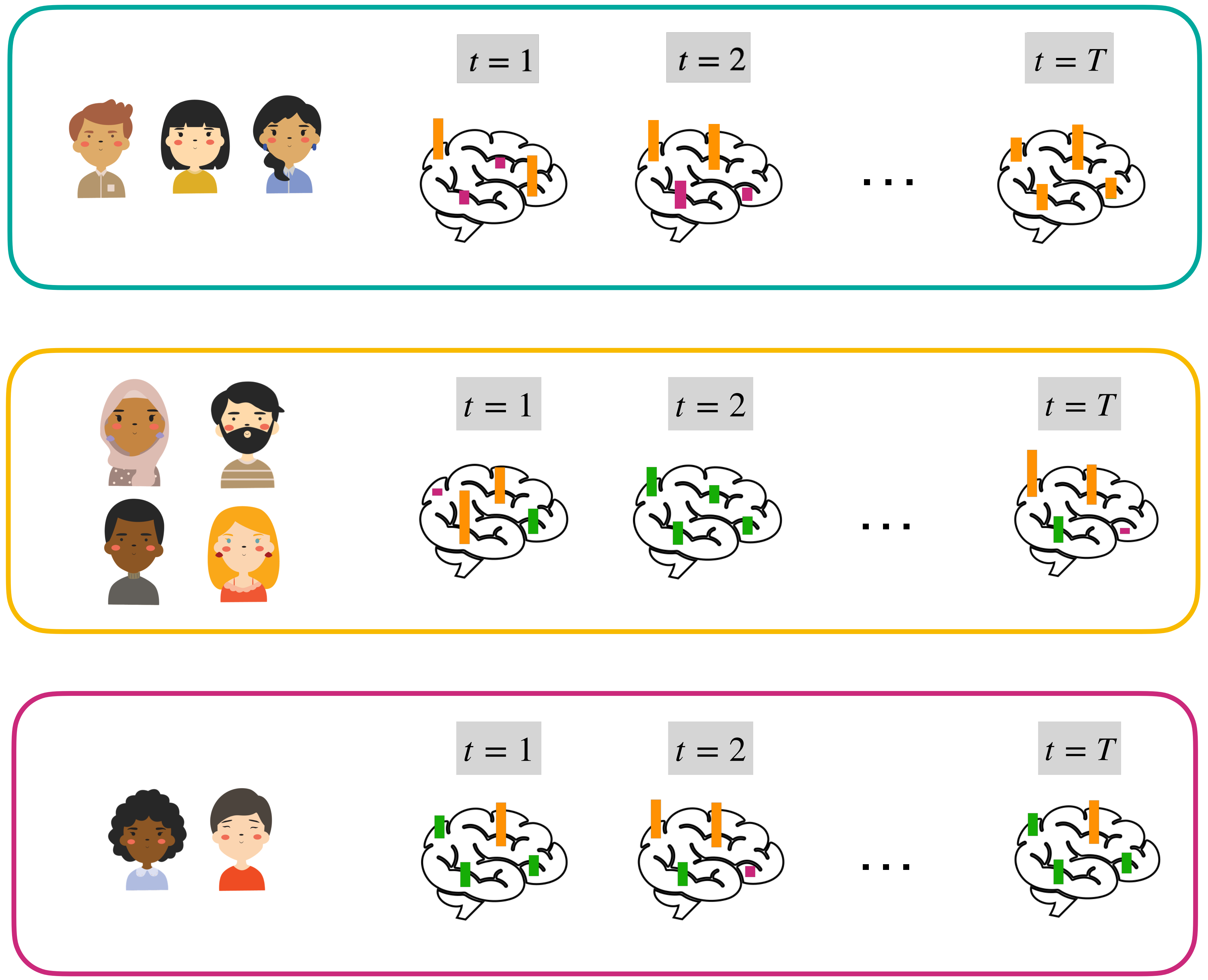
Bayesian temporal biclustering with applications to multi-subject neuroscience studies



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July 5 2024, ISBA World Meeting

Collaborators

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Megan Peters (UCI Cognitive Sciences)

Funding

HPI Hasso Plattner Institut
IT Systems Engineering | Universität Potsdam

Hasso Plattner Institute in Machine Learning and Data Science at UCI

Motivating data

Many studies observe **multiple units** over time and collect **a range of measurements** on each unit at **specific time intervals**

Application field	Units	Measurements
Climate studies	Locations	Meteorological variables
Economic studies	Countries	Economic indicators
Neuroscience studies	Subjects	Brain regions' signals
…	…	…

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Functional Magnetic Resonance Imaging (fMRI)

Electroencephalogram (EEG)

Motivating data (1)

- fMRI study conducted at UC Riverside Center for Advanced Neuroimaging
- Multiple subjects undergo 12.8 m experiment of alternating between
  - 18-sec squeeze blocks (SQ1-SQ5) when dominant hand brought to chest and ball is squeezed at maximum grip strength
  - resting blocks (RS1-RS5)

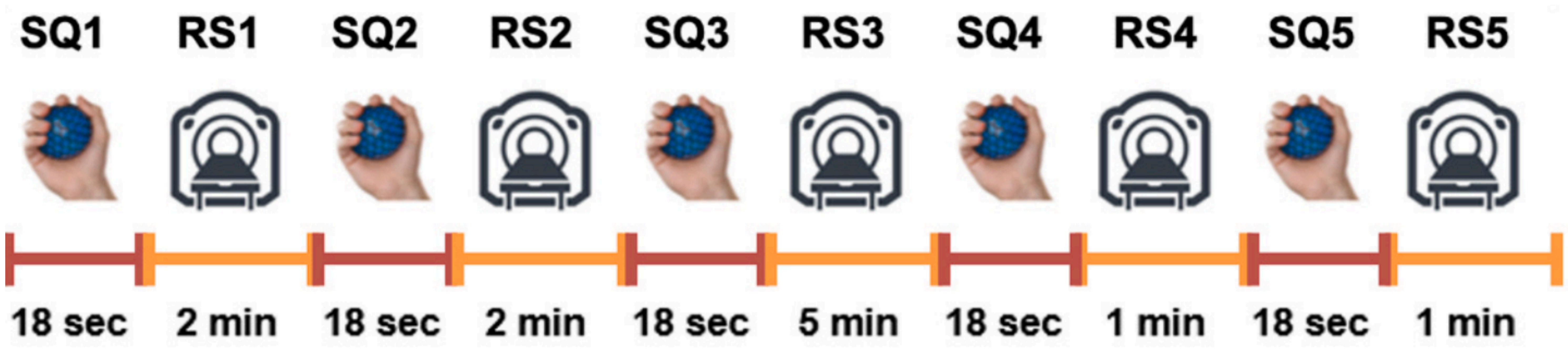


Image credit: Hussain, Sana, et al. (2023)

Motivating data (1)

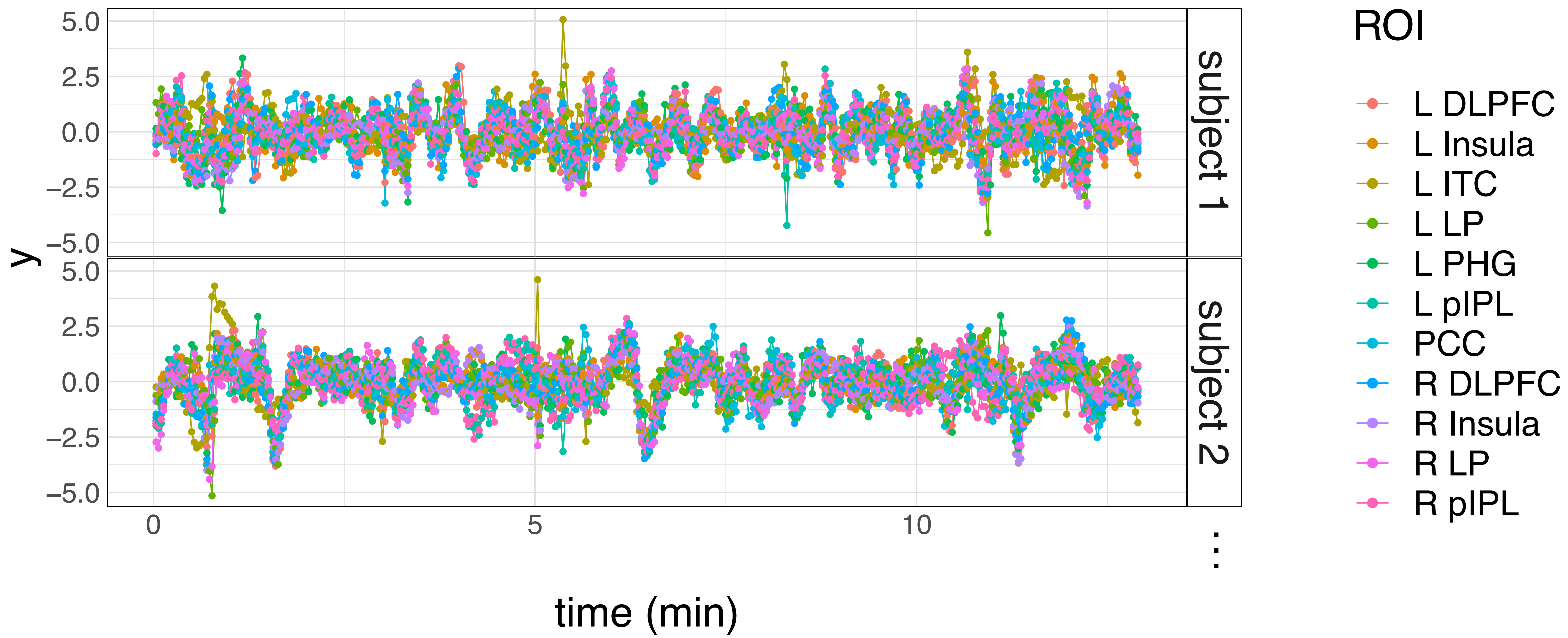
- Blood Oxygenation Level Dependent (BOLD) time-series from 23 subjects
- 11 regions of interest (ROIs), chosen from the Default Mode Network (associated with resting) or the Salience Network (allocating response to stimuli)

Y_{irt} : BOLD signal

subject $i = 1, \ldots, N$

ROI $r = 1, \ldots, R$

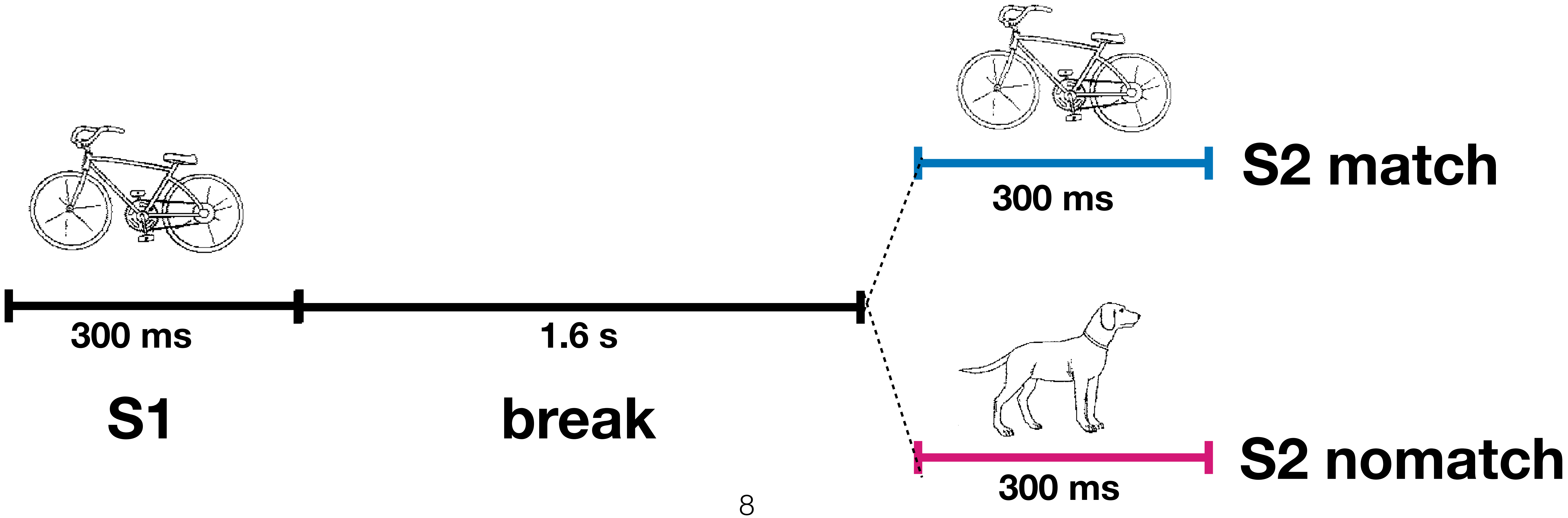
time $t = 1, \ldots, T$



Motivating data (2)

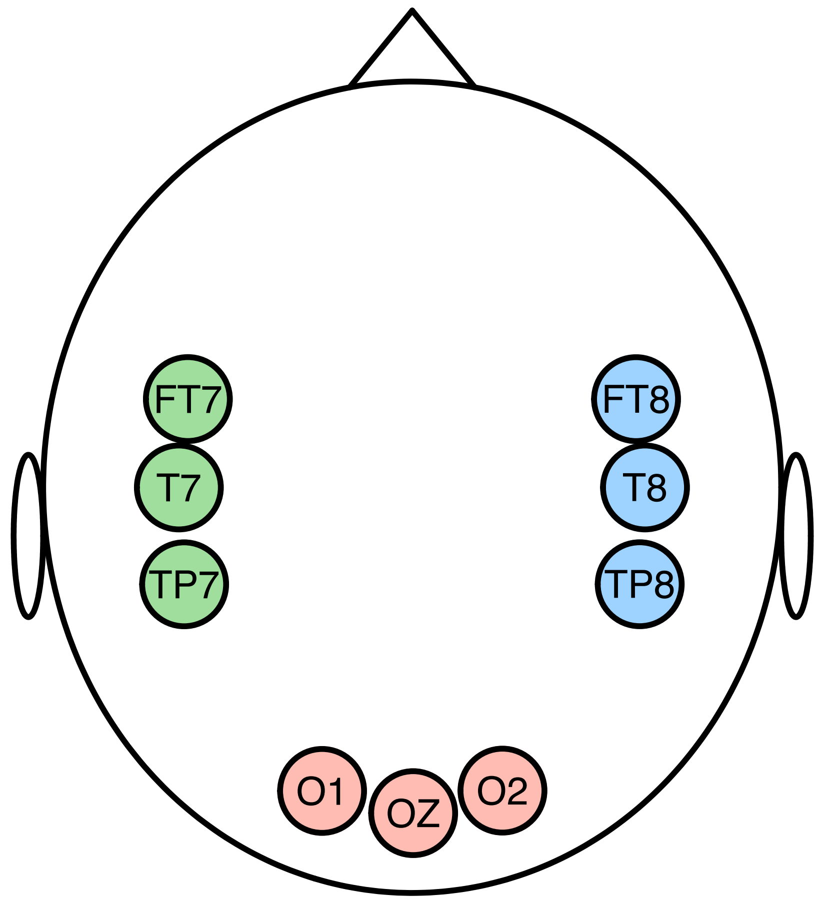
- EEG dataset publicly available on the UCI Machine Learning Repository
- Multiple subjects undergo multiple trials in which they are shown
  - a first picture (S1)
  - a picture identical to first (S2 match) or semantically different (S2 nomatch)

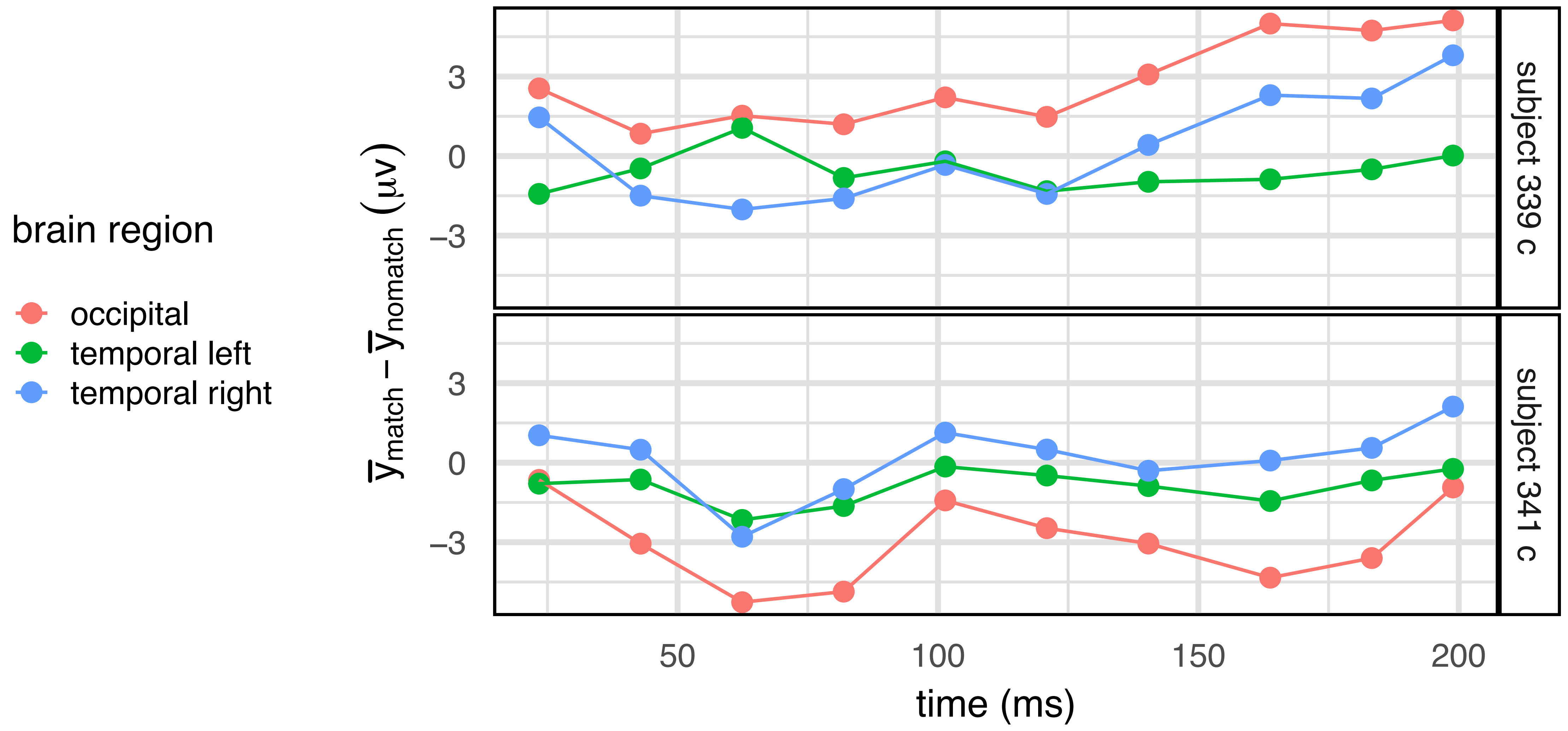
Images from Snodgrass & Vanderwart (1980)



Motivating data (2)

- Event Related Potentials (ERP) time-series (averaged across trials) from 121 subjects
- ERP averaged across electrodes in left temporal region and in right temporal region (memory) and occipital region (receptive to visual stimuli)
- ERP difference of S2 match and S2 nomatch conditions -> remove subject-specific variability





Research questions

- What patterns of brain-region activation are there in any given moment of the experiment? — *Brain region clusters*
- How do patterns of brain-region activation change during the experiment? — *Dynamic brain region clusters*
- How do patterns of brain-region activation vary across subjects? — *Subject clusters*

Within subject *Across subjects*

Prior relevant work

Prior relevant work

BICLUSTERING

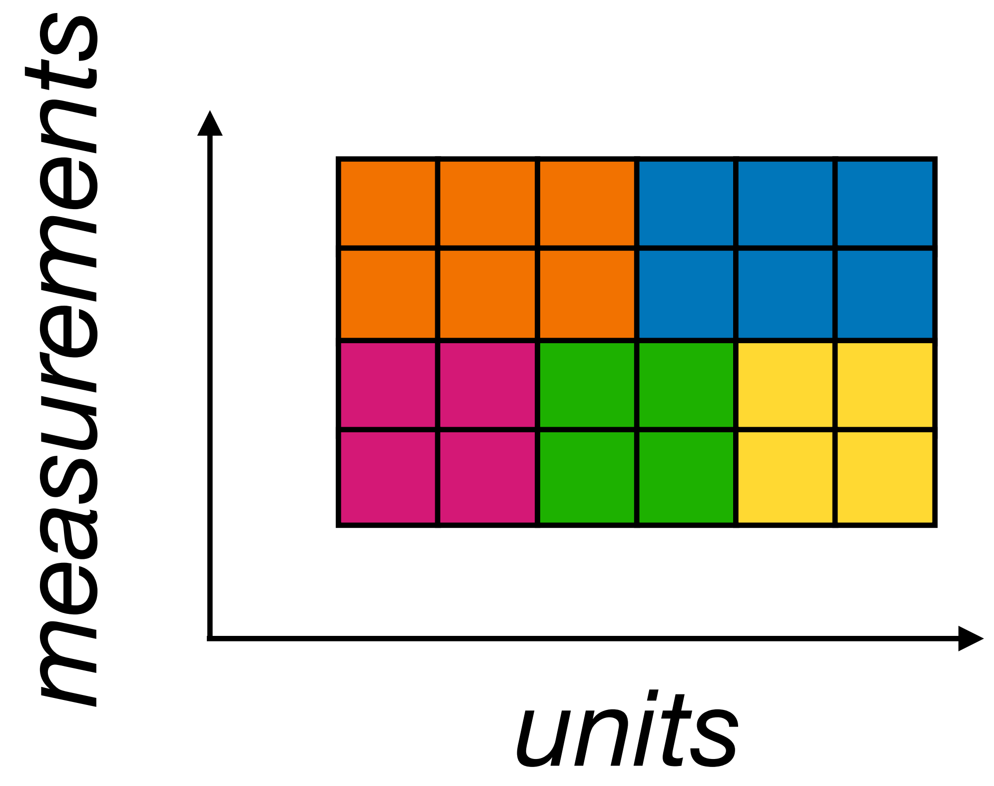
Nonparametric Bayesian Model for Local Clustering With Application to Proteomics (Lee et al. 2013, JASA)

+ *Murua and Quintana (2022, BA)*

Multiple units ✅

Multiple measurements ✅

Time ❌



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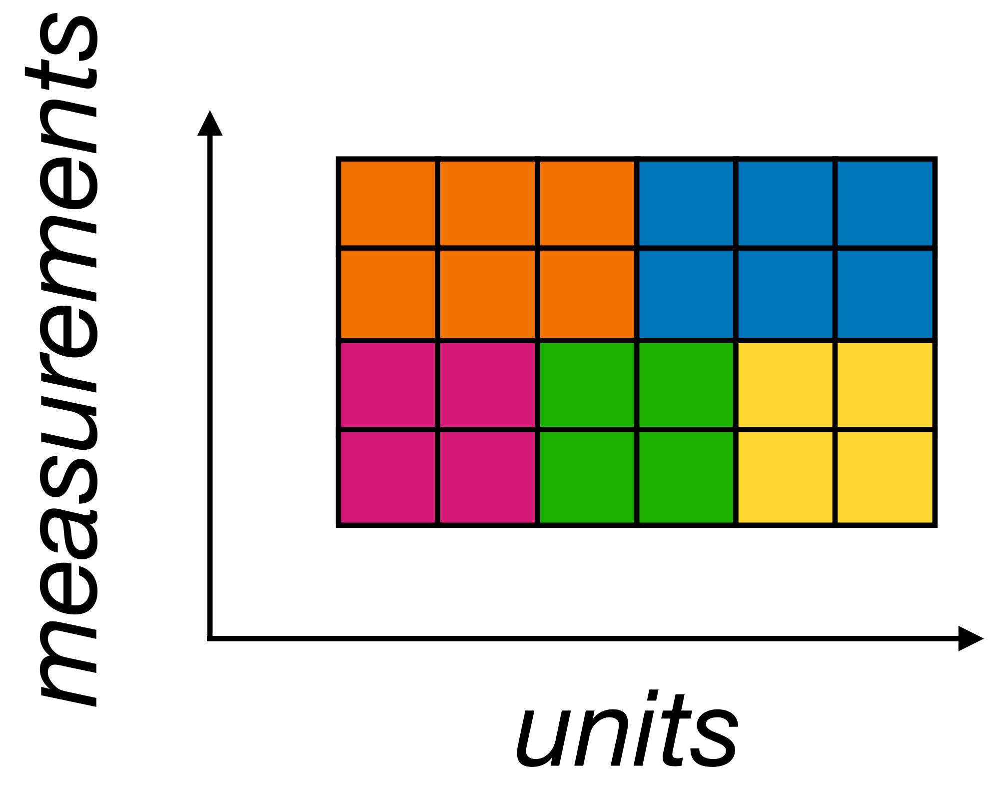


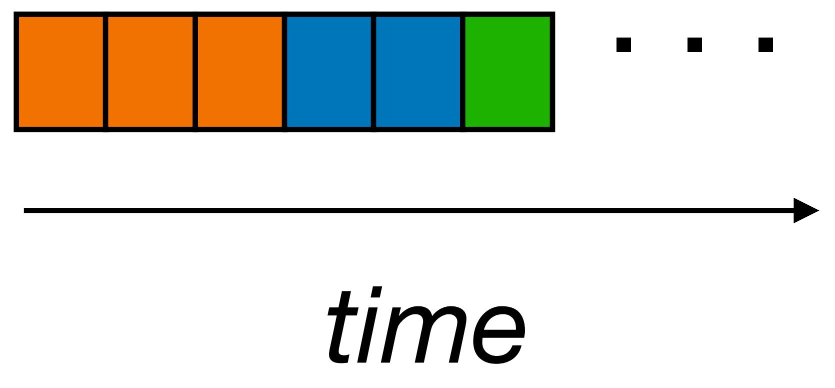
TIME-SERIES CLUSTERING

A Sticky HDP-HMM with Applications to Speaker Diarization (Fox et al. 2011, AOAS)

Multiple units ❌

Multiple measurements ❌

Time ✅



Prior relevant work

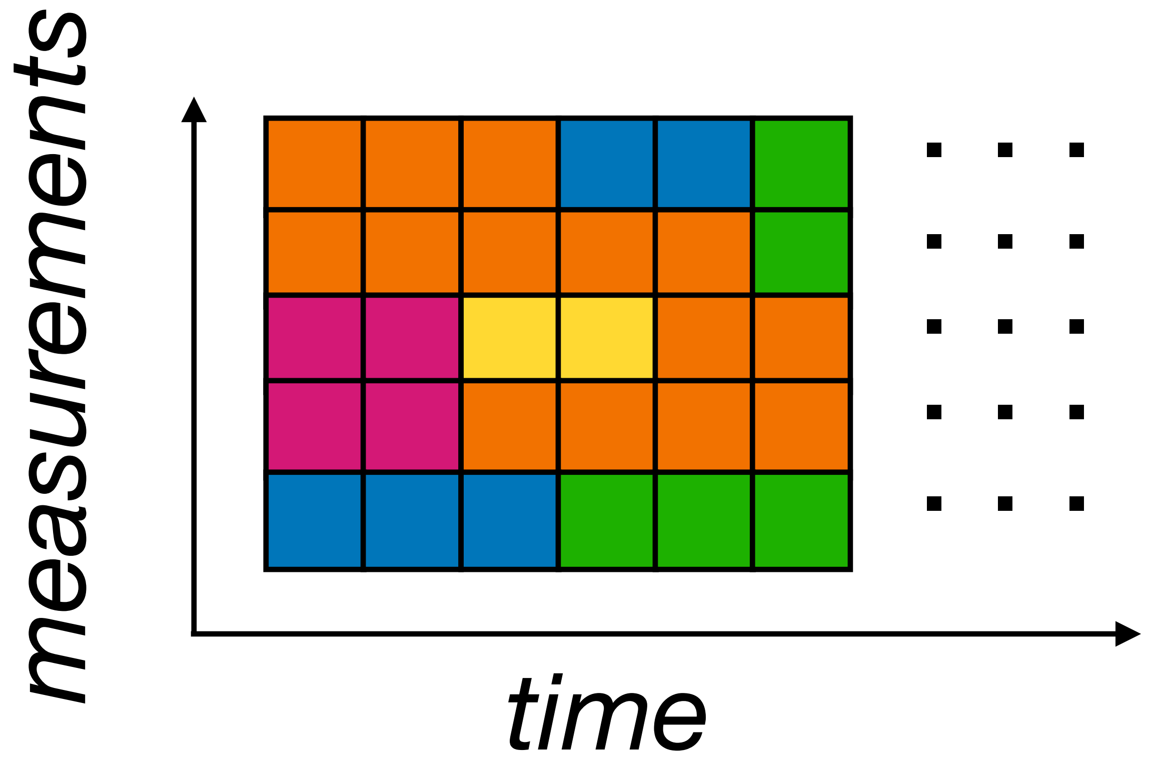
MULTIVARIATE TIME-SERIES CLUSTERING

Dependent Modeling of Temporal Sequences of Random Partitions (Page et al. 2022, JCGS)

Multiple units ❌

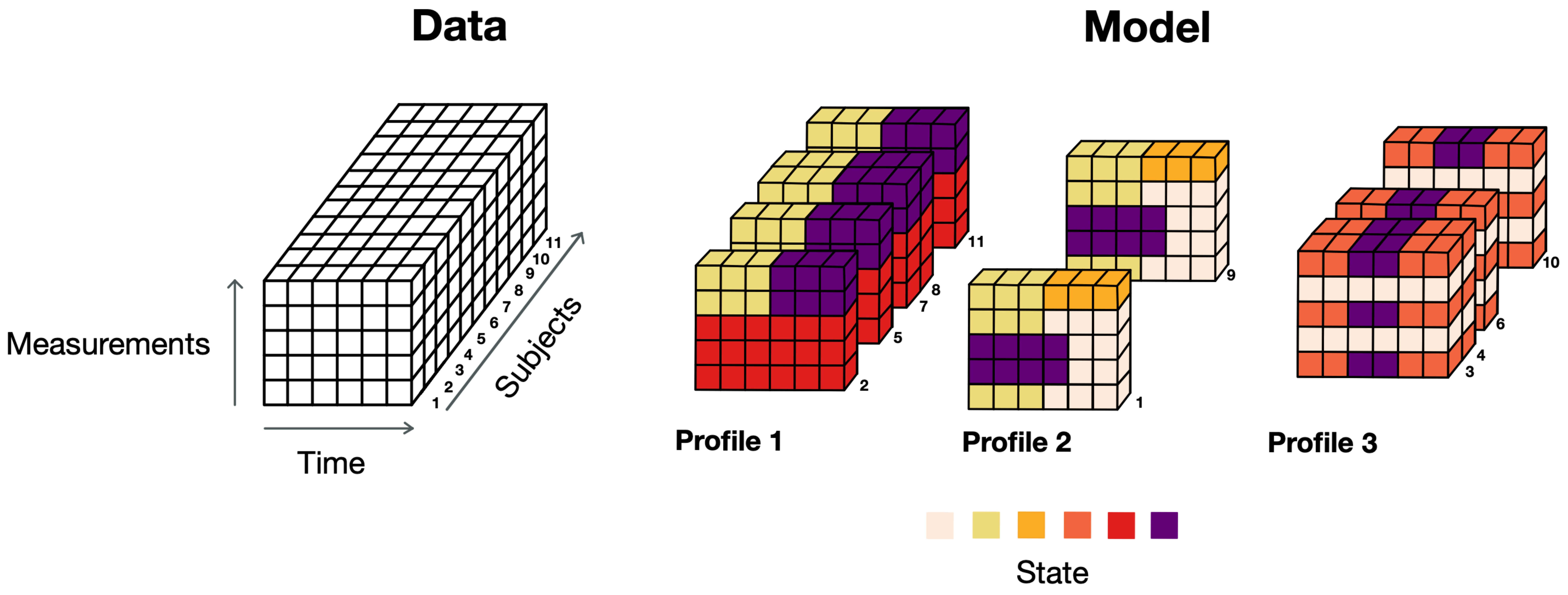
Multiple measurements ✅

Time ✅



Overview of our framework

MULTI-SUBJECT, MULTIVARIATE TIME-SERIES CLUSTERING

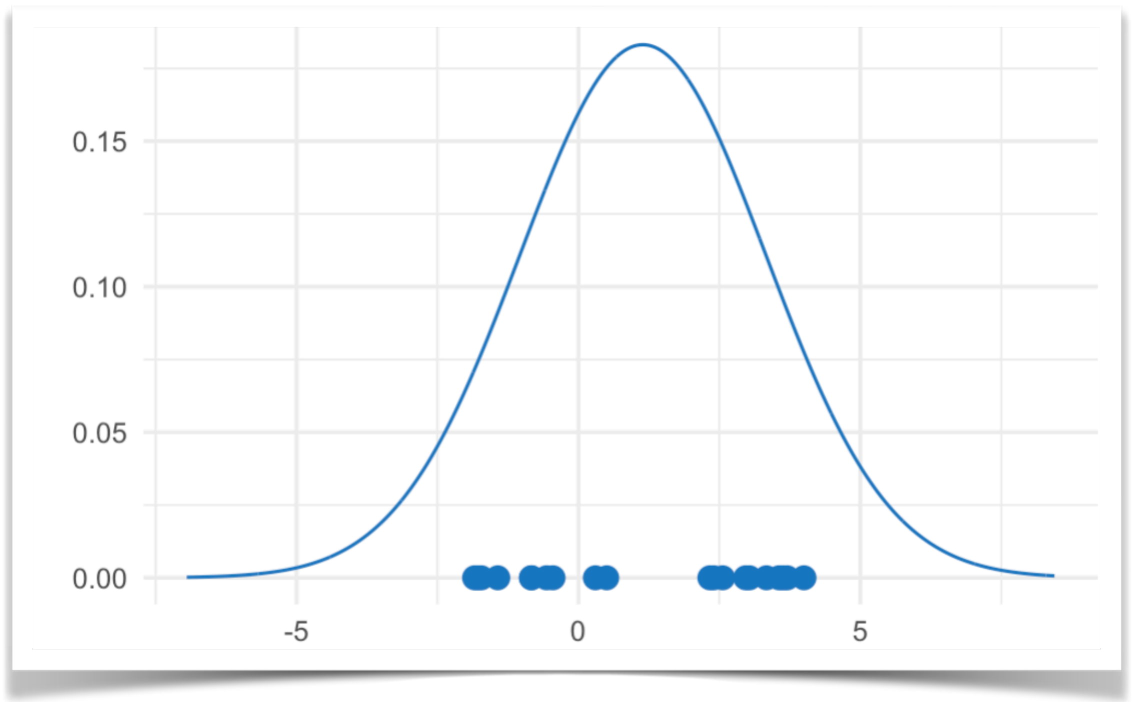


Temporal biclustering model

Clustering all brain regions for one subject and first time step

Data

Y_r for ROI $r = 1, \ldots, R$



Clustering all brain regions for one subject and first time step

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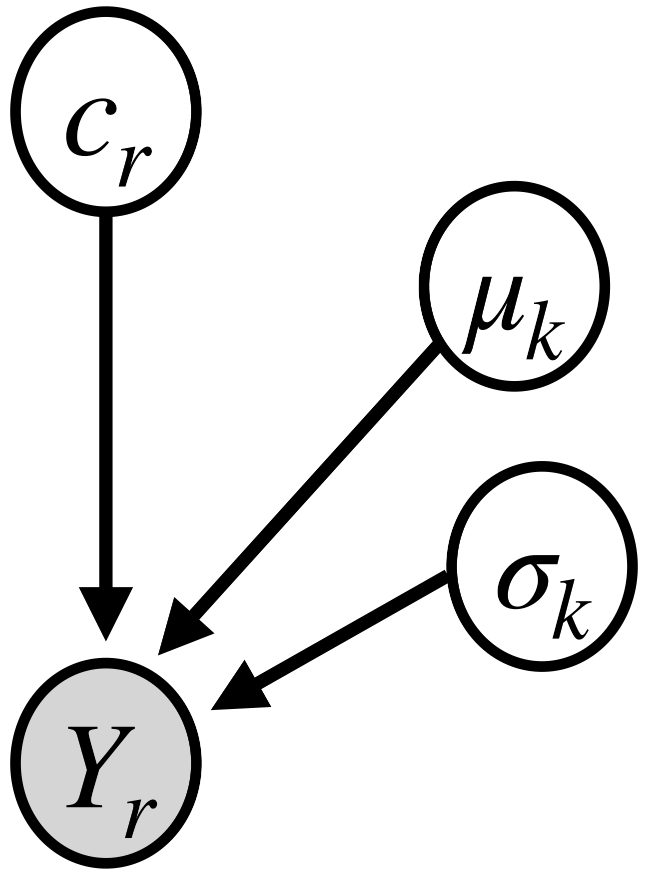
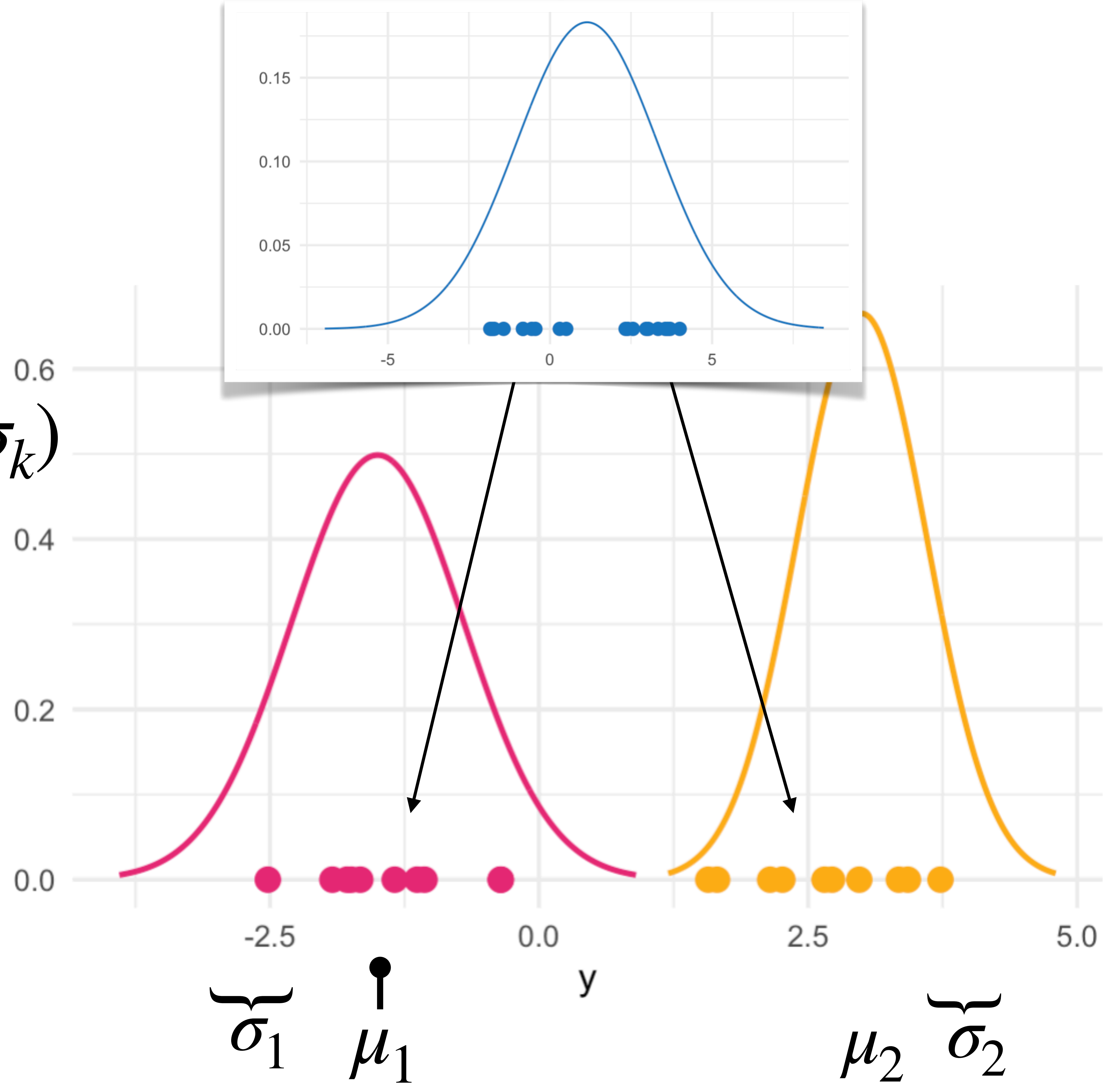
Y_r for ROI $r = 1, \ldots, R$

Statistical model



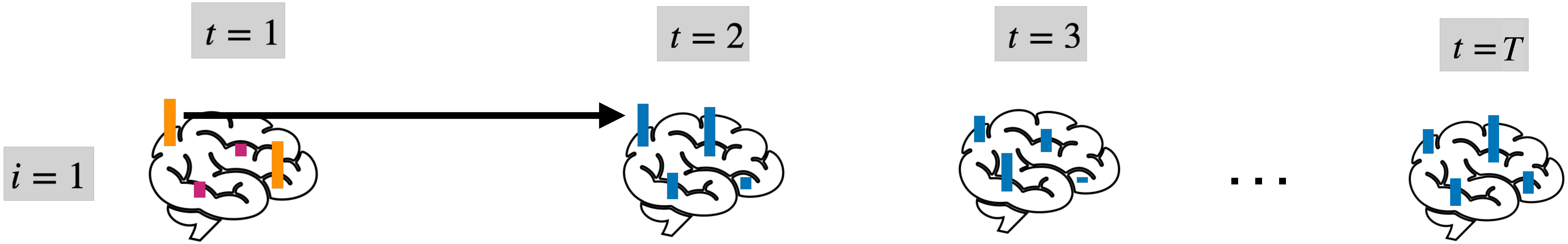
$Y_r \mid c_r = k \sim$ Student-t(μ_k, σ_k)

Inferred activation pattern



Brain region clusters (dynamic)

How can we model the way clustering changes over time?



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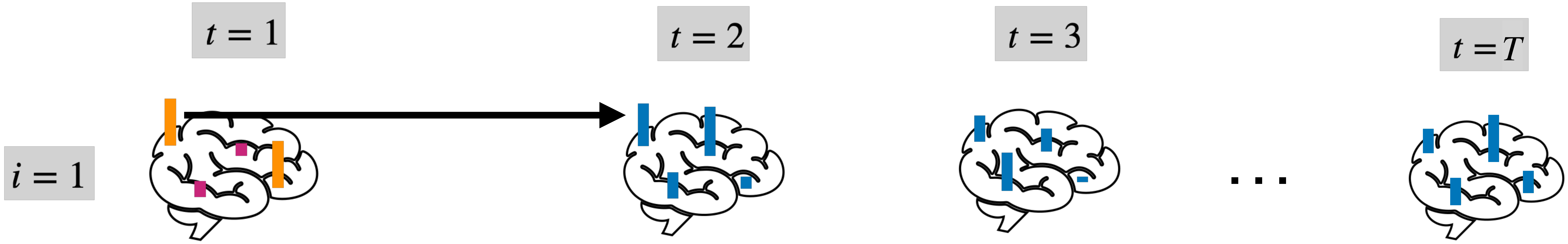

with probability α_2 : $\quad c_{r2} = c_{r1}$

with probability $1 - \alpha_2$: $\quad c_{r2} \sim$ Categorical$(p_1, \dots, p_K)$

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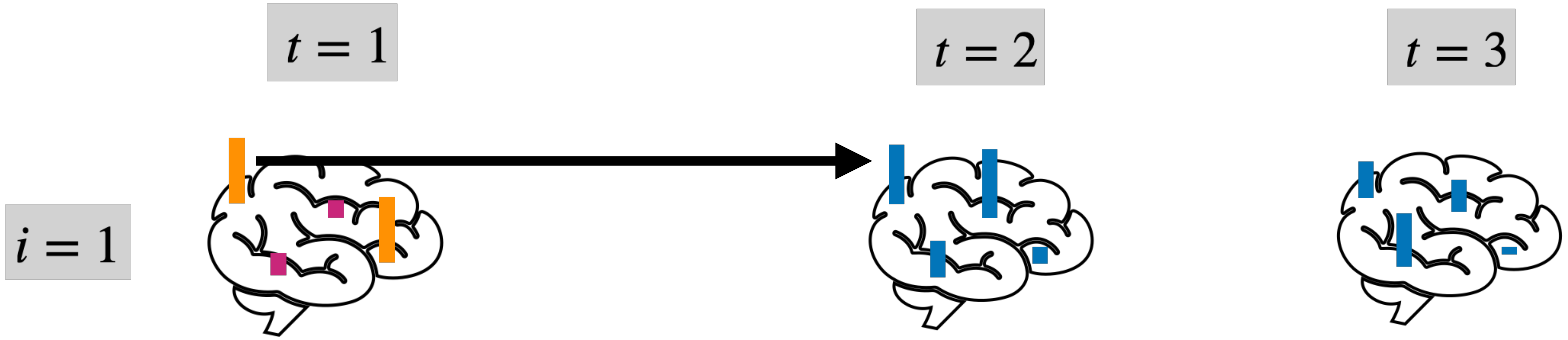

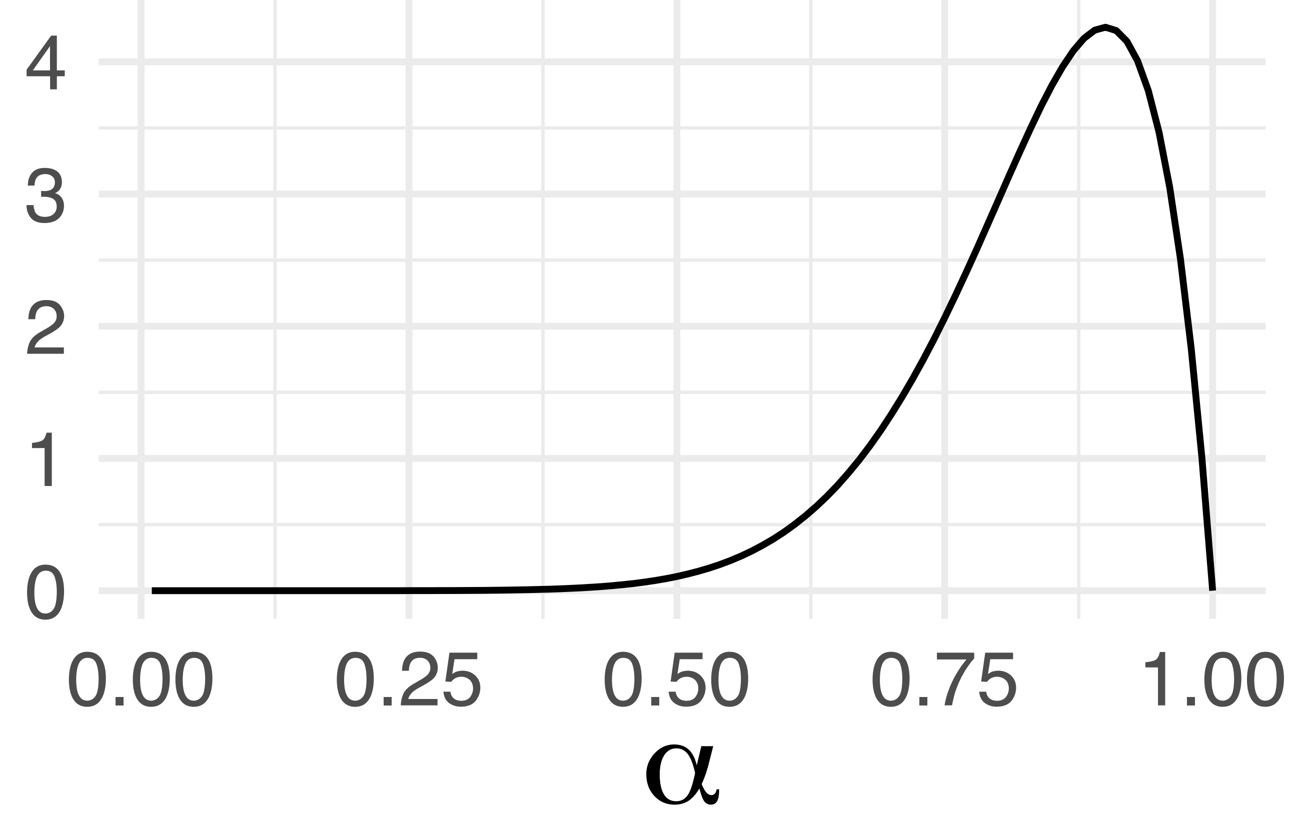

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$$\alpha_t \sim \text{Beta}(10,2)$$

Large α_t encourages smooth dynamics!

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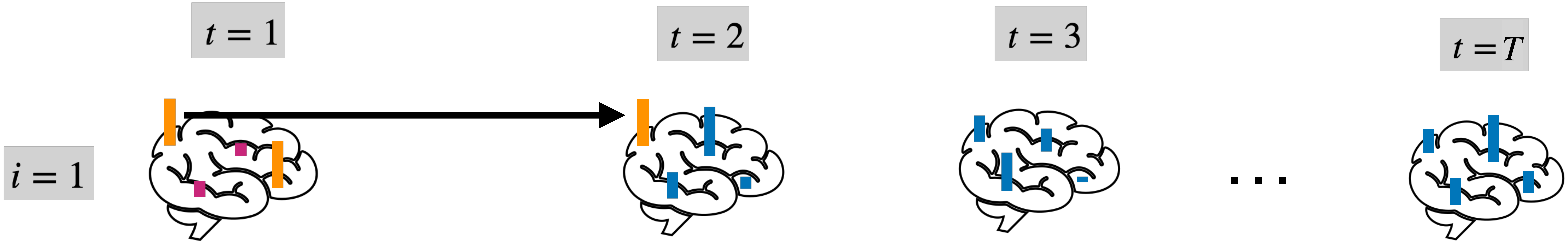

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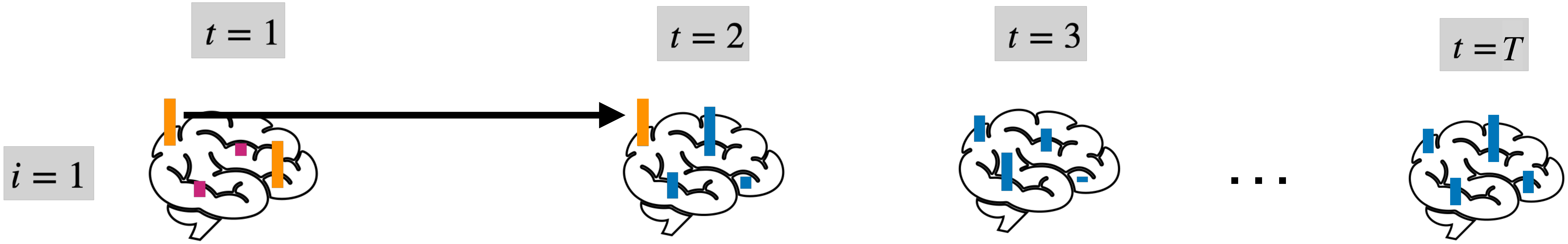

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Prior on $\mathbf{p} = (p_1, \dots, p_K)$ *such that active number of clusters can:*

- *be learned from data*
- *differ across time and subjects*

Brain region clusters (dynamic)

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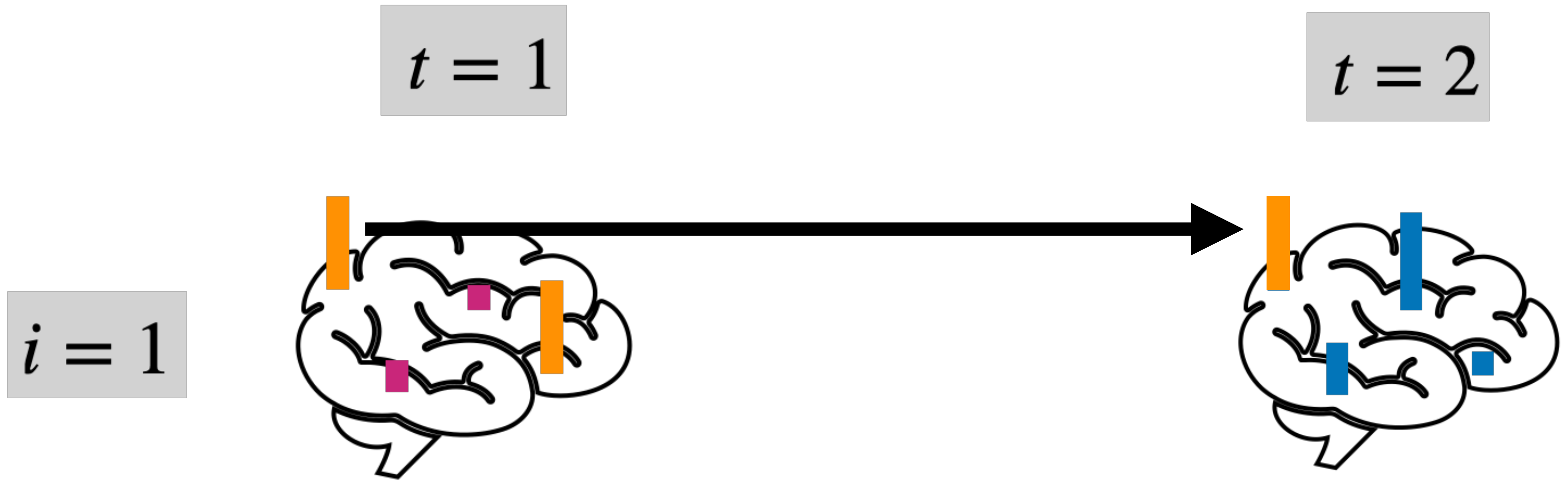

$$\boldsymbol{p} \mid \boldsymbol{p}_0 \sim \text{Dirichlet}(\phi\, \omega_{01}, \ldots, \phi\, p_{0K}),$$

$$\boldsymbol{p}_0 \mid \eta \sim \text{Dirichlet}\left(\frac{\eta}{K}, \ldots, \frac{\eta}{K}\right)$$

$$\eta \sim \text{Gamma}(d_1, d_2)$$

[Finite approx. of Hierarchical Dirichlet Process]

(Malsiner-Walli et al. 2016 Stat. Comput.)

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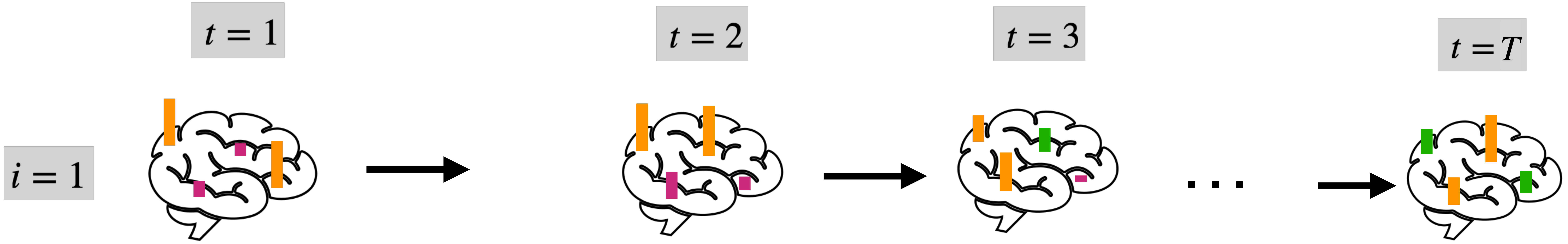

with probability α_T : $\quad c_{rT} = c_{r,T-1}$

with probability $1 - \alpha_T$: $\quad c_{rT} \sim$ Categorical$(p_1, \ldots, p_K)$

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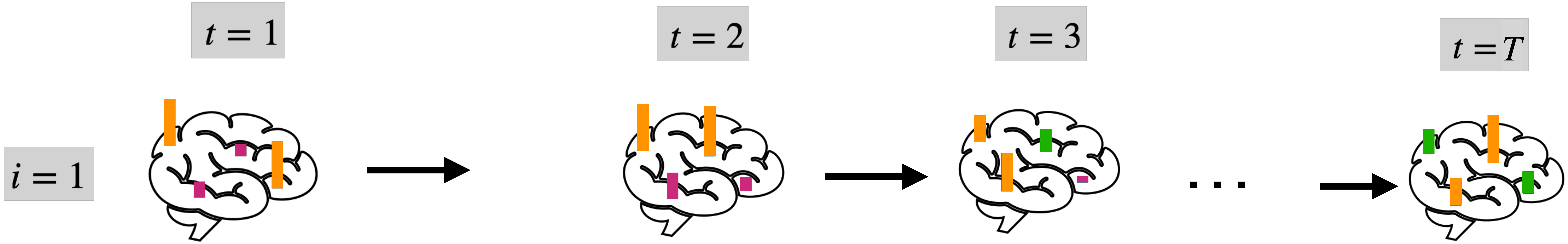

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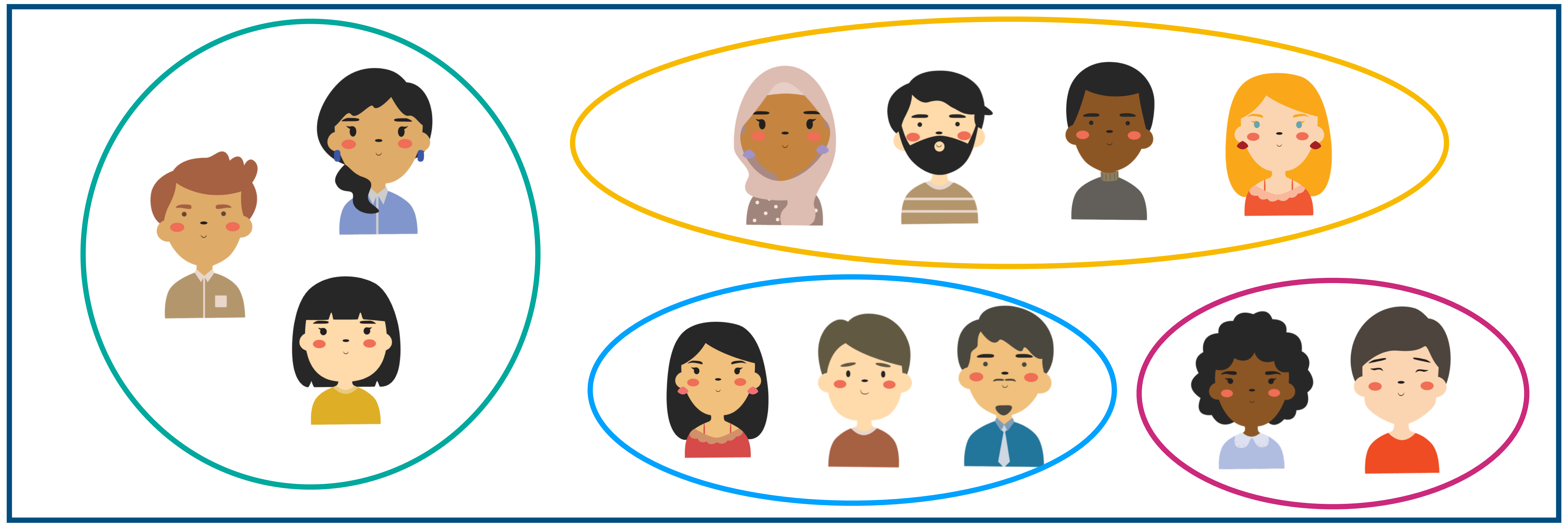
Adapted from the **Temporal Random Partition Model (Page et al. 2022, JCGS)**

Subject clusters

So far: brain regions clusters, over time.. for a single subject!

What about clusters of subjects?

Data



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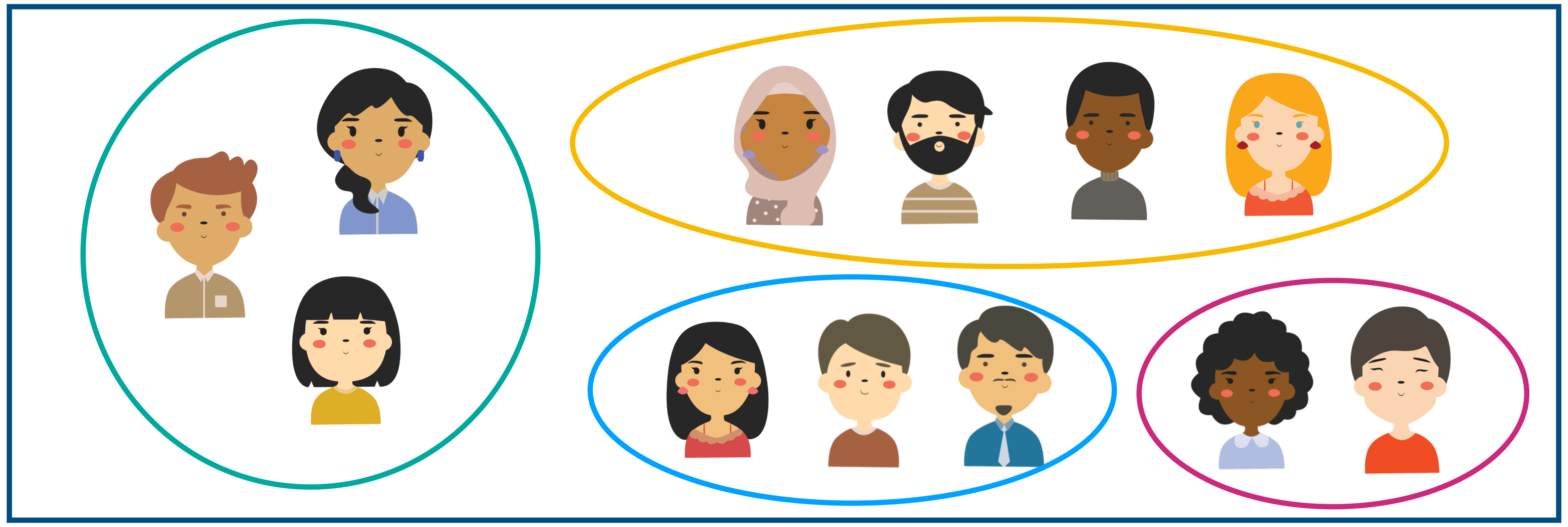
Data + **Inference on profiles** →



💡 **Profile**: specific **sequence of brain-region clusters** during the experiment

Subject clusters

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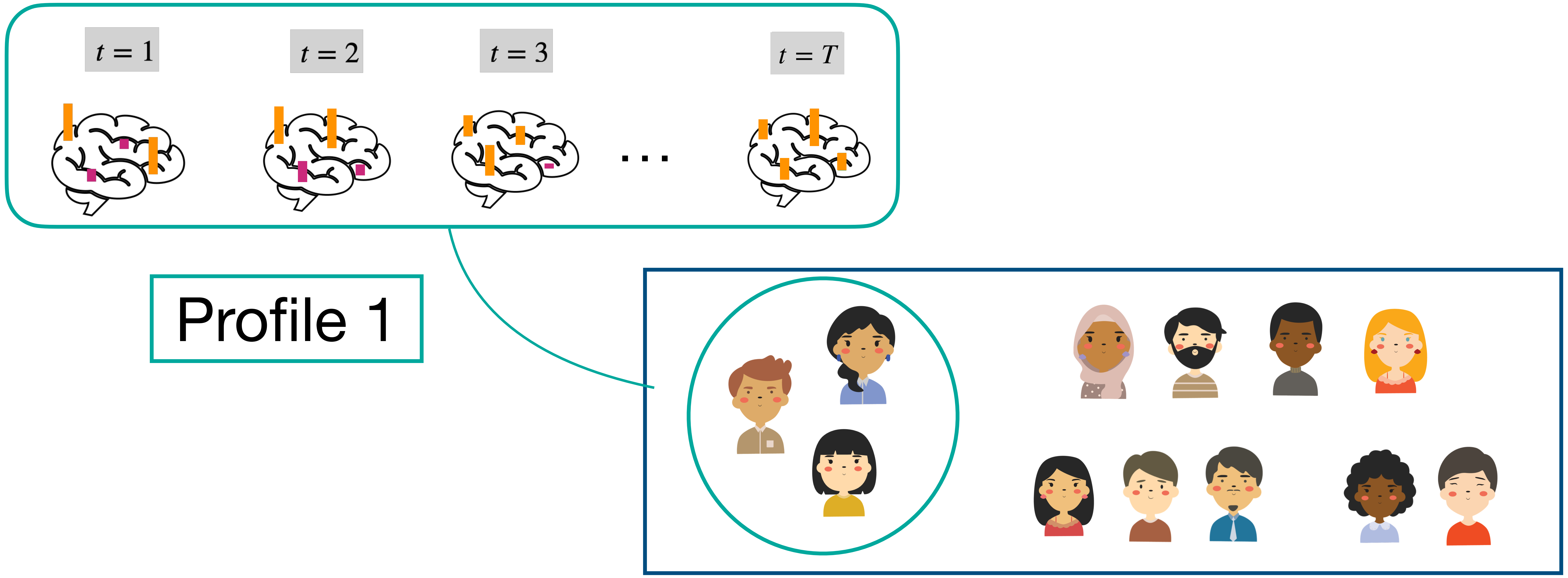

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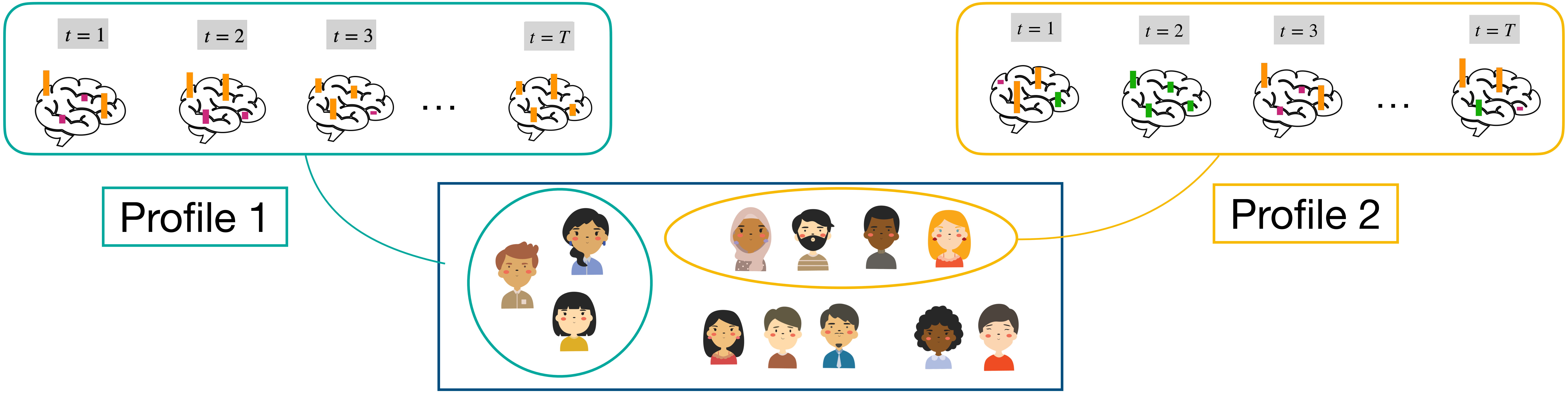

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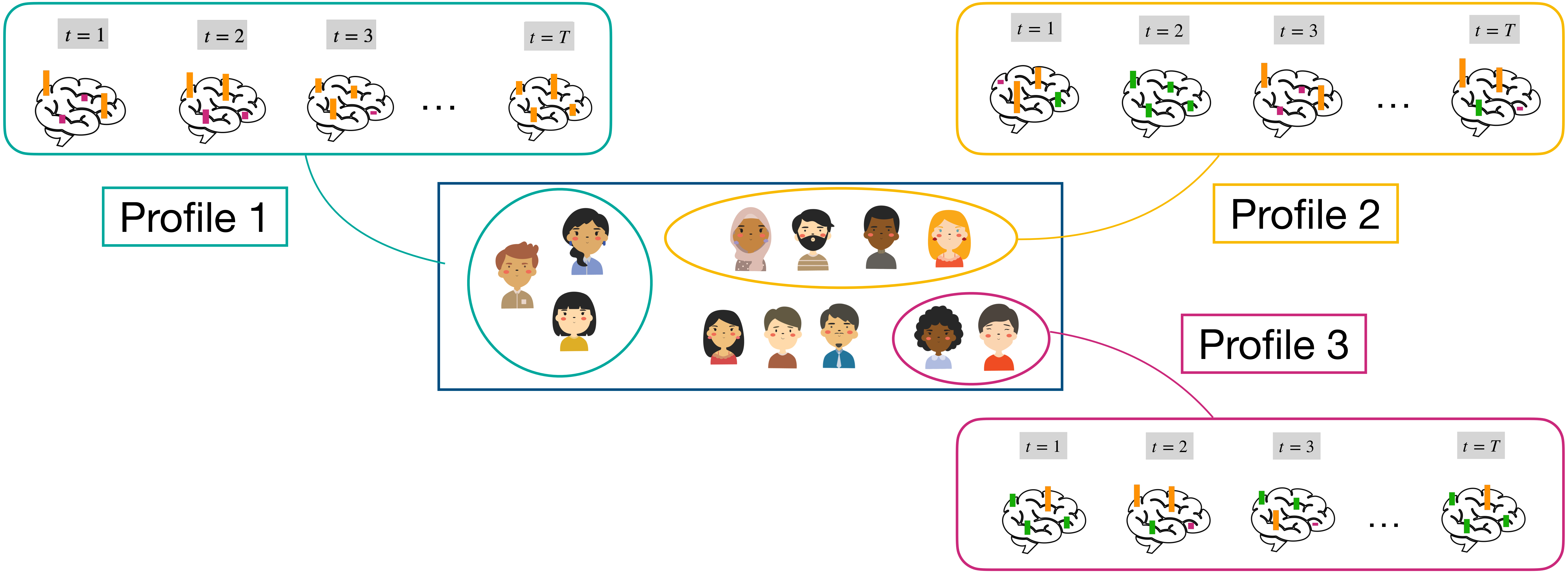

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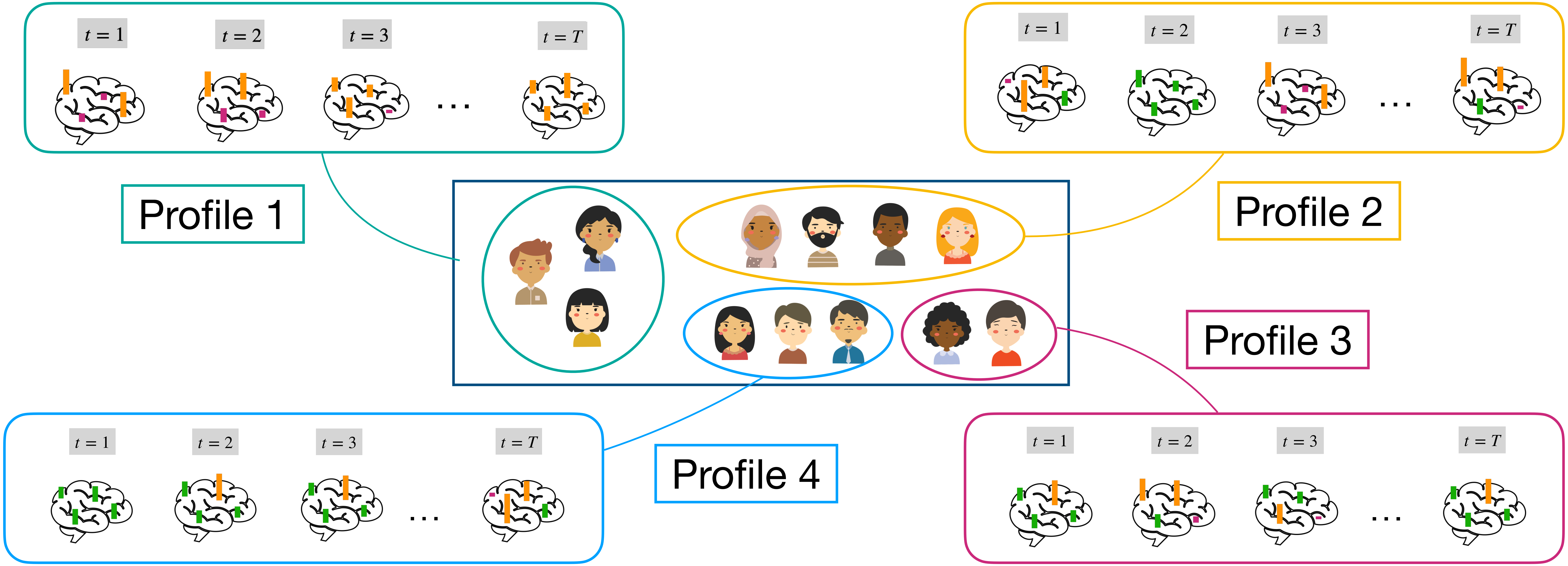

Full model

For subject i, brain region r and time t

Y_{irt}

Full model

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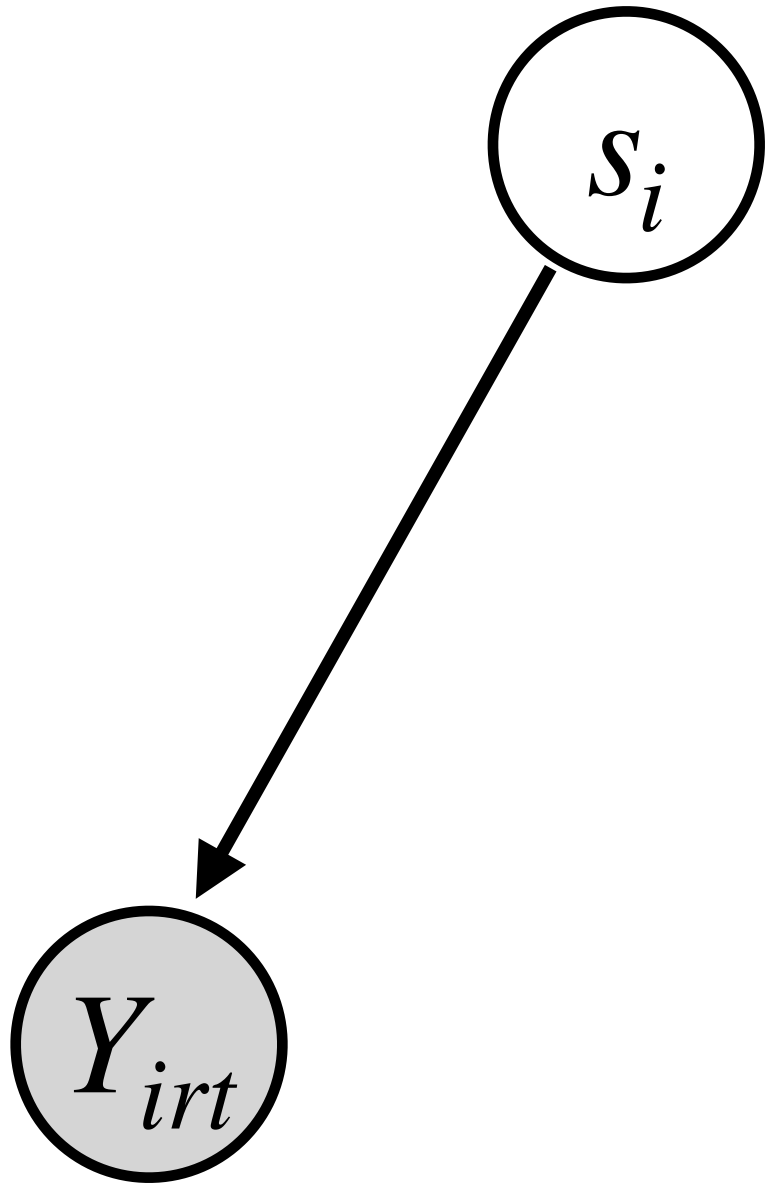
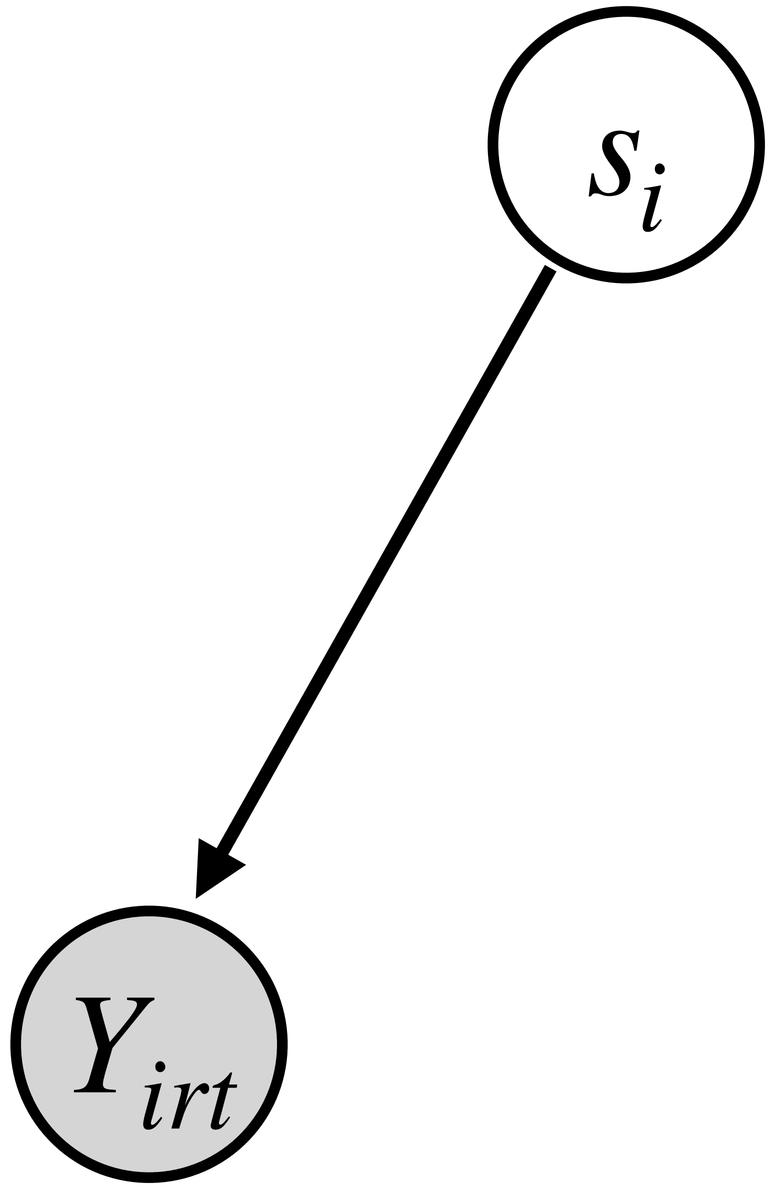


Profile of subject i

Full model

For subject i, brain region r and time t



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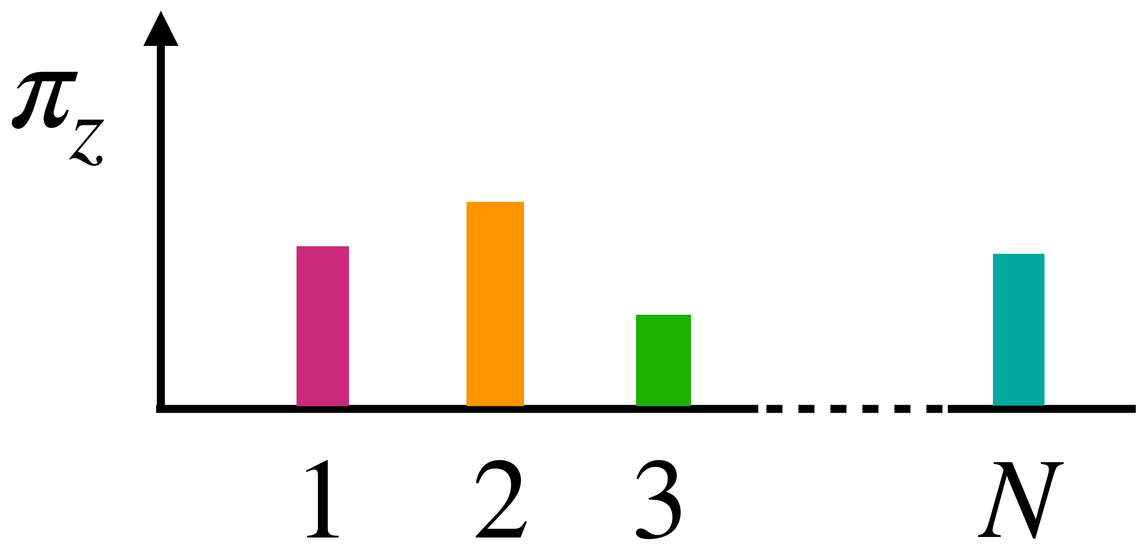

$$s_i \sim \text{Categorical}(\pi_1, \ldots, \pi_N)$$

$$\pi \sim \text{Dirichlet}\left(\frac{\varepsilon}{N}, \ldots, \frac{\varepsilon}{N}\right)$$

$$\varepsilon \sim \text{Gamma}(b_1, b_2)$$

Sparse Finite Mixture

[Finite approximation of Dirichlet Process]

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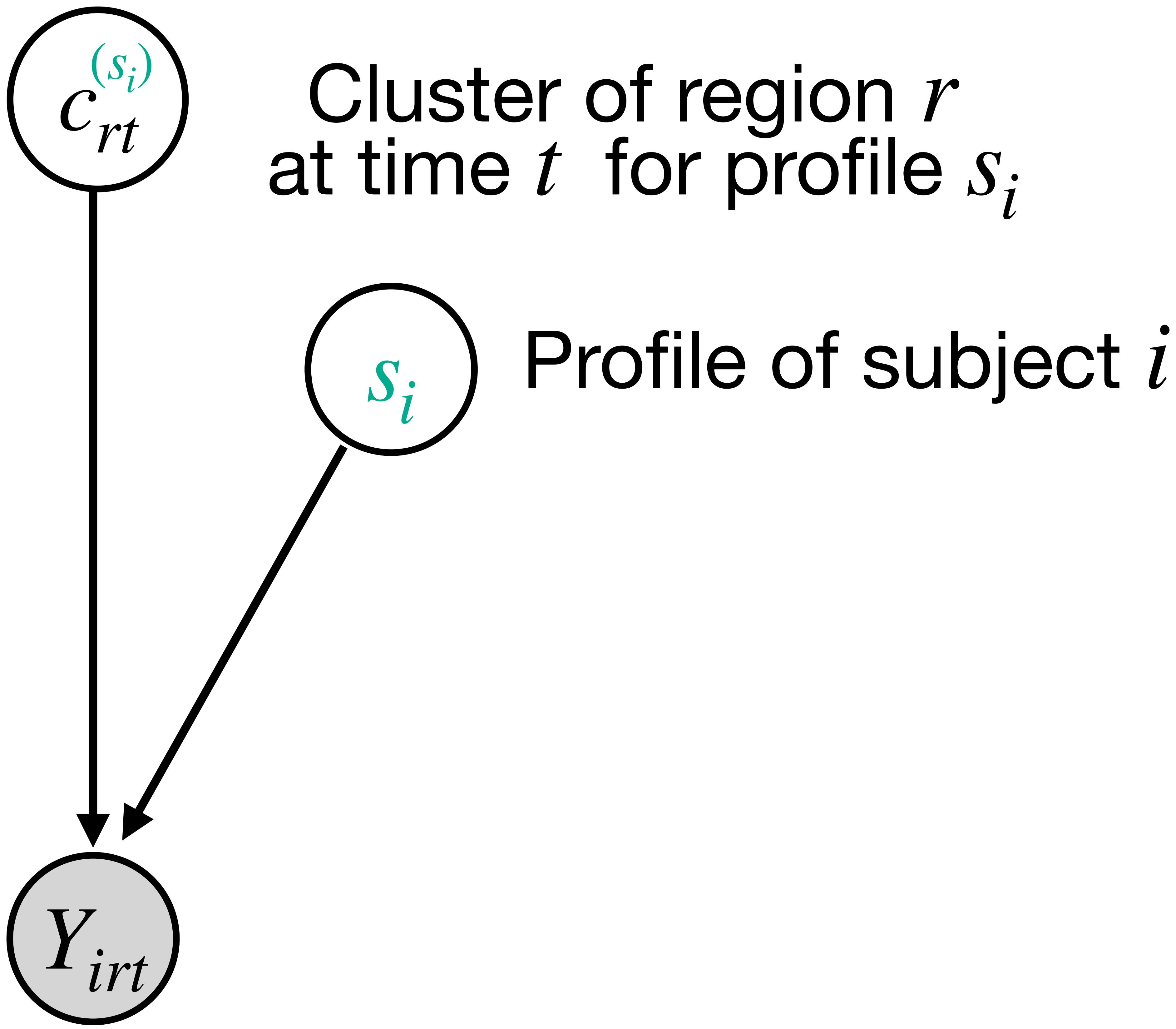

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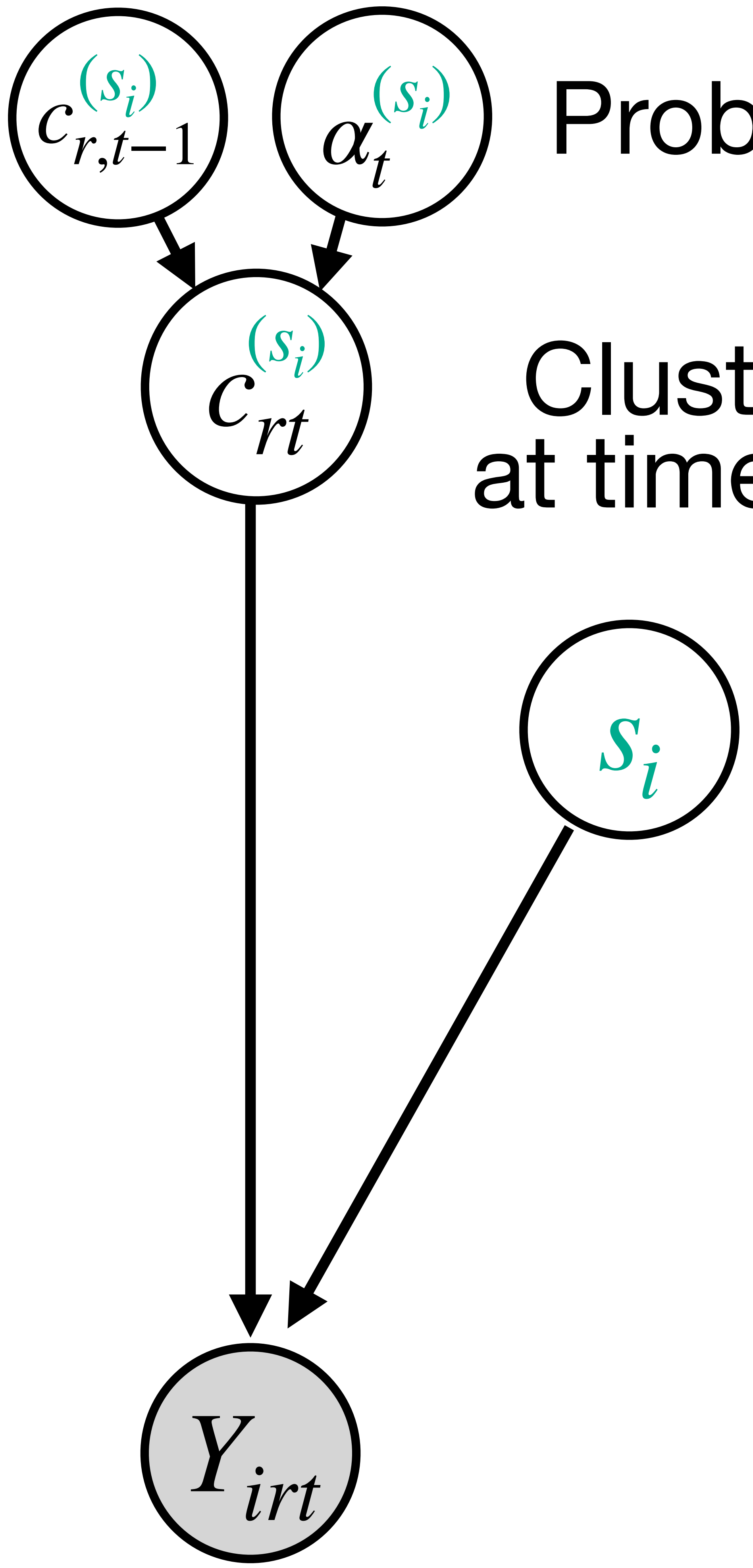


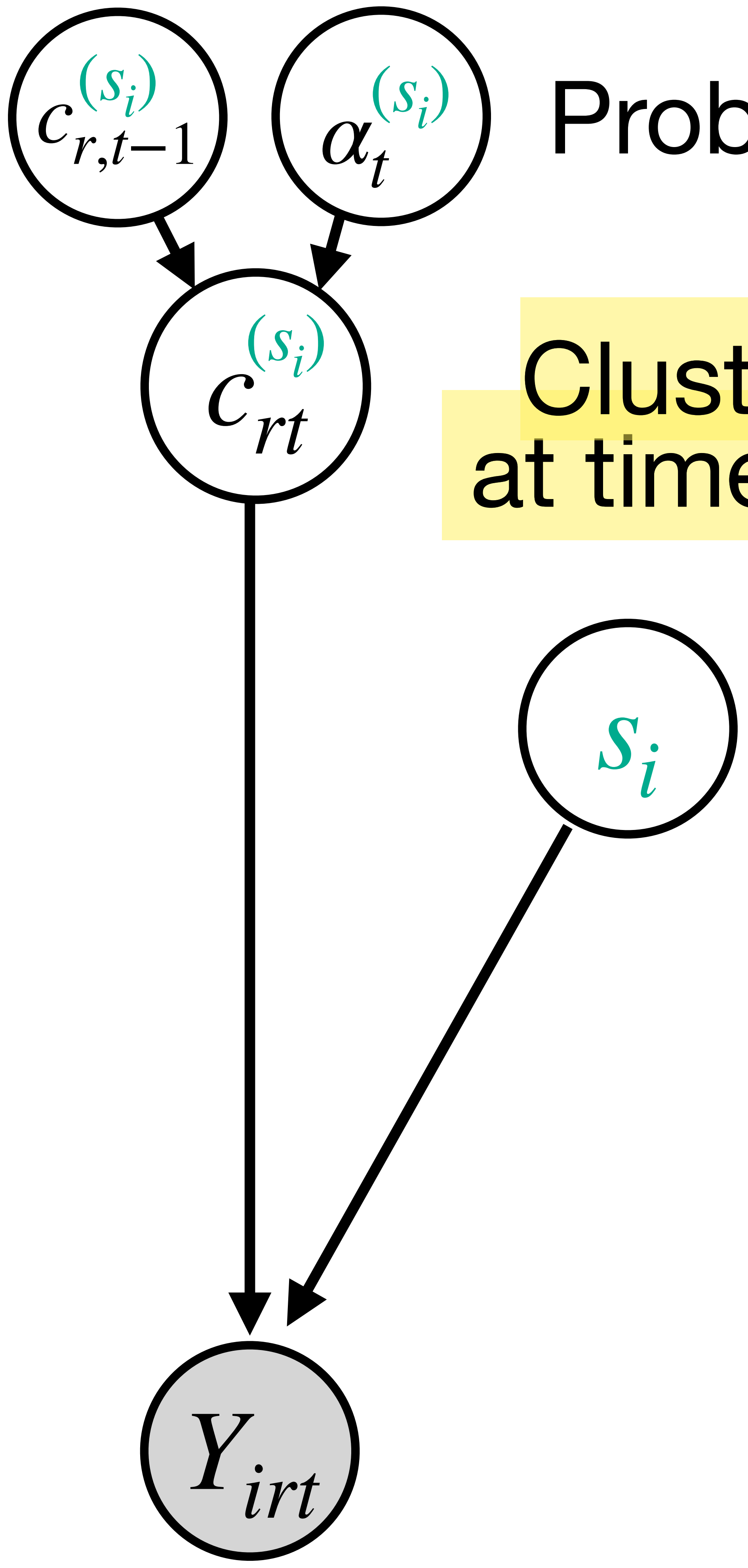
Probability that a cluster persists over time

Cluster of region r at time t for profile s_i

Profile of subject i

Full model

For subject i, brain region r and time t



Probability that a cluster persists over time

Cluster of region r at time t for profile s_i

$$\begin{cases} \text{with probability } \alpha_t^{(s_i)} & c_{r,t}^{(s_i)} = c_{r,t-1}^{(s_i)} \\ \text{with probability } 1 - \alpha_t^{(s_i)} & c_{r,t}^{(s_i)} \sim \text{Categ}\left(p_1^{(s_i)}, \ldots, p_K^{(s_i)}\right) \end{cases}$$

Profile of subject i

$$\boldsymbol{p}^{(s_i)} \mid \boldsymbol{p}_0 \sim \text{Dirichlet}(\phi\, \omega_{01}, \ldots, \phi\, p_{0K}),$$

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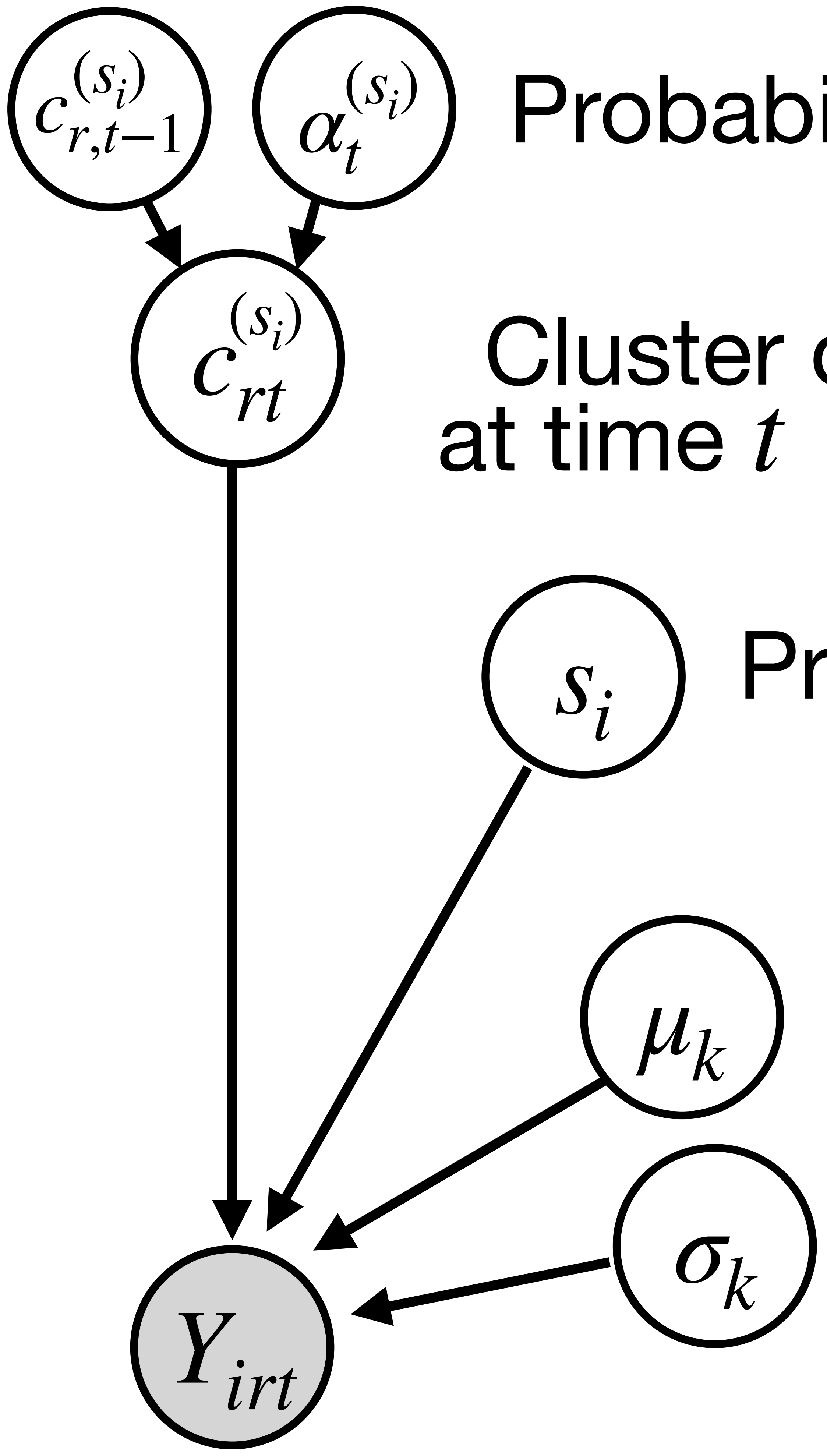

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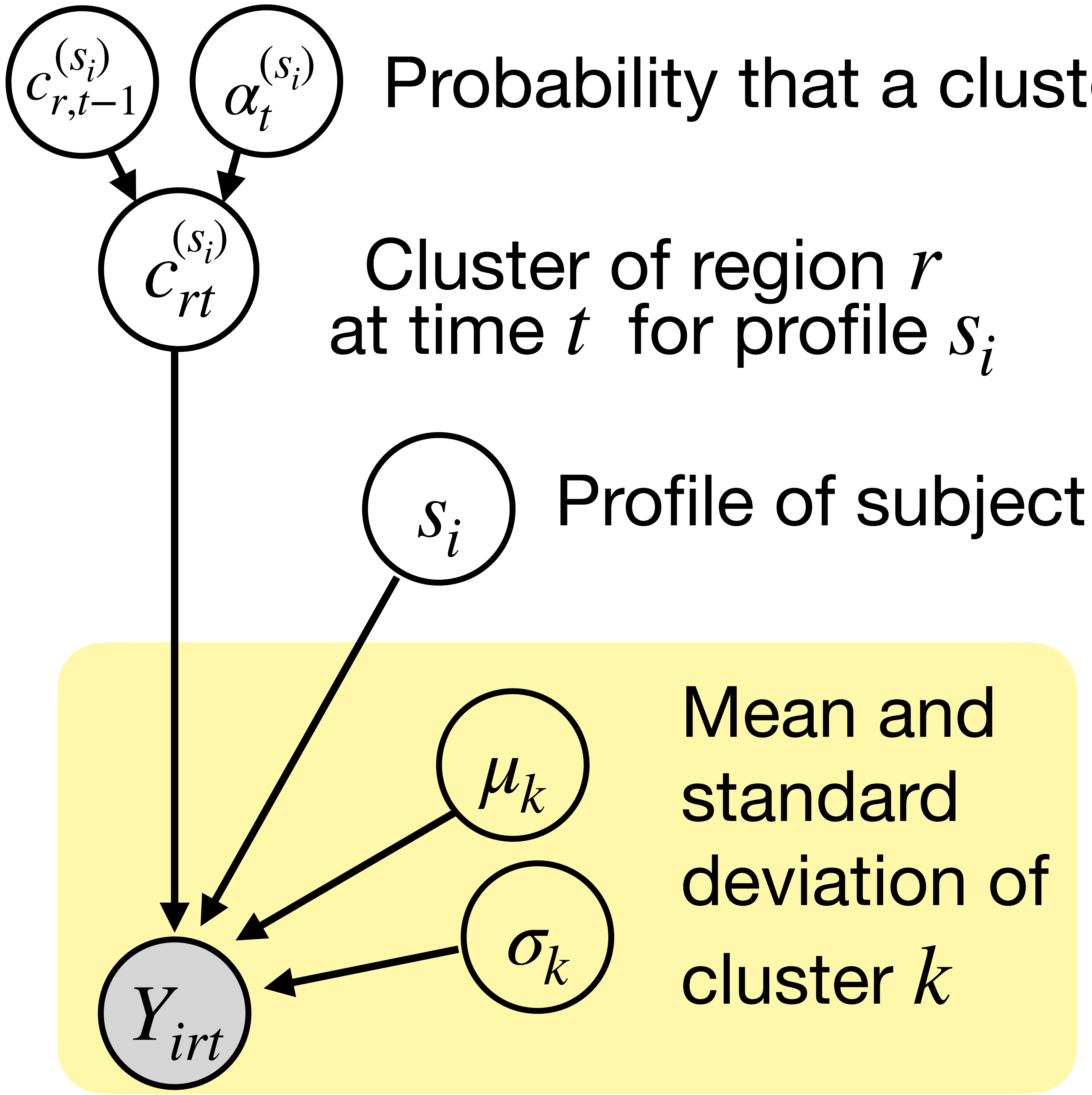
Profile of subject i

Mean and standard deviation of cluster k

Full model

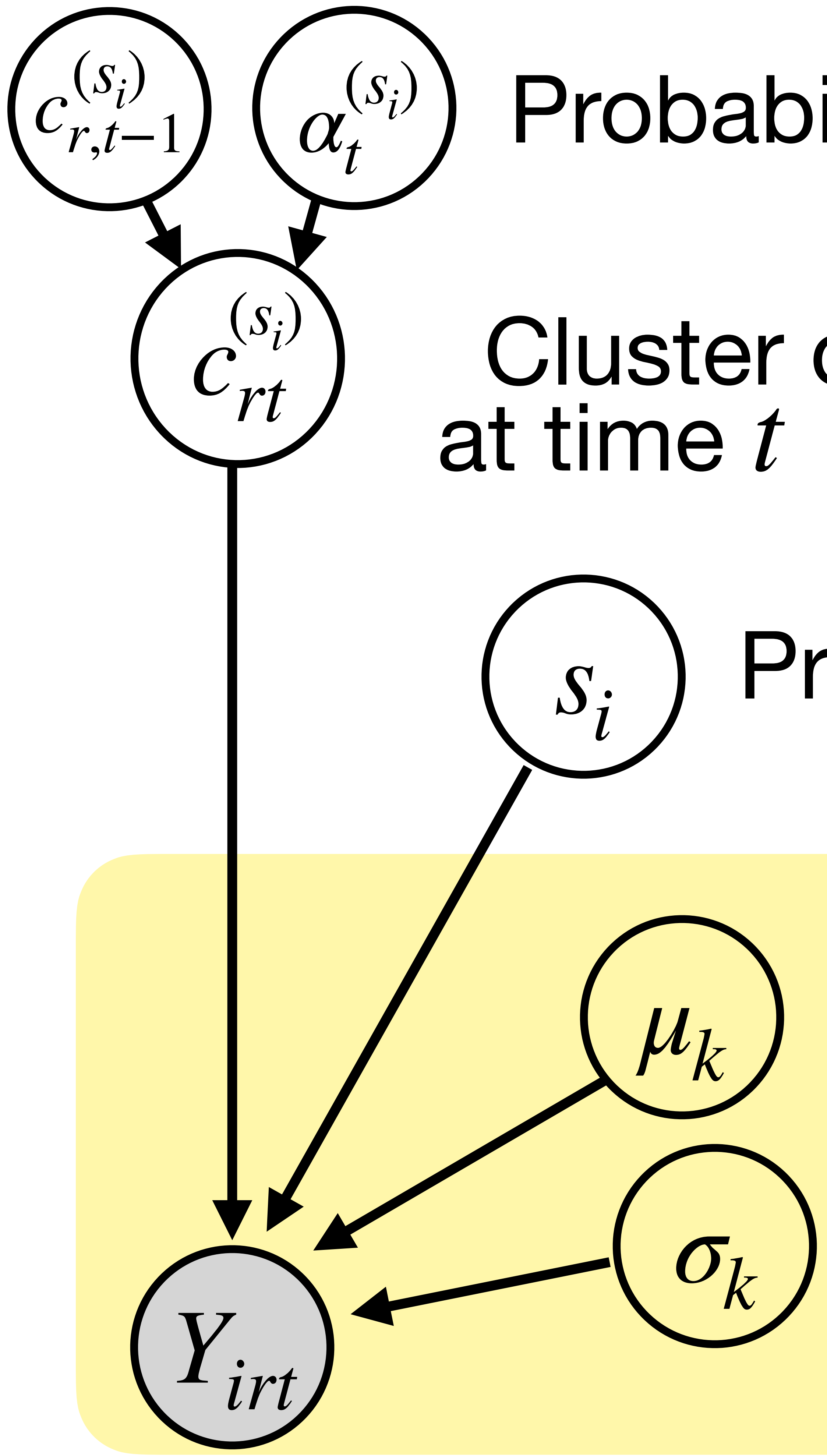
For subject i, brain region r and time t



$$Y_{irt} \mid s_i = z, c_{rt}^{(z)} = k, \mu_k, \sigma_k \sim \text{Student-t}(\mu_k, \sigma_k)$$

Full model

For subject i, brain region r and time t



Probability that a cluster persists over time

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Mean and standard deviation of cluster k

$$Y_{irt} \mid s_i = z, c_{rt}^{(z)} = k, \mu_k, \sigma_k \sim \text{Student-t}(\mu_k, \sigma_k)$$

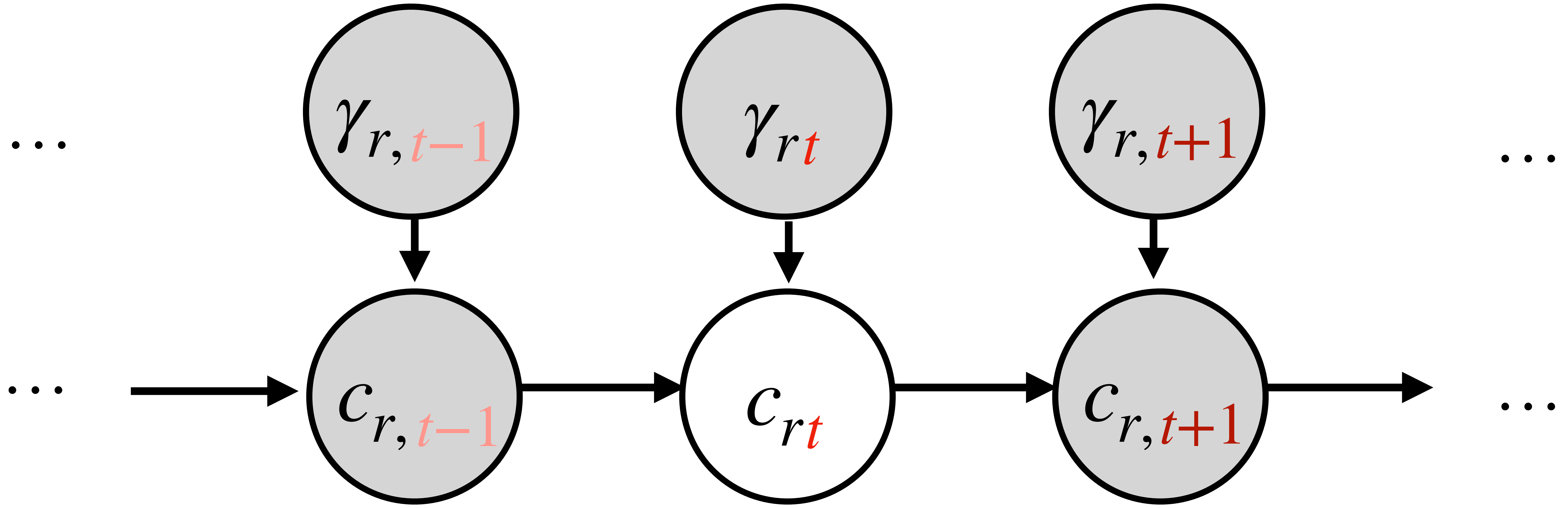
$$\Downarrow$$

$$Y_{i,r,t} \mid c_{r,t}^{(s_i)} = k, \mu_k, V_{i,r,t} \overset{\text{ind}}{\sim} \text{Normal}(\mu_k, V_{i,r,t})$$

$$V_{i,r,t} \mid c_{r,t}^{(s_i)} = k, \sigma_k^2 \overset{\text{iid}}{\sim} \text{Inv-}\chi^2(\nu, \sigma_k^2)\,.$$

Posterior Inference

- We design a MCMC for posterior inference, mostly using Gibbs updates
- Crucial step is the update of cluster-assignment sequence $(c_{r,1}^{(z)}, \ldots, c_{r,T}^{(z)})$ for each profile z and region r
- For the case with no profiles, Page et al. (2022) propose a marginal sampler
  - Let $\gamma_{r,t} = 1$ with probability α_t (so $\gamma_{r,t}$ is an indicator of cluster persistence)
  - Marginal updates are conditional on past, present and future persistence indicators and cluster assignments



Block update of region clusters

- We design update of cluster-assignment sequences *in block:*
  - Update persistence indicators and cluster assignments together and sequentially, only conditioned on the past

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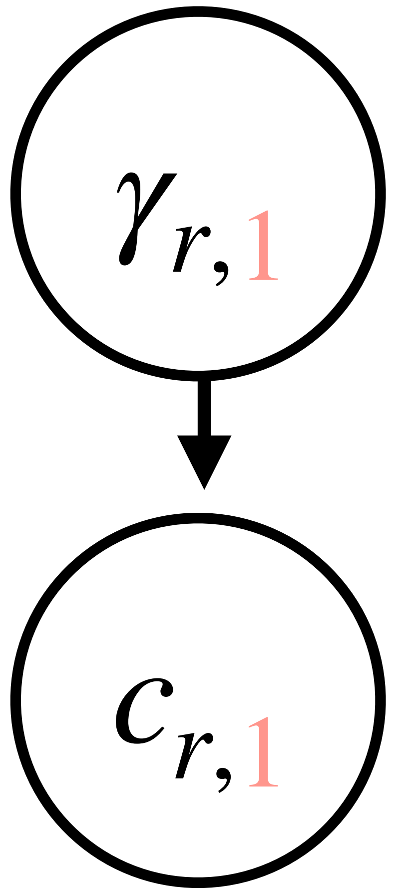

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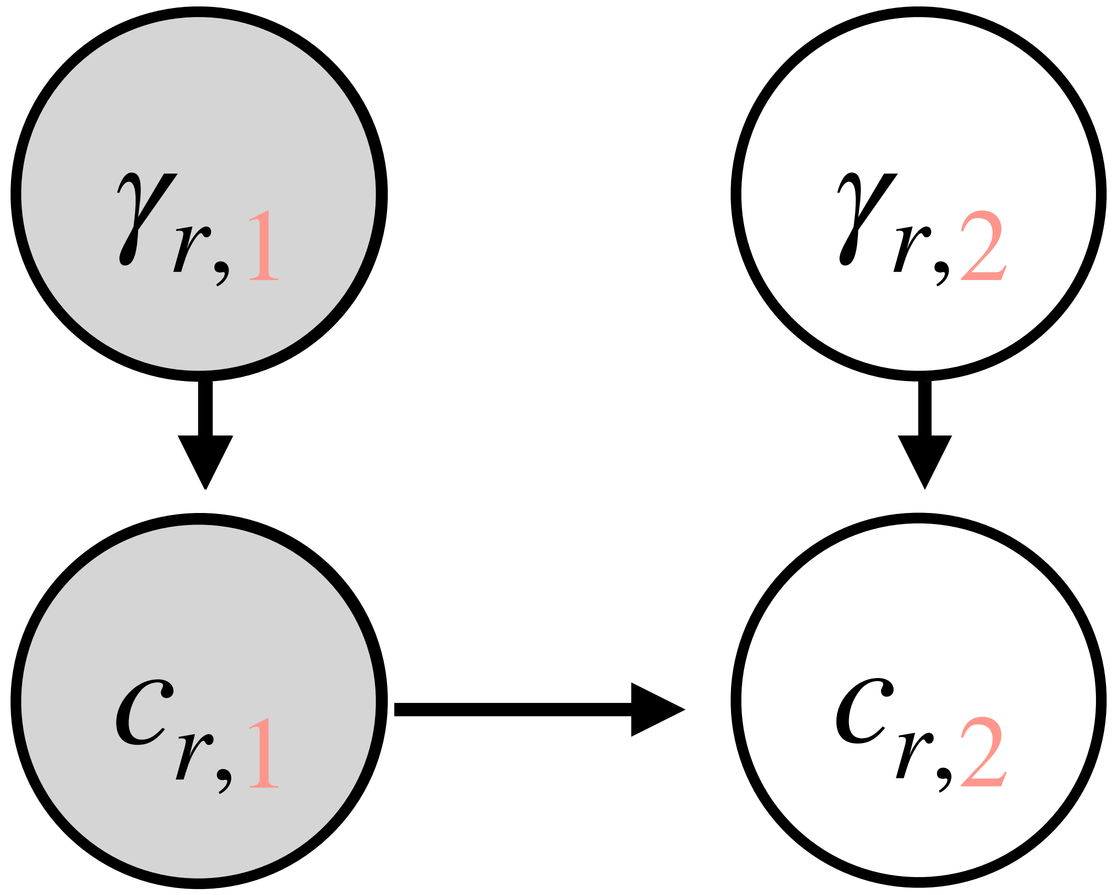

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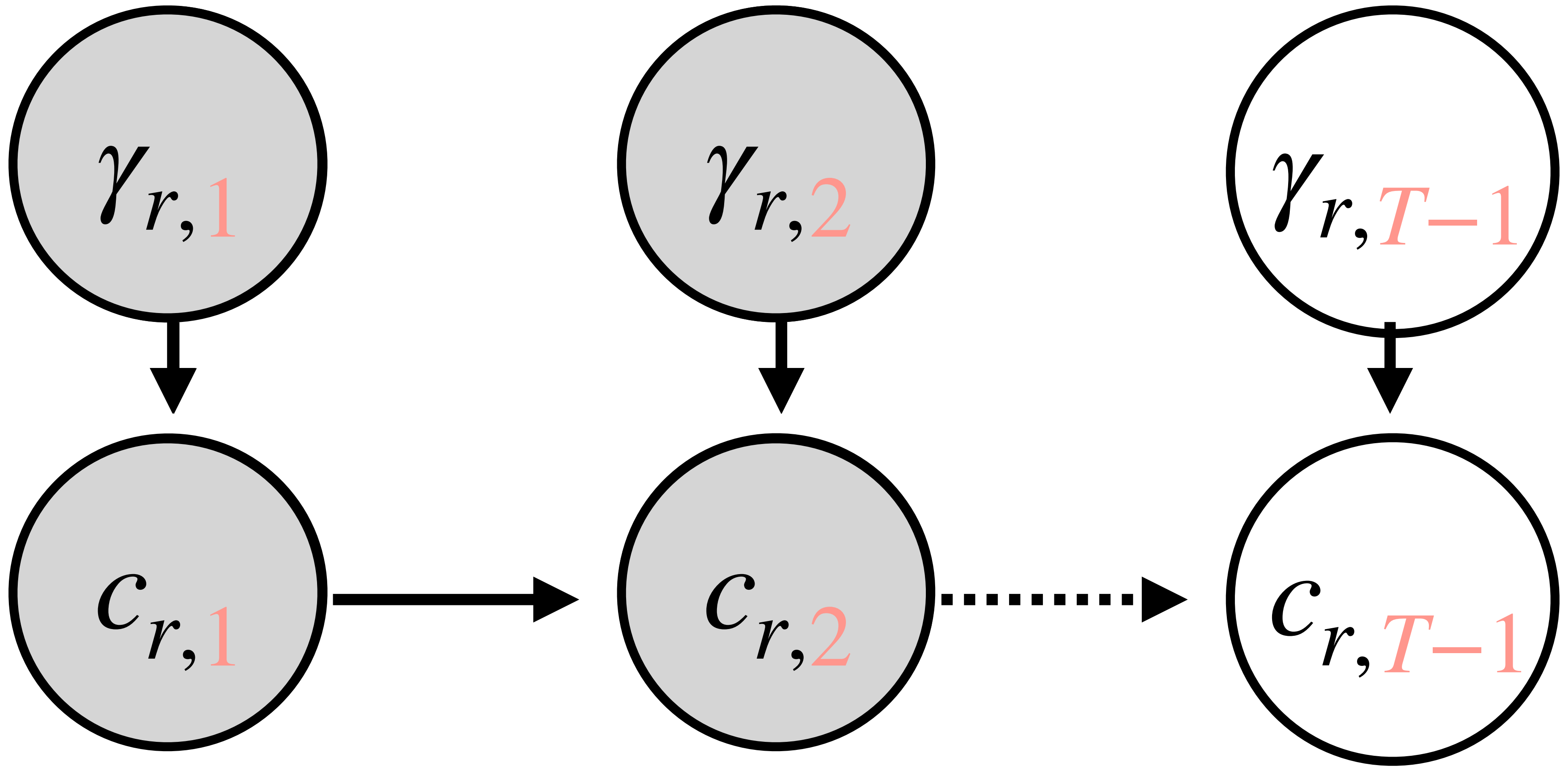

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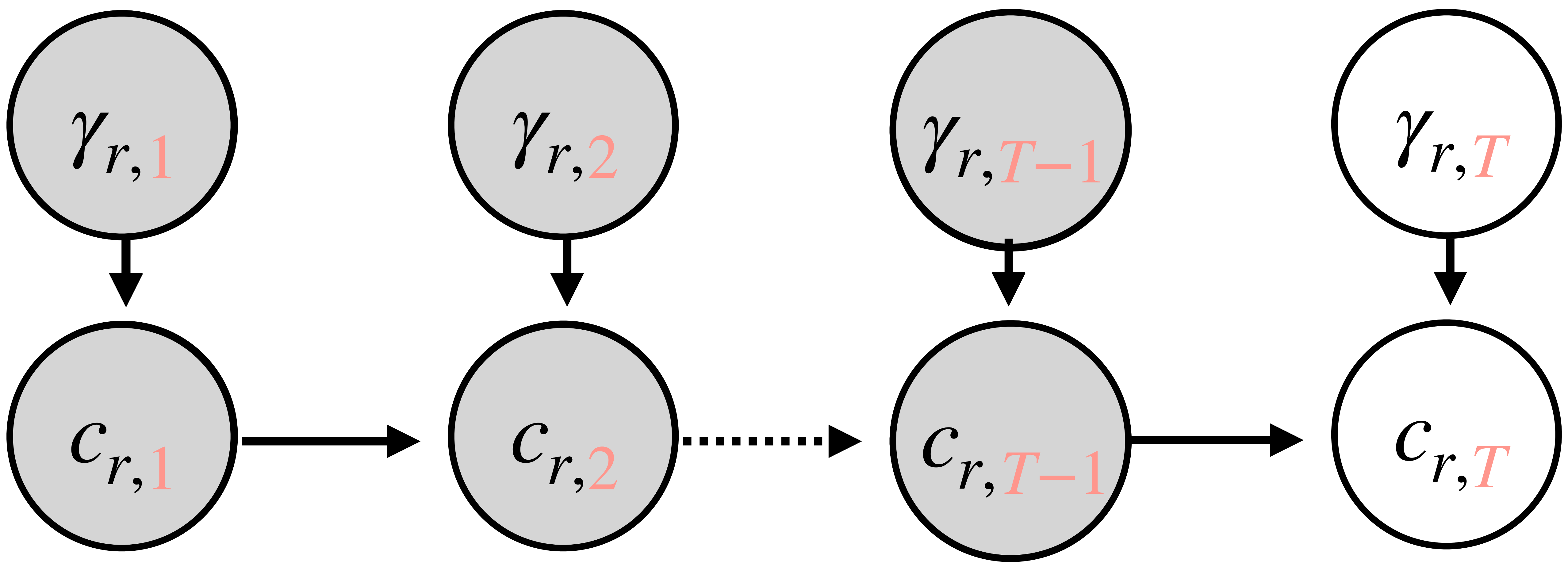
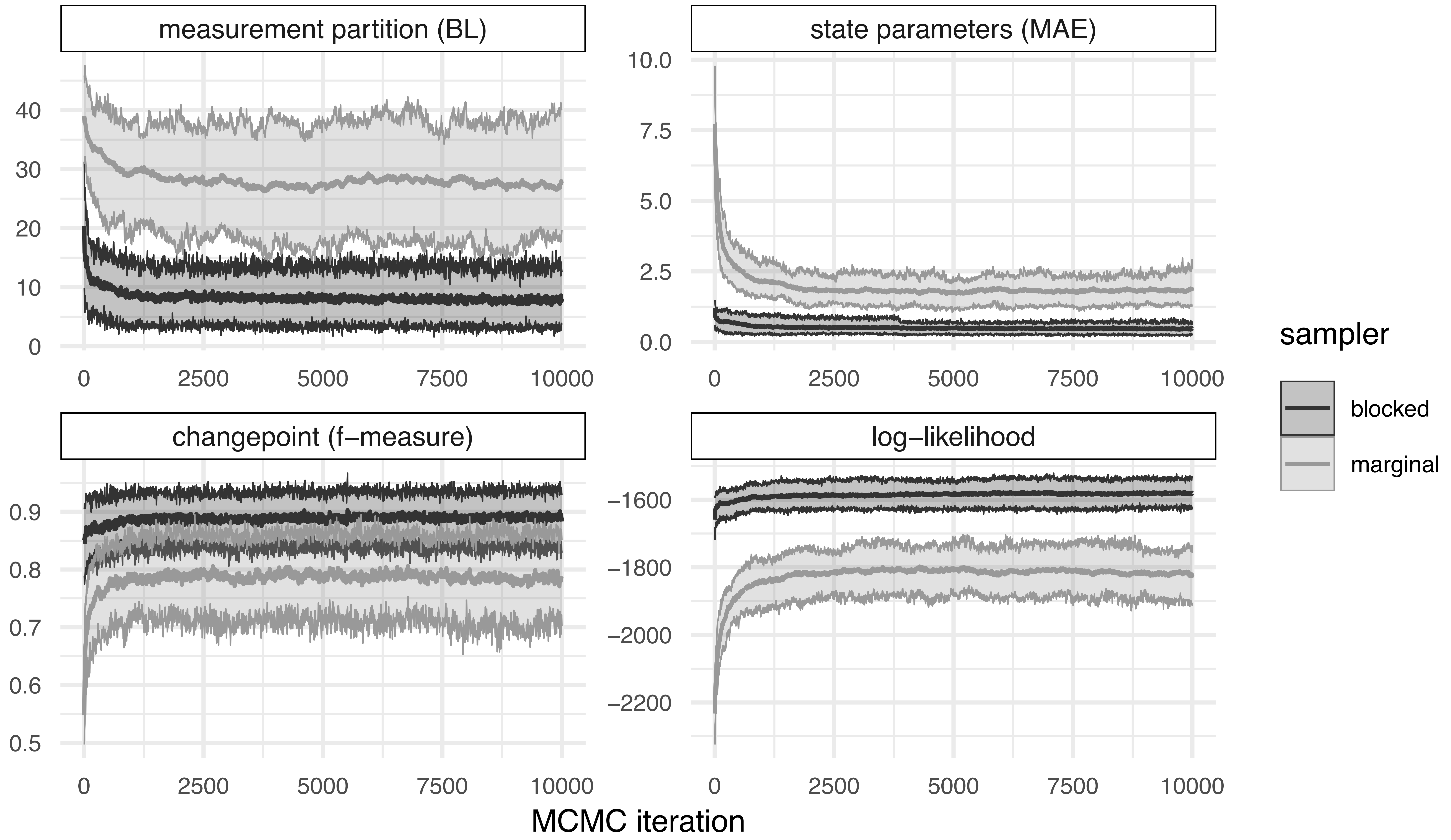
- We design update of cluster-assignment sequences *in block:*
  - Update persistence indicators and cluster assignments together and sequentially, only conditioned on the past

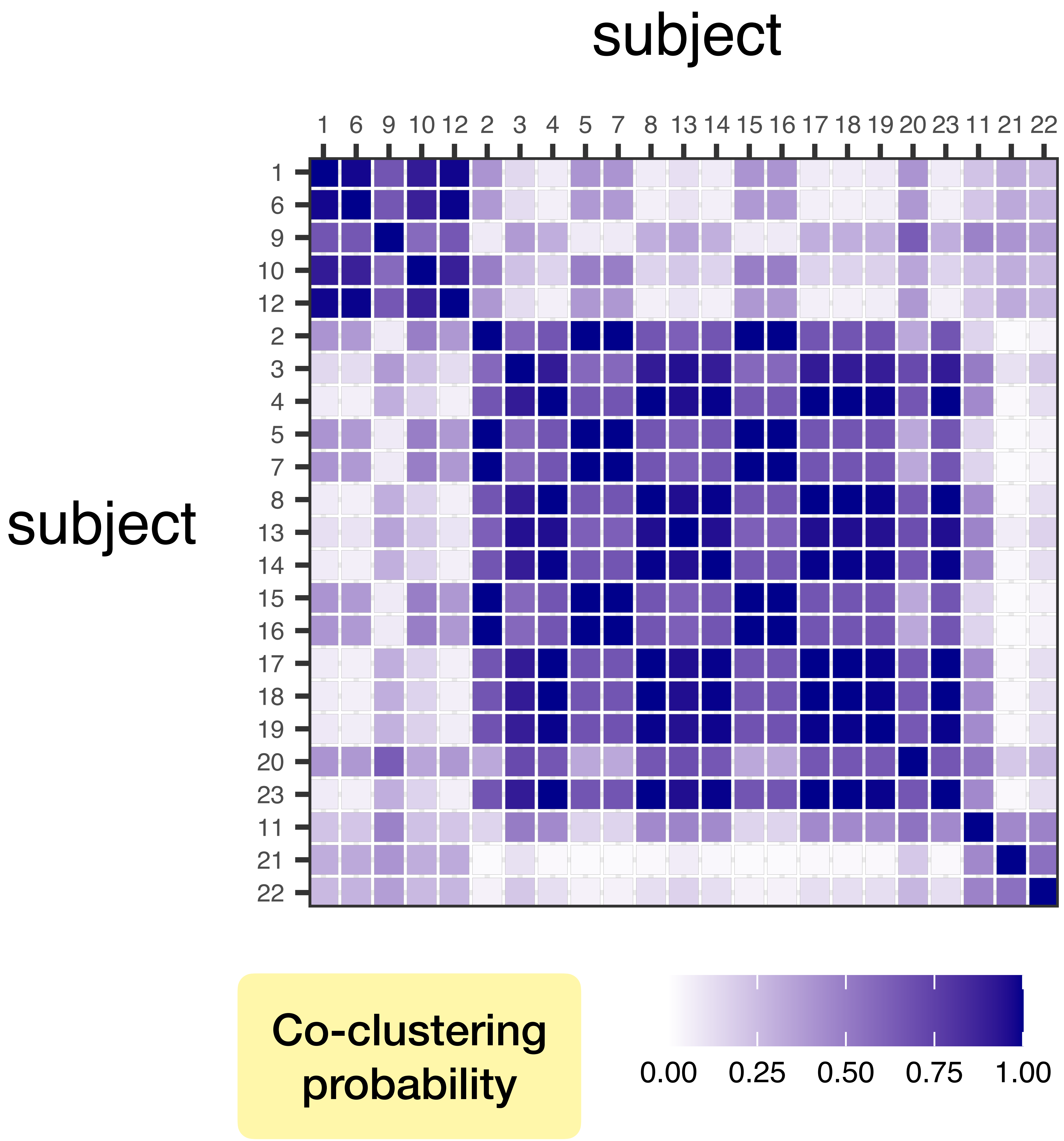


Blocked vs. Marginal sampler

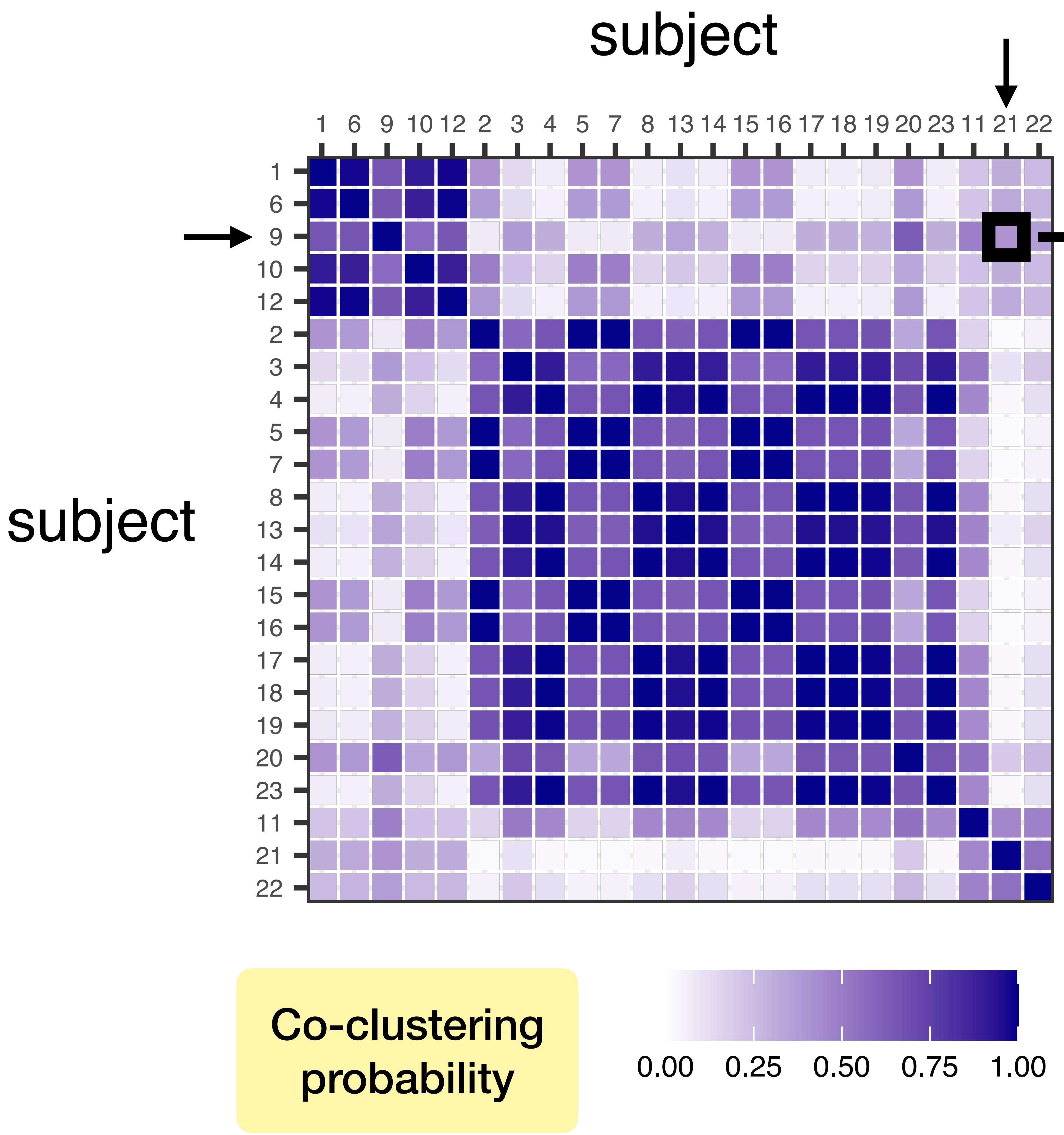


Application to neuroscience studies

fMRI data - profiles

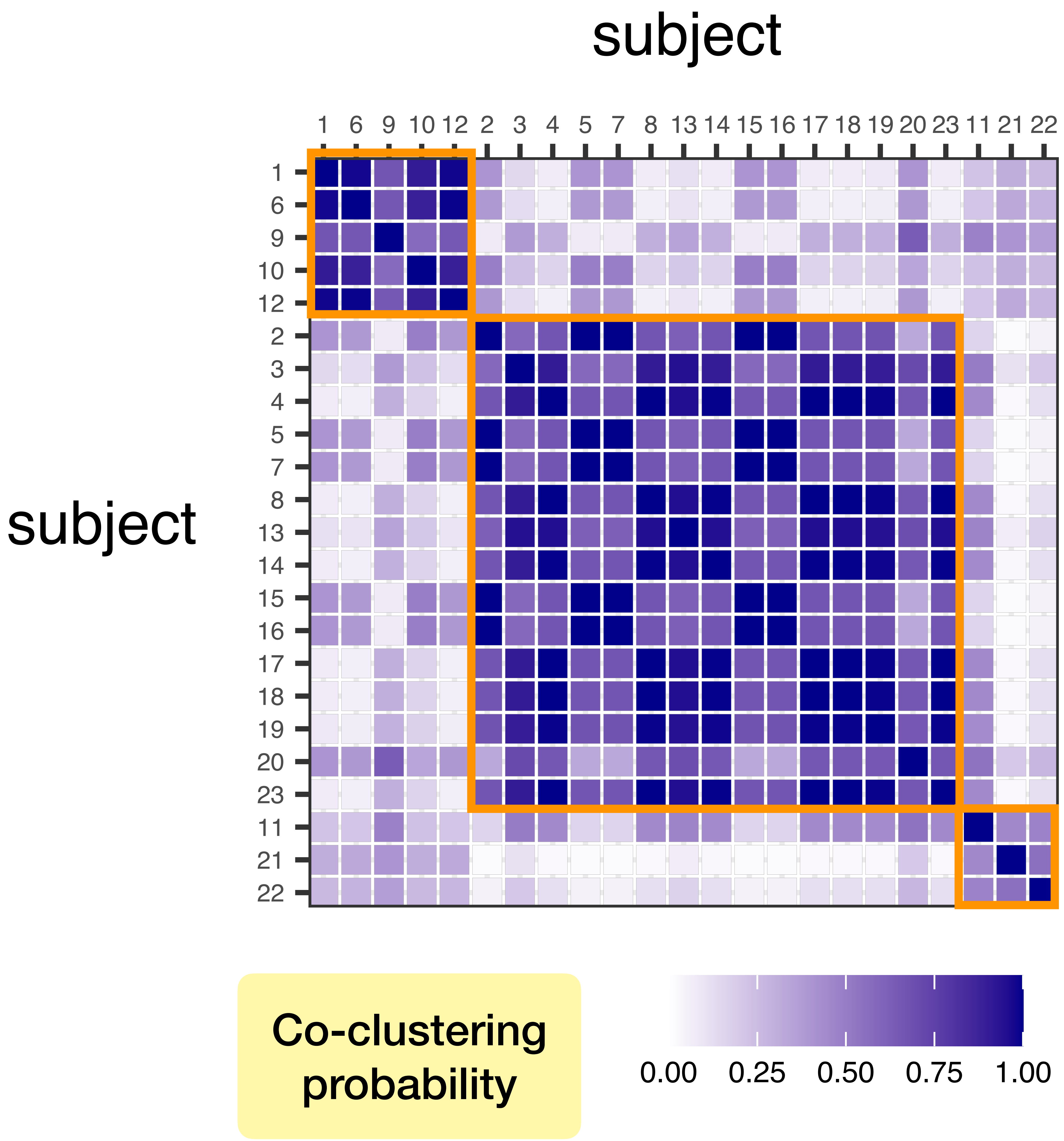


fMRI data - profiles



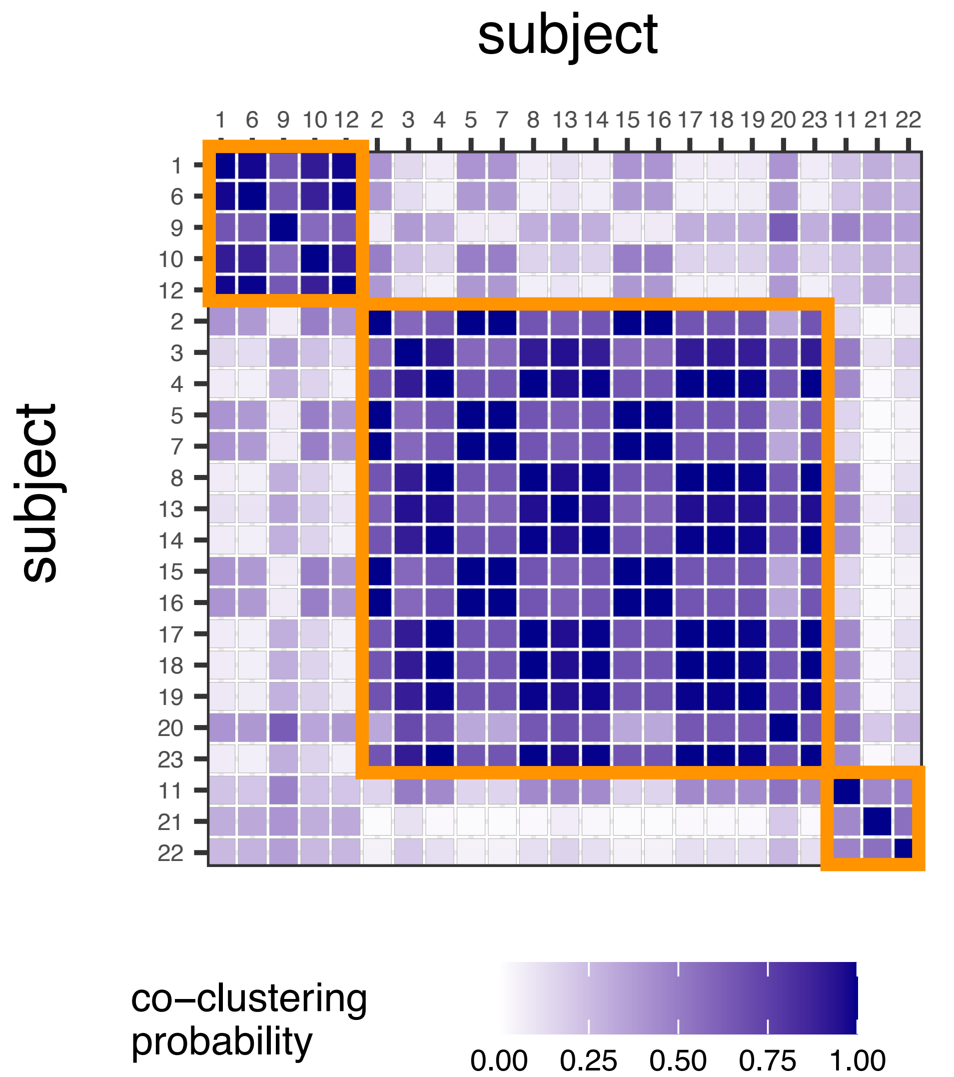
Probability that subject 9 and 21 have the same profile

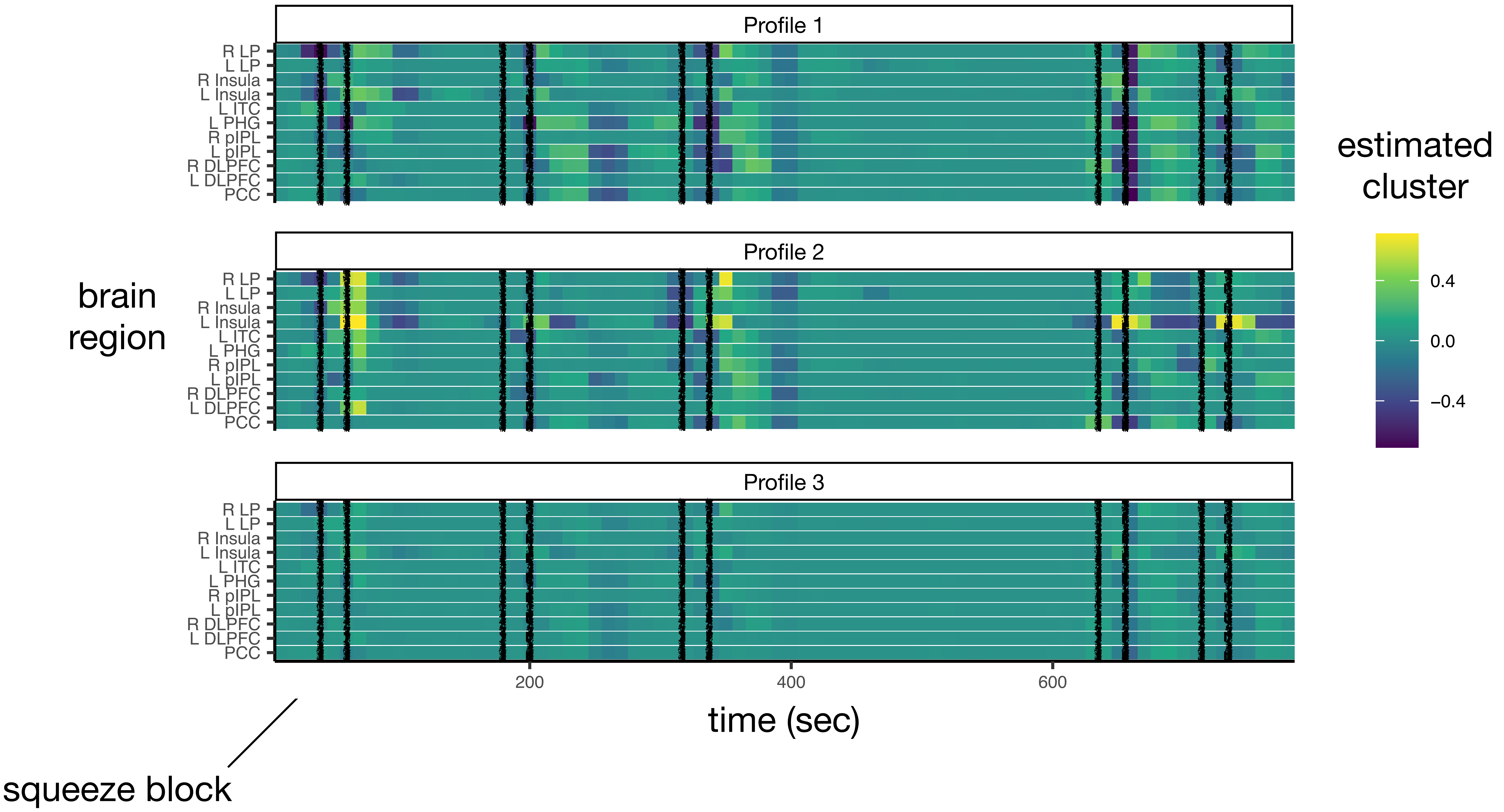
fMRI dataset - profiles



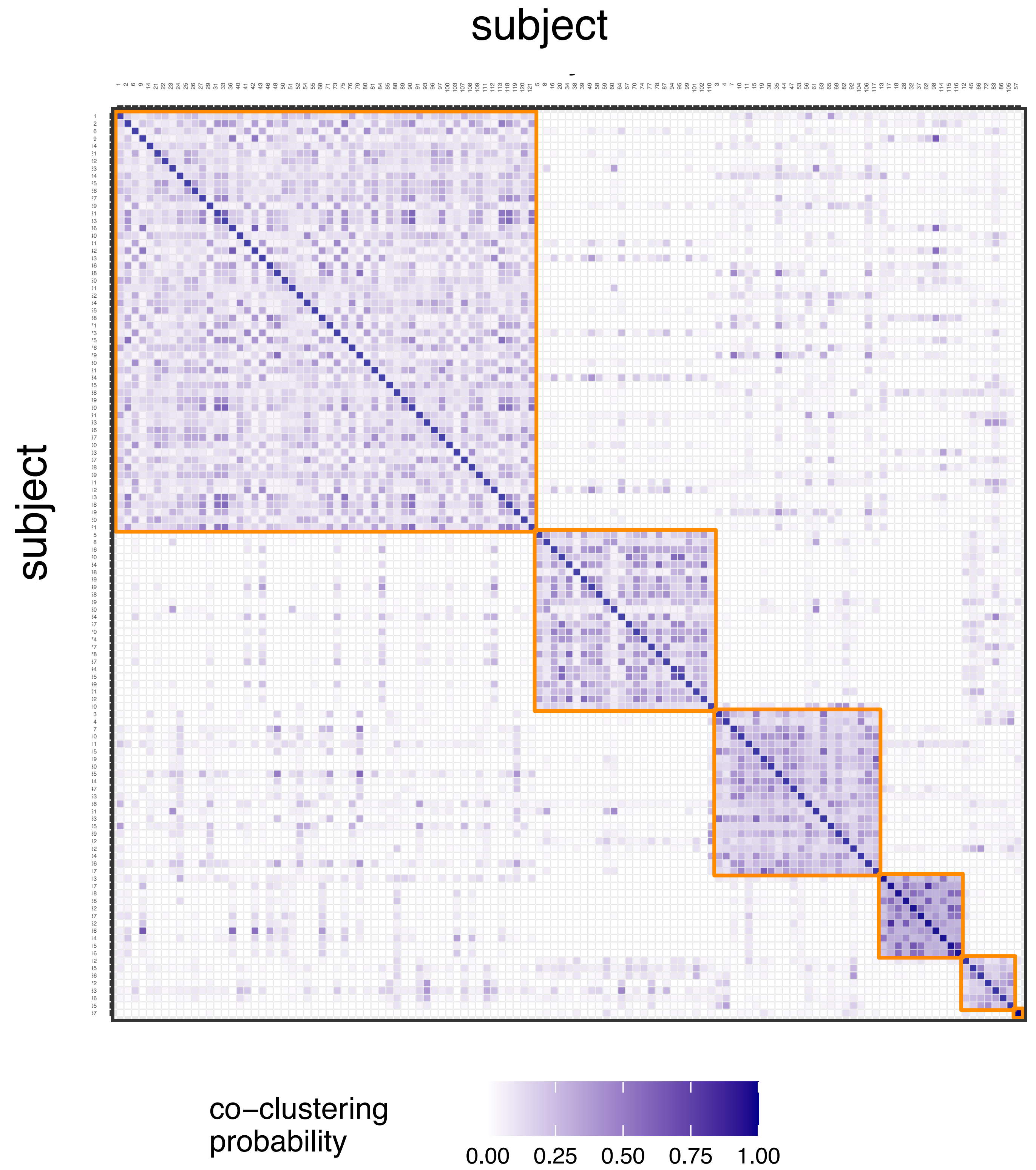
Estimate 3 profiles of subjects

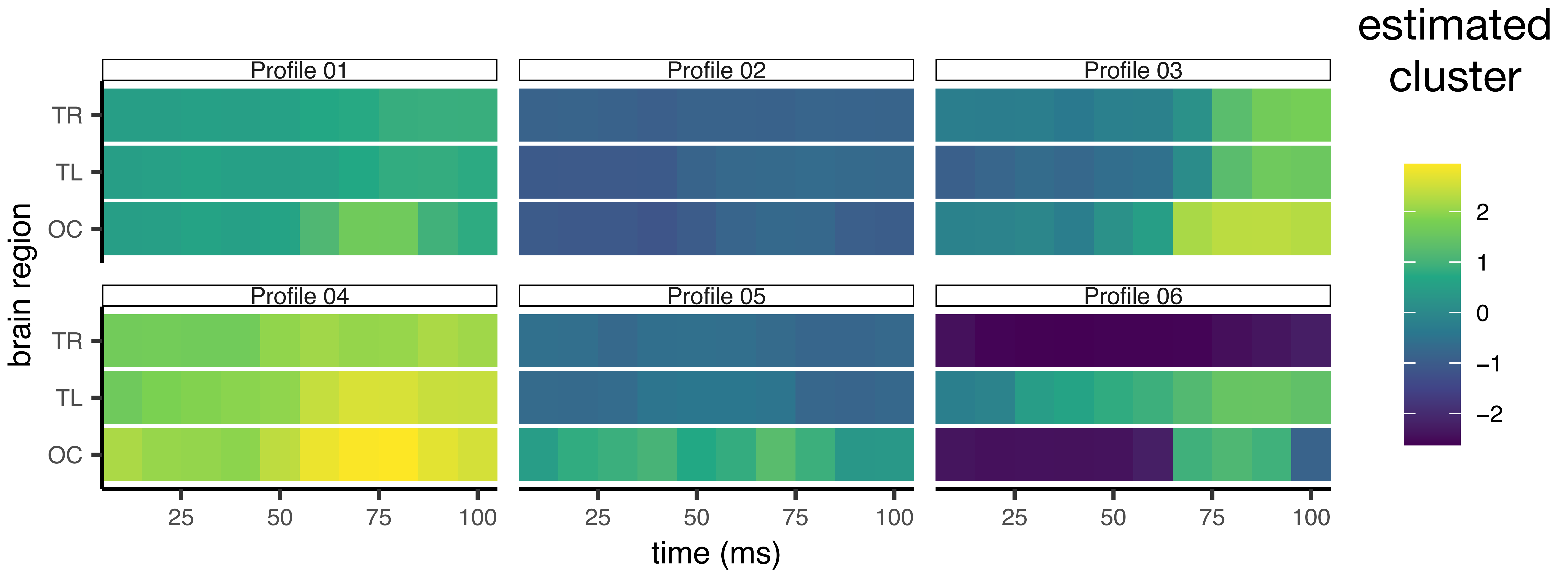
fMRI dataset - brain region clusters



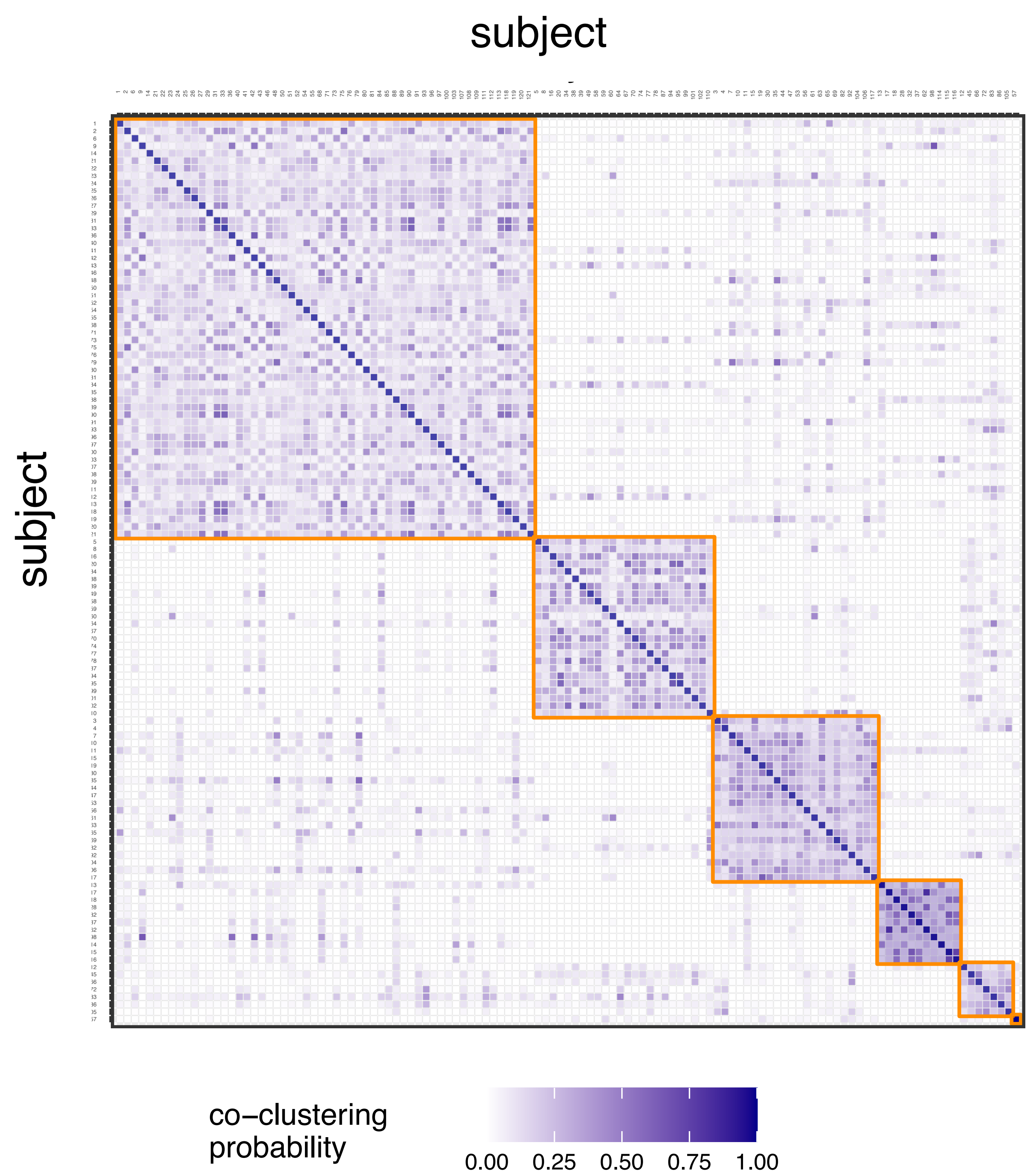


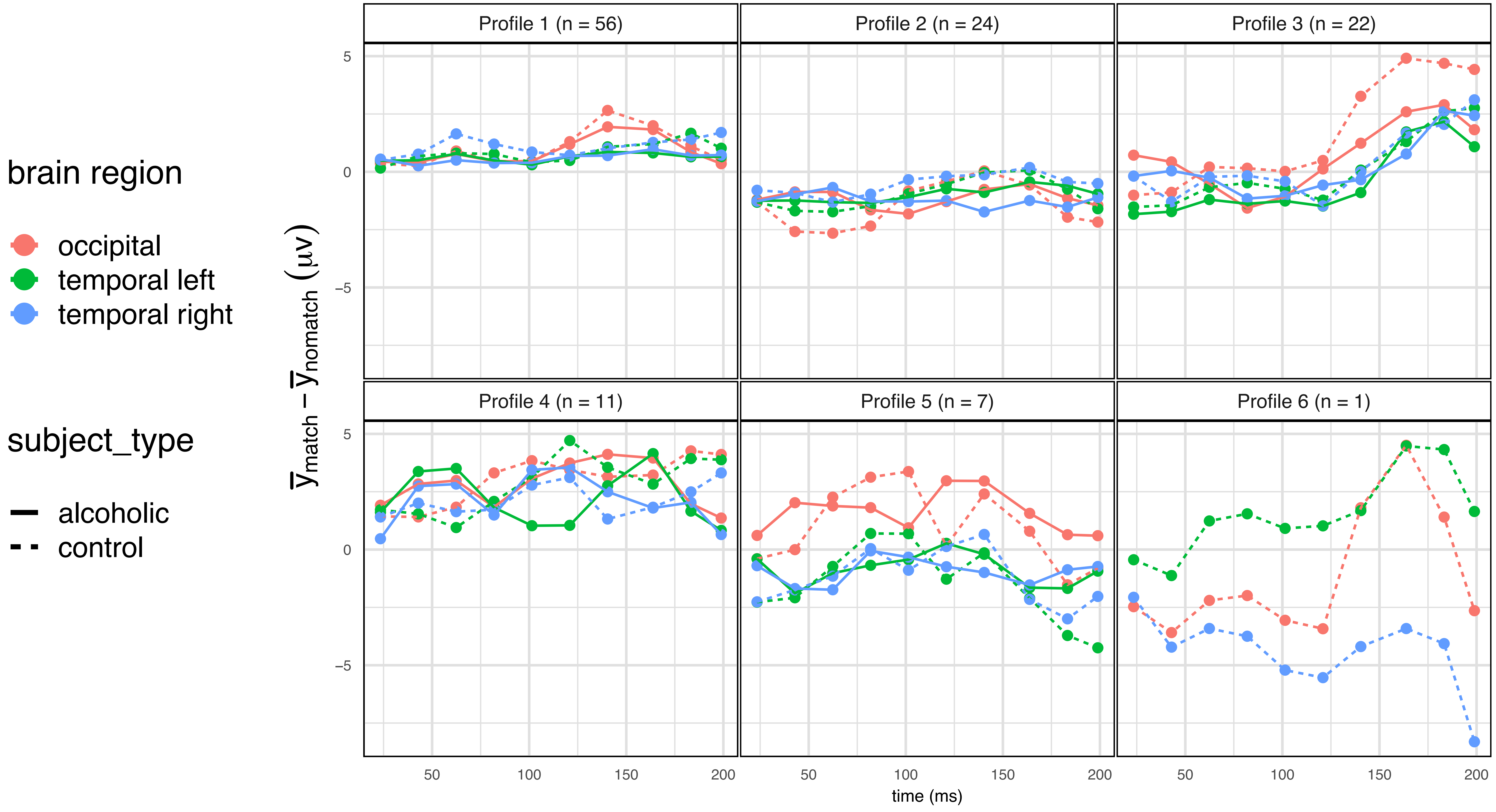
EEG dataset - brain region clusters





EEG dataset - brain region clusters





Discussion

Contributions

- Define a framework for time-varying partitions of measurements nested within time-invariant partitions of subjects

- Derive a MCMC block update for efficient exploration of state-sequence assignments

- Neuroscience applications: model identifies potential sub-populations within a given cohort based on neural profiles

Future directions

- Incorporate time-invariant covariates (e.g. subjects' characteristics)

- Allow for measurements to be observed at different time intervals for different subjects

- Include more measurements: using random effects (Kim and Smyth 2006), allowing there to be sets of irrelevant measurements (Lee et al. 2013) or using variable selection methods (Tadesse and Vannucci 2021)

- Allow subjects to change profile, e.g. multi-view clustering (Franzolini et al, 2023)

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Preprint: https://arxiv.org/abs/2406.17131

Questions?

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