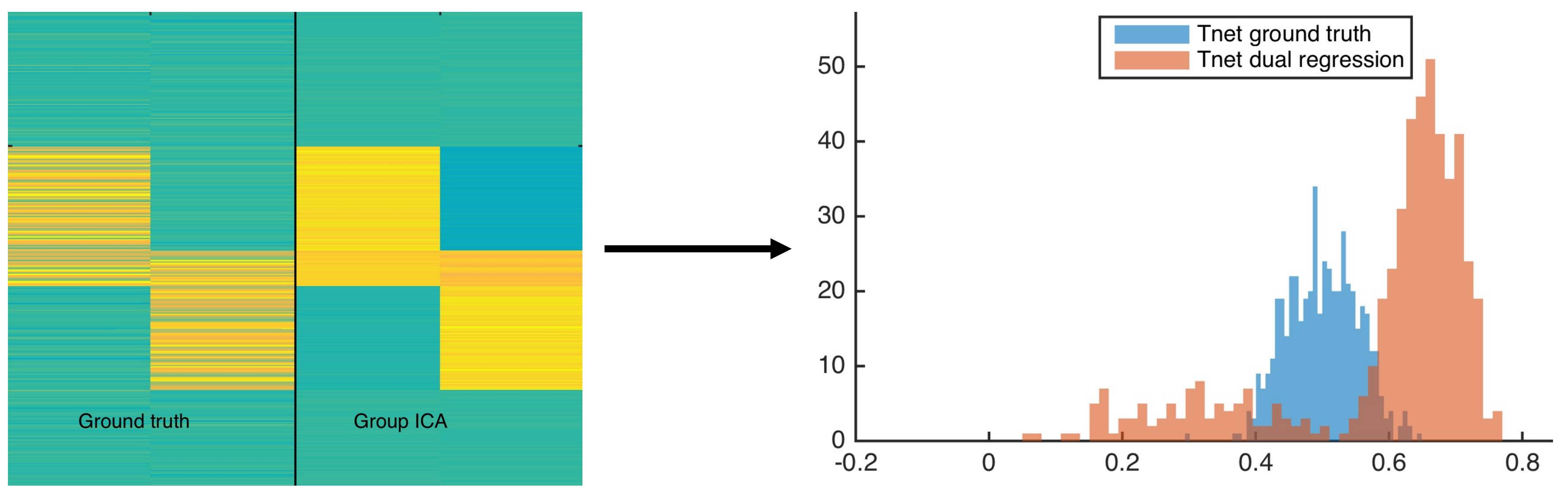
- Assumption of spatial mode independence results in failure to capture genuine mode overlaps
- This leads to a model mixing signals across multiple modes
- And mis-represent spatial correlations as functional correlations.

Cross-Subject Network Overlap



if missed

Biased estimation of functional connectivity

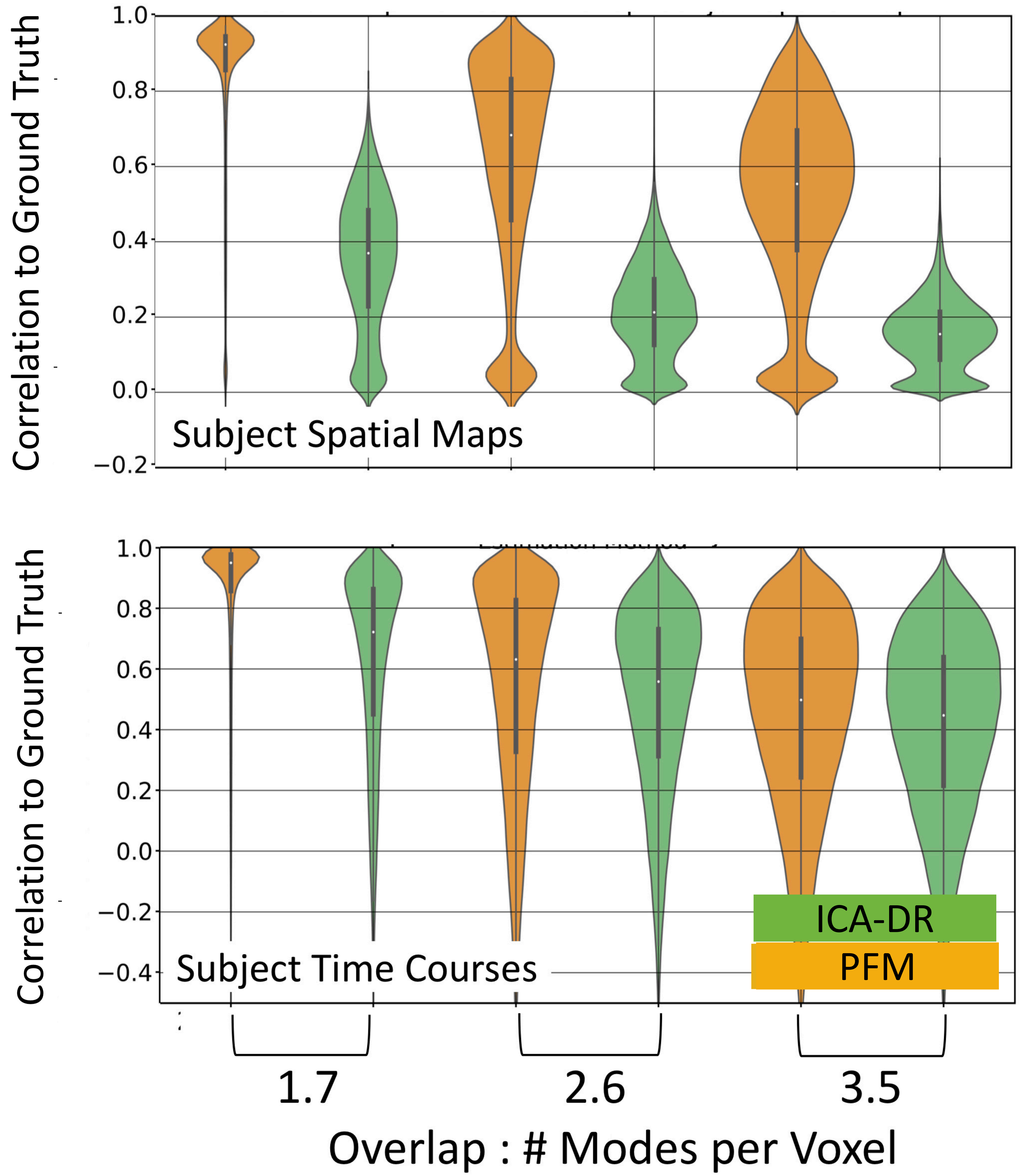


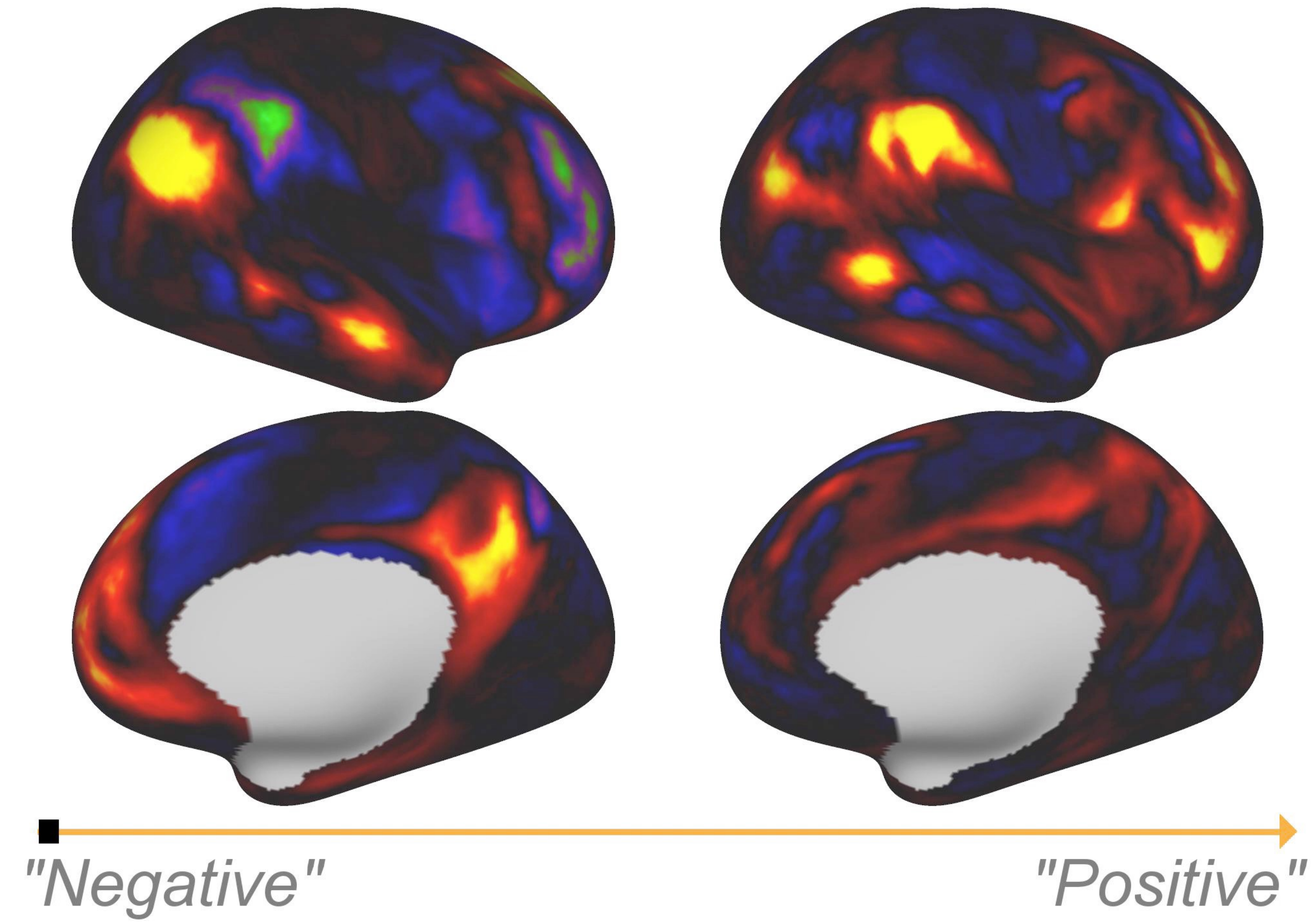
Based on Bijsterbosch et al., 2019

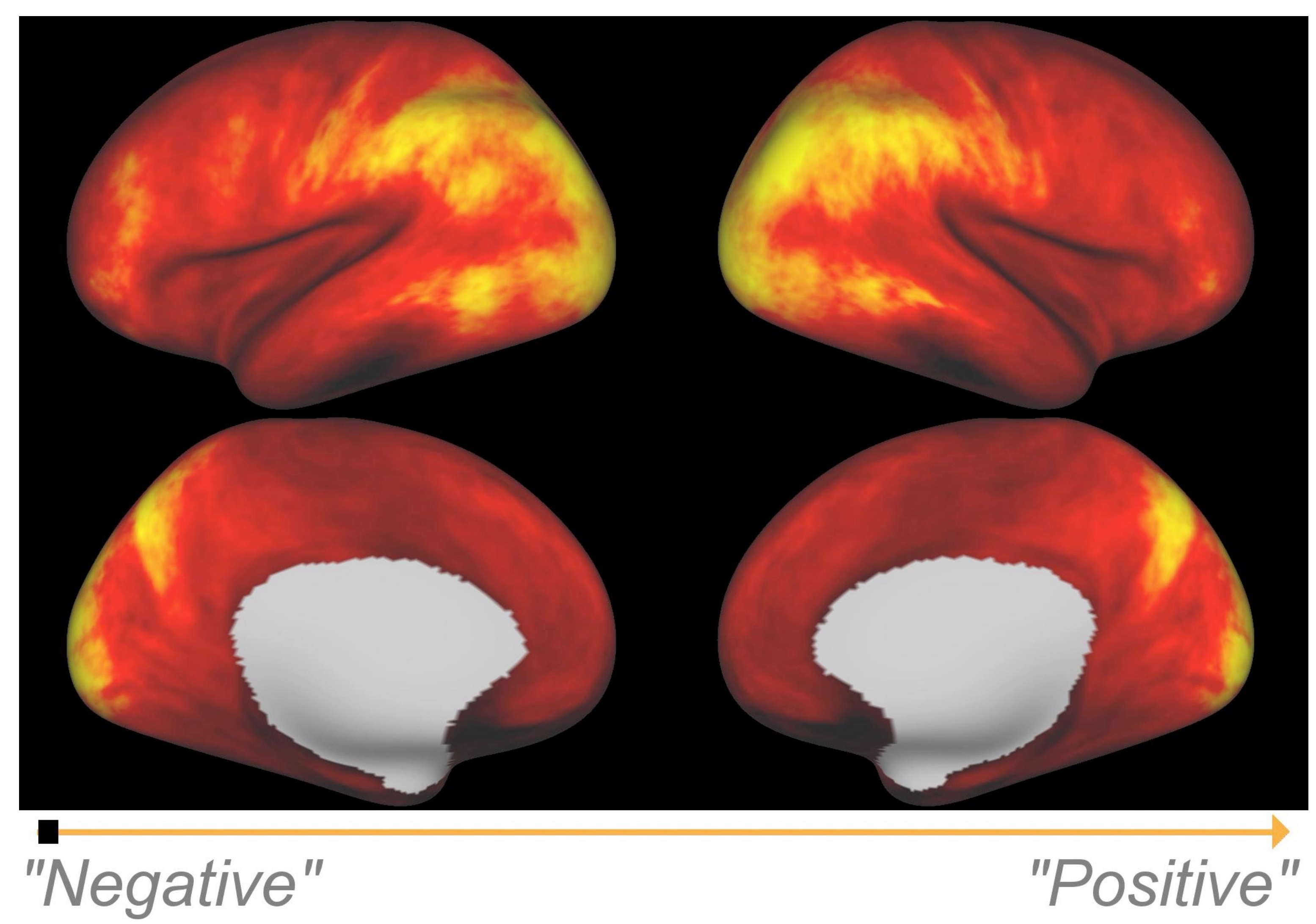
Two PFM features can help circumvent this problem

- Allowing spatial and/or temporal correlation between modes
- Defining hierarchy on both Spatial maps and Temporal NetMats

Comparing PFM and Dual Regression for different degrees of spatial overlap



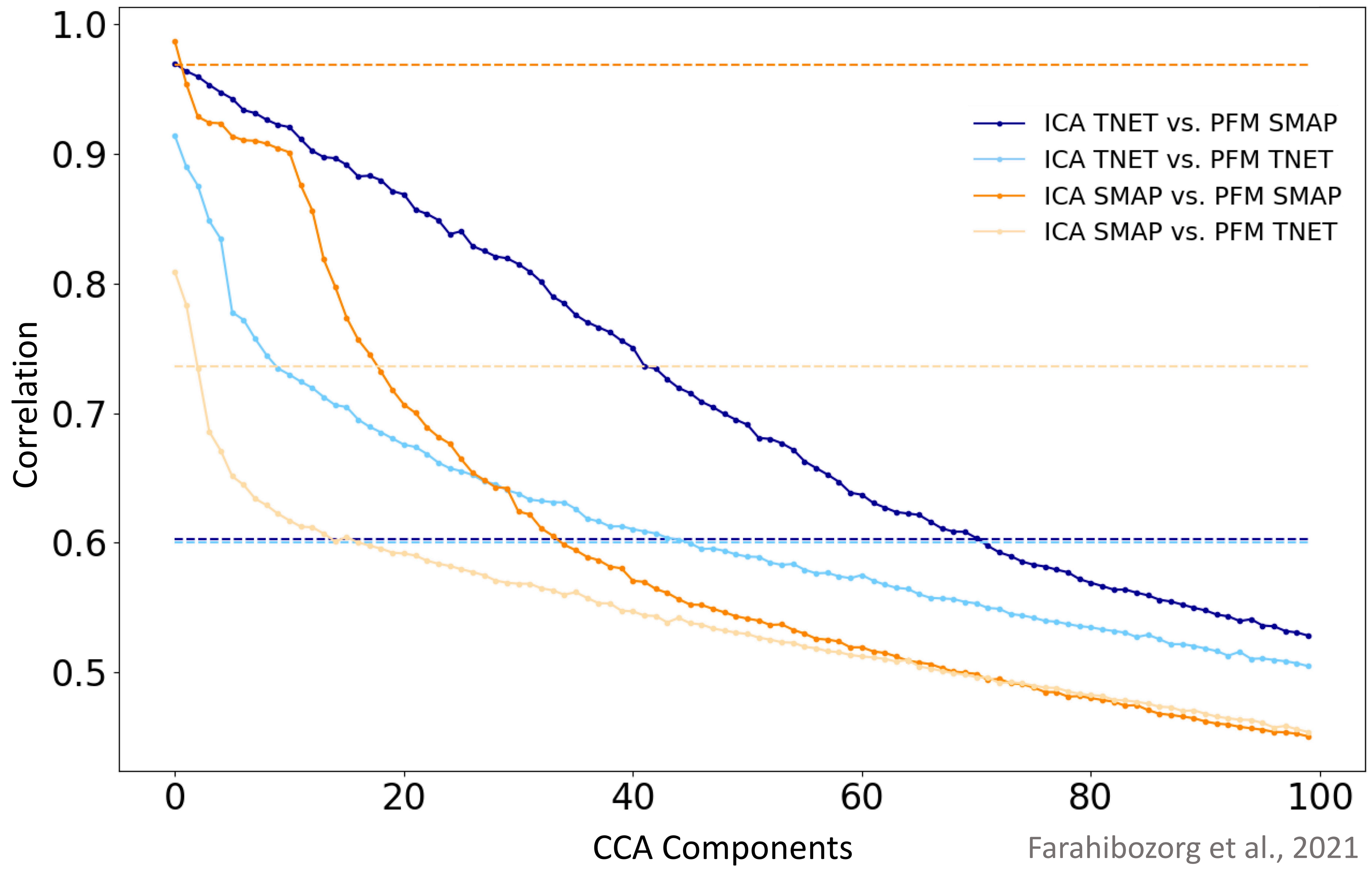




Based on Farahibozorg et al., 2021

Subject variability in spatial versus temporal domains

- Therefore, biased estimation of functional connectivity means that sources of subject variability that are **spatial** in nature, will be misrepresented as **temporal connectivity variations**.
    - To depict this, we can use Canonical Correlation Analysis (CCA) to measure **shared cross-subject variance** between
        - PFM spatial maps (SMAP) and ICA spatial maps and temporal NetMats (TNET)
        - PFM TNETs and ICA SMAPs and TNETs



Farahibozorg et al., 2021

- Therefore, what ICA-Dual Regression reflects predominantly onto TNETs, is shared between PFM SMAPs and TNETs.

Part 2 summary - In this lecture we learned that:

1. PFMs do not require the modes to be spatially and/or temporally independent.
   - Therefore, in practice, spatial and temporal NetMats end up somewhere between Spatial and Temporal ICA
2. Effect of dimensionality on PFM and spatial ICA are different
   - At lower dimensions (e.g. 25), there is a good overlap between group-level PFMs and MELODIC spatial maps
   - At higher dimensions:
     - Distributed ICA modes are split into multiple non-overlapping components;
     - Distributed PFMs are maintained and fine-grained modes are added.
3. Disentangling subject variability in spatial versus temporal brain function is challenging. Following PFM features address this challenge:
   - Explicit subject modelling
   - Bidirectional hierarchy
   - Allowing spatial and/or temporal correlation between modes
   - Defining hierarchy on both Spatial maps and Temporal NetMats

Thank you!