Probabilistic Functional Modes (PROFUMO): Modelling brain networks in populations and individuals

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FSL Course

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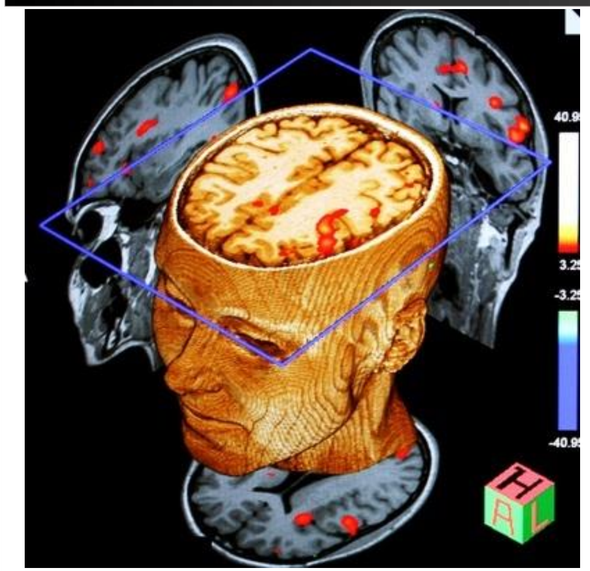
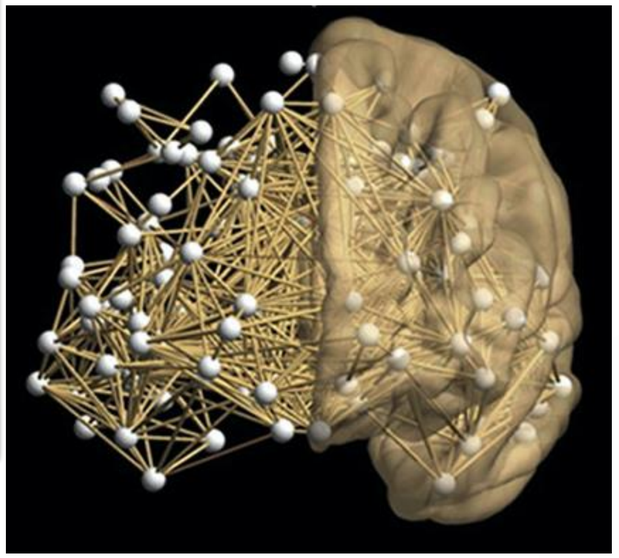
Aim: Population-Informed Personalised Brain Mapping

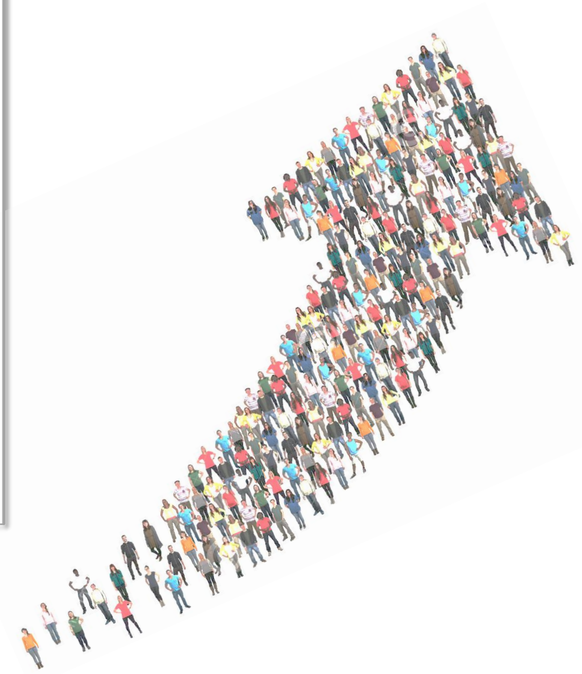
Non-Invasive Functional Brain Imaging



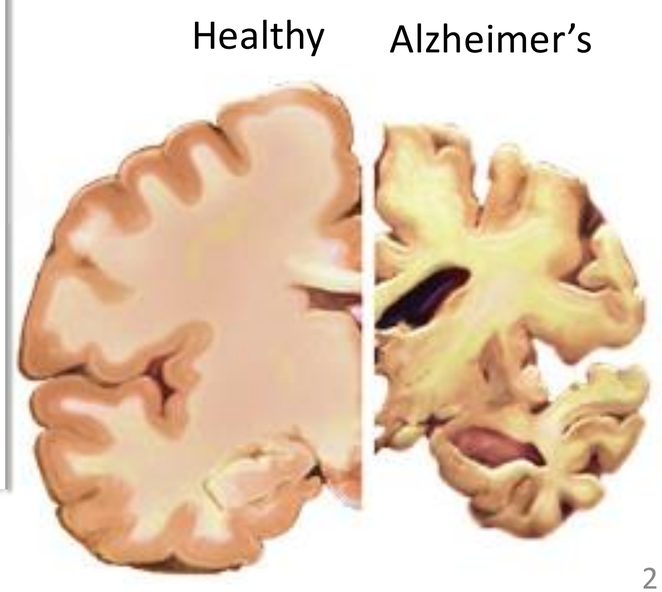
Network Modelling



Cross-Individual Variability



Personalised Disease Prediction



Outline

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   - Modes of the brain function
   - Group-average vs subject-specific modelling
   - Probabilistic Functional Modes

2. Model properties and outputs of PROFUMO
   - How does the model work?
   - What are the key outputs?

3. Example applications to big data
   - Characterising multiscale brain modes and predicting phenotypes
   - Characterising subgroups

4. Model Variants and Software

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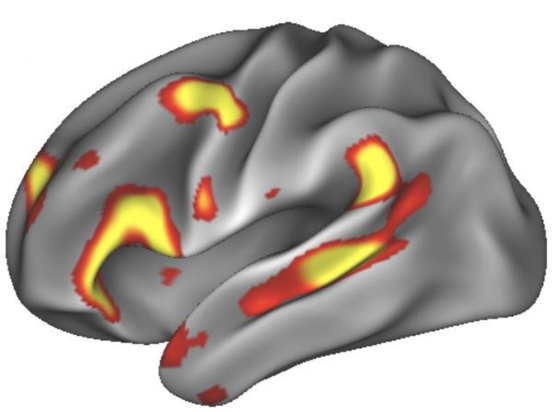
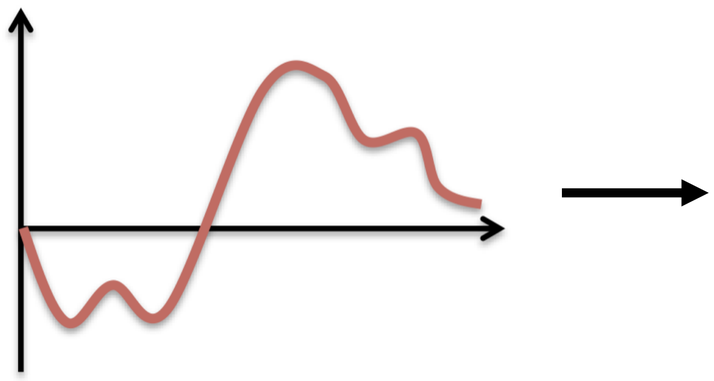
Background

Modes of brain function

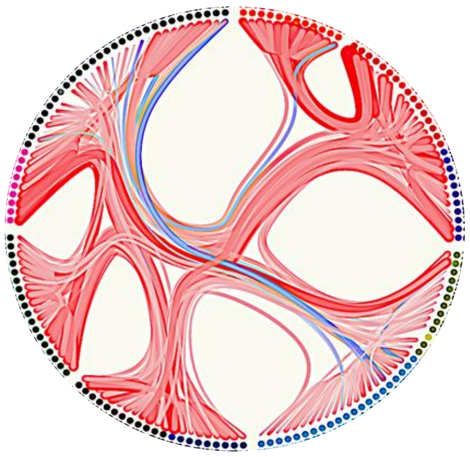
Spatial Configuration
(Topography)



Time Courses



Temporal Correlation
(Functional Connectivity)

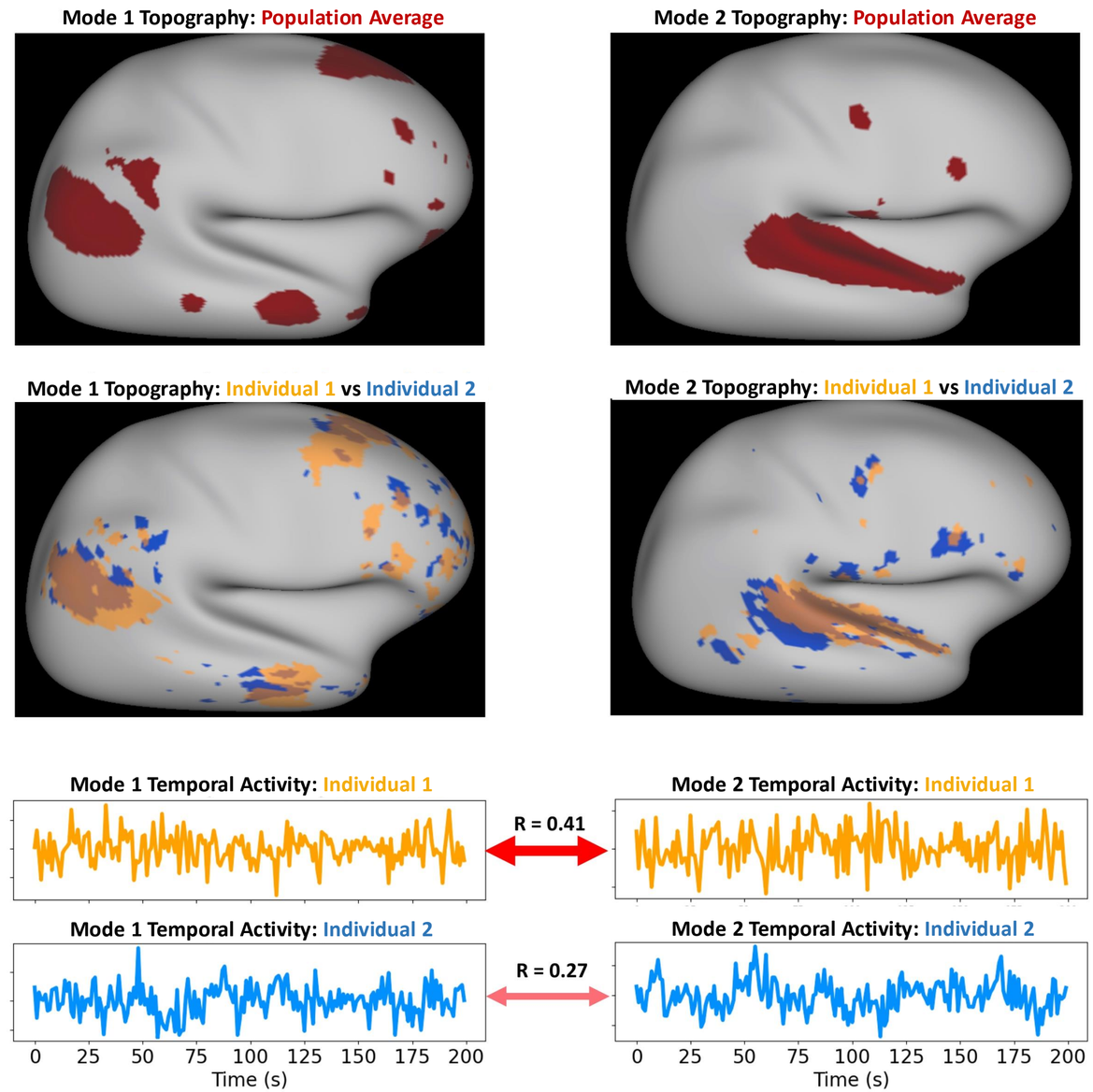


- Functional mode -> a set of brain regions that share a common time course.
- Can be estimated from resting-state data (i.e., resting-state networks or RSNs) or task data.

Functional modes vary across individuals

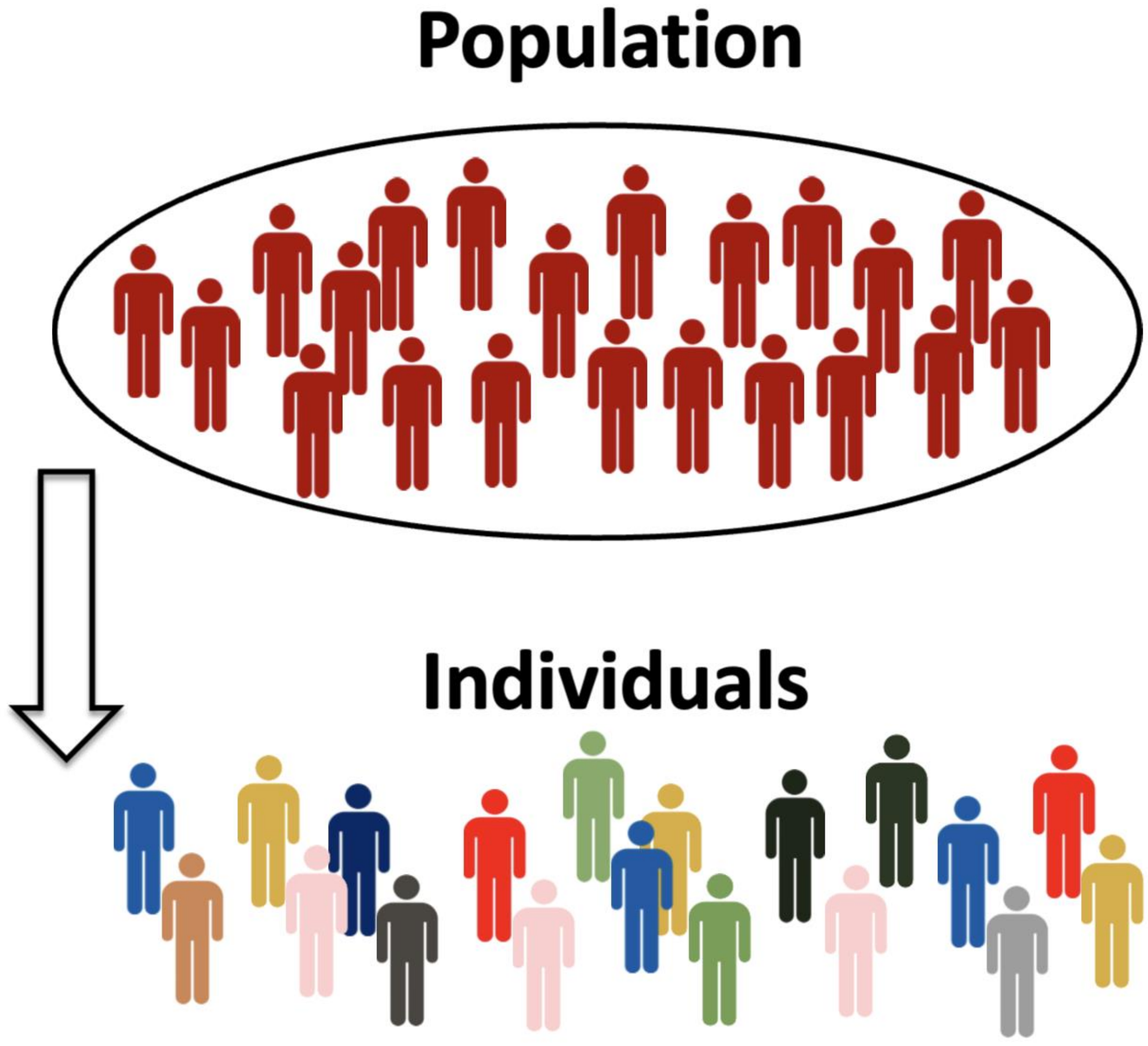
- Inter-subject variability of **mode topographies** and **functional connectivity** is meaningfully predictive of personalised traits and pathology, like a diagnostic assay for the brain.

- We need new tools that can accurately capture this variability and provide more accurate fMRI-based biomarkers of diseases.



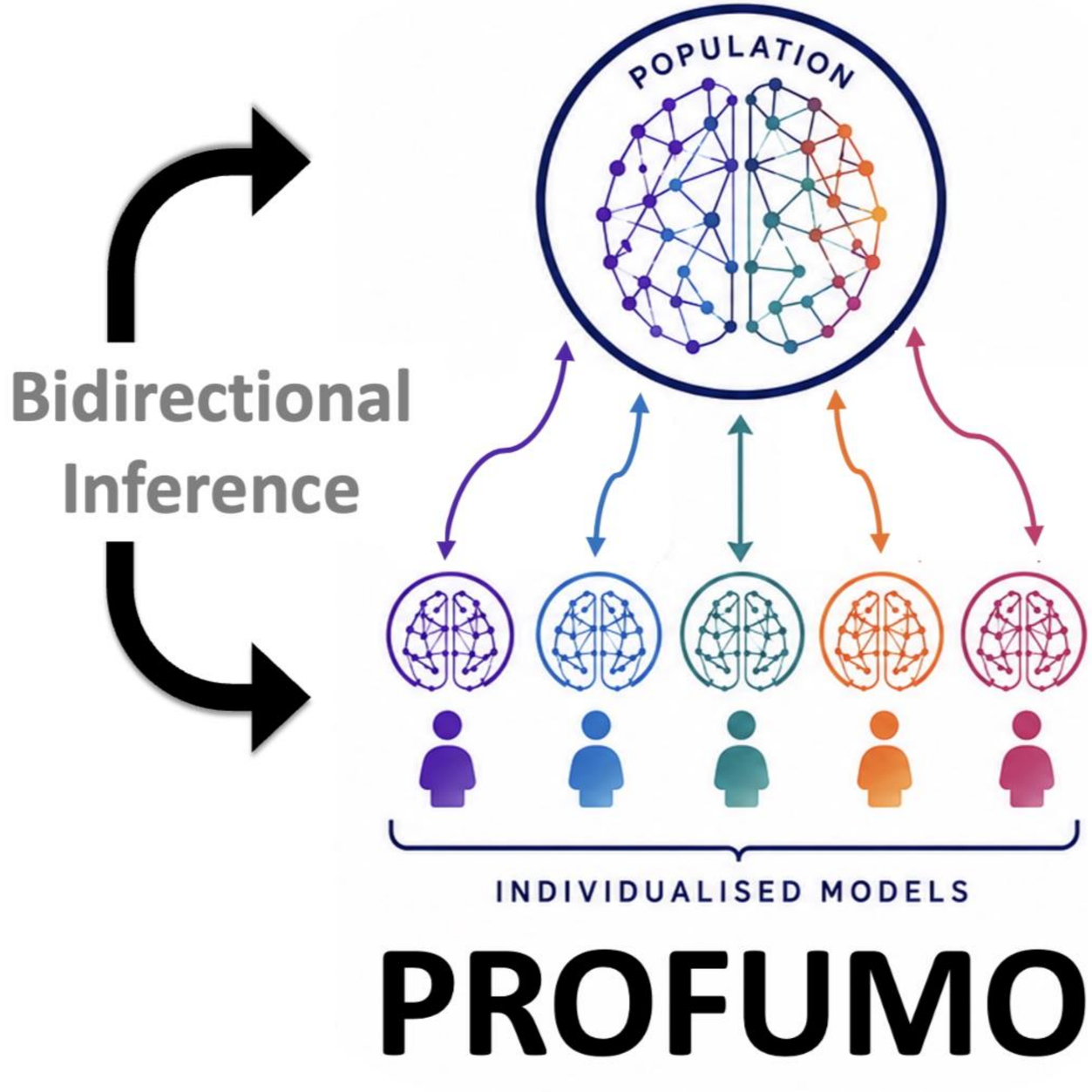
Standard techniques for functional mode modelling

Standard techniques for functional mode modelling rely on population averages, thus biasing individual estimates towards group means, and missing meaningful cross-individual variability that is linked to cognition and disease.



Probabilistic Functional Model (PROFUMO)

PROFUMO places individual variability at the core of network modelling, using patterns of population variation to inform fully individualised brain networks and vice versa.



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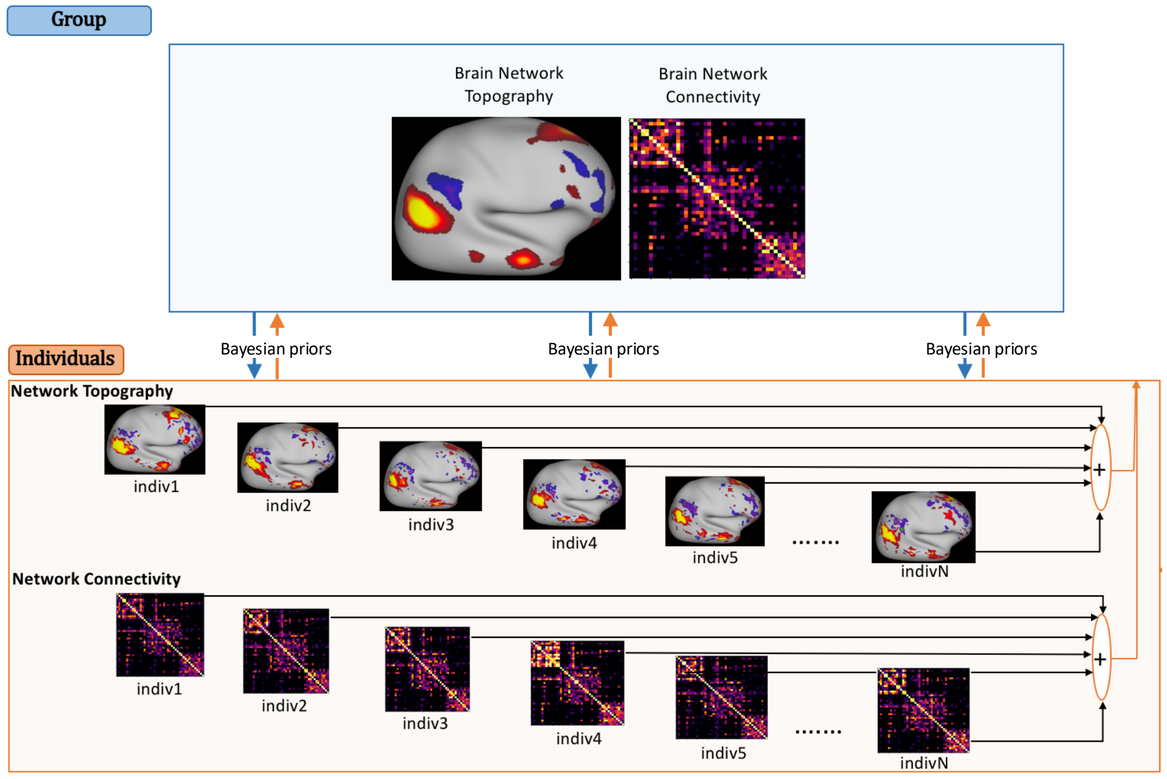
Model properties and outputs of PROFUMO

How does the model work?

PROFUMO: A Hierarchical Bayesian framework

- The model will:
  1. Use priors from group-level modelling to regularise subject-specific estimations.
  2. Use accumulated posterior evidence across subject to update the group
  3. Iterate steps 1&2 until convergence

❖ Functional modes that are estimated using PROFUMO are called PFMs.



Subject-specific decomposition

- Let us assume that we have fMRI data from a subject ‘s’ and recording session ’r’.
- We do the following matrix factorisation for this subject:

$$D^{sr} = P^{s} H^{sr} A^{sr} + \varepsilon^{sr}$$

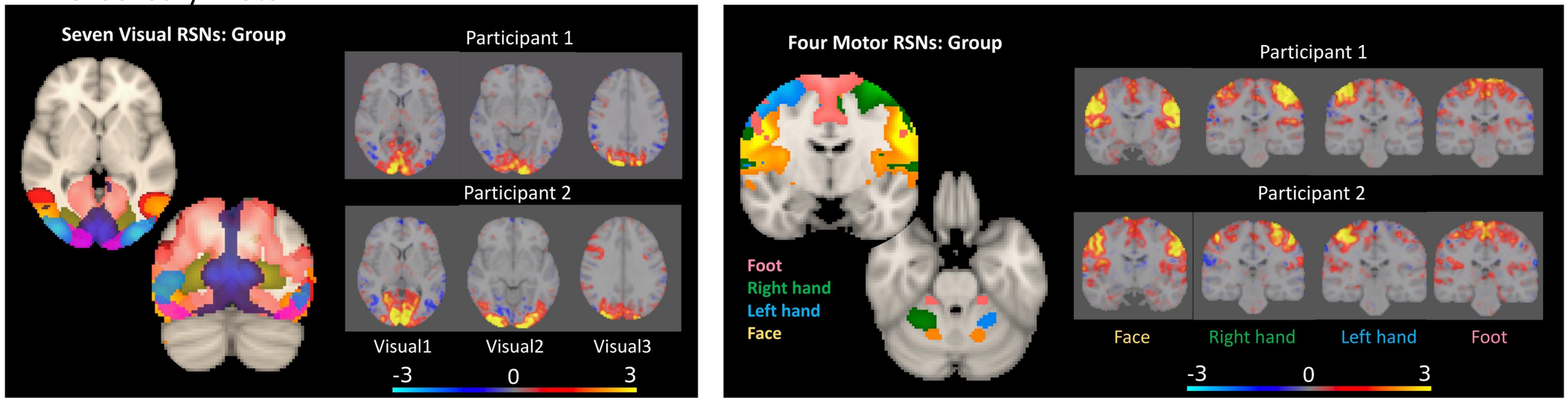
$\mathbf{D}^{sr}$	$\mathbf{P}^{s}$	$\mathbf{H}^{sr}$	$\mathbf{A}^{sr}$	$\boldsymbol{\varepsilon}^{sr}$	And α^{s}
fMRI data	Spatial maps	Mode amplitudes	Time courses	Residuals	Temporal correlation
$(N_v \times N_t)$	$(N_v \times N_m)$	$(N_m \times N_m)$	$(N_m \times N_t)$		$(N_m \times N_m)$

- A probabilistic formulation used together with Variational Bayesian inference, with group model providing prior distributions, to optimise the model fit to the data.

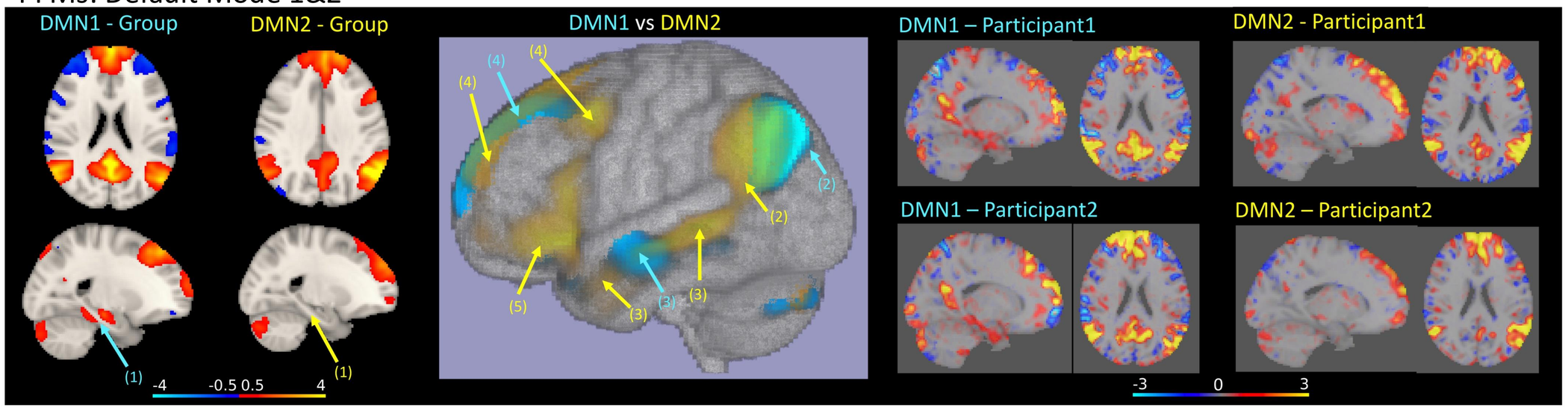
PROFUMO outputs

a) Spatial Maps: Group-level and Subject-level

PFMs: Sensory-Motor

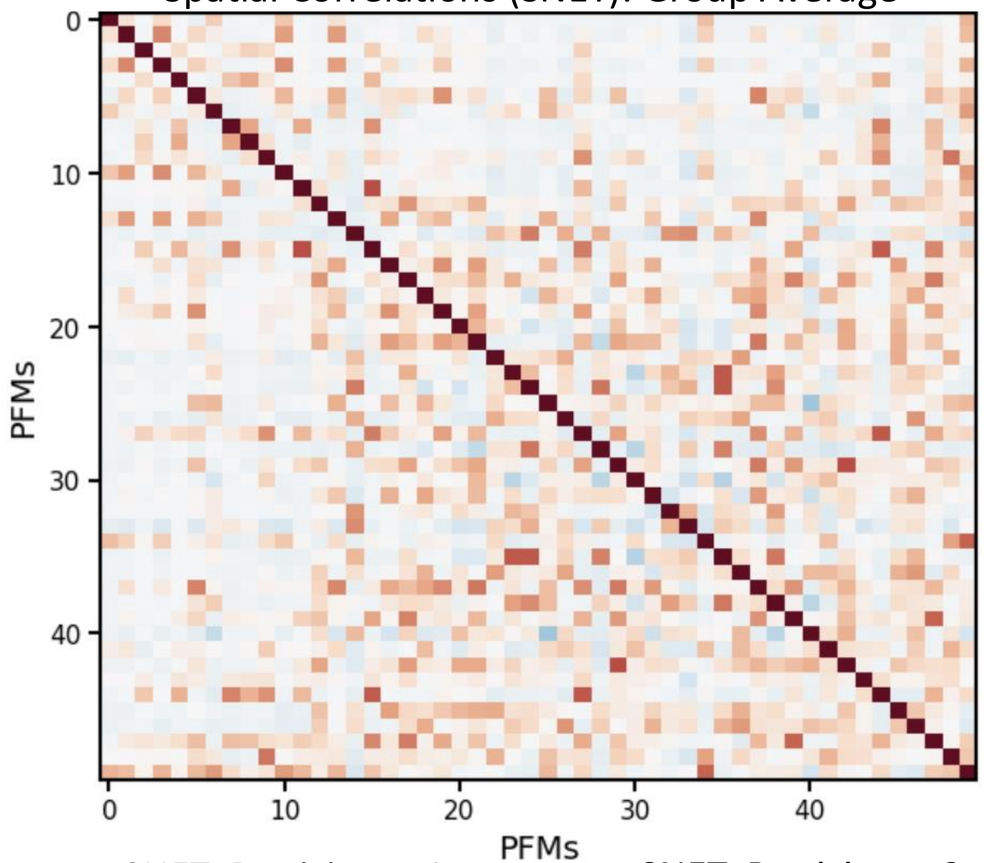


PFMs: Default Mode 1&2

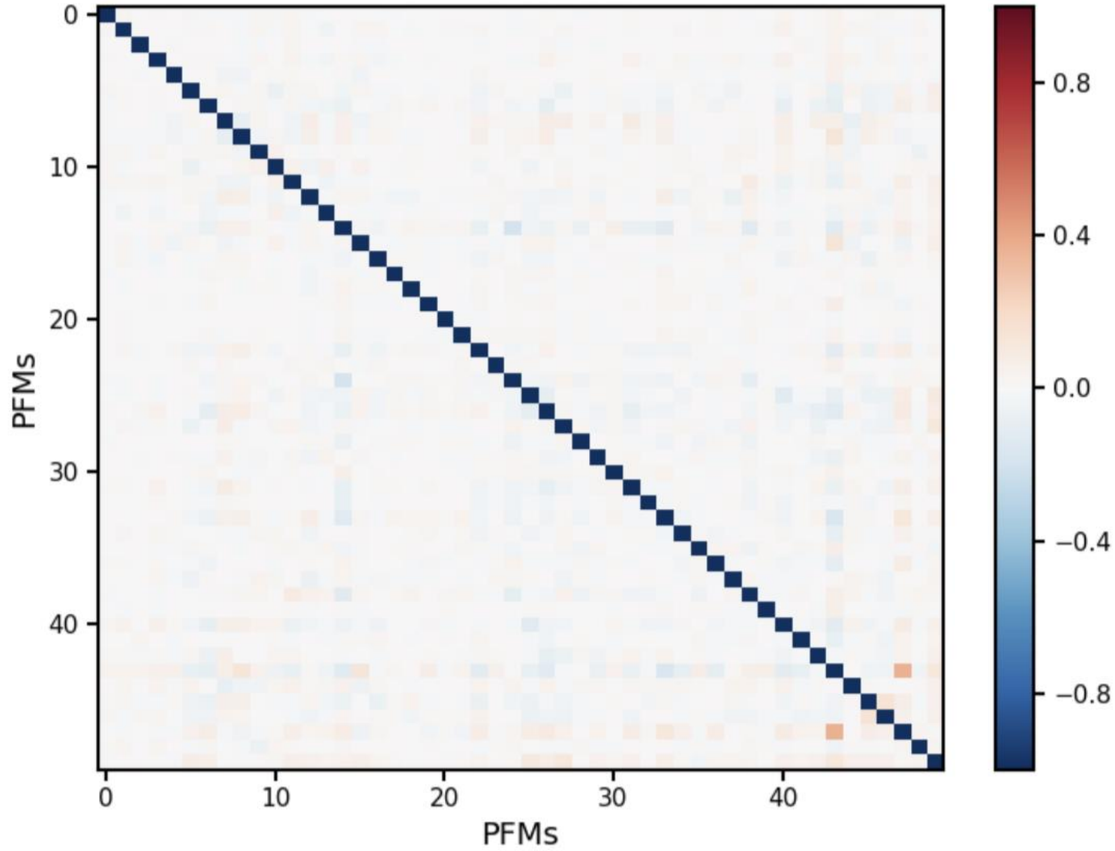


b) Spatial and Temporal Connectivity: Group-level and subject-level

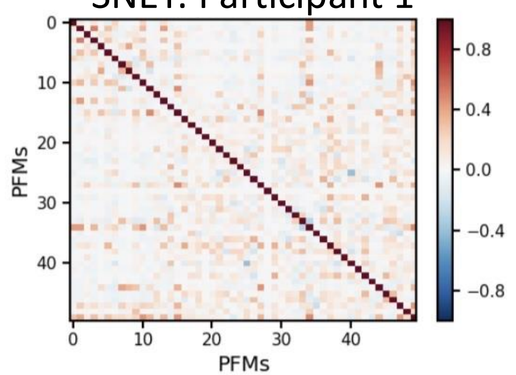
Spatial Correlations (SNET): Group Average



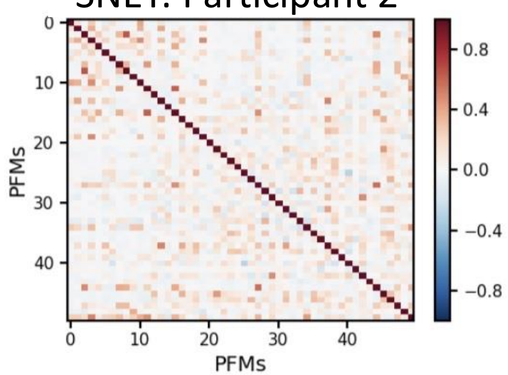
Partial Temporal Correlations (TNET): Group Average



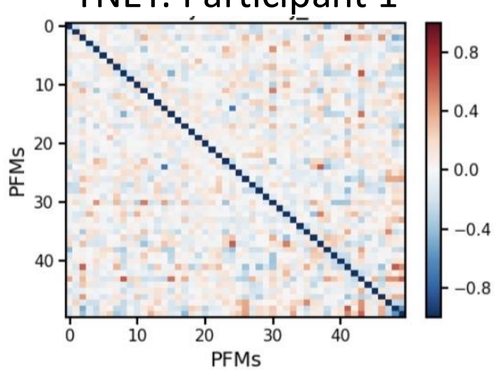
SNET: Participant 1



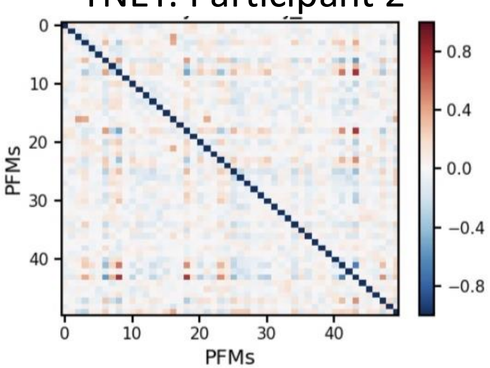
SNET: Participant 2



TNET: Participant 1

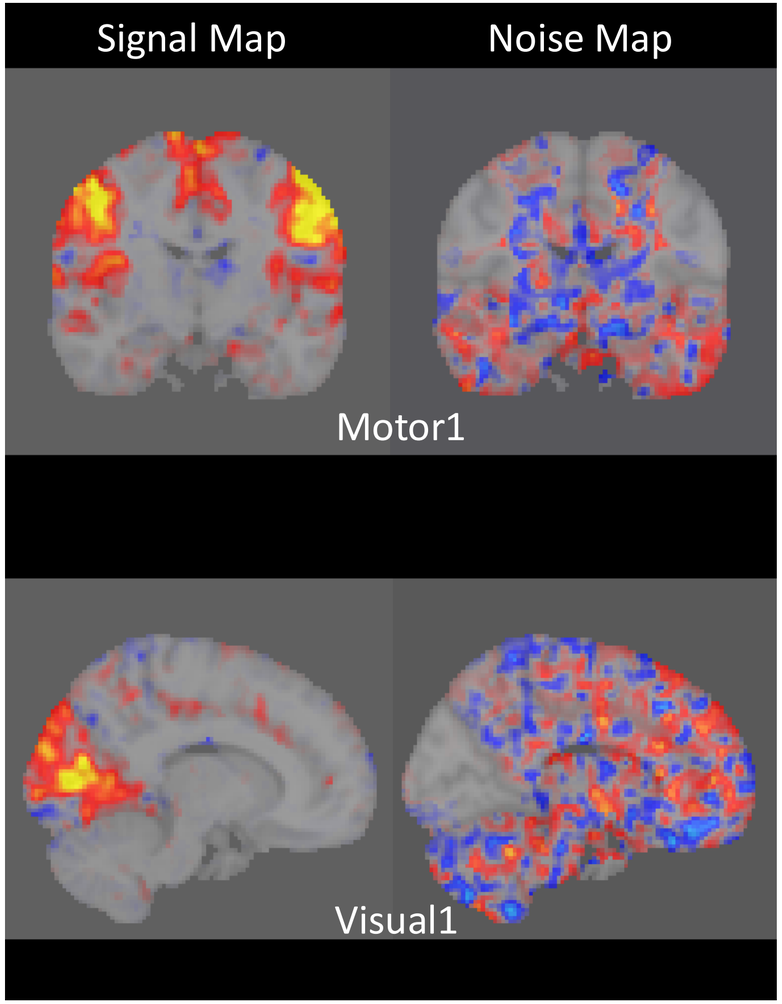


TNET: Participant 2

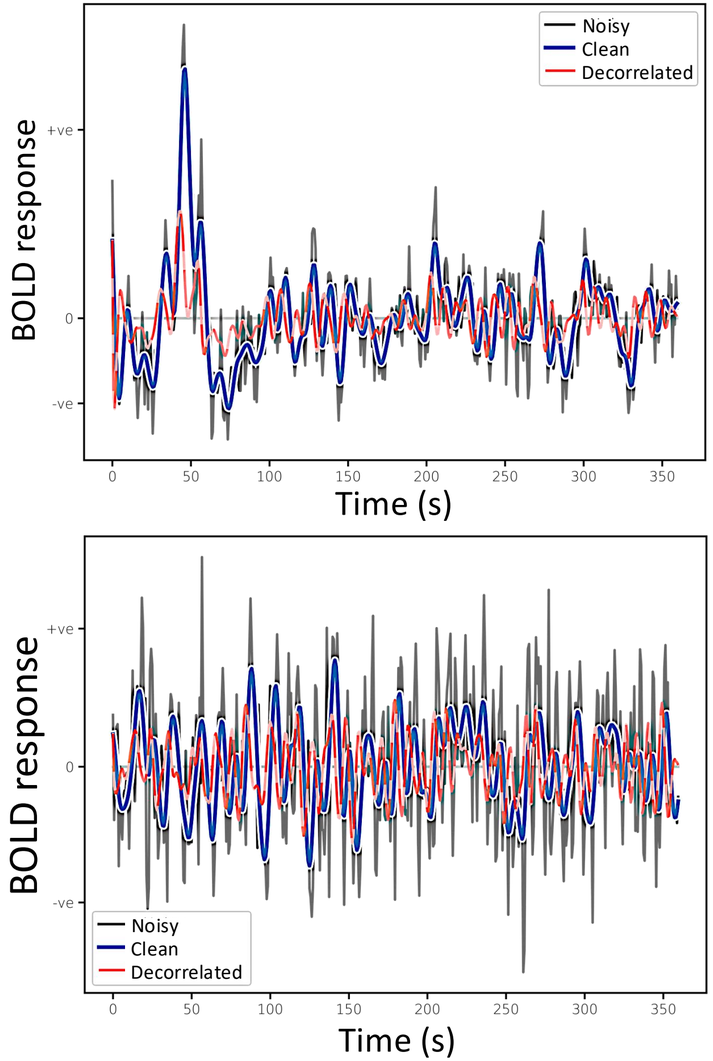


c) Signal vs Noise separation in subject spatial maps and time courses

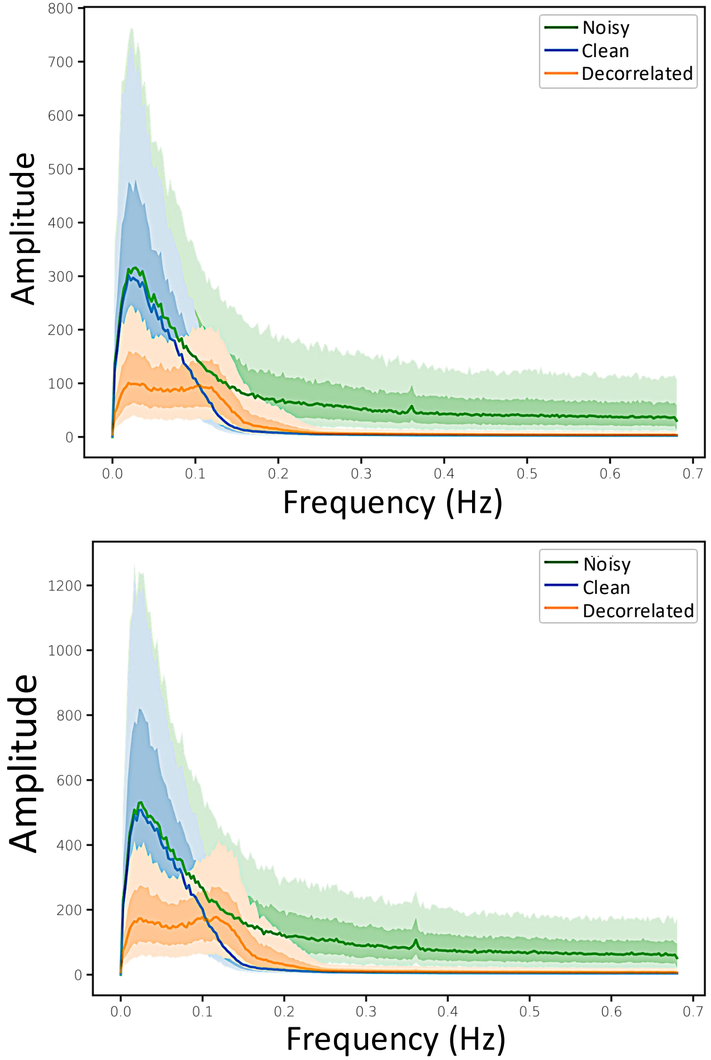
Spatial Maps: Example Participant



Time courses: Example Participant



Power Spectra: Example Participant



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Example applications to big data

Multiscale Brain Modes

Large-scale networks vs fine-grained parcels

Functional modes have been characterised using two distinct approaches in previous literature:

1- Large-scale Networks

- Span multiple regions
- Long-range connections
- Low-dimensional (~20-30 networks)

Smith et al., 2009

2- Fine-grained Parcels

- Contiguous to one or a few regions
- Short-range connections
- High-dimensional (100-1000 parcels)

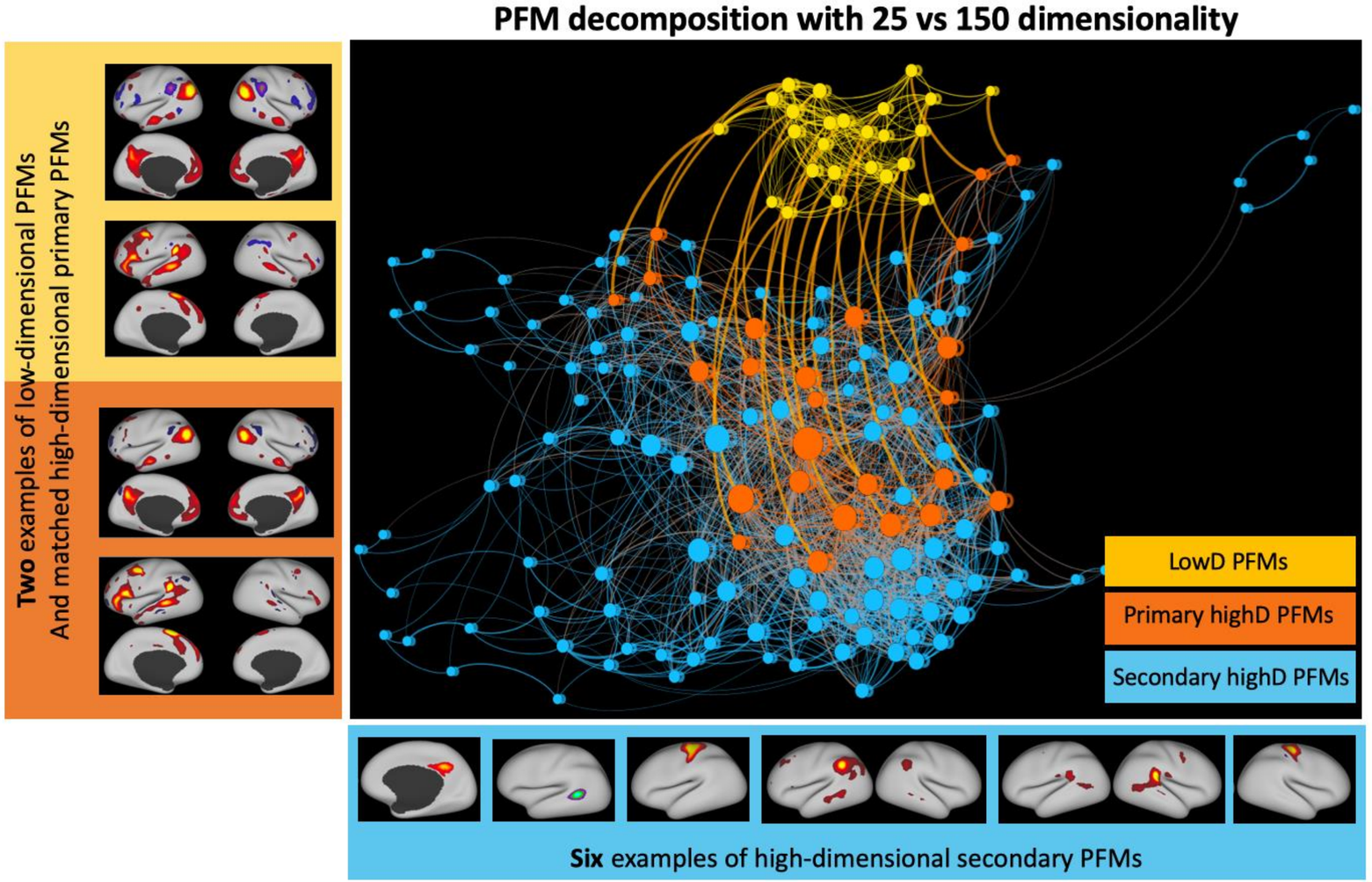
Shaefer et al., 2018

Multiscale brain modes:

By applying the model to HCP or UK Biobank, we found that high-dimensional (150) PFMs consist of:

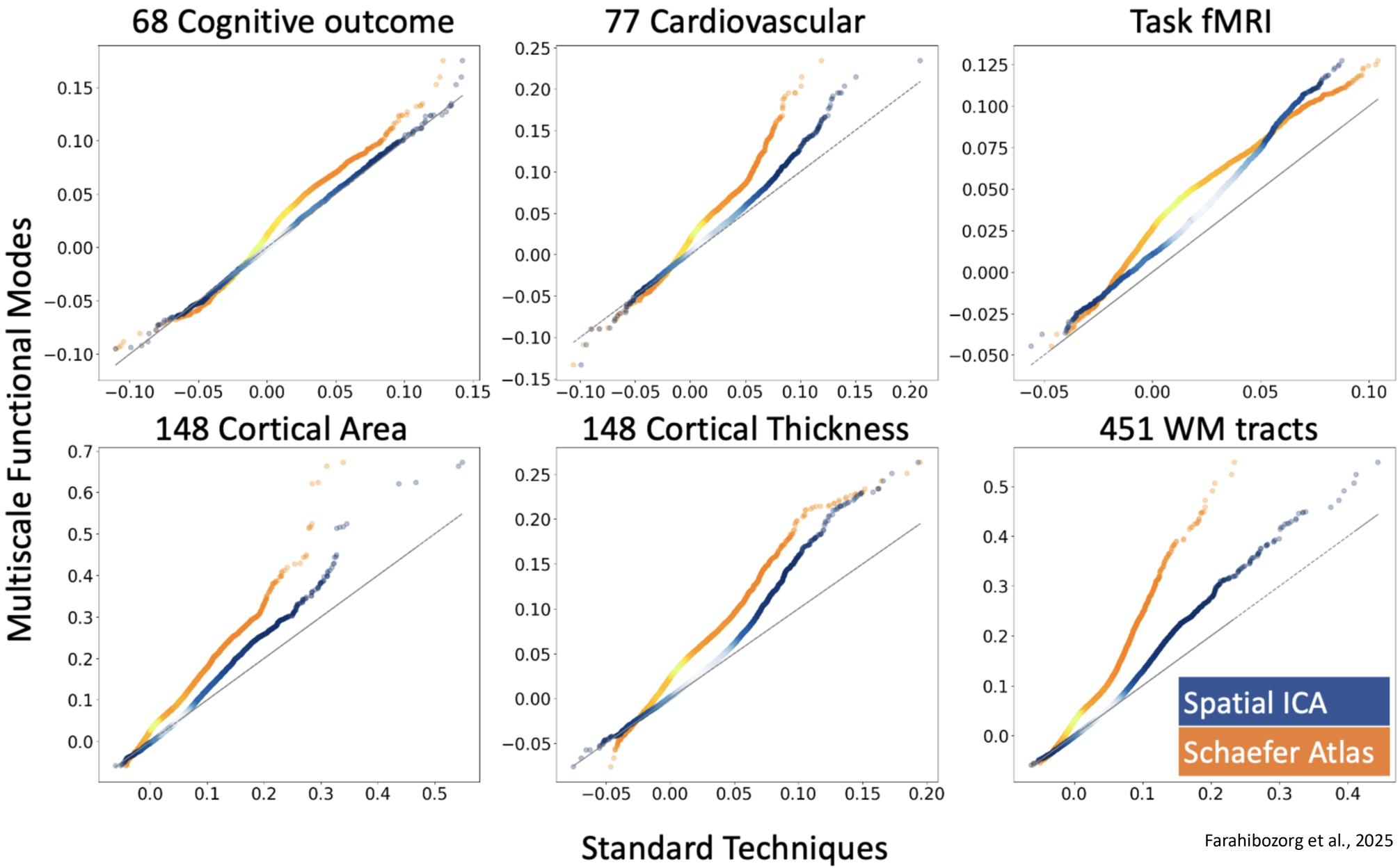
- *primary highD* (orange), 25 modes from high-dimensional decomposition with clear one-to-one match to lowD.
- *Secondary HighD* (blue) denote the remaining 125 RSNs from high-dimensional decomposition that appear with increased dimensionality.

This new representation can be used to characterise inherent global-local connectivity, in space and time.



Farahibozorg et al., 2025

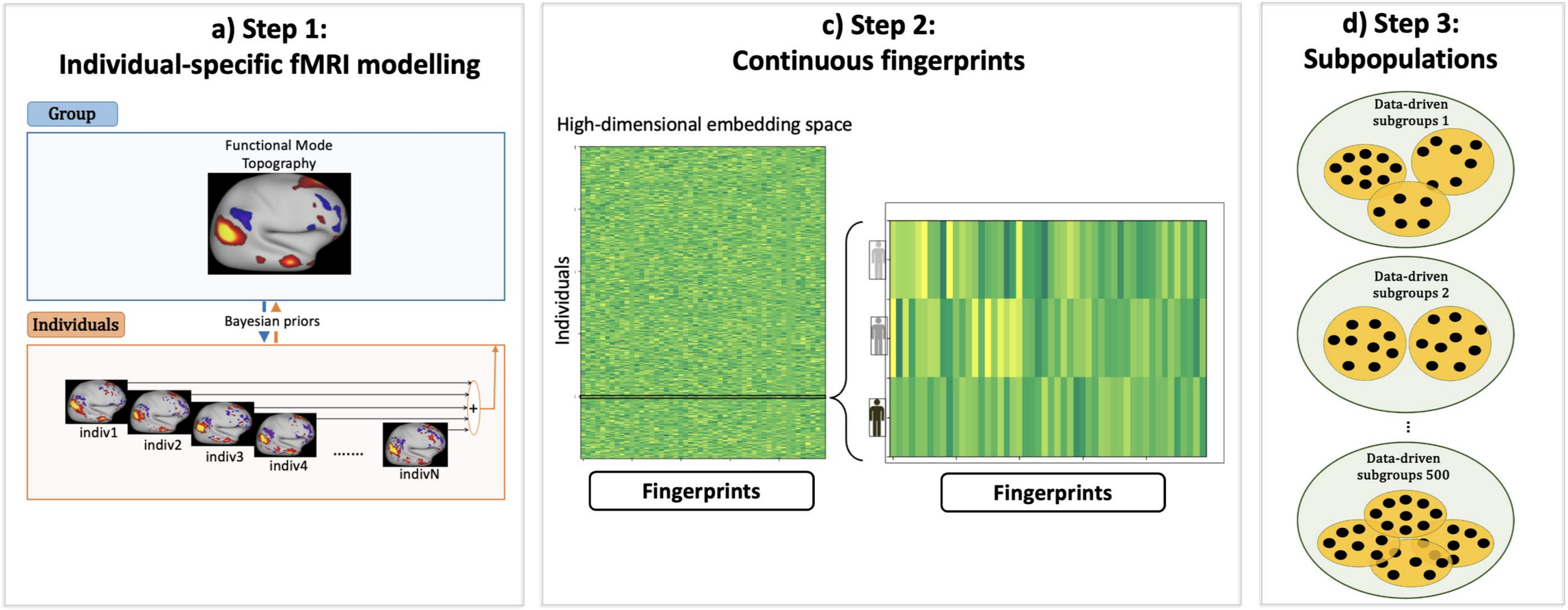
Phenotype predictions: Multiscale Functional Modes vs Standard Techniques



Farahibozorg et al., 2025

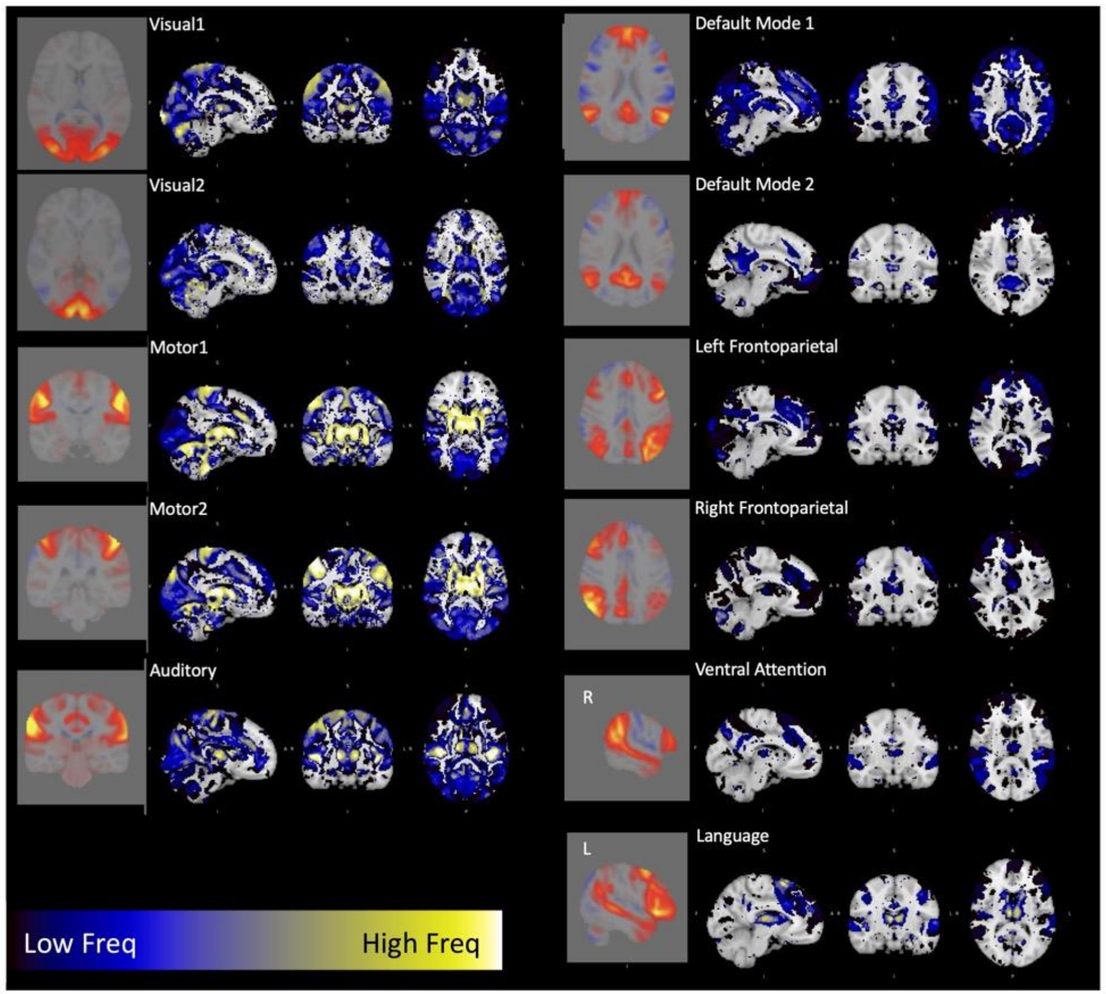
Subgroup discovery based on PFM Spatial Maps

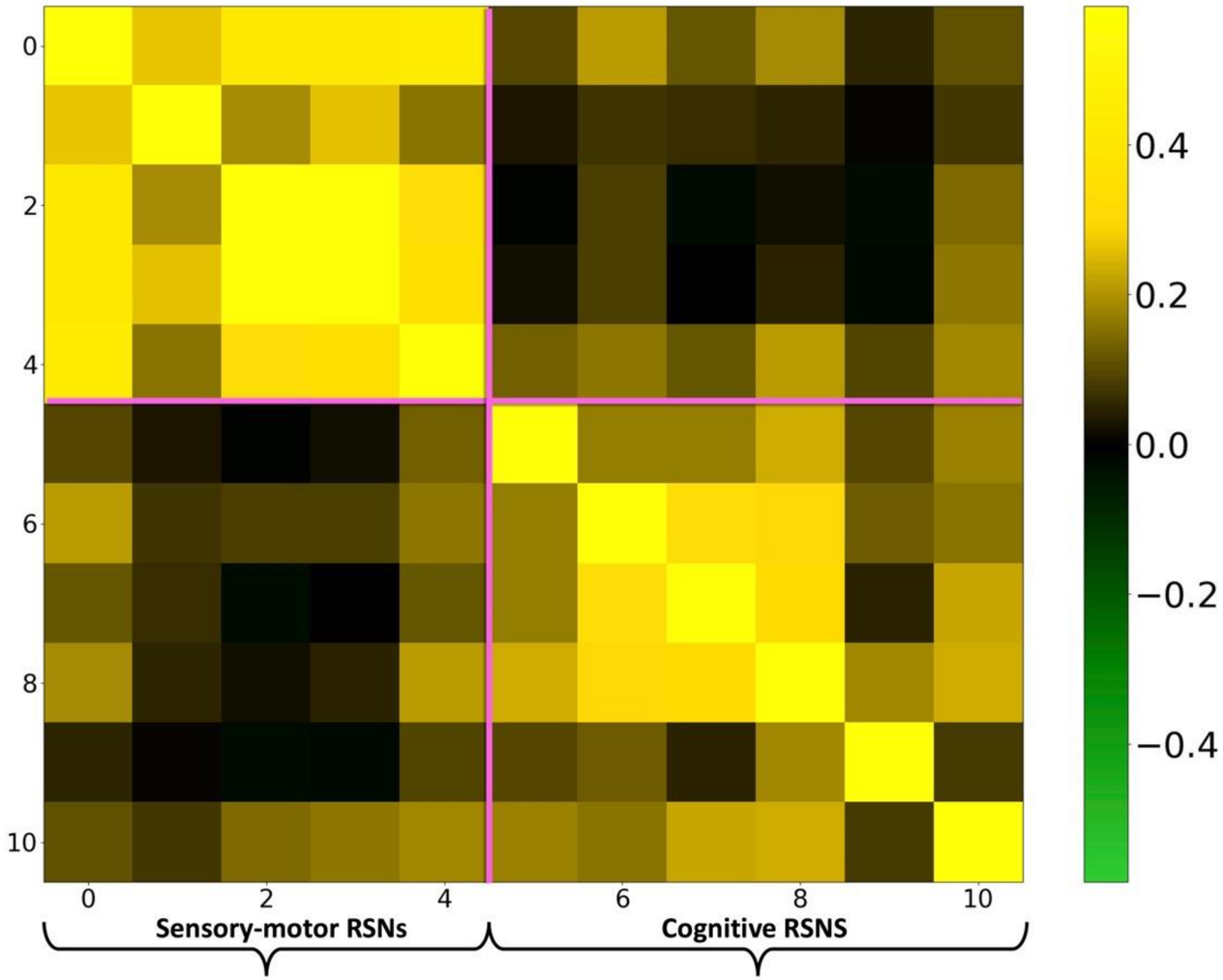
Subject-specific modes -> fingerprints -> subgroups



- Feature reduction techniques were used to extract fingerprints from spatial maps
- Fingerprint features were used as input to Gaussian Mixture Modelling to identify subgroups

Spatial Maps of Subgroup Differences





Farahibozorg et al., in prep

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Model Variants and Software Package

Three Variants of PROFUMO

cPROFUMO

Classic PROFUMO uses Variational Bayesian (VB) inference to find a solution for the probabilistic model described above.

WHEN TO USE?

Small to medium-sized datasets (e.g., 20 up to 500 subjects), and when group model is to be inferred based on own data.

sPROFUMO

Stochastic PROFUMO uses stochastic VB, dividing subjects from big data into small batches, updating the group model across batches, and using it for regularisation of the subjects.

WHEN TO USE?

Large datasets (100s to tens of 1000s), and when group model is to be inferred based on own data.

pPROFUMO

Predefined PROFUMO keeps the spatiotemporal group-level parameters fixed as priors, and only estimates subject-level parameters.

WHEN TO USE?

Any sample size – a pre-existing group model required. Pretrained models can be obtained from our public HCP or UK Biobank results or trained locally.

Software Package

- Git repository: https://git.fmrib.ox.ac.uk/profumo/profumo/-/tree/sprofumo-cpp-clean
- Upcoming FSL tool

Thank you!