the framework of:

Probabilistic Functional Modes

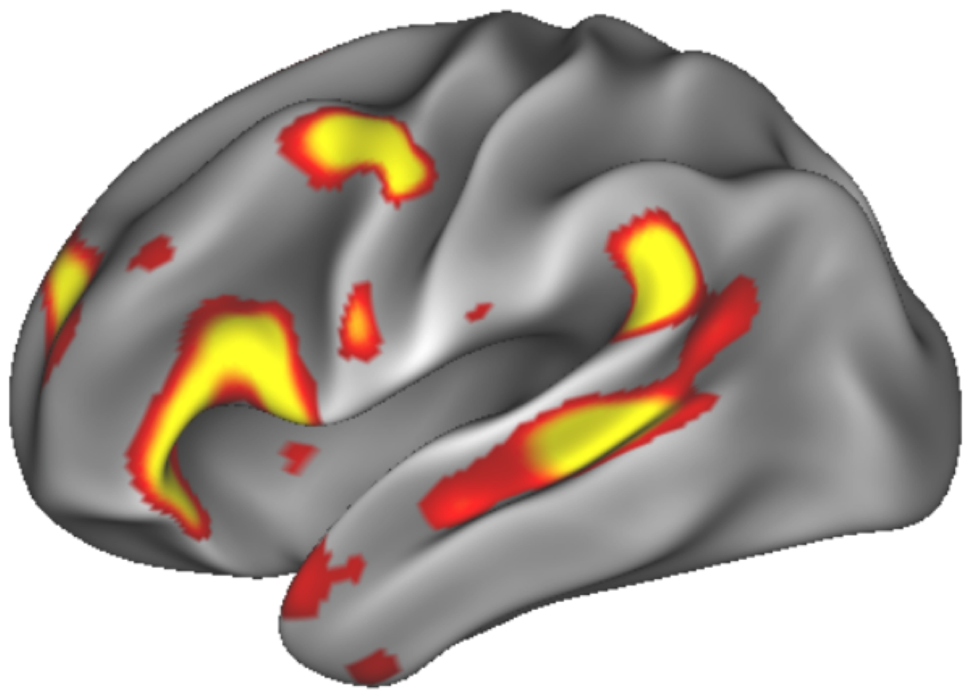
part 1

Three lectures on FSL tool Probabilistic Functional Modes

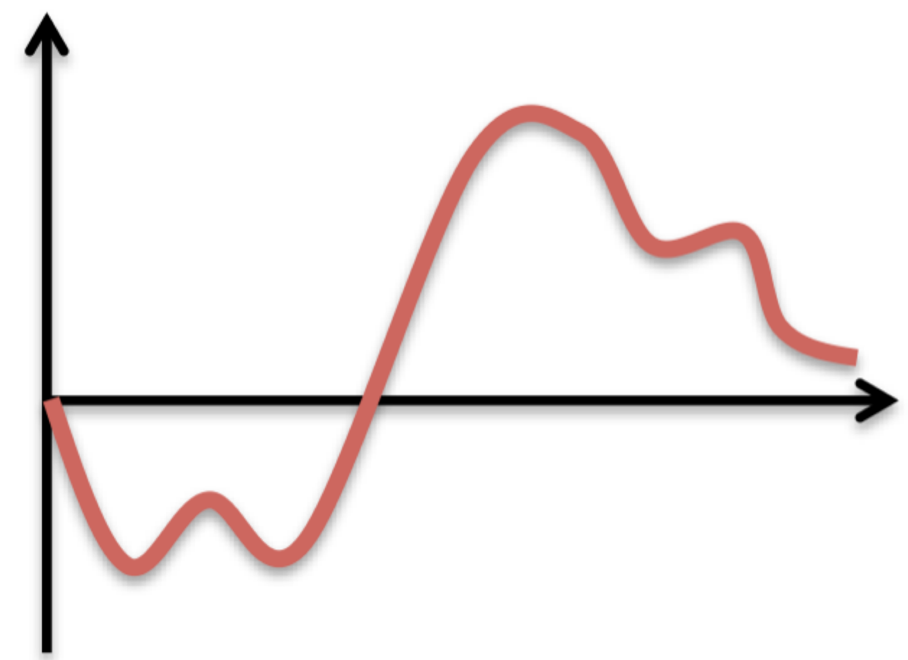
- Description of PFM framework and its key features.
- PFM Network Matrices, comparison to ICA, and interpretability of functional connectivity.
- PFMs for big data and prediction of individualistic traits.

Modes of brain function

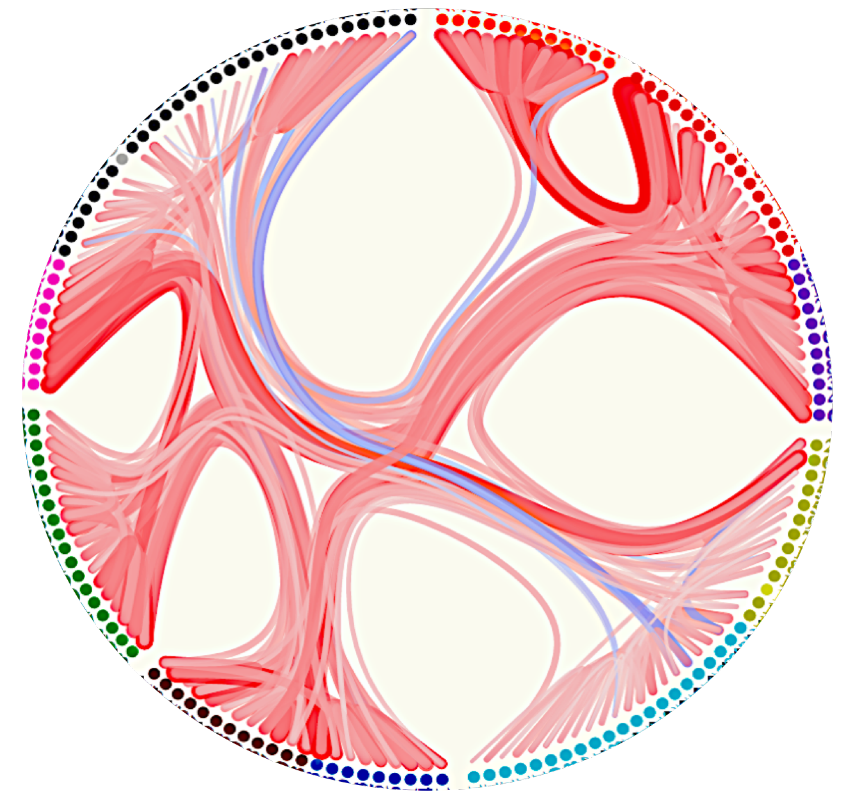
Spatial Configuration
(Topography)



Time Courses



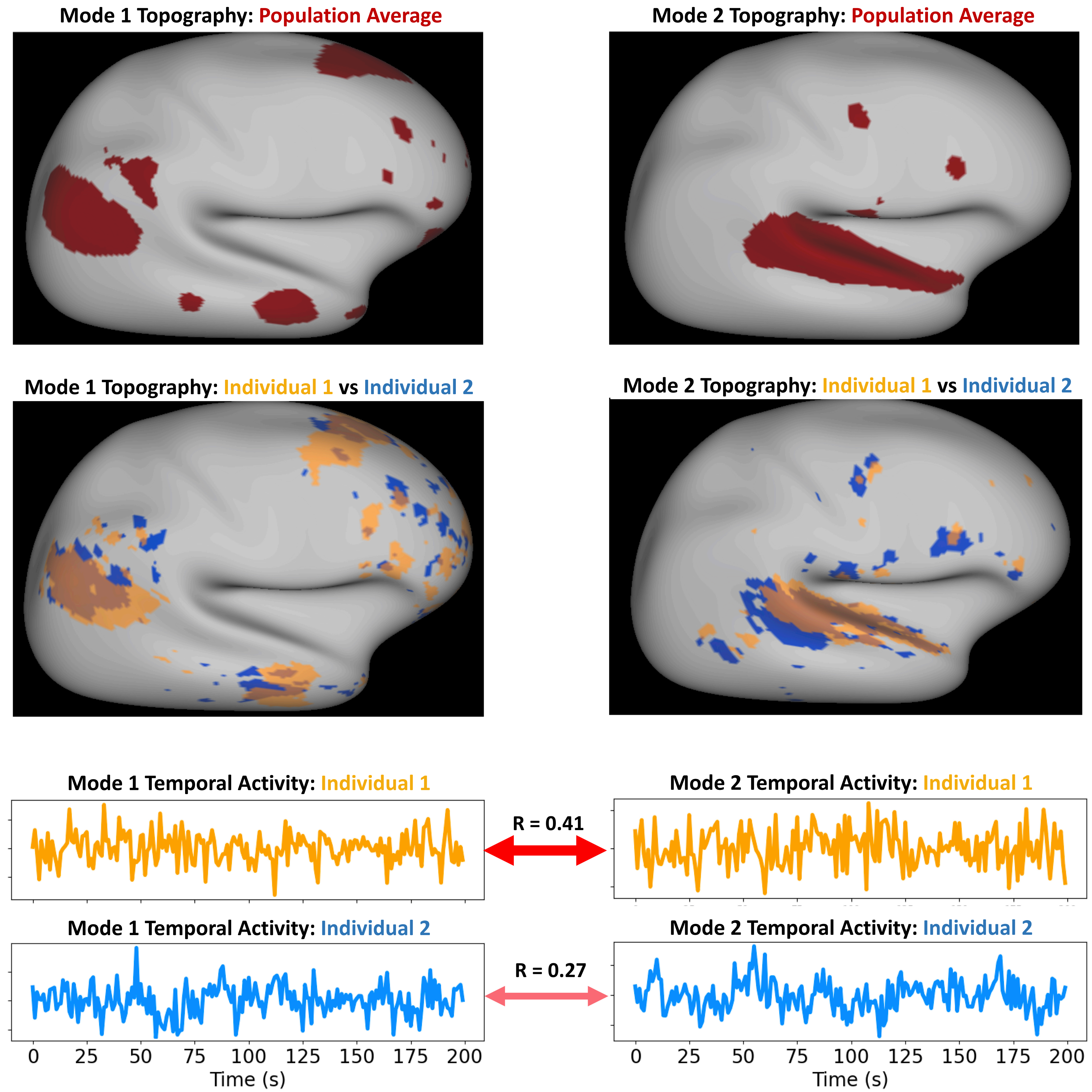
Temporal Correlation
(Functional Connectivity)



- 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.

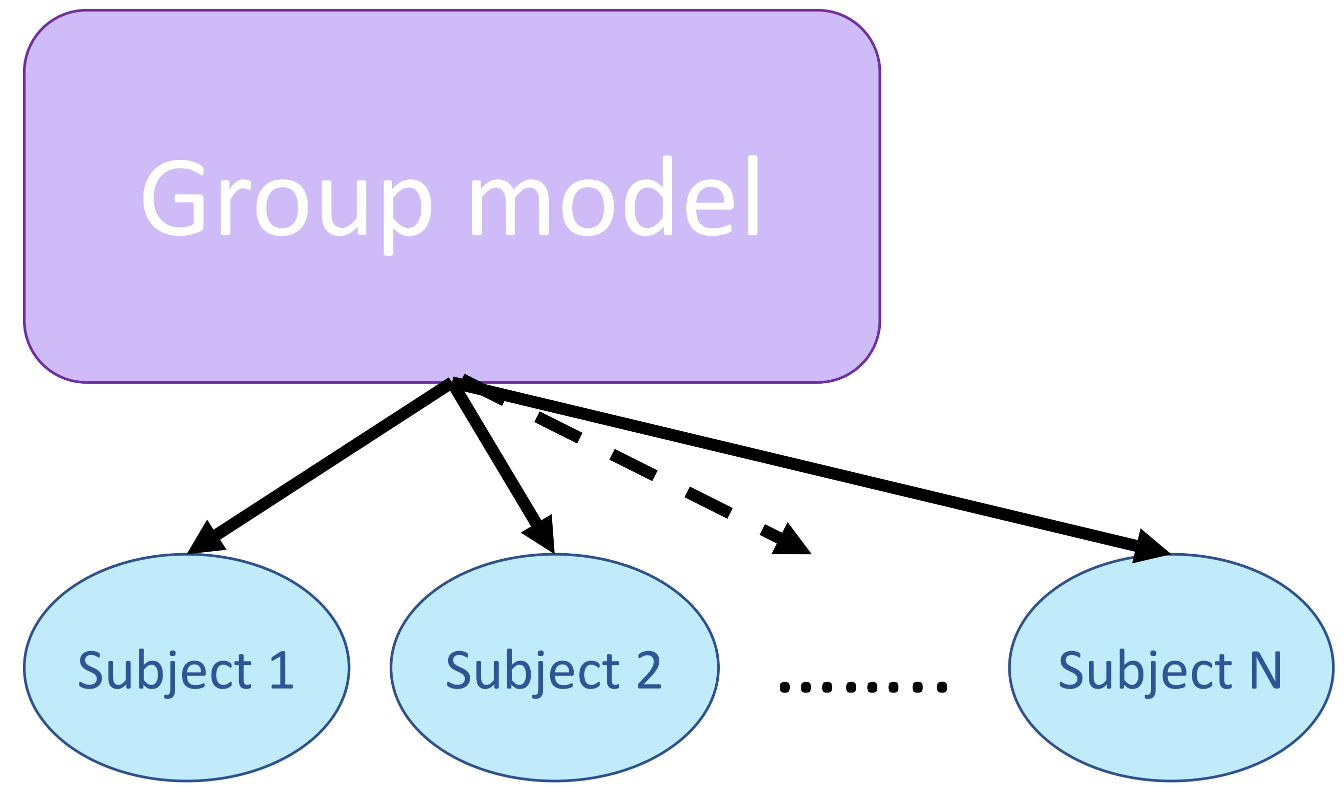
Functional modes vary across individuals

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

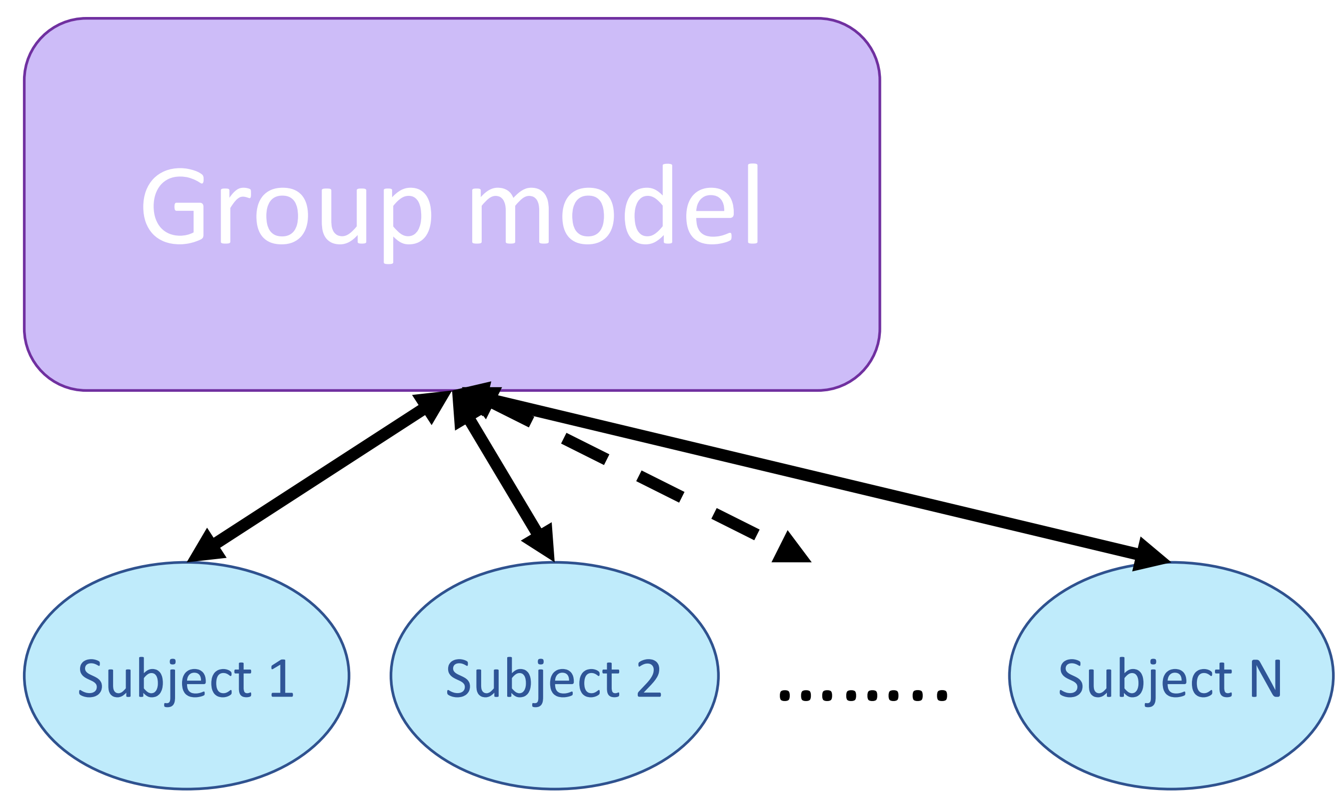


Current standard technique: Group ICA + Dual Regression

- Subject-specific mode estimation typically follows two separate steps:
  1. Group-level ICA
  2. Group-ICA mapped onto subject fMRI timeseries via multiple regressions
- Explicit subject modelling: No
- Directionality: Unidirectional
- Limited ability for capturing cross-individual variability



➢ Recent advances include estimating modes simultaneously and hierarchically for the population and individuals

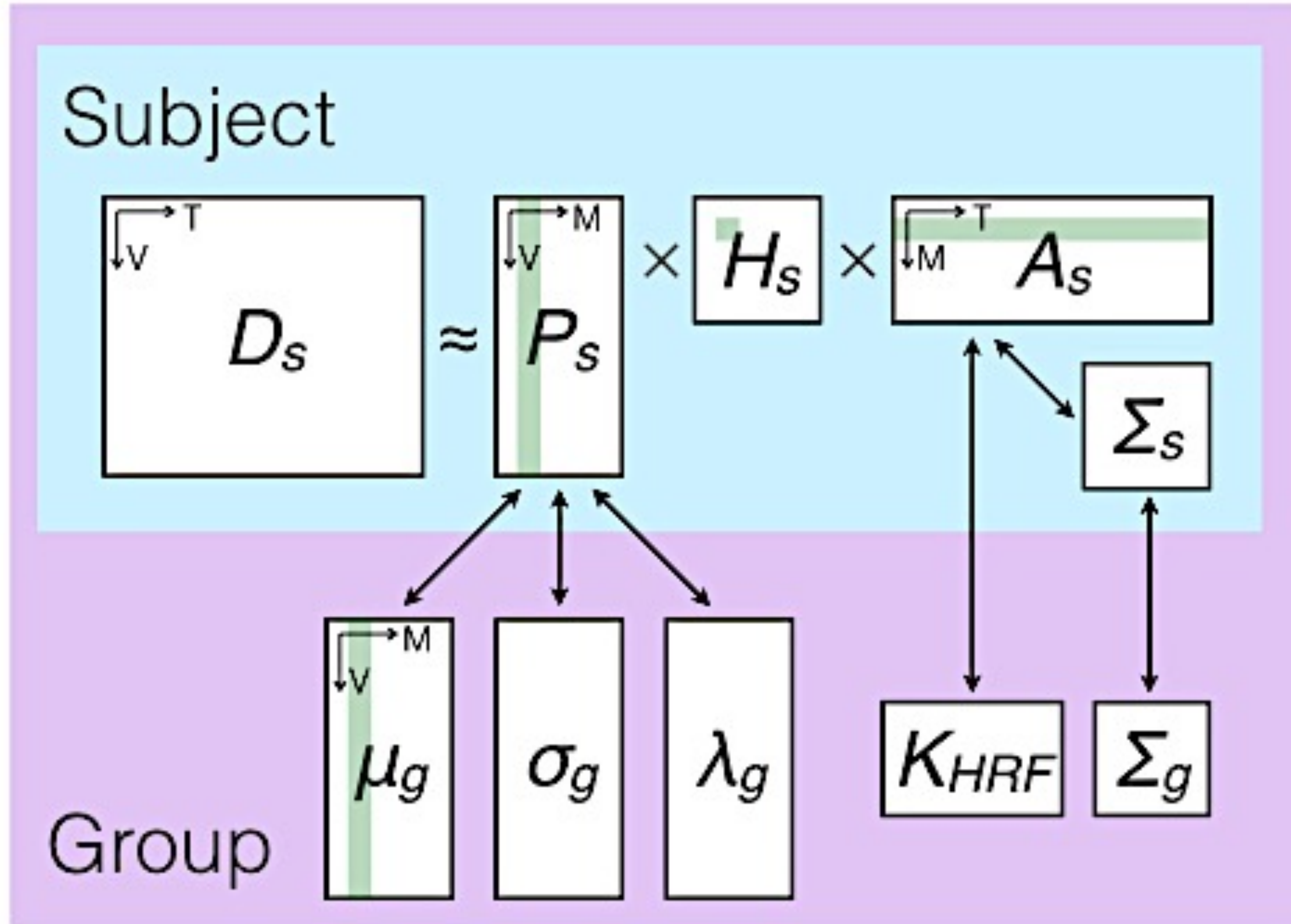


Probabilistic Functional Modes (PFMs)

- Simultaneous modelling of population and individuals

  1. Group-level modes used for top-down regularisation of individuals

  2. Individual-specific modes used for bottom-up regularisation of the group



Based on Harrison et al., 2015

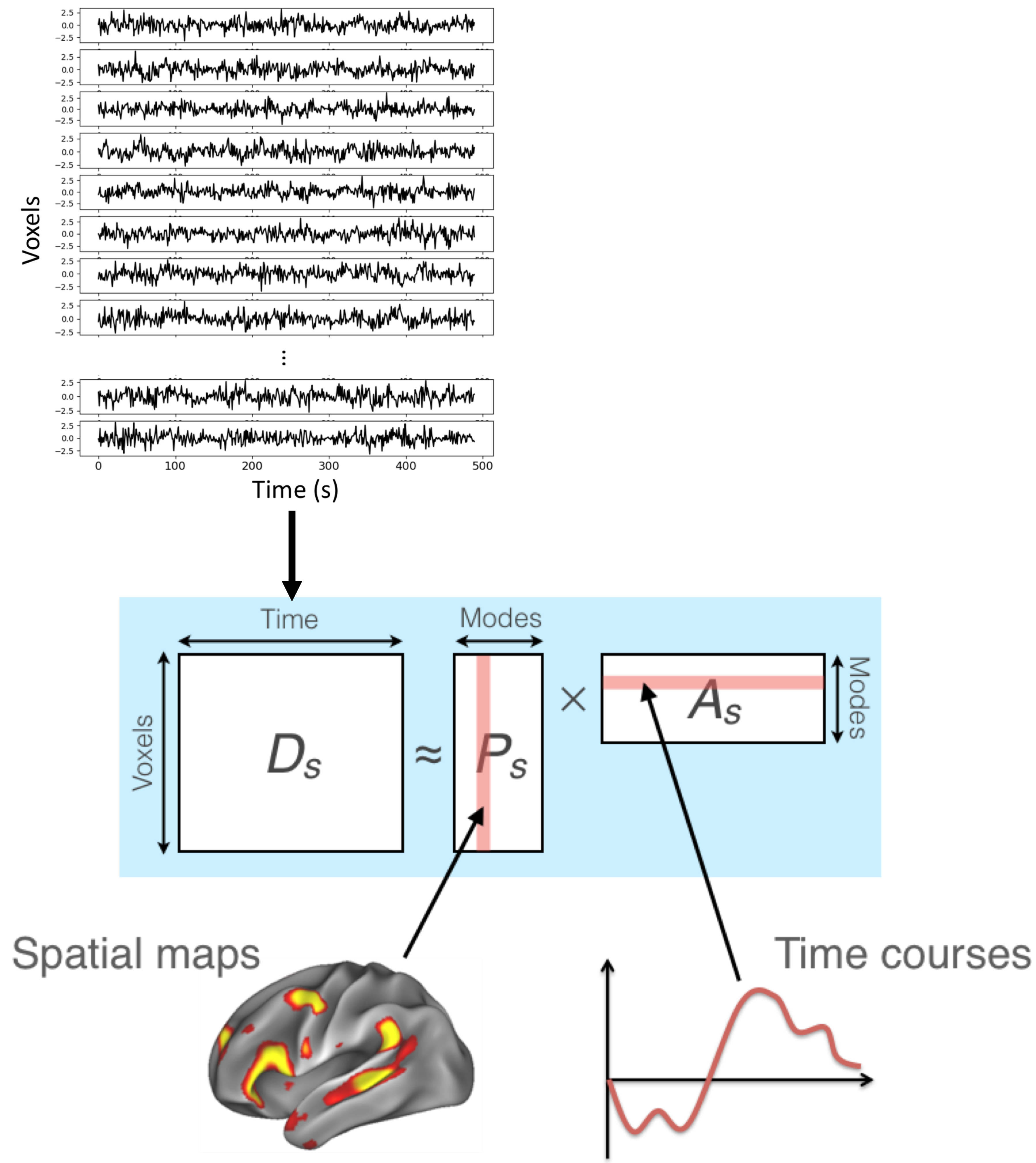
- Explicit subject modelling: Yes
- Directionality: Bidirectional
- Aim is to improve cross-individual variability modelling

How does the model work?

Reconstructing functional modes using Matrix Factorisation

- FMRI data (N_{Voxel} x N_{Time}) is factorised into a set of functional modes. Modes are characterised by:

1. Spatial Maps (N_{Voxel} x N_{Mode})
    - Spatial configuration or Topography
2. Time course (N_{Mode} x N_{Time})
    - Activity over time
3. Functional Connectivity (N_{mode} x N_{mode})
    - Temporal correlation between modes (NetMat)



Based on Harrison et al. 2015

Subject-specific decomposition in PFMs

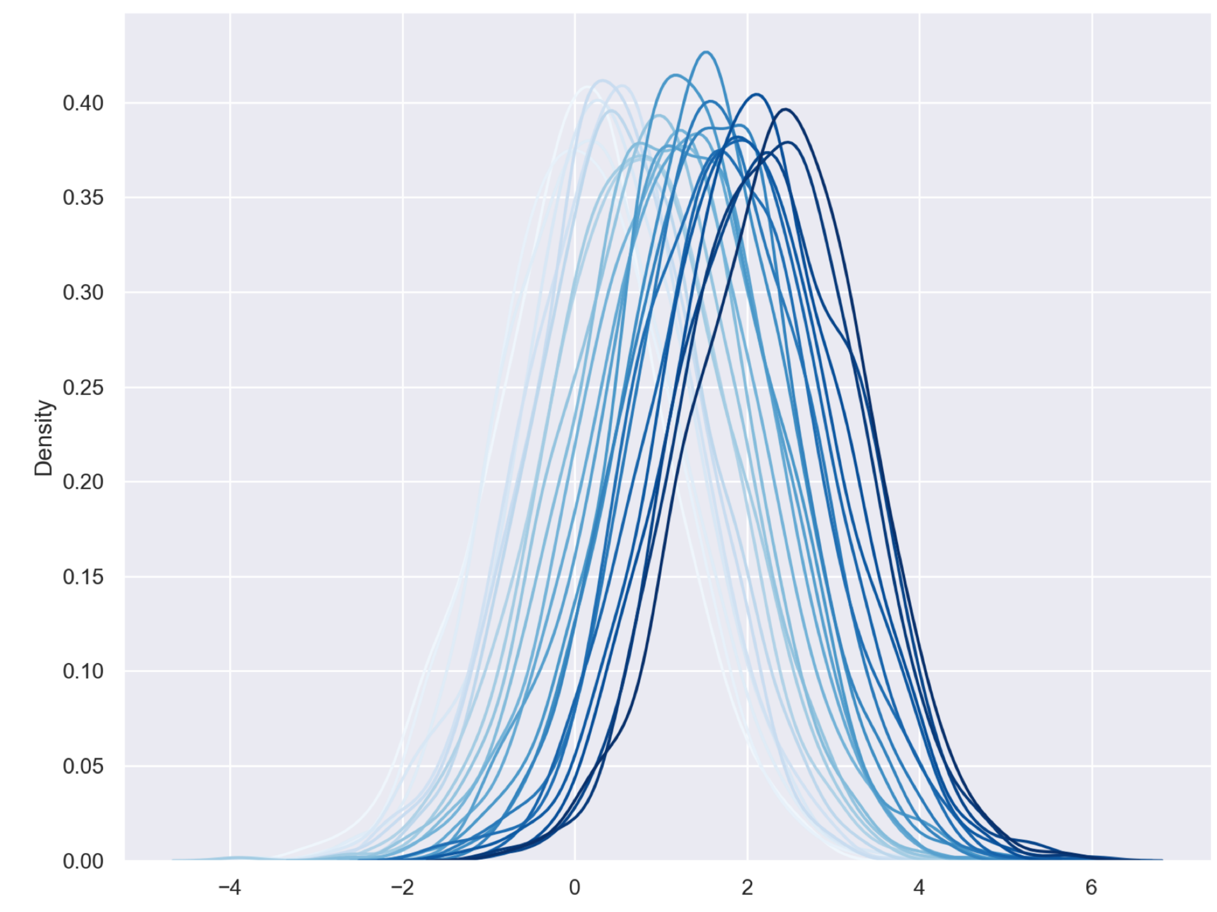
- Let us assume that we have fMRI data from a subject ‘s’ and recording session ’r’.
- We do the following matrix factorisation for this subject:

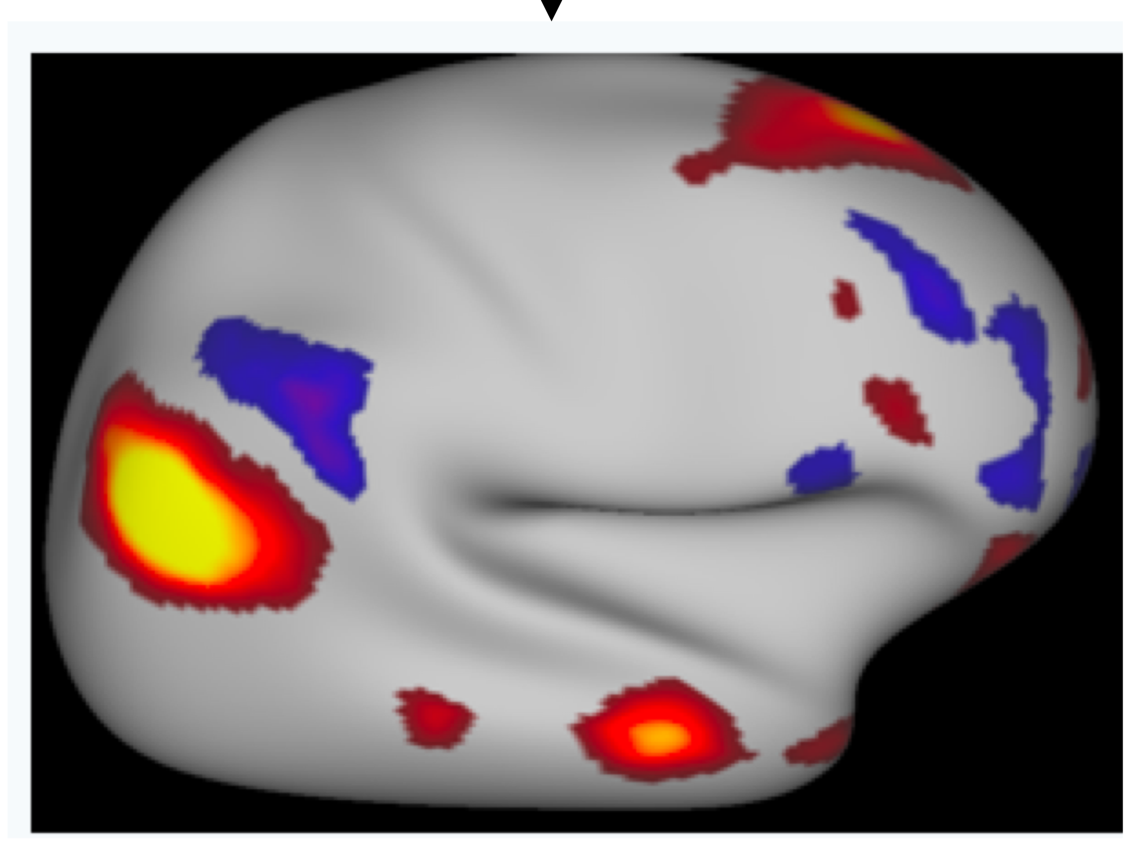
$$\boldsymbol{D} = \boldsymbol{P}\ \boldsymbol{H}\ \boldsymbol{A} + \boldsymbol{\varepsilon} \qquad \textbf{(1)}$$

- Where: D -> preprocessed data;
- P -> spatial maps of modes;
- A -> time courses of modes;
- H -> amplitudes of mode activity over time;
- ε -> residuals;
- α -> partial temporal correlation (i.e., connectivity) between timeseries of A.

Probabilistic formulation

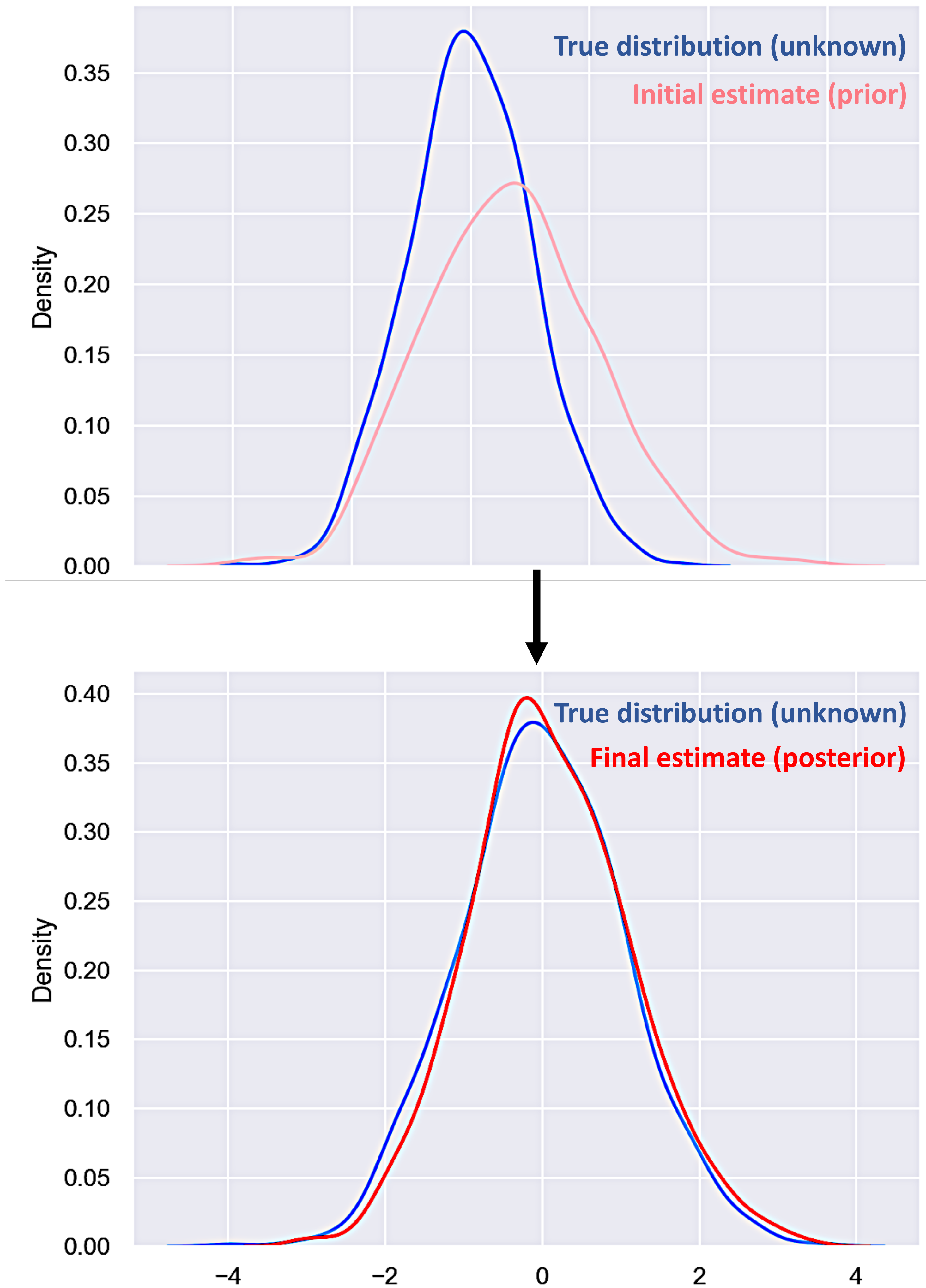
- We use a data-driven probabilistic approach to approximate a solution to Equation 1.
- Our aim is to estimate a probability distribution for each of the model's spatial and temporal variables, for each subject and the group.
  - For this purpose, we define what types of distributions we expect for each model element.
  - For example, distributions for voxel-wise spatial maps are set to be Gaussian.
  - Model should be able to estimate relevant parameters (e.g. mean and variance) to characterise these distributions to explain the observed data.





Variational Bayesian solution to probabilistic framework

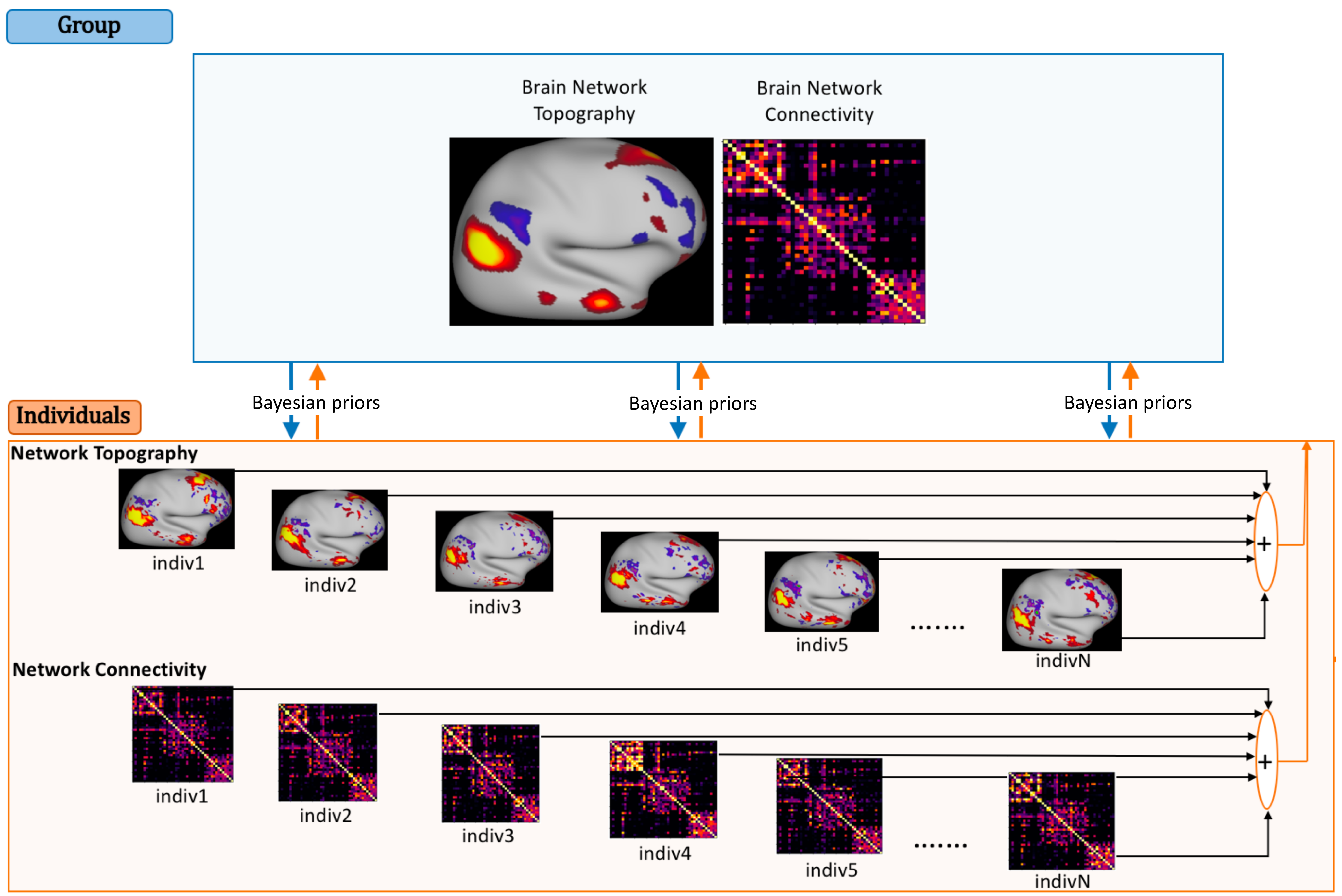
- To achieve this optimisation goal, we use Bayesian inference:
  1. Assume that there are ”true” distributions in the data, which we do not know.
  2. We start with an initial estimate (prior).
  3. We optimise the distribution using a technique called variational Bayes (VB).
  4. Without knowing the true distribution, with VB inference we can derive and optimise a lower bound for the marginal likelihood of the data given the model (see Harrison et al., 2015 for technical details of inference).



- **Question: Where do we get the prior distributions from?**

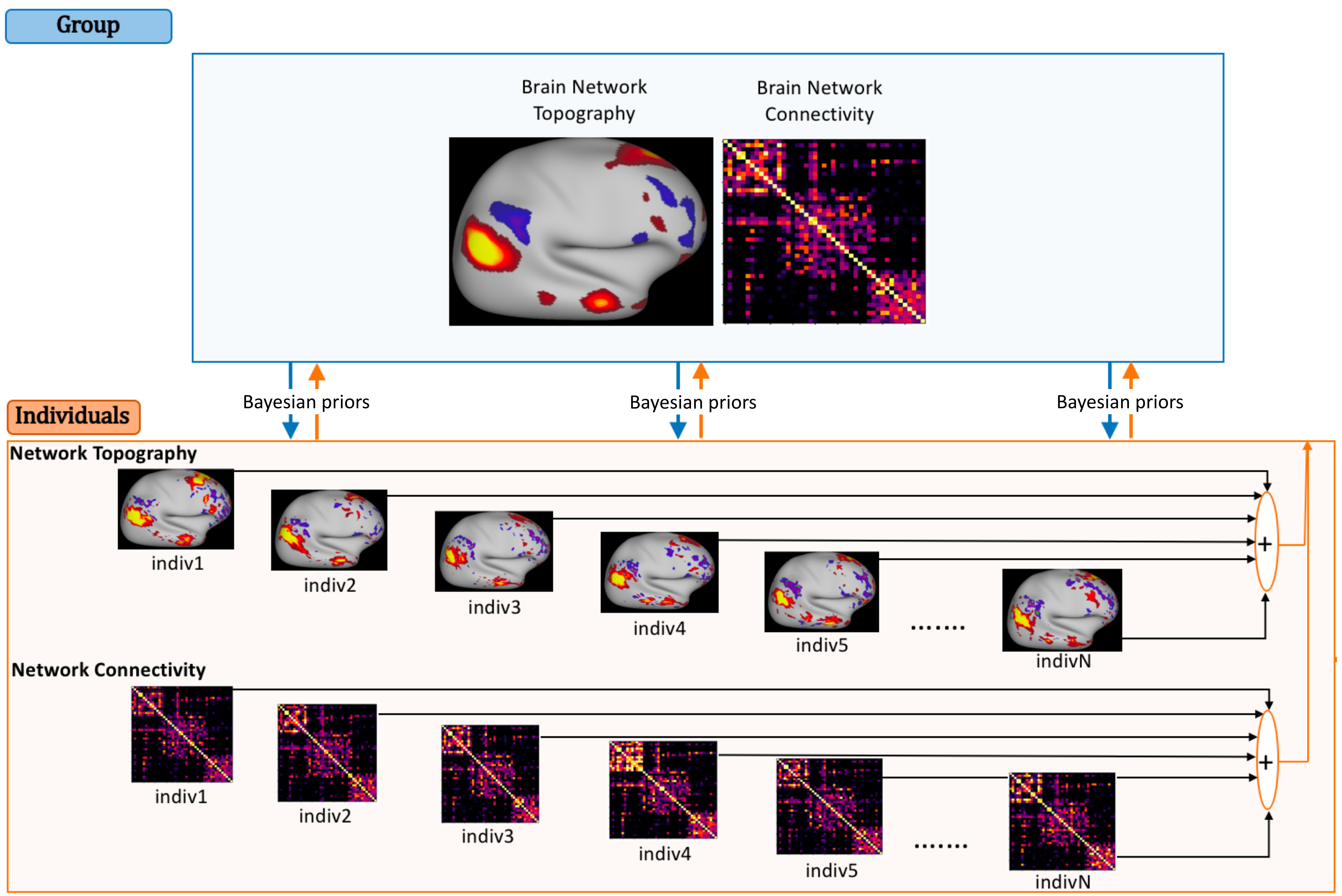
Hierarchical solution to the probabilistic Bayesian framework

- Therefore, the model will:
  1. Compute an initial set of group-level modes
  2. Use priors from group-level modelling to regularise subject-specific estimations.
  3. Use accumulated posterior evidence across subject PFMs to update the group
  4. Iterate steps 2&3 until convergence



Hierarchical solution to probabilistic framework

- To define the priors and optimise the subject-specific networks, the model works around these ideas:
    1. The general spatial layout of the modes correspond across individuals, e.g. default mode network occupies roughly the same regions;
    2. The general organisation of functional connectivity between the modes corresponds across individuals.
    3. No group-level priors on time courses, but time course amplitudes are also defined hierarchically.

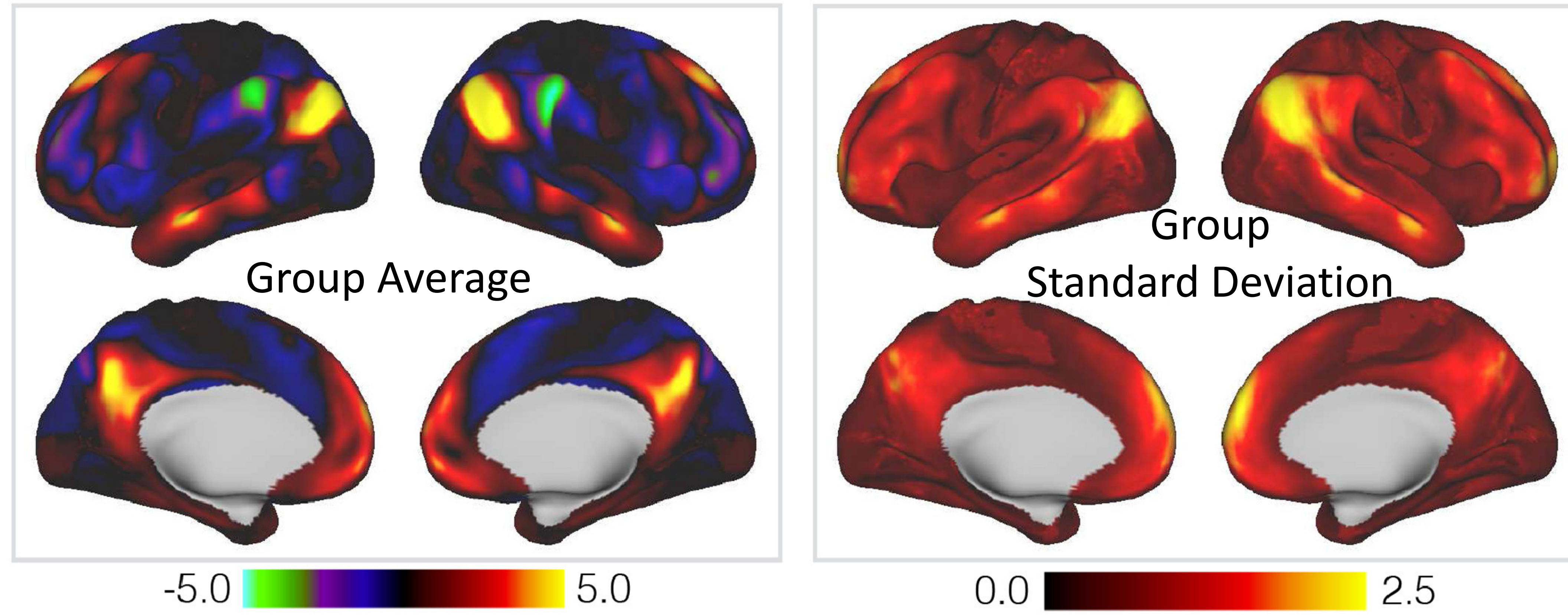


What are the key features of PFM?

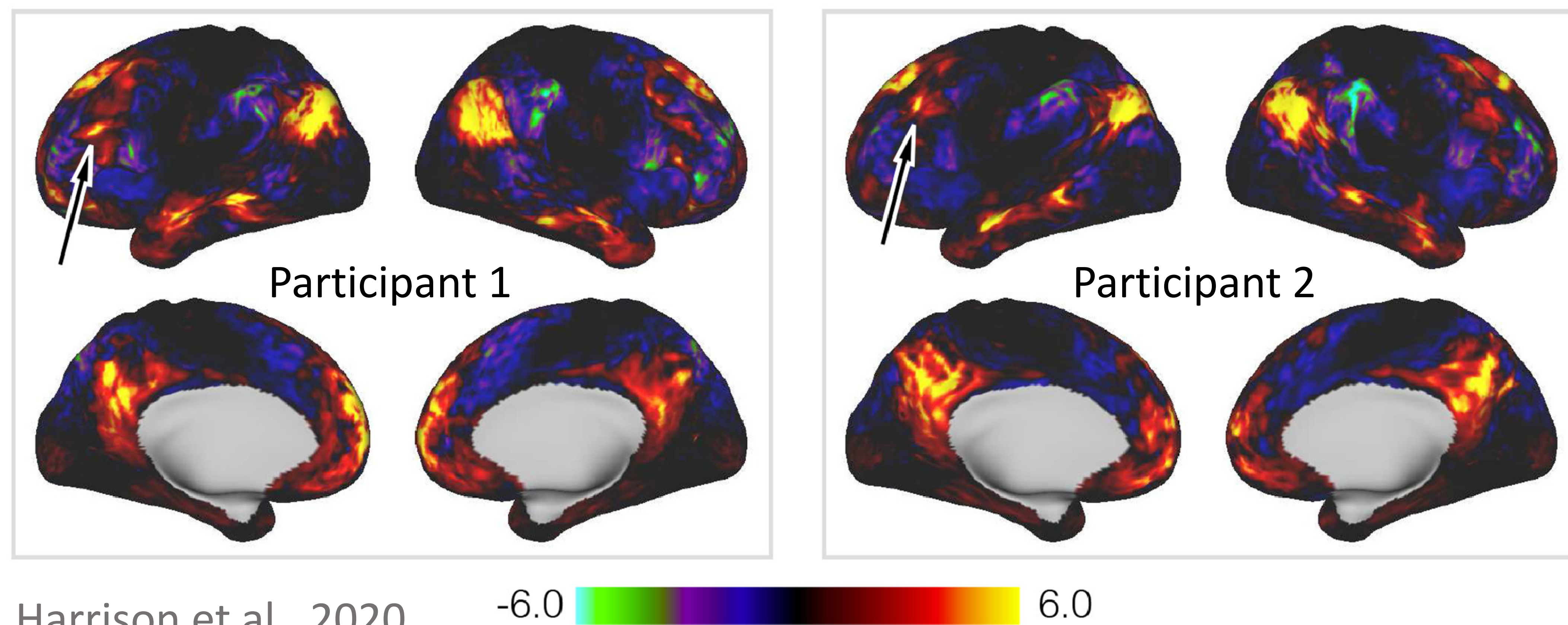
1) Simultaneous group and subject modelling

PFMs optimise group-level and subject-level mode estimations in a unified iterative process, which allows for bidirectional flow of information between population and individuals, leading to:

1. Group-model learning richer population variations



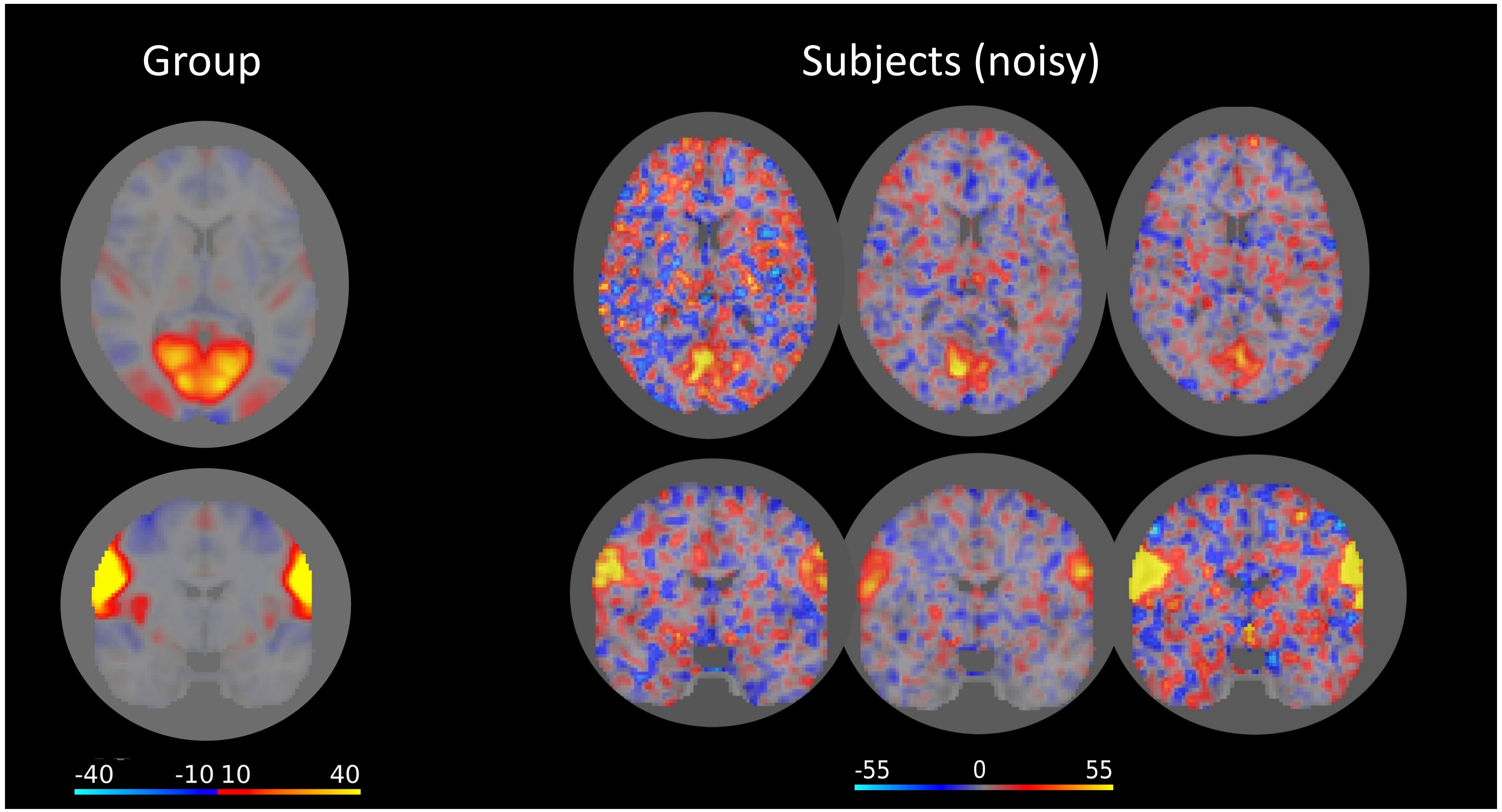
2. Accurate capturing of subject-specific deviations from the group



Harrison et al., 2020

2) Separating *spatial* signal from background noise for subject-specific modes- continued

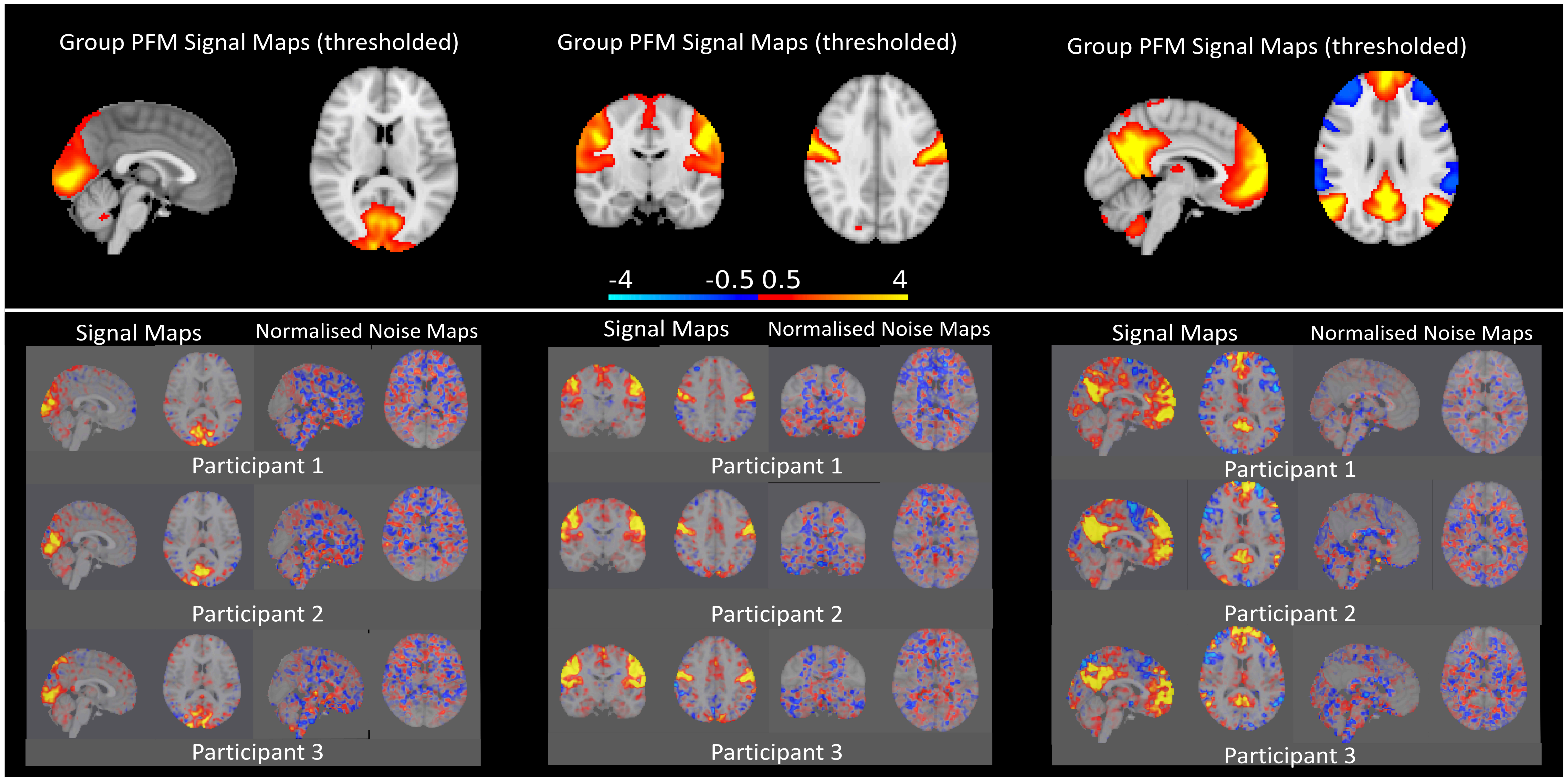
- Non-invasive recordings in fMRI means that data can be noisy
  - In group-level estimations, noise can be cancelled by averaging across individuals
  - Estimating clean modes for individual subjects can be very challenging



2) Separating *spatial* signal from background noise for subject-specific modes

To resolve this, PFMs use mixture modelling of each functional mode for each subject

- Each mode is summarised with **two** Gaussian distributions
- One distribution capturing signal, another capturing background noise

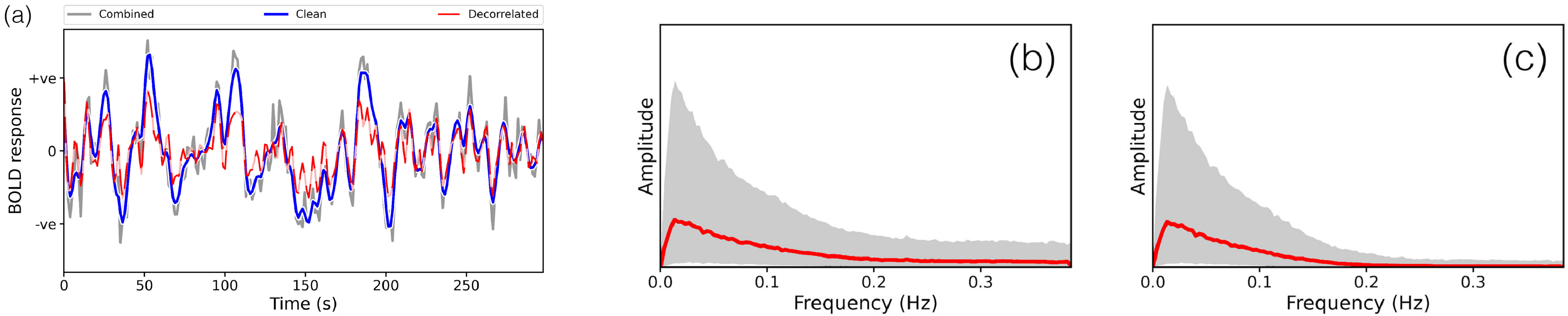


Based on Harrison 2020, Farahibozorg 2021

3) Separating *temporal* signal from background noise for subject-specific modes

Similarly, mode timecourses are separated into signal and noise subparts

- Signal part is constrained by a Haemodynamic Response Function (HRF)
- Noise part is modelled with a Gaussian distribution



Harrison et al., 2020

Part 1 summary - in this lecture we learned that:

1. PFMs provide a unified framework to model population and every individual simultaneously
   - This is done via an iterative process, where group model is used for subject-specific regularisation and vice versa
2. To achieve this, PFMs use hierarchical Bayesian inference
   - We define probability distributions over spatio-temporal mode characteristics
   - Our aim is to optimise these distributions to explain the data, thus obtaining probabilistic functional modes
   - Hierarchy defined over spatial maps and functional connectivity (NetMats)
3. This framework provides the following advantages:
   - Group model capturing more variability
   - More accurate modelling of subject deviation from the group
   - Separating spatial and temporal Signal from background Noise to obtain 'clean' subject modes

Thank you!