the framework of:

Probabilistic Functional Modes

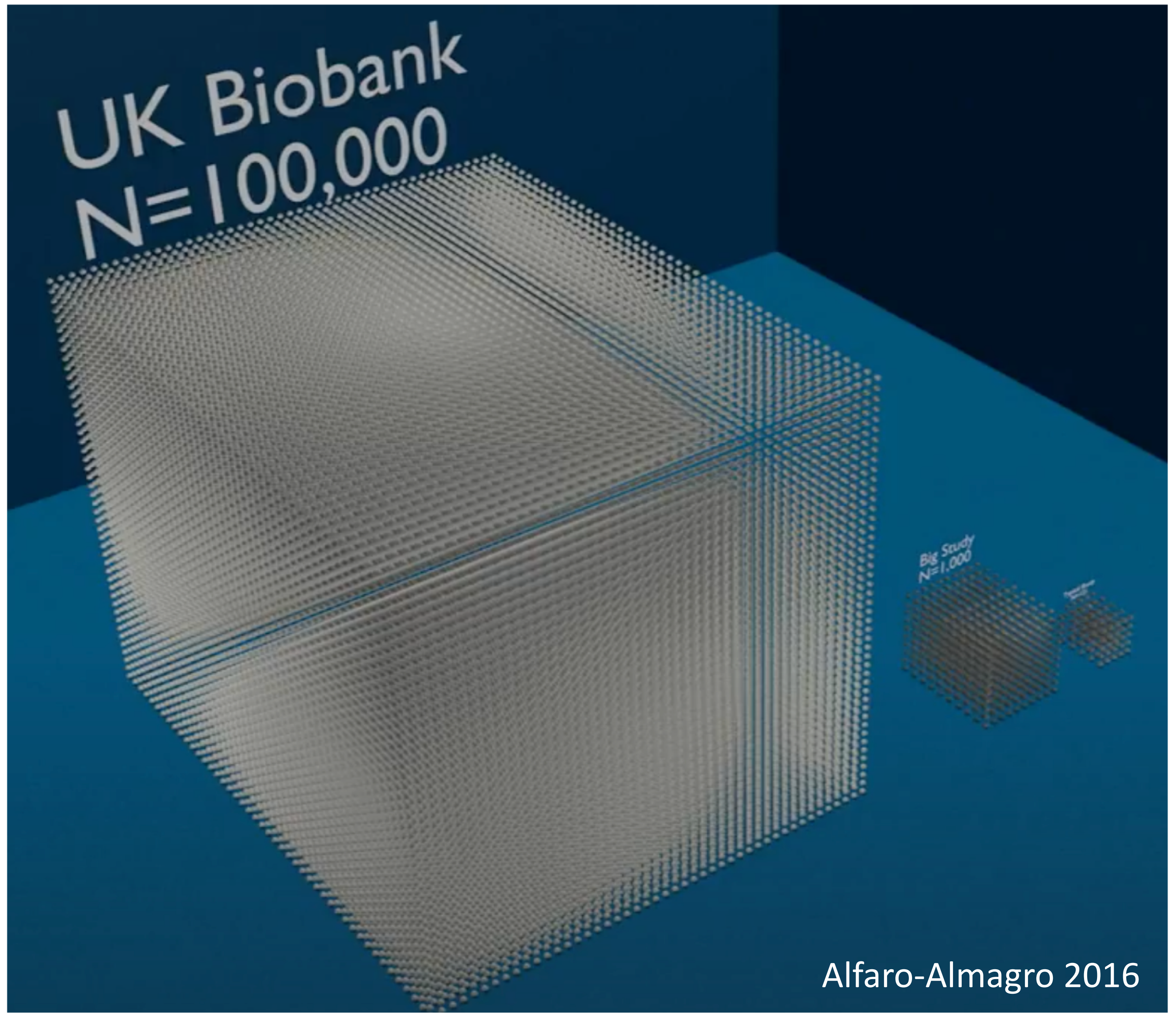
part 3

- 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

Functional brain network discovery from big data

- Big fMRI data such as UK Biobank, HCP, ABCD, etc. provide *population-scale* imaging:
  - Detailed mapping of the brain function and disorders beyond conventional Neuroimaging data;
  - Functional network/mode discovery in population and individuals.

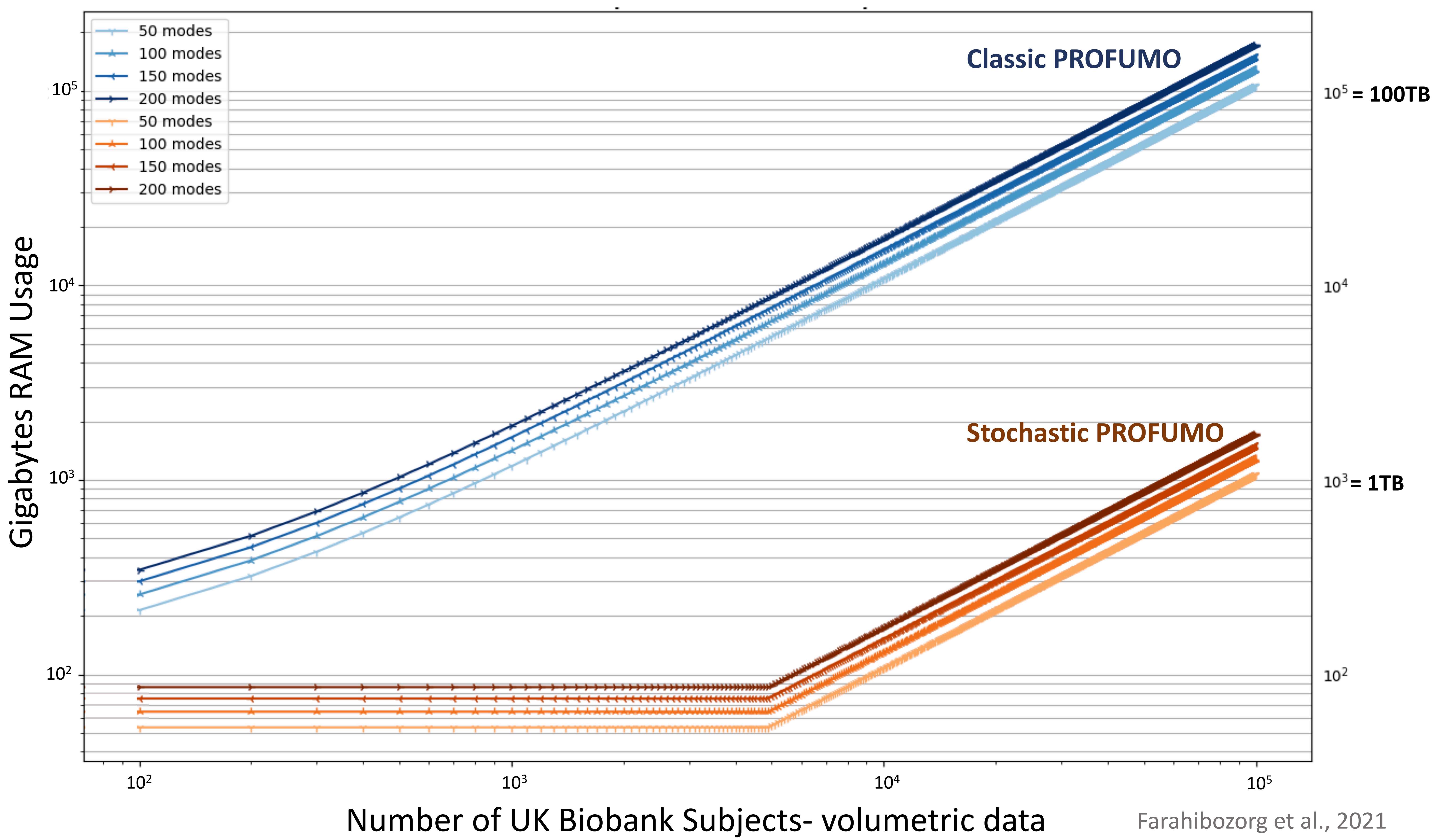
- Large populations are typically more heterogeneous:
  - A key usefulness of hierarchical functional mode modelling in PFMs can be to characterise these big heterogeneous populations.



Stochastic Probabilistic Functional Modes

for big data

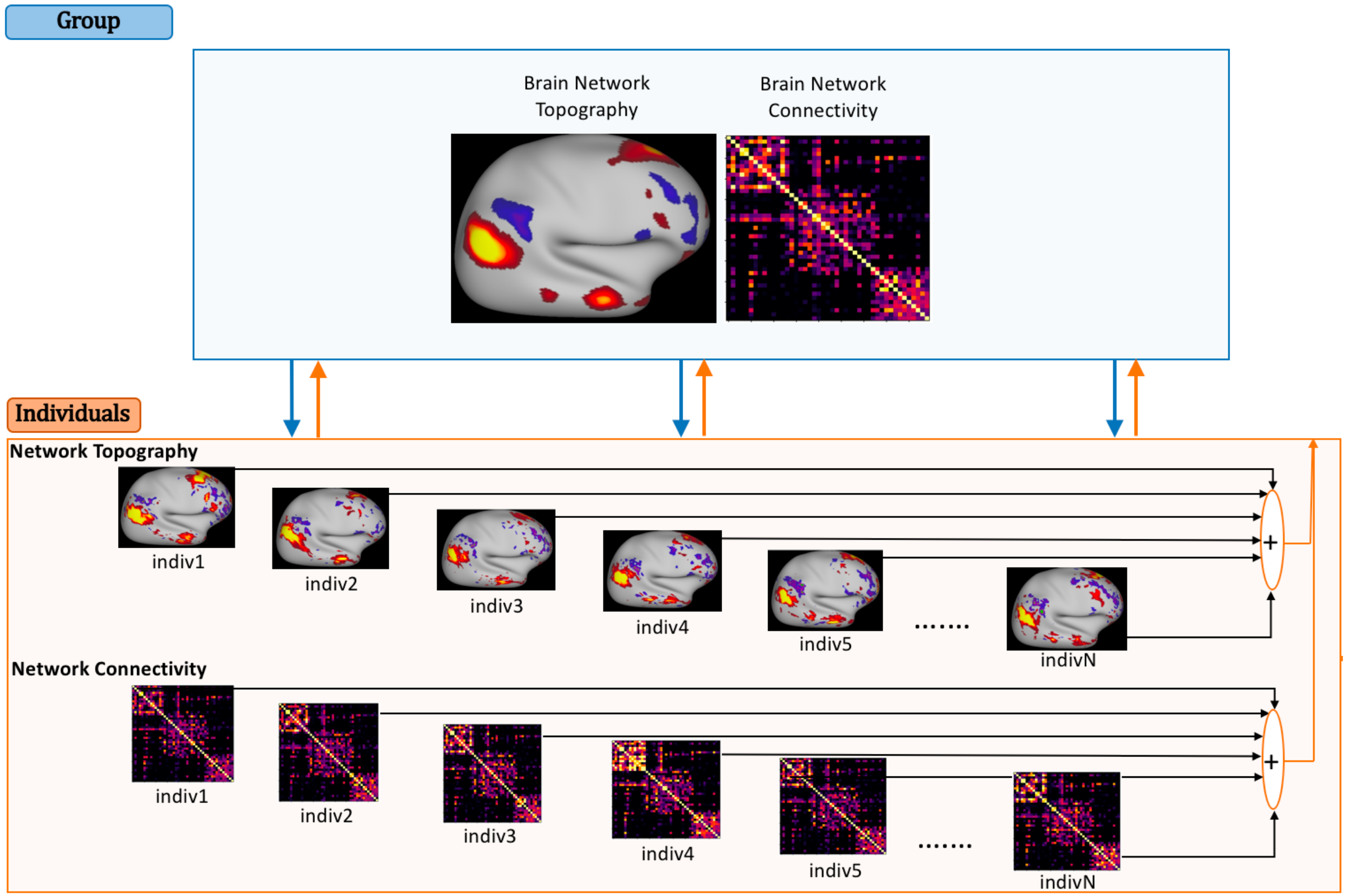
Computational demand of classic vs stochastic PROFUMO



Farahibozorg et al., 2021

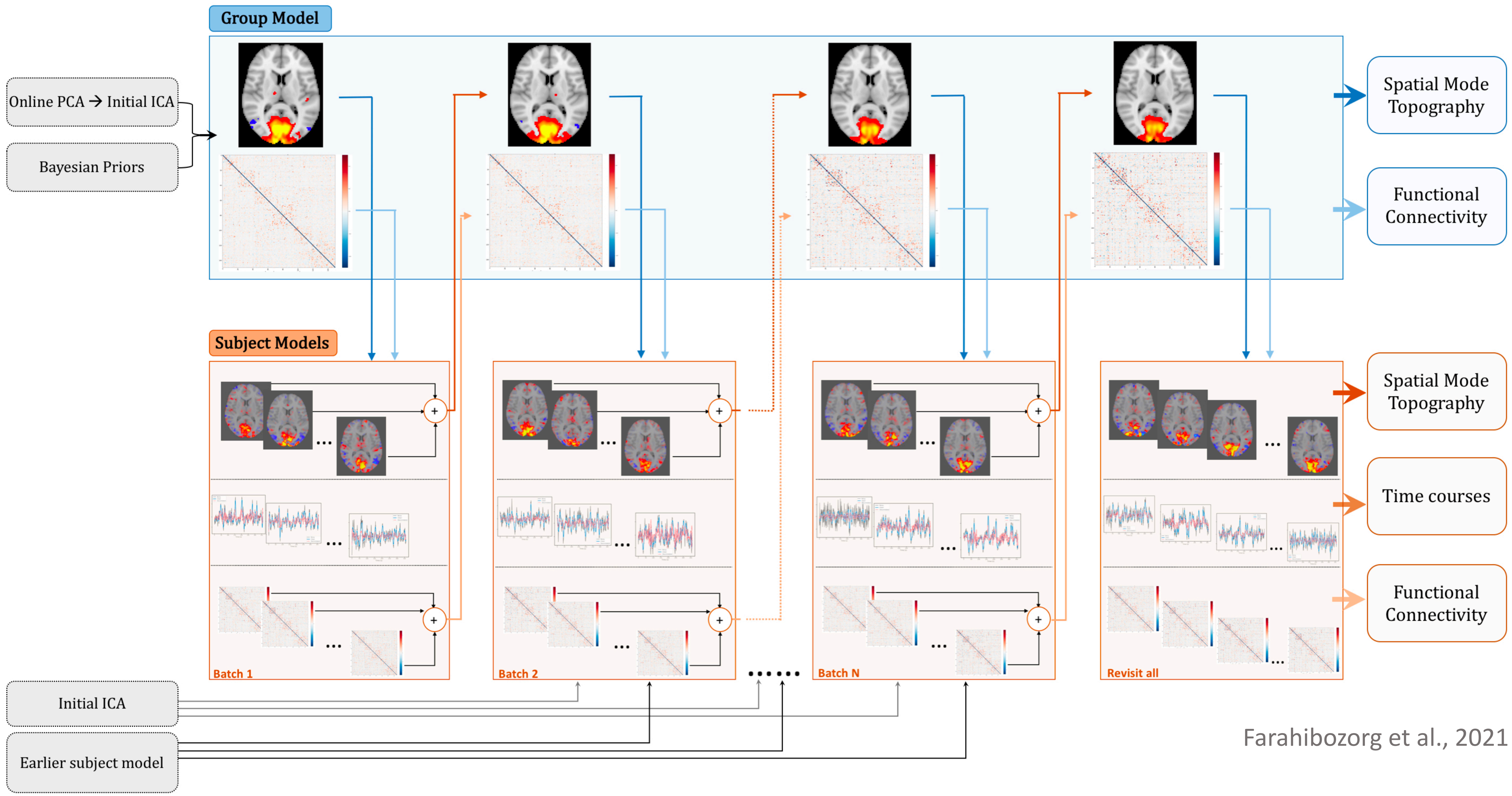
- Running classic PROFUMO on thousands of subjects, e.g. UK Biobank is computationally intractable.
- Stochastic PROFUMO recently proposed to resolve this issue.

Stochastic Probabilistic Functional Modes- *similarities* to classic PROFUMO



- Estimates functional brain networks for individuals from large populations
- Builds upon PROFUMO (Harrison 2020) and modifies the model to be able to characterise big populations e.g. UK Biobank (Farahibozorg 2021):
  - Simultaneous and hierarchical modelling of the population and every subject
  - Builds Bayesian hierarchies on spatial maps and functional connectivity (temporal NetMats)

Stochastic Probabilistic Functional Modes- *differences* to classic PROFUMO



Farahibozorg et al., 2021

- Visits only a small subset of population in each model update iteration
  - A group model that is representative of the entire population
  - Subjects that are aligned with the group regardless of when they have been visited
  - Convergence obtained for both the group and the individuals
- Uses stochastic variational Bayesian inference
- Can be expected to accommodate more population heterogeneity

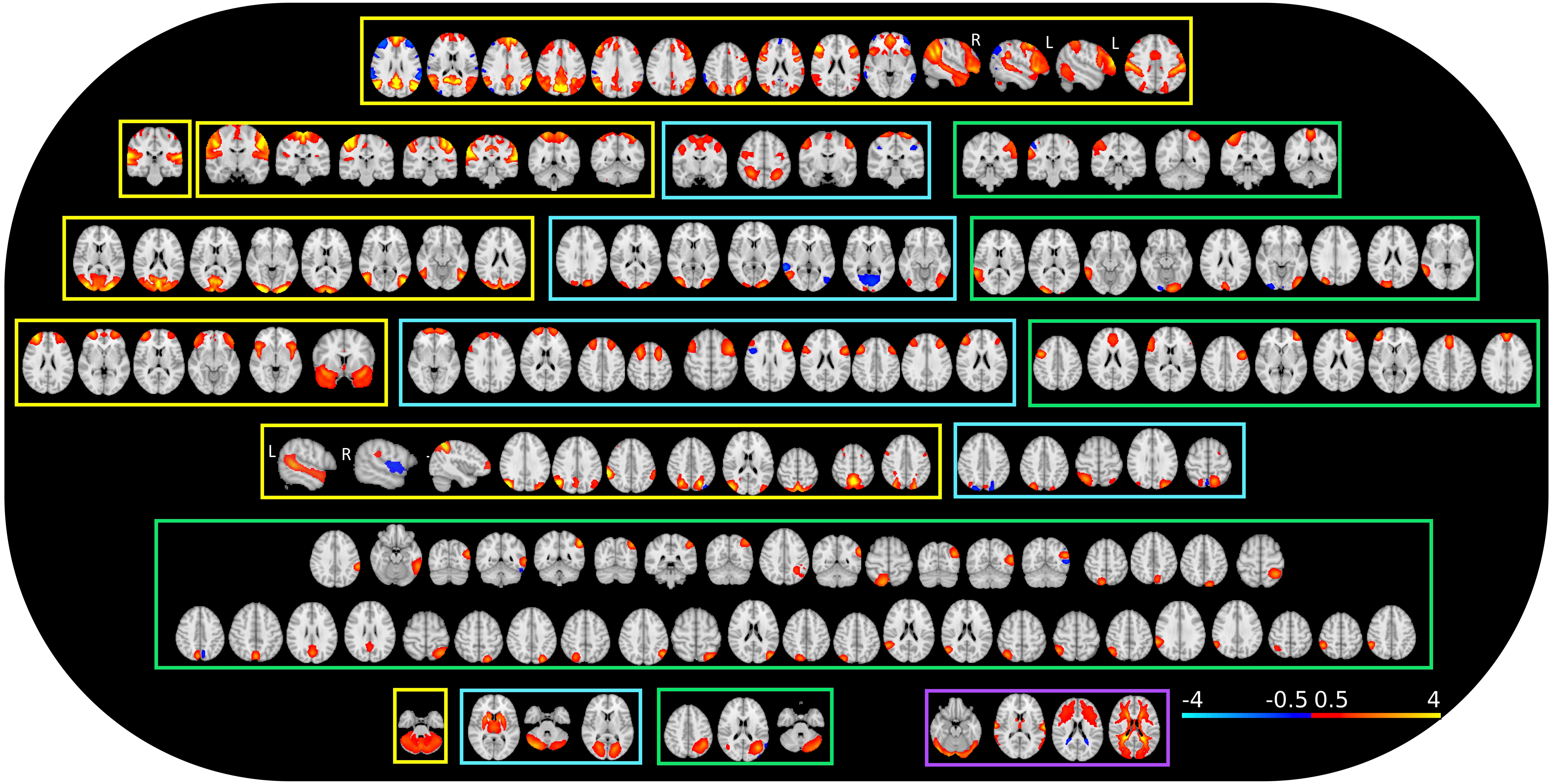
Some applications of PFMs to date

- Detailed mapping of brain function using big fMRI data
- Predicting cognitive outcome based on individualised functional modes
- Predicting a person’s brain response to task based on resting state networks

Detailed mapping of the brain function

by applying PFMs to big data

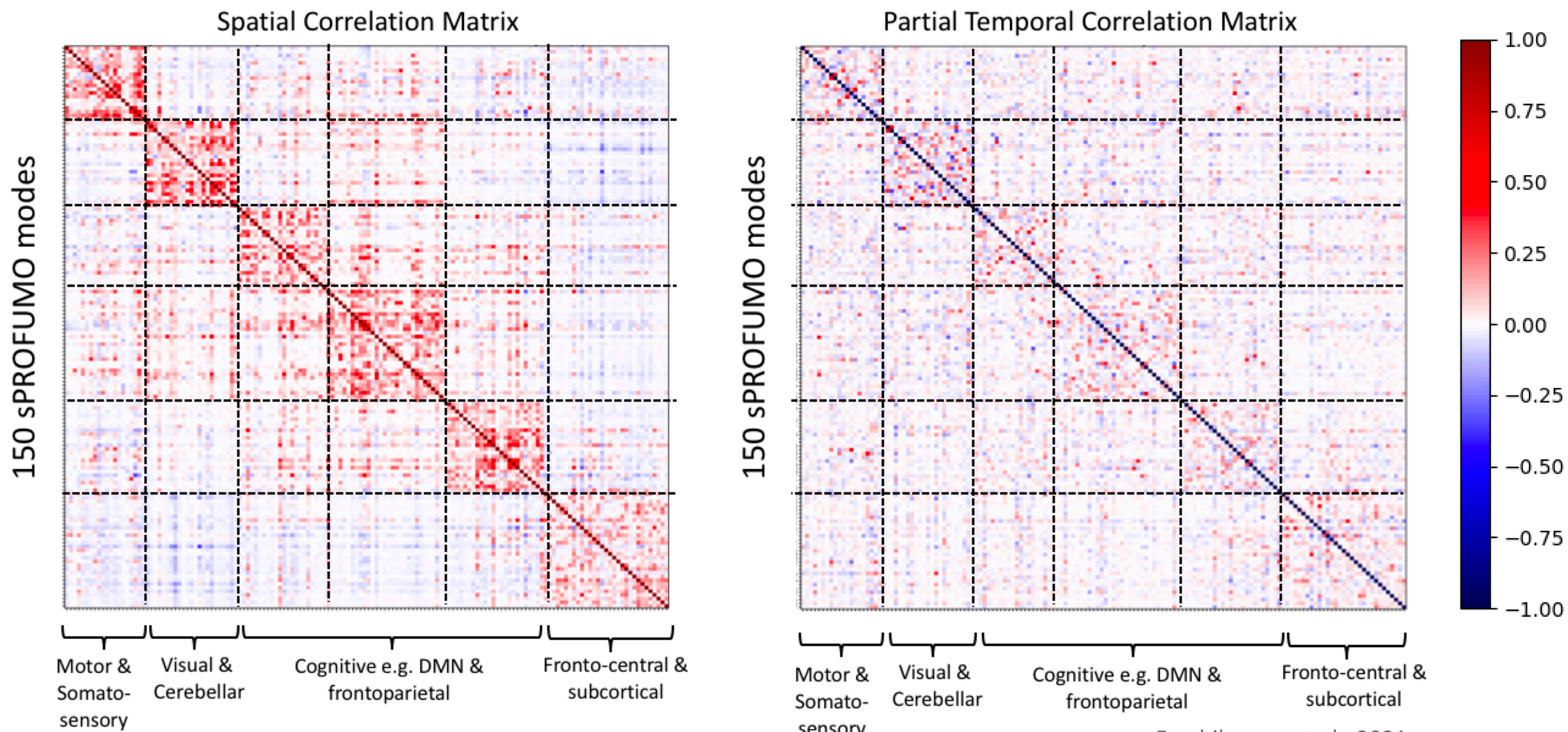
150 PFMs based on 5000 UK Biobank subjects



Farahibozorg et al., 2021

- 150 PFMs reconstructed based on 5000 UK Biobank subjects
- Provides a high dimensional soft functional parcellation of the brain
- Three categories of RSNs: high-SNR (yellow) and low-SNR (blue) large-scale RSNs, and parcel-like RSNs (green):
  - Category 1 (yellow) found at lower dimensions, categories 2&3 added as we increase dimensionality

NetMats: Spatial and Temporal correlations between 150 PFMs



Farahibozorg et al., 2021

- The spatial NetMats cluster into 6 distinct clusters of modes.
- Modes within each cluster are also more temporally correlated, but temporal NetMats are generally sparser
- While no restriction on spatial vs temporal independence, behaviour closer to temporal ICA

Predicting cognitive outcome using PFMs

Functional modes can be used to predict individualistic traits

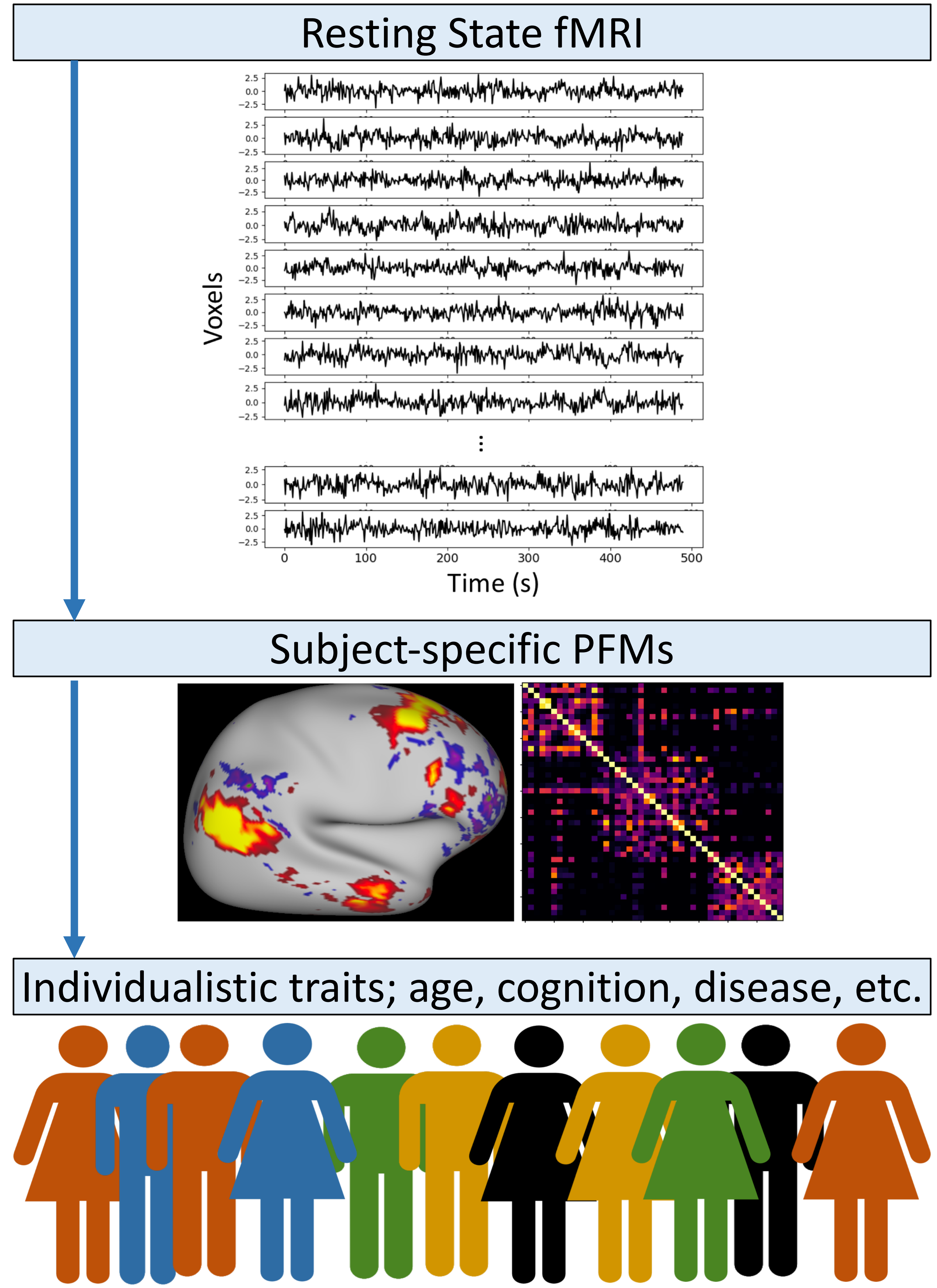
To predict cross-individual trait variability from mode variability we can:

1. Summarise model elements
   i. Spatial configuration (spatial maps);
   ii. Spatial overlaps (spatial NetMats);
   iii. Temporal connectivity (temporal NetMats);

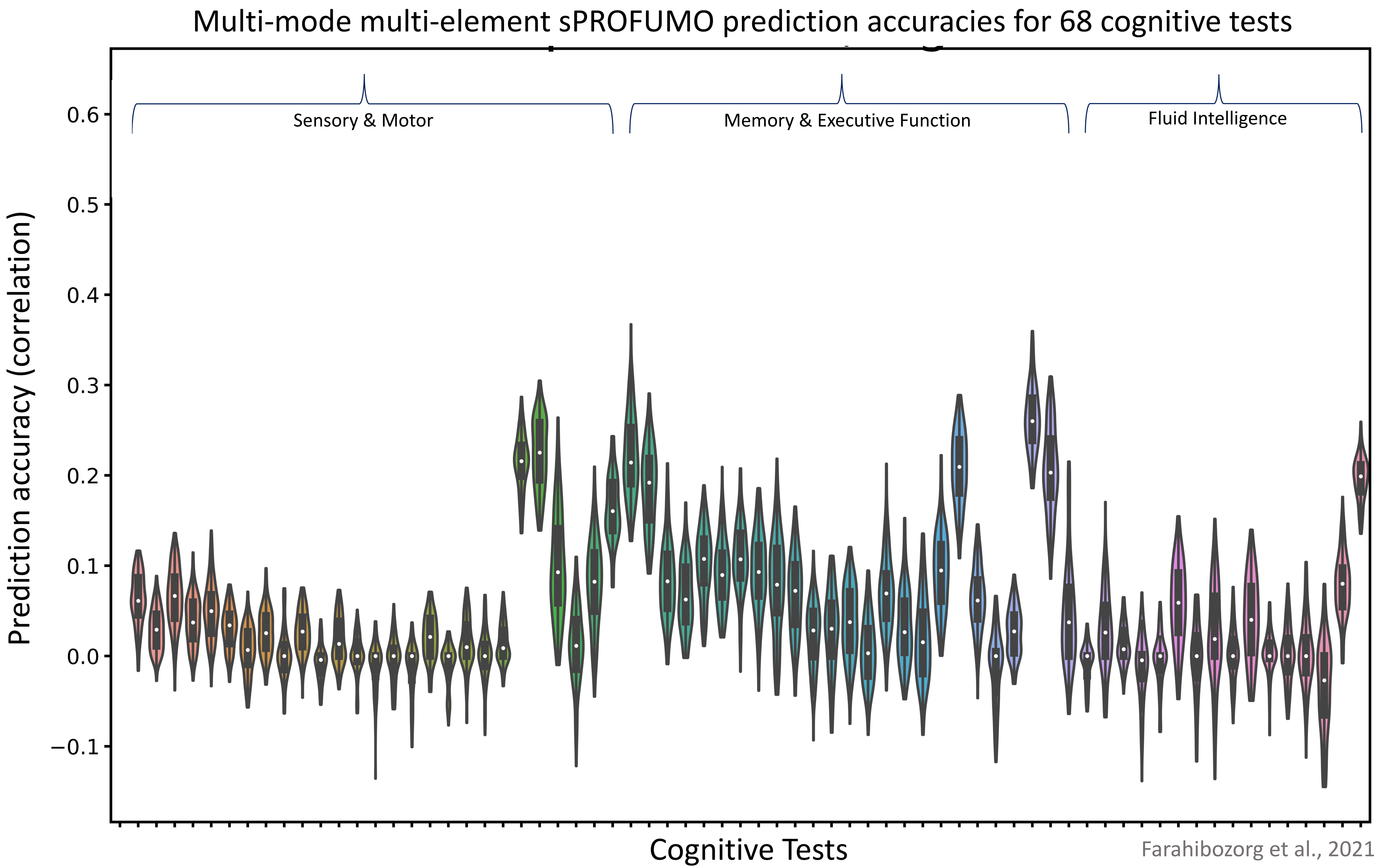
2. Use traits (e.g. cognitive scores) from UK Biobank as targets
   - For example, how well a person performed memory function, reaction time or executive function tests

3. Use Elastic net regression with cross-validation to predict cognitive scores based on PFM variations
   - Identify best-predicting PFMs

4. Compare PFMs performance to ICA-Dual Regression

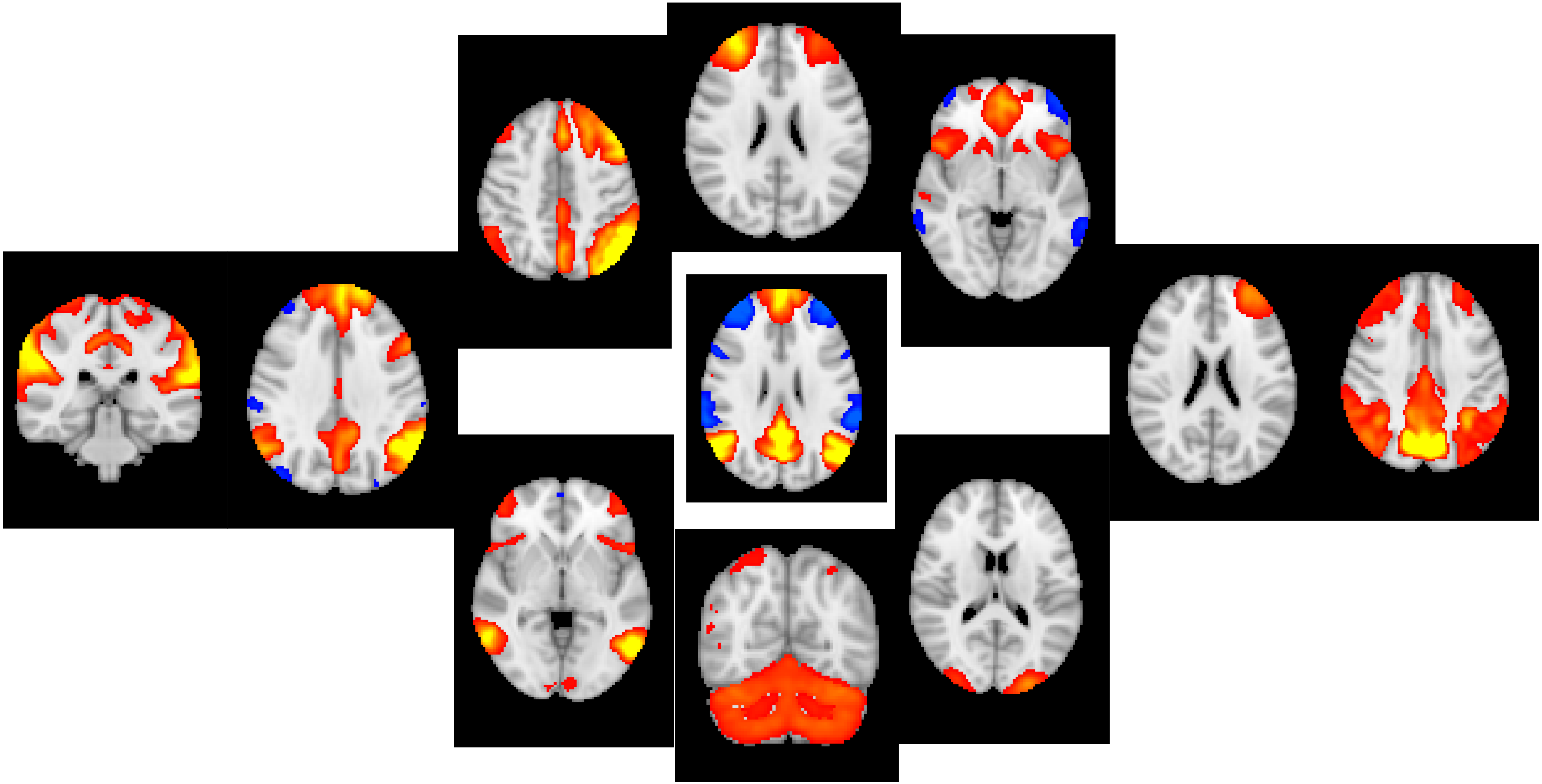


Predicting cognitive scores based on PFMs



Farahibozorg et al., 2021

Top PFMs predictive of cognitive function

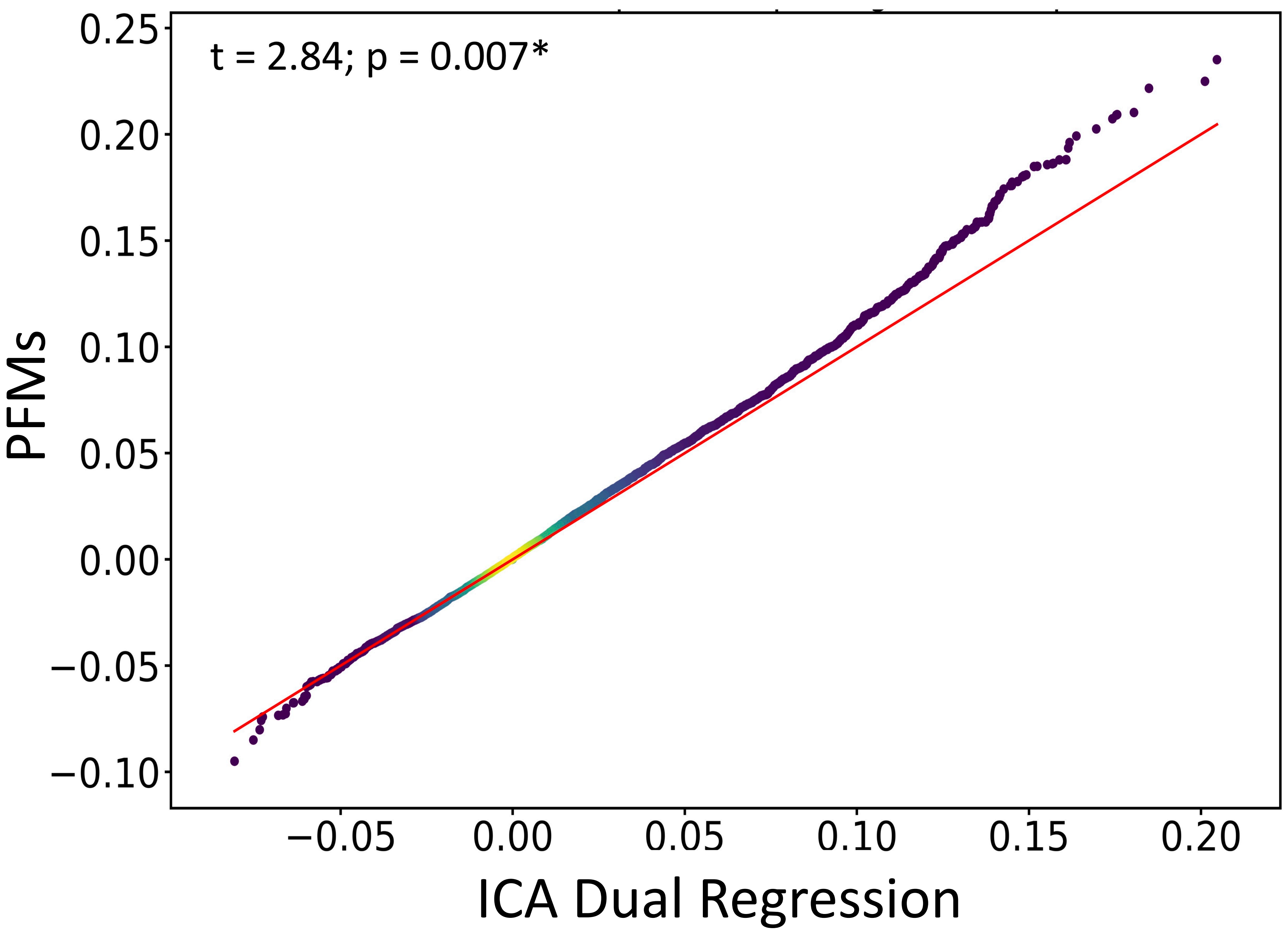


Comparison of PFM and ICA-Dual Regression predictions

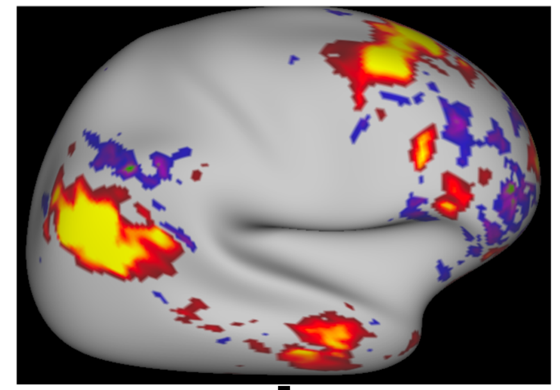
PFM vs. ICA-Dual Regression for predicting phenotypes

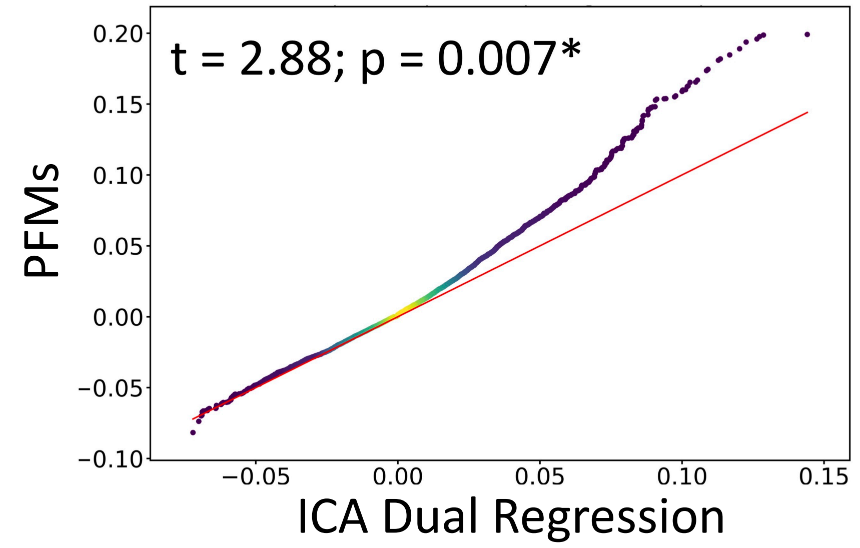
(1) Full network

predict cognitive score

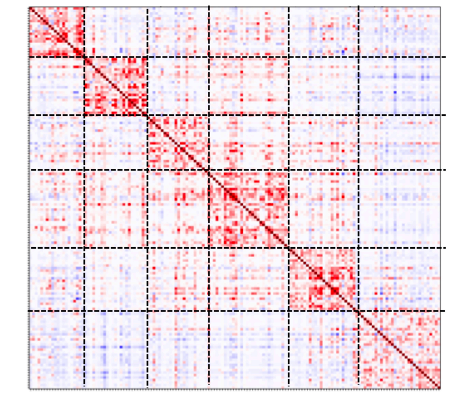


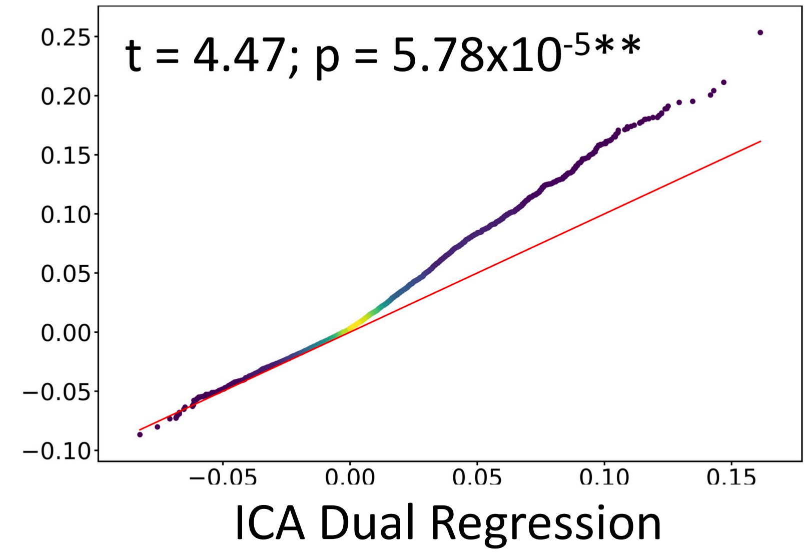
(2) Spatial Maps



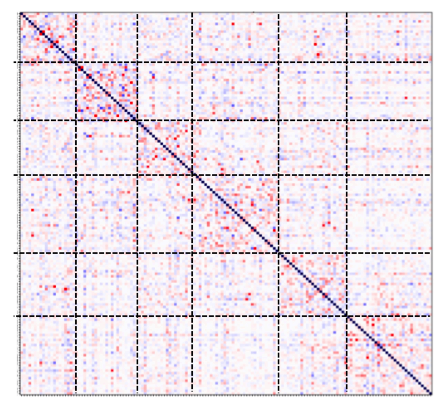


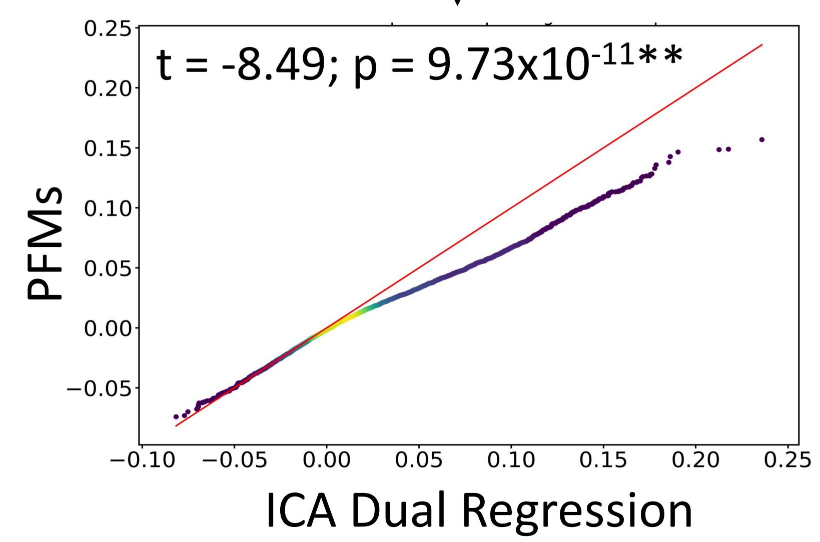
(3) Spatial NetMat





(4) Temporal NetMat





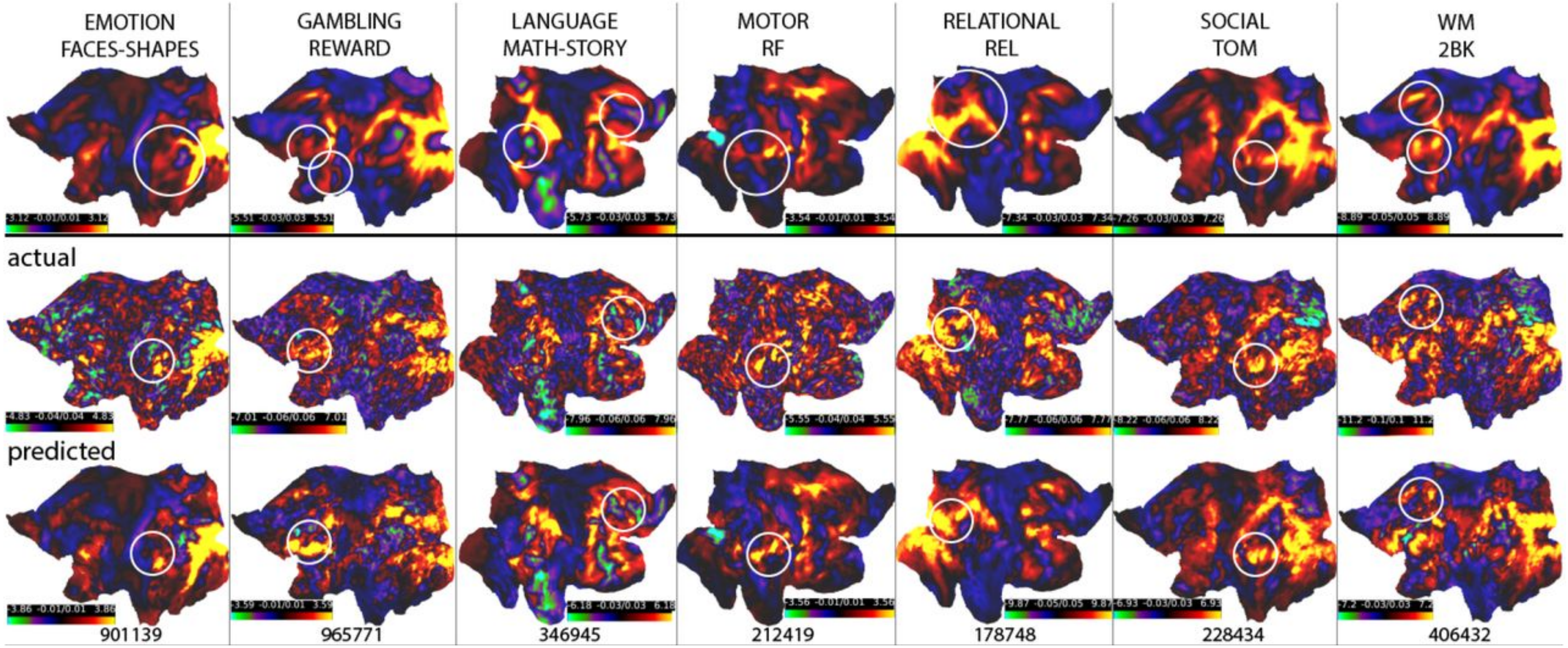
- This is related to what we learned in PFM lecture 2: Entanglement of spatial and temporal variations affects interpretability of functional connectivity

Based on Farahibozorg et al., 2021

Predicting brain response to different tasks based on resting state PFMs

Resting-state PFMs to predict task-induced activity

- Each person's brain responds uniquely to a cognitive task, e.g. emotion processing, working memory tests or listening to stories;
- Individualistic resting state modes have been shown to be able to predict these unique task responses (Tavor et al., 2016);
- Zheng et al. (2021), recently showed that, compared with standard techniques, PFMs improve our ability to predict task response from resting state networks.



Zheng et al., 2021

Part 3 summary - In this lecture we learned that:

1. The most recent version of PFMs, stochastic Probabilistic Functional Modes has been proposed to enable us to obtain individualistic brain function mapping for tens of thousands of individuals in big data populations
   - This enables us to realise the potential of the PFM framework for modelling population heterogeneity

2. Based on stochastic PFMs, high-dimensional PFMs were reconstructed based on resting state fMRI
   - These are divided into three categories of RSNs

3. These high-dimensional PFMs can improve our ability to predict individualistic traits; e.g. cognition and behaviour, or unique response of each person’s brain to cognitive tasks.

Thank you!