Practical Tutorial G: Advanced Models of Connectivity - part 1

Hierarchical Unsupervised Generative Embedding (HUGE)

Yu Yao

Translational Neuromodeling Unit

Universität Zürich[UZH]

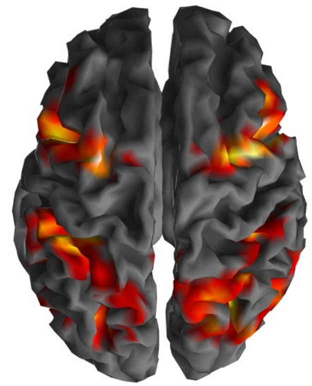
ETH Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Computational Psychiatry Course 2019

Zurich | 6th September 2019

Contents

DCM for fMRI



fMRI

Model inversion:
Estimating
neuronal
mechanisms

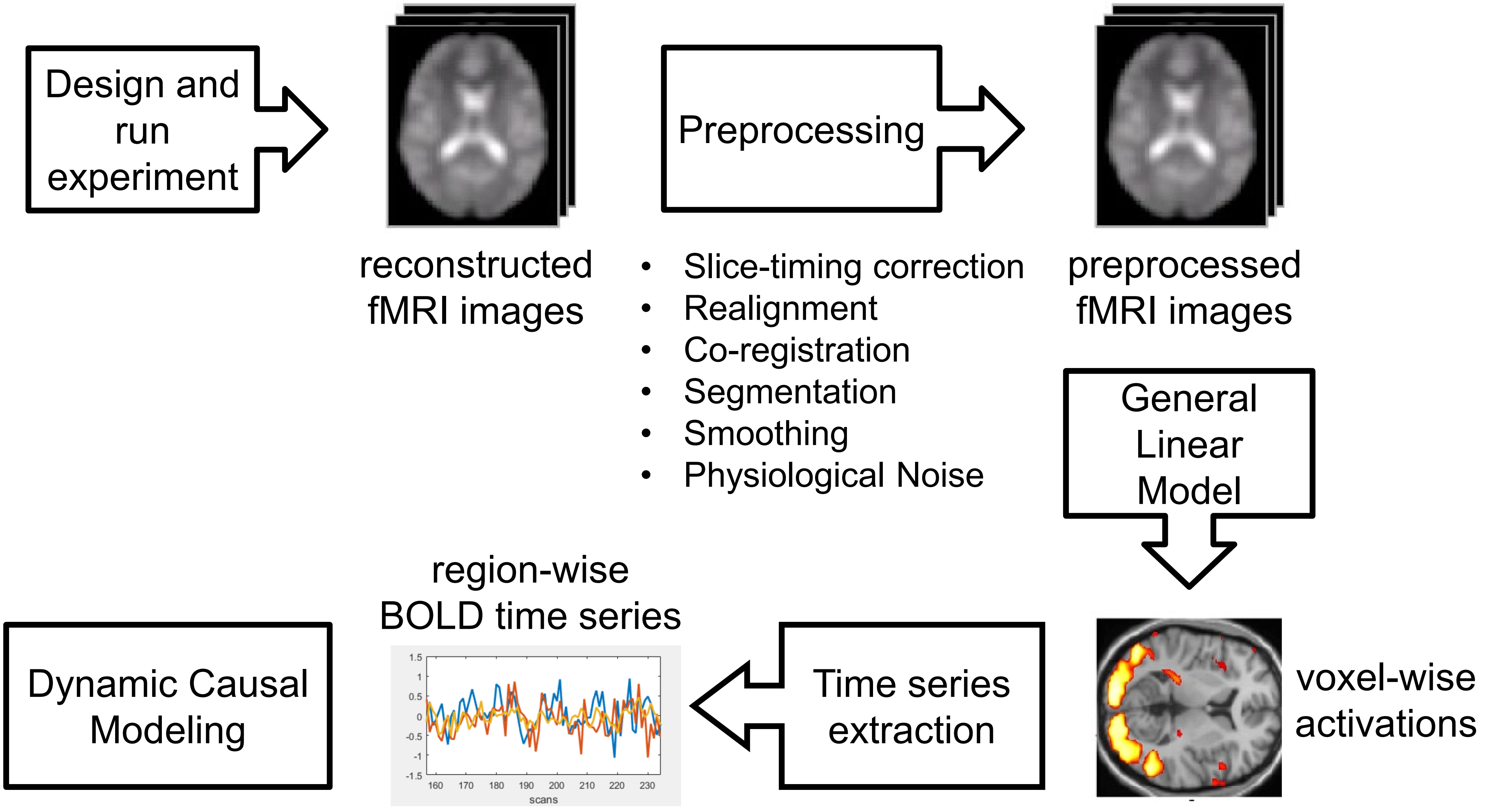
Forward model:
Predicting
measured activity

$$y = g(x, \theta) + \varepsilon$$

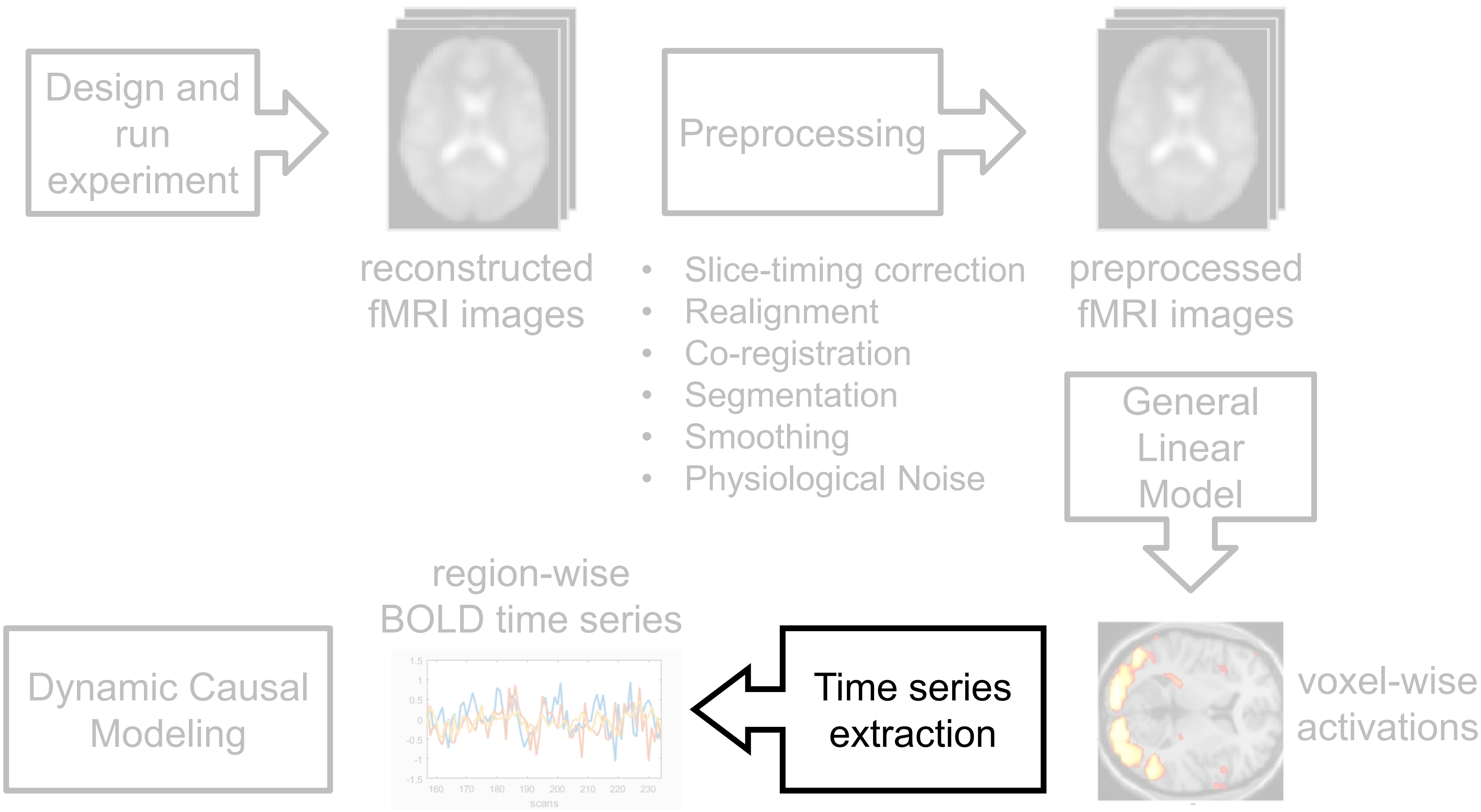
$$\frac{dx}{dt} = f(x, u, \theta)$$

Neural state equation:
Describing neuronal
dynamics

The standard fMRI Pipeline



The standard fMRI Pipeline



Time Series Extraction

- Identification of region of interest:
  - e.g.: Group-level activation, Anatomical atlas, …
  - DCM network structure
  - Research question and experimental design

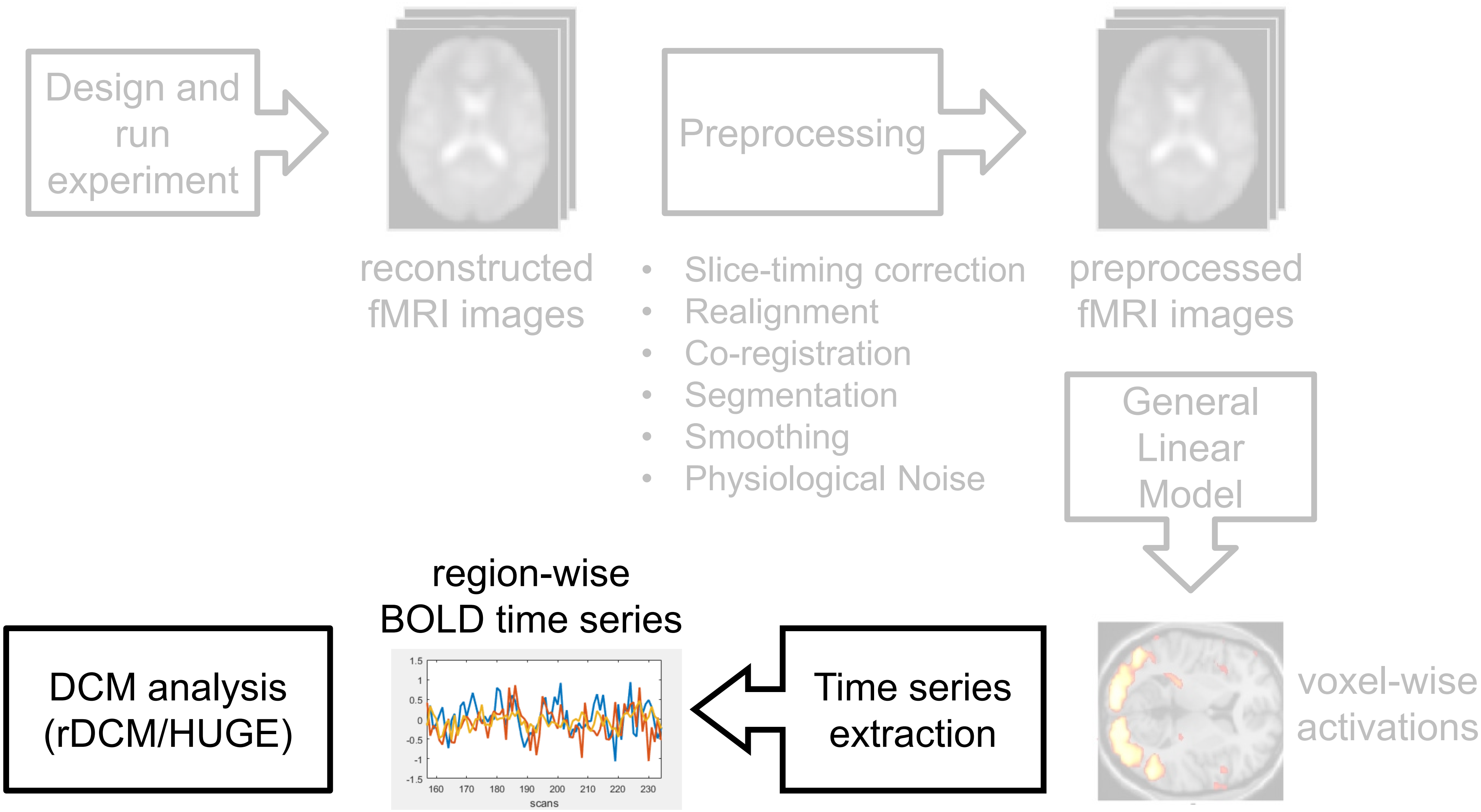
Time Series Extraction

- Identification of region of interest:
  - e.g.: Group-level activation, Anatomical atlas, …
  - DCM network structure
  - Research question and experimental design
- Check for sufficient activation across population
  - Make sure there is activation in all regions of interest across all individuals.
  - Exclude subjects if necessary.

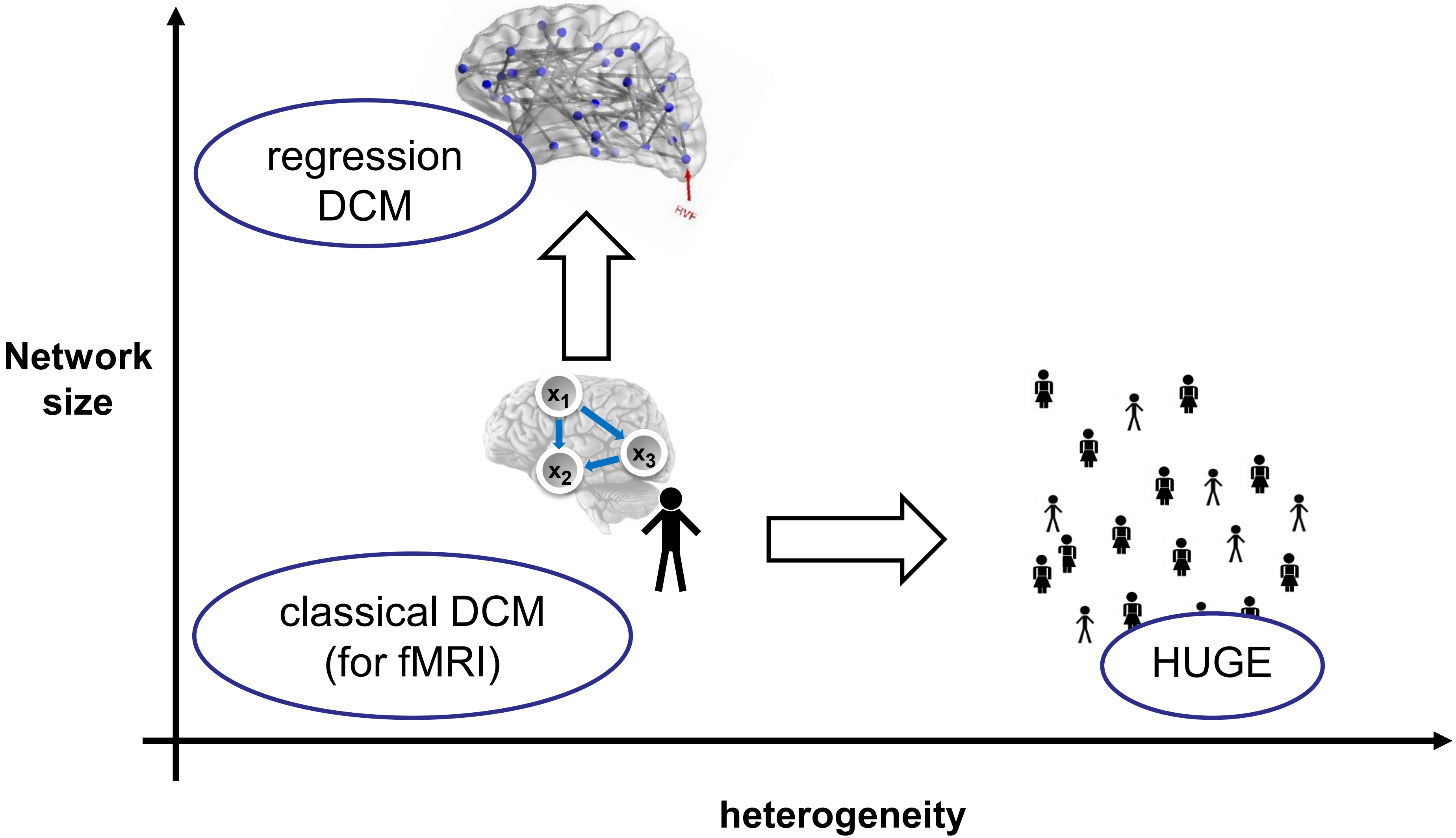
Time Series Extraction

- Identification of region of interest:
  - e.g.: Group-level activation, Anatomical atlas, …
  - DCM network structure
  - Research question and experimental design
- Check for sufficient activation across population
  - Make sure there is activation in all regions of interest across all individuals.
  - Exclude subjects if necessary.
- Extraction of time series for each region:
  - Average activity in all voxels belonging to the region.
  - SPM: singular value decomposition

The standard fMRI Pipeline



Introduction



Introduction

Hierarchical Unsupervised Generative Embedding **(HUGE)**:

1. Empirical Bayes:

Use data to inform prior distribution.

2. Stratification of heterogeneous cohorts:

Find subgroups in heterogeneous cohorts.

Introduction

Friston et al. (2016)
NeuroImage

Parametric Empirical Bayes

Hierarchical Unsupervised Generative Embedding (HUGE)

Joint estimation of individual and group-level DCM parameters.

Do the above for multiple (sub)groups at once.

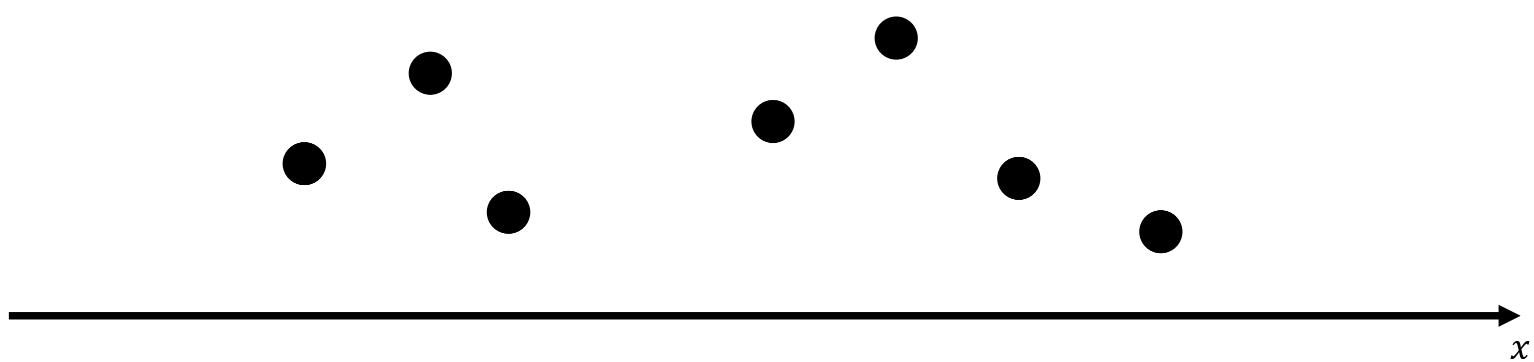
Find out which subject belongs to which group.

Yao et al. (2018)
NeuroImage

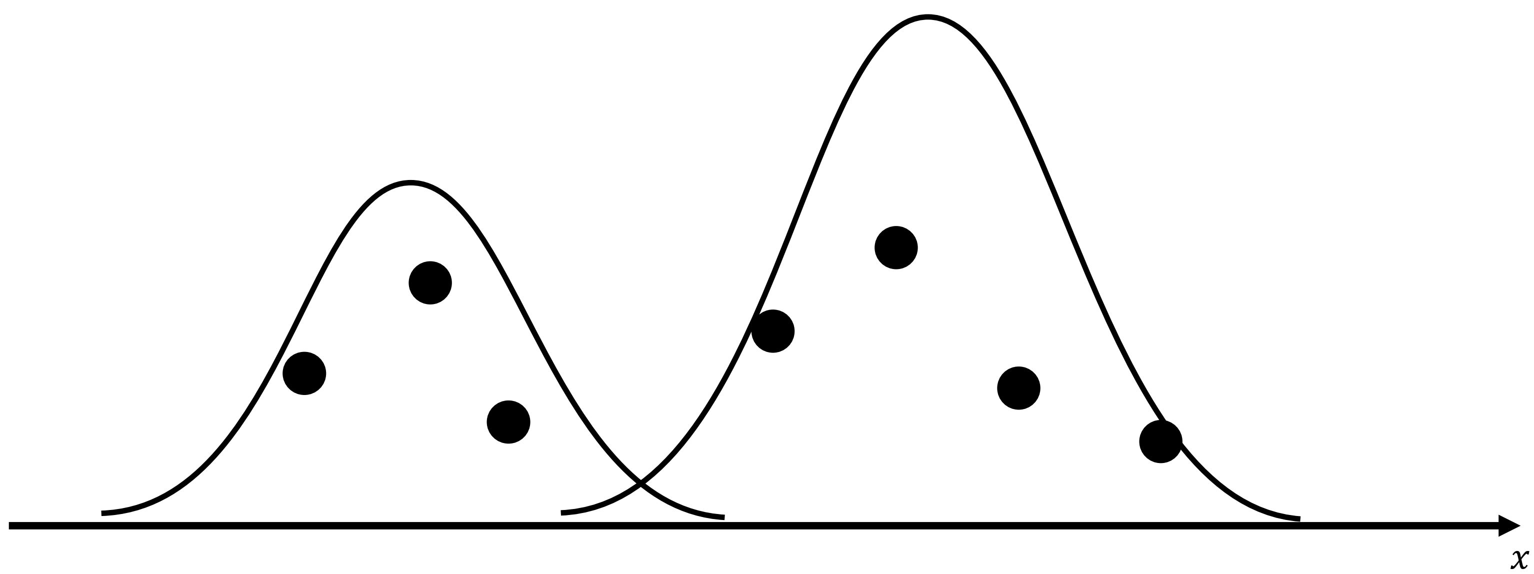
Generative Embedding

Brodersen et al. (2014)
NeuroImage: Clinical

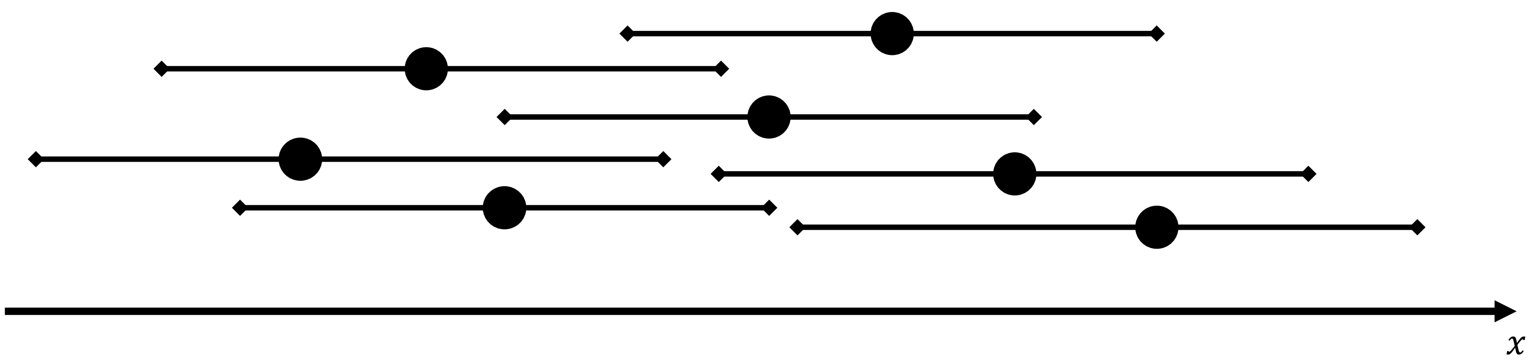
Clustering Latent Variables



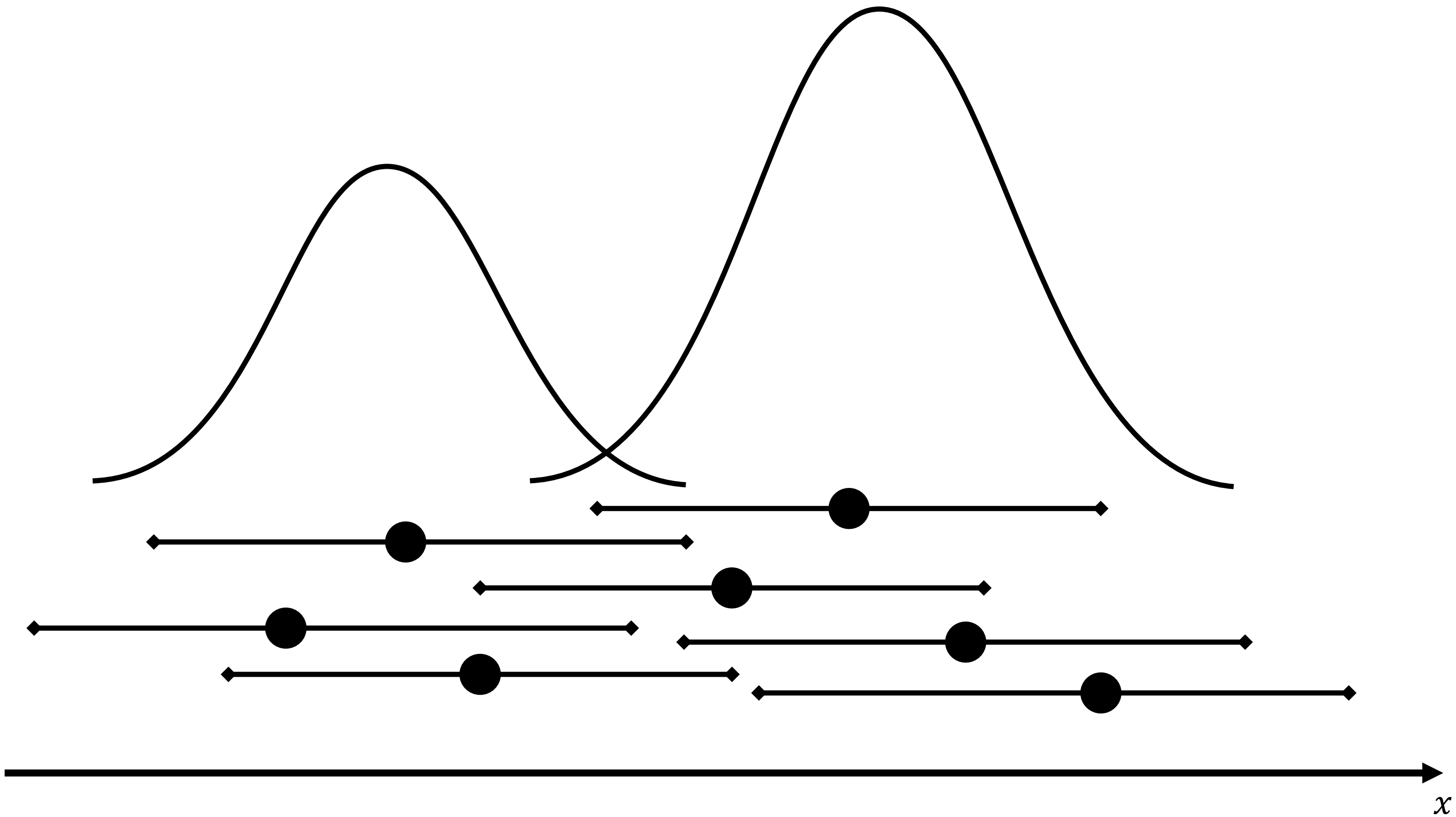
Clustering Latent Variables



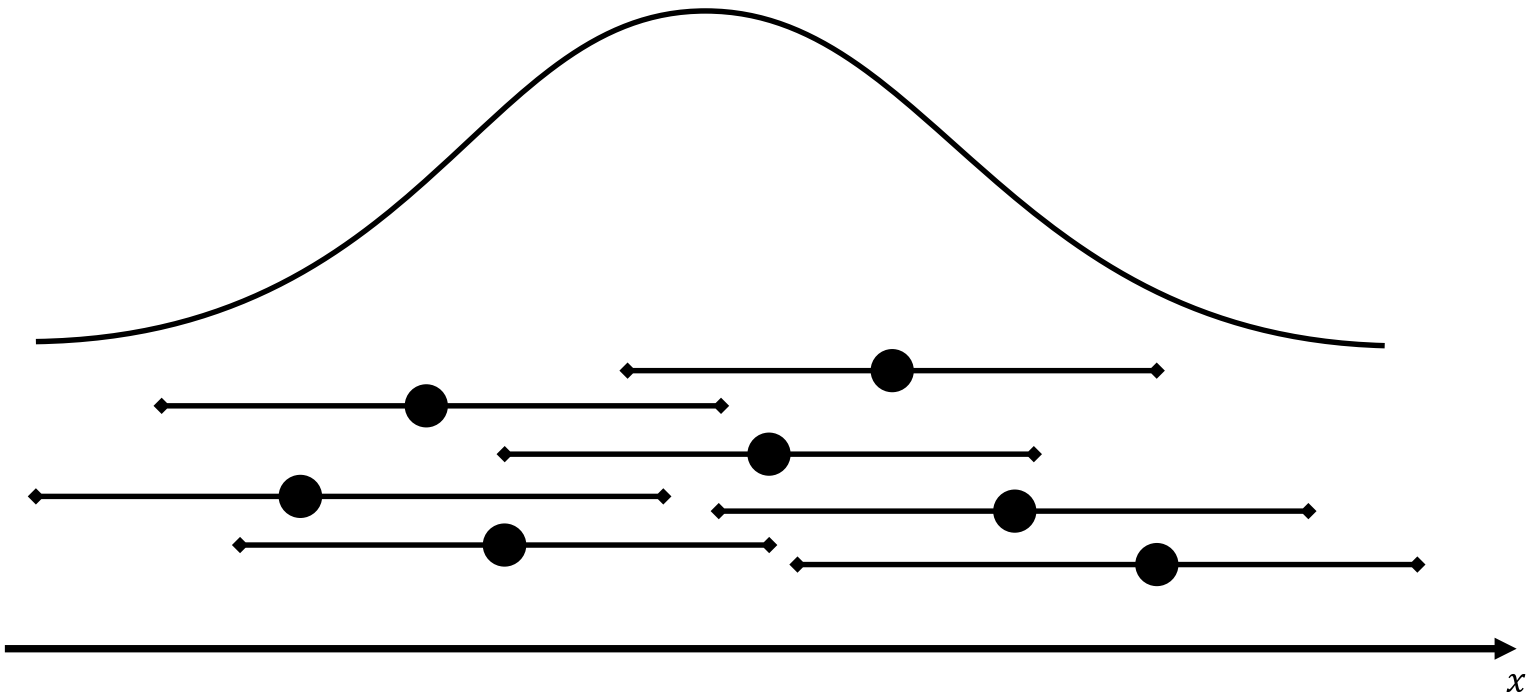
Clustering Latent Variables



Clustering Latent Variables

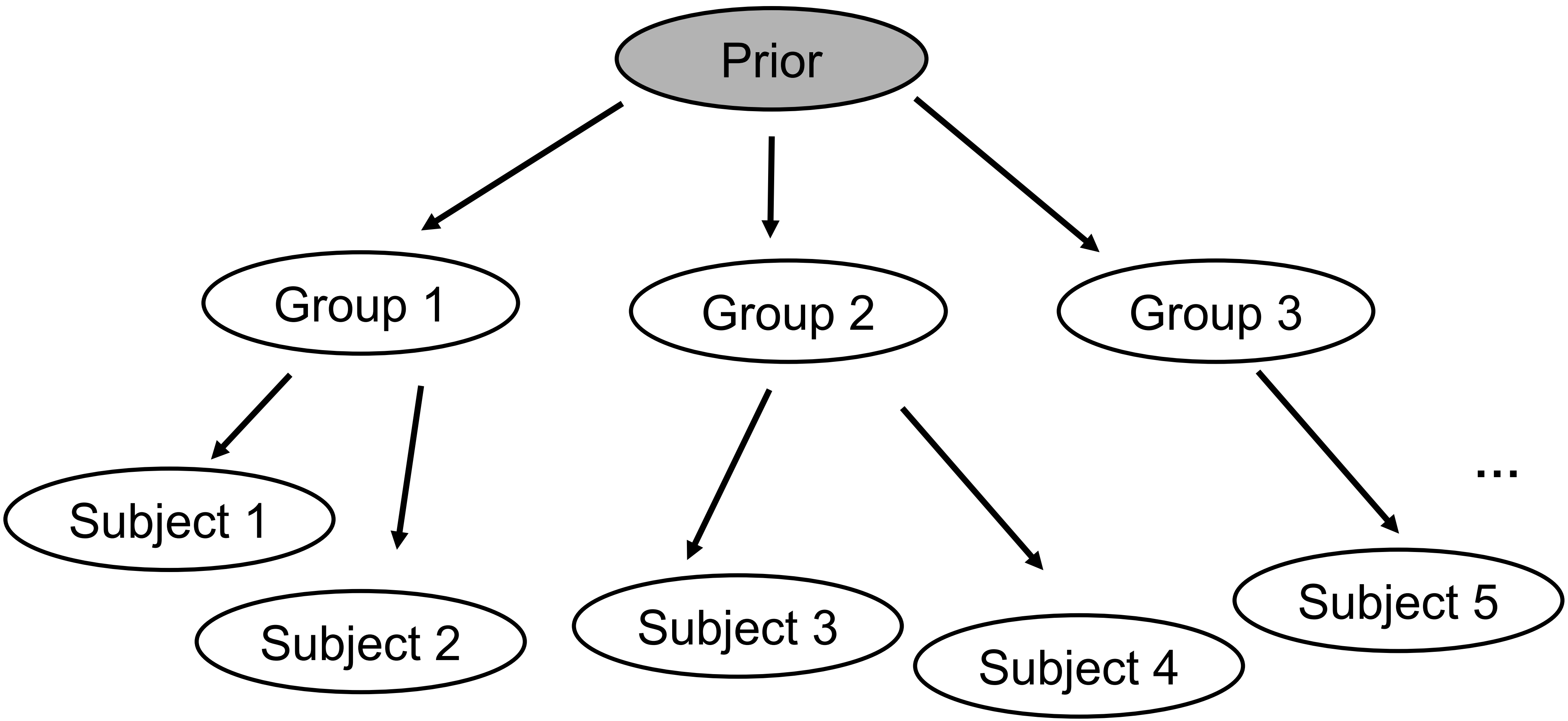


Clustering Latent Variables



A Unified Model for Empirical Bayes and Stratification

A generative, hierarchical model for unsupervised learning



A Unified Model for Empirical Bayes and Stratification

A generative, hierarchical model for unsupervised learning

Mixture of Gaussian: Population consists of several (Gaussian) clusters.

$$\mu_1\Sigma_1,\ldots,\mu_K\Sigma_K \sim prior\left(m_0, S_0\right)$$

DCM network parameters: Each subject is modelled by one of the clusters.

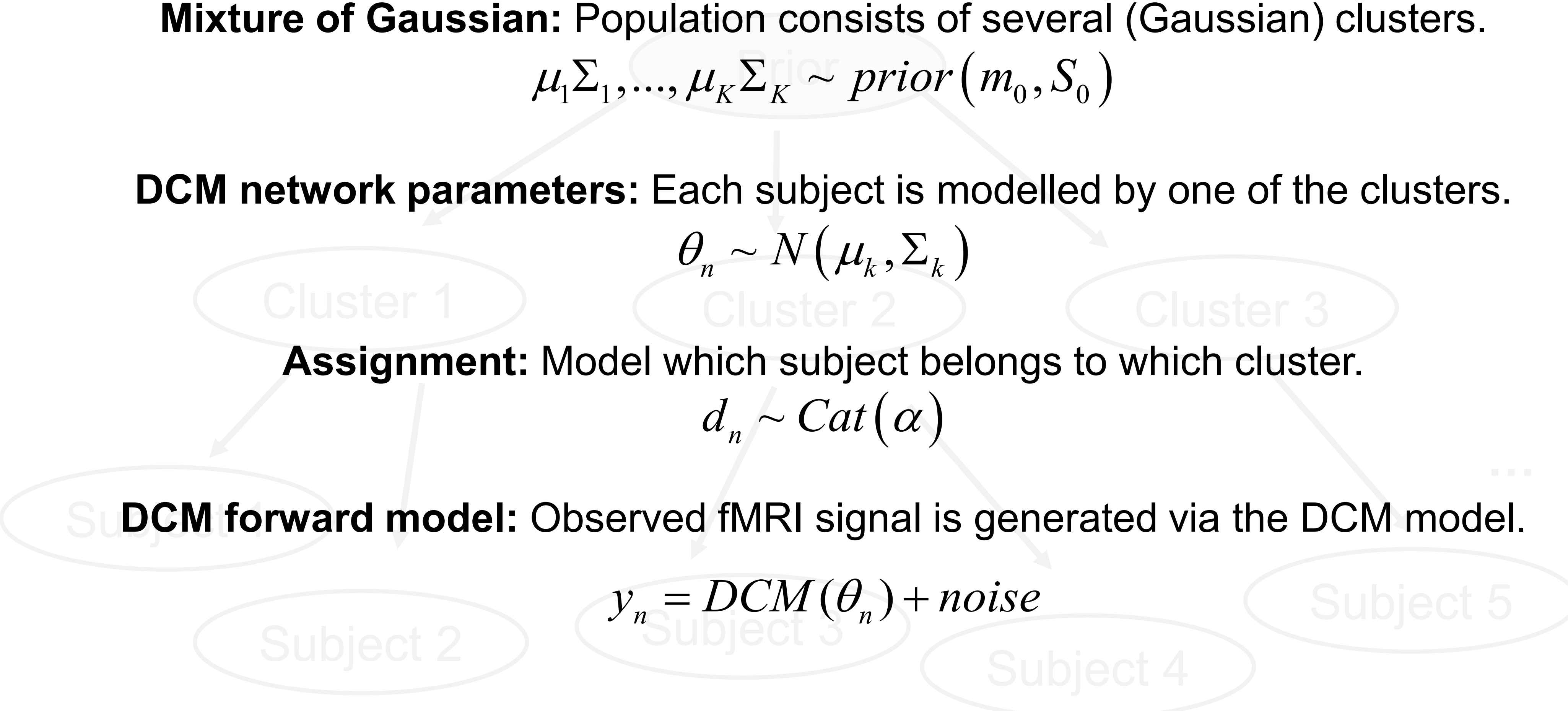
$$\theta_n \sim N\left(\mu_k, \Sigma_k\right)$$

Assignment: Model which subject belongs to which cluster.

$$d_n \sim Cat\left(\alpha\right)$$

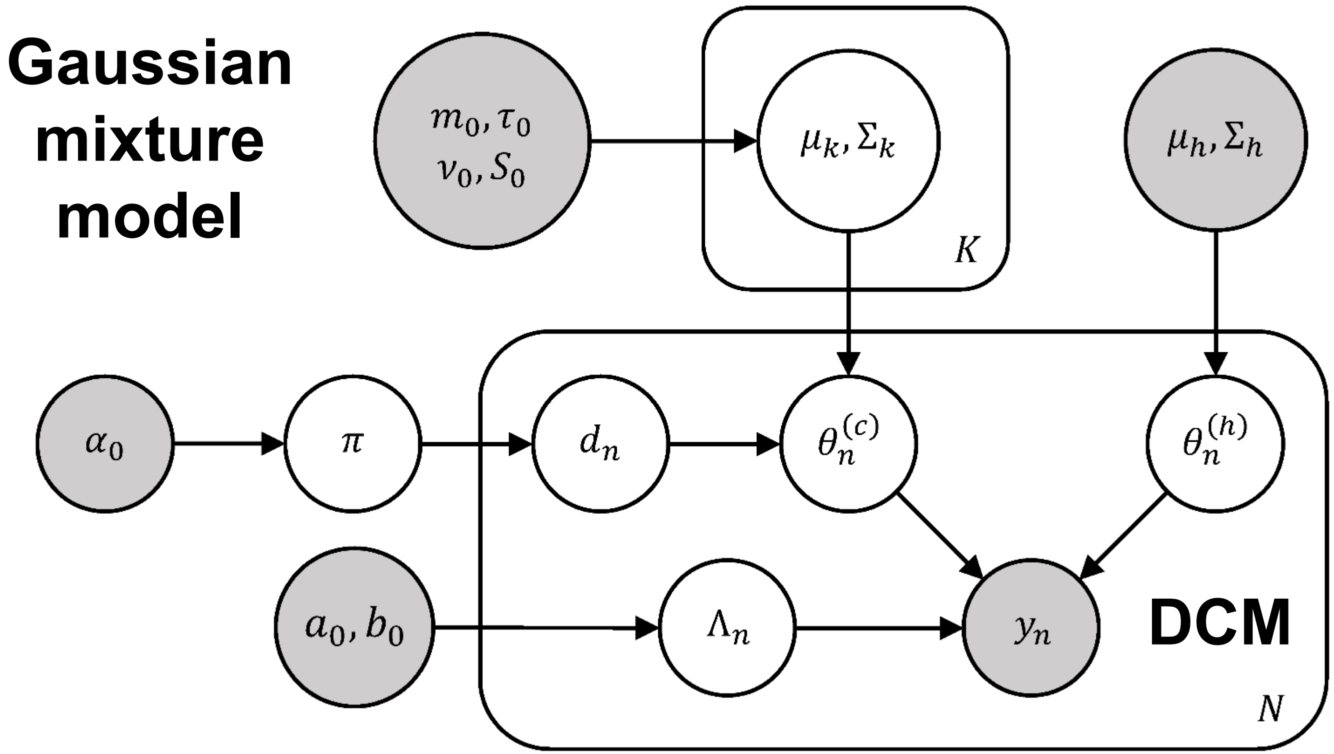
DCM forward model: Observed fMRI signal is generated via the DCM model.

$$y_n = DCM\left(\theta_n\right) + noise$$



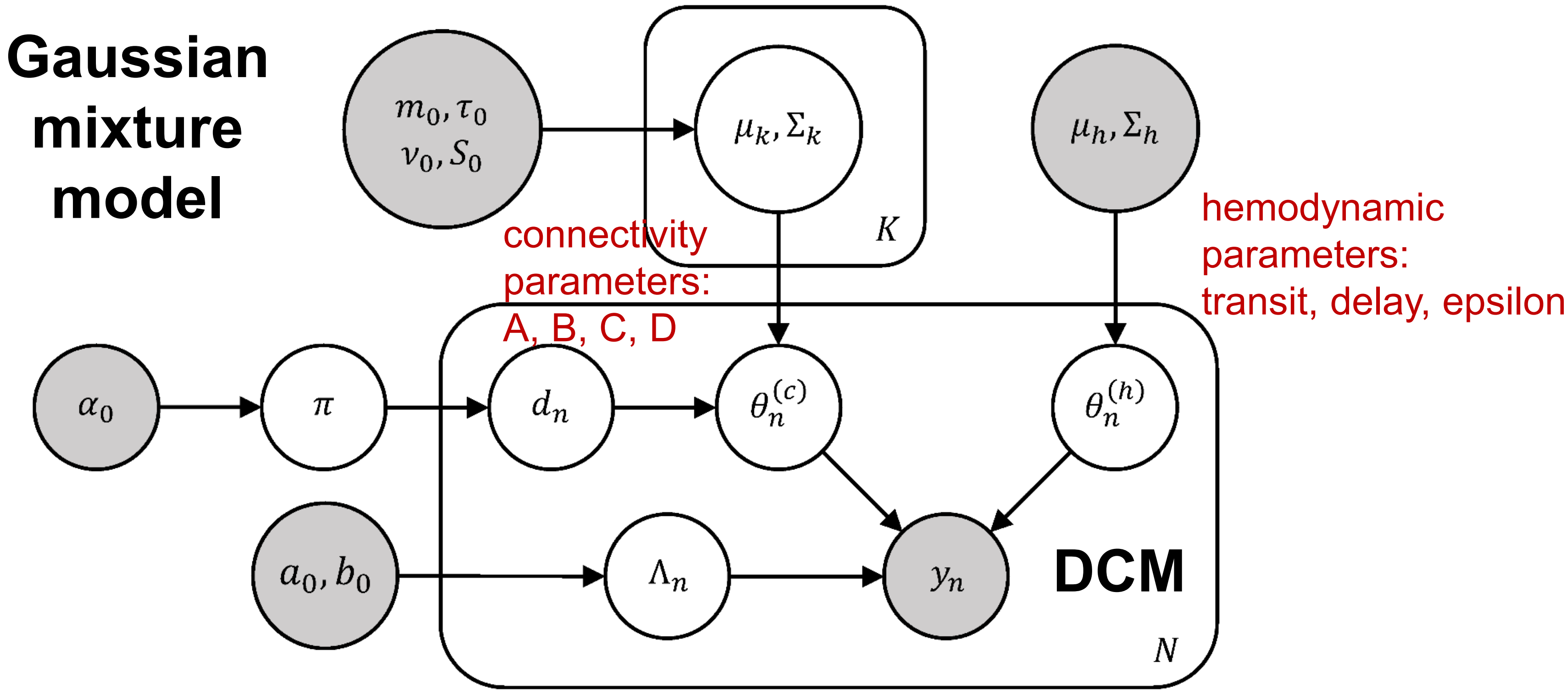
A Unified Model for Empirical Bayes and Stratification

A generative, hierarchical model for unsupervised learning



A Unified Model for Empirical Bayes and Stratification

A generative, hierarchical model for unsupervised learning



Variational Update Equations for HUGE

Auxiliary Variables:

$$q_k = \sum_{n=1}^{N} q_{nk}$$

$$\boldsymbol{\mu}_{ck} = \frac{1}{q_k}\sum_{n=1}^{N} q_{nk}\boldsymbol{\mu}_{c_n}$$

$$\Sigma_{ck} = \sum_{n=1}^{N} q_{nk}\Sigma_{c_n}$$

$$\varepsilon_n = \boldsymbol{y}_n - g(\boldsymbol{\mu}_n)$$

$$G_n = \frac{\partial}{\partial\boldsymbol{\theta}_n} g(\boldsymbol{\mu}_n)$$

$$b'_{nr} = \varepsilon_n^T Q_r \varepsilon_n + \operatorname{tr}\left(G_n^T Q_r G_n \Sigma_n\right)$$

$$\bar{\lambda}_{nr} = \frac{a_{nr}}{b_{nr}}$$

$$\Lambda'_n = \begin{pmatrix} \sum_{k=1}^{K} q_{nk}\nu_k\bar{\Sigma}_k^{-1} & 0 \\ 0 & \Sigma_h^{-1} \end{pmatrix}$$

$$\boldsymbol{\mu}'_n = \left(\sum_{k=1}^{K} q_{nk}\nu_k\bar{\Sigma}_k^{-1}\bar{\boldsymbol{\mu}}_k,\ \Sigma_h^{-1}\boldsymbol{\mu}_h\right).$$

Cluster Weighs:

$$\boldsymbol{\alpha}[k] = \boldsymbol{\alpha}_0[k] + q_k$$

Noise Precision:

$$a_{nr} = a_{0r} + \frac{q_r}{2}$$

$$b_{nr} = b_{0r} + \frac{b'_{nr}}{2}.$$

DCM Parameters:

$$\Sigma_n^{-1} = G_n^T\bar{\Lambda}_n G_n + \Lambda'_n \quad \text{and}$$

$$\boldsymbol{\mu}_n = \Sigma_n\left(G_n^T\bar{\Lambda}_n(\varepsilon_n + G_n\boldsymbol{m}_n) + \boldsymbol{\mu}'_n\right).$$

$$\Sigma_n = \begin{pmatrix} \Sigma_{c_n} & \dots \\ \dots & \Sigma_{h_n} \end{pmatrix}$$

$$\boldsymbol{\mu}_n = (\boldsymbol{\mu}_{c_n}^T, \boldsymbol{\mu}_{h_n}^T)^T$$

Σ_{c_n}: $p_c \times p_c$
Σ_{h_n}: $p_h \times p_h$
$\boldsymbol{\mu}_{c_n}$: $p_c \times 1$
$\boldsymbol{\mu}_{h_n}$: $p_h \times 1$

Cluster Mean and Covariance:

$$\bar{\boldsymbol{\mu}}_k = \frac{q_k\boldsymbol{\mu}_{ck} + \tau_0\bar{\boldsymbol{\mu}}_0}{q_k + \tau_0},$$

$$\tau_k = q_k + \tau_0,$$

$$\nu_k = q_k + \nu_0,$$

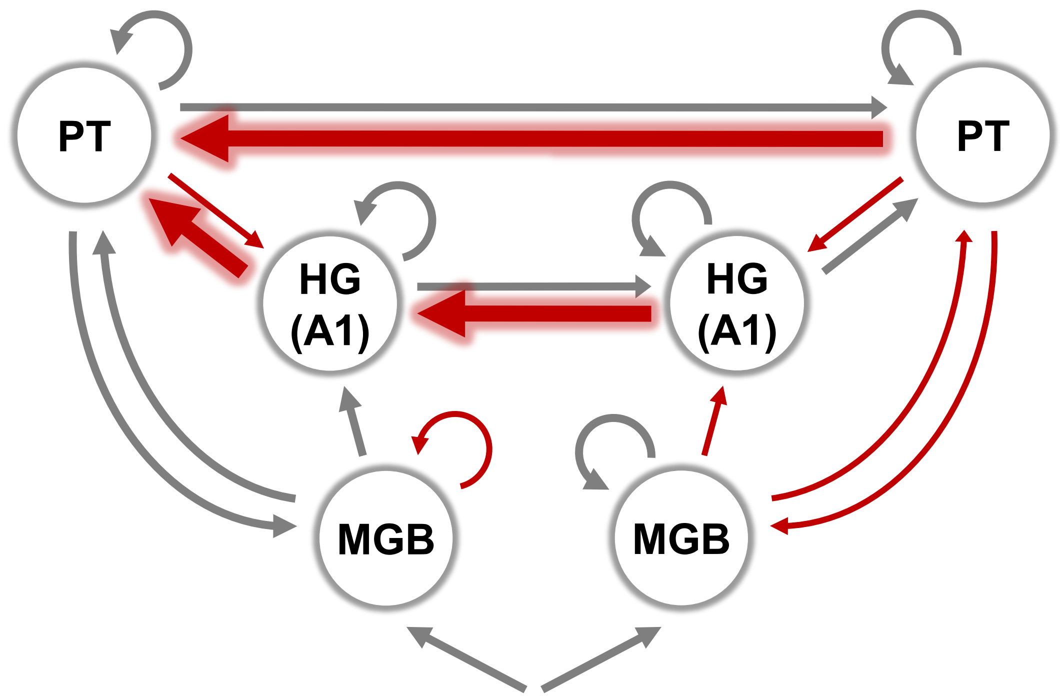
$$\bar{\Sigma}_k = \Sigma_{ck} + \sum_{n=1}^{N} q_{nk}(\boldsymbol{\mu}_{c_n} - \boldsymbol{\mu}_{ck})(\boldsymbol{\mu}_{c_n} - \boldsymbol{\mu}_{ck})^T + \frac{q_k\tau_0}{q_k + \tau_0}(\boldsymbol{\mu}_{ck} - \bar{\boldsymbol{\mu}}_0)(\boldsymbol{\mu}_{ck} - \bar{\boldsymbol{\mu}}_0)^T + \bar{\Sigma}_0.$$

Assignments:

$$\log q_{nk} = -\frac{1}{2}\log|\bar{\Sigma}_k| + \frac{1}{2}\sum_{i=1}^{p_c}\Psi\left(\frac{\nu_k + 1 - i}{2}\right) - \frac{p_c}{2\tau_k} - \frac{\nu_k}{2}\operatorname{tr}(\bar{\Sigma}_k^{-1}\Sigma_{c_n}) - \frac{\nu_k}{2}(\boldsymbol{\mu}_{c_n} - \bar{\boldsymbol{\mu}}_k)^T\bar{\Sigma}_k^{-1}(\boldsymbol{\mu}_{c_n} - \bar{\boldsymbol{\mu}}_k) + \Psi(\boldsymbol{\alpha}[k]) + const$$

Example: Aphasia Study

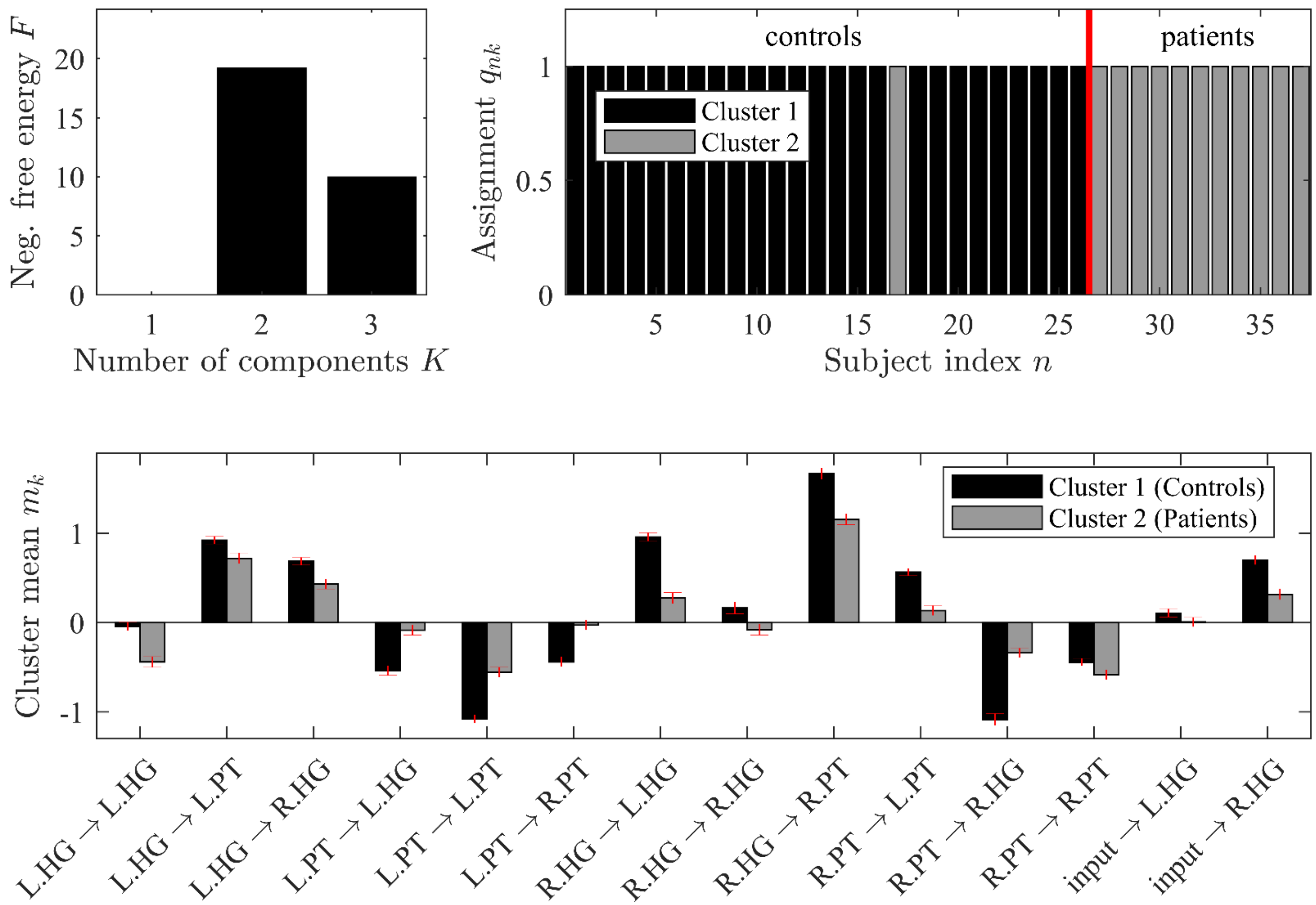
- Aphasic patients (N=11) vs. controls (N=26)
- passive speech listening
- 6-region DCM of auditory areas
- SVM Classification on DCM parameters (supervised learning): Patients vs Control achieved balanced accuracy of 98%



Brodersen et al. 2011, *PLoS Comput. Biol.*

Example: Aphasia Study

HUGE (unsupervised) achieved a balanced purity of 96%



Yao et al. (2018)
NeuroImage

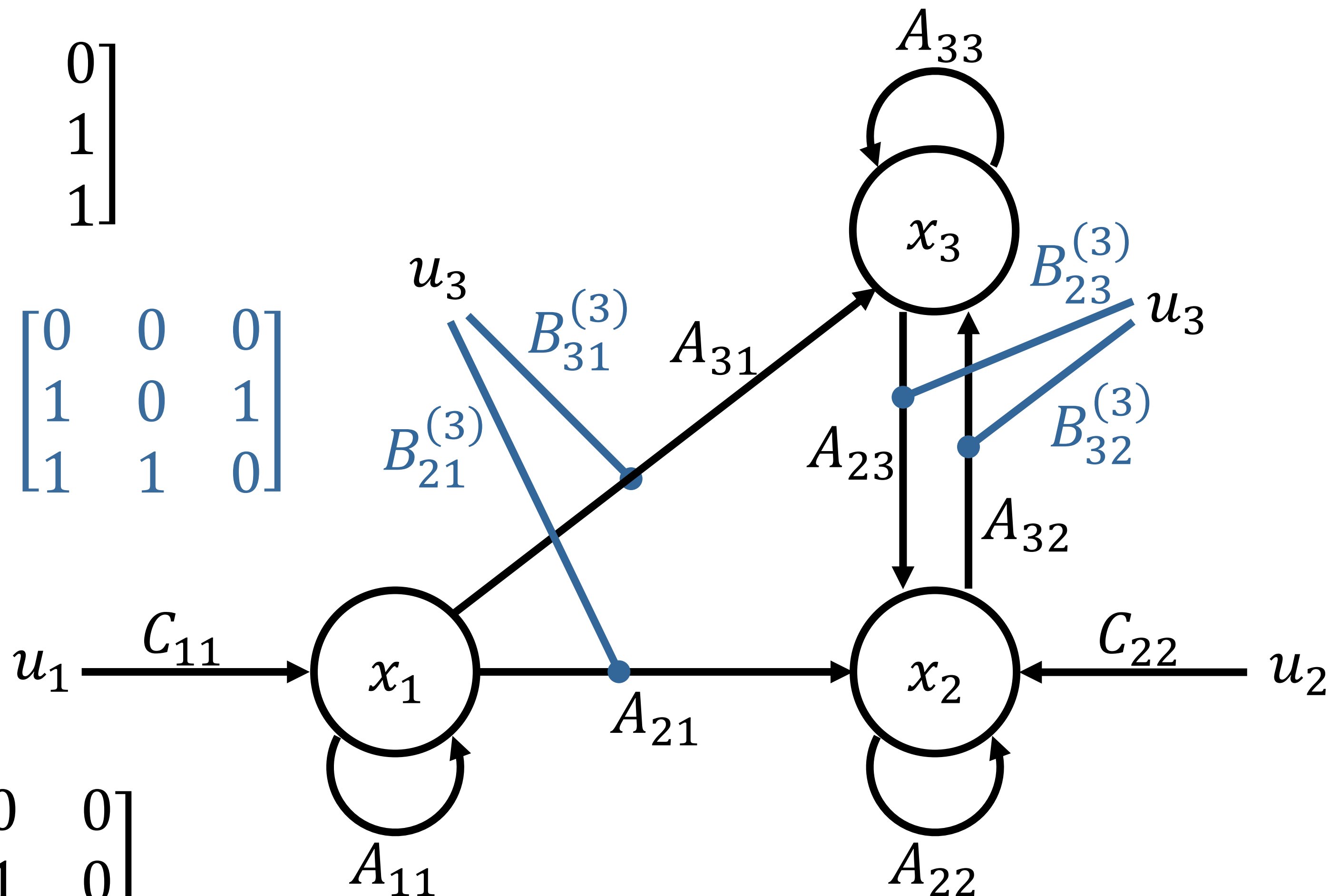
Matlab Demo

open **`tapas_huge_demo.mlx`**

DCM Network Structure

$$a = \begin{bmatrix} 1 & 0 & 0 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{bmatrix}$$

$$b(:,:,3) = \begin{bmatrix} 0 & 0 & 0 \\ 1 & 0 & 1 \\ 1 & 1 & 0 \end{bmatrix}$$



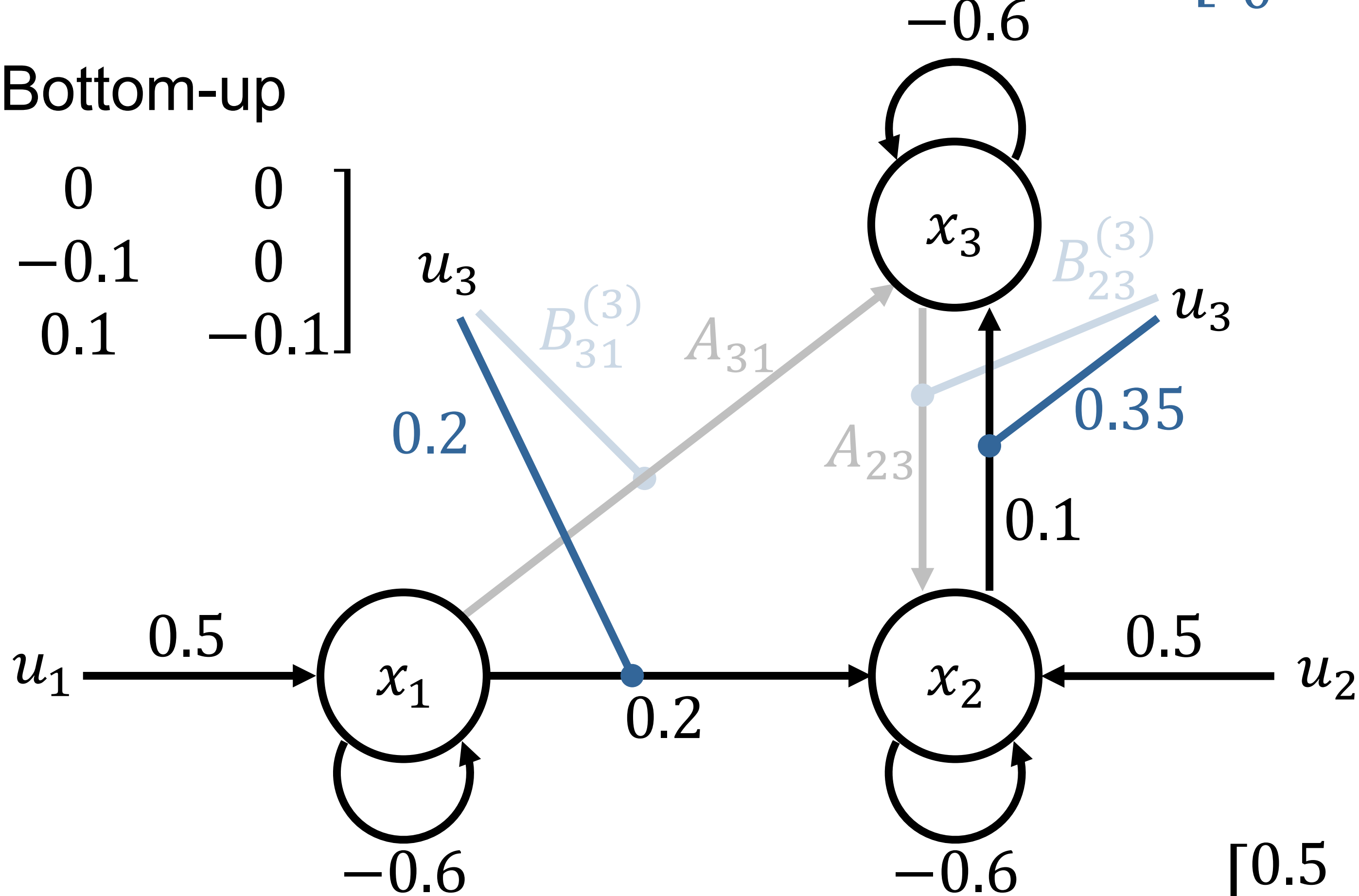
$$c = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

DCM Network Structure

$$B(:,:,3) = \begin{bmatrix} 0 & 0 & 0 \\ 0.2 & 0 & 0 \\ 0 & 0.35 & 0 \end{bmatrix}$$

Group 1: Bottom-up

$$A = \begin{bmatrix} -0.1 & 0 & 0 \\ 0.2 & -0.1 & 0 \\ 0 & 0.1 & -0.1 \end{bmatrix}$$



$$C = \begin{bmatrix} 0.5 & 0 & 0 \\ 0 & 0.5 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

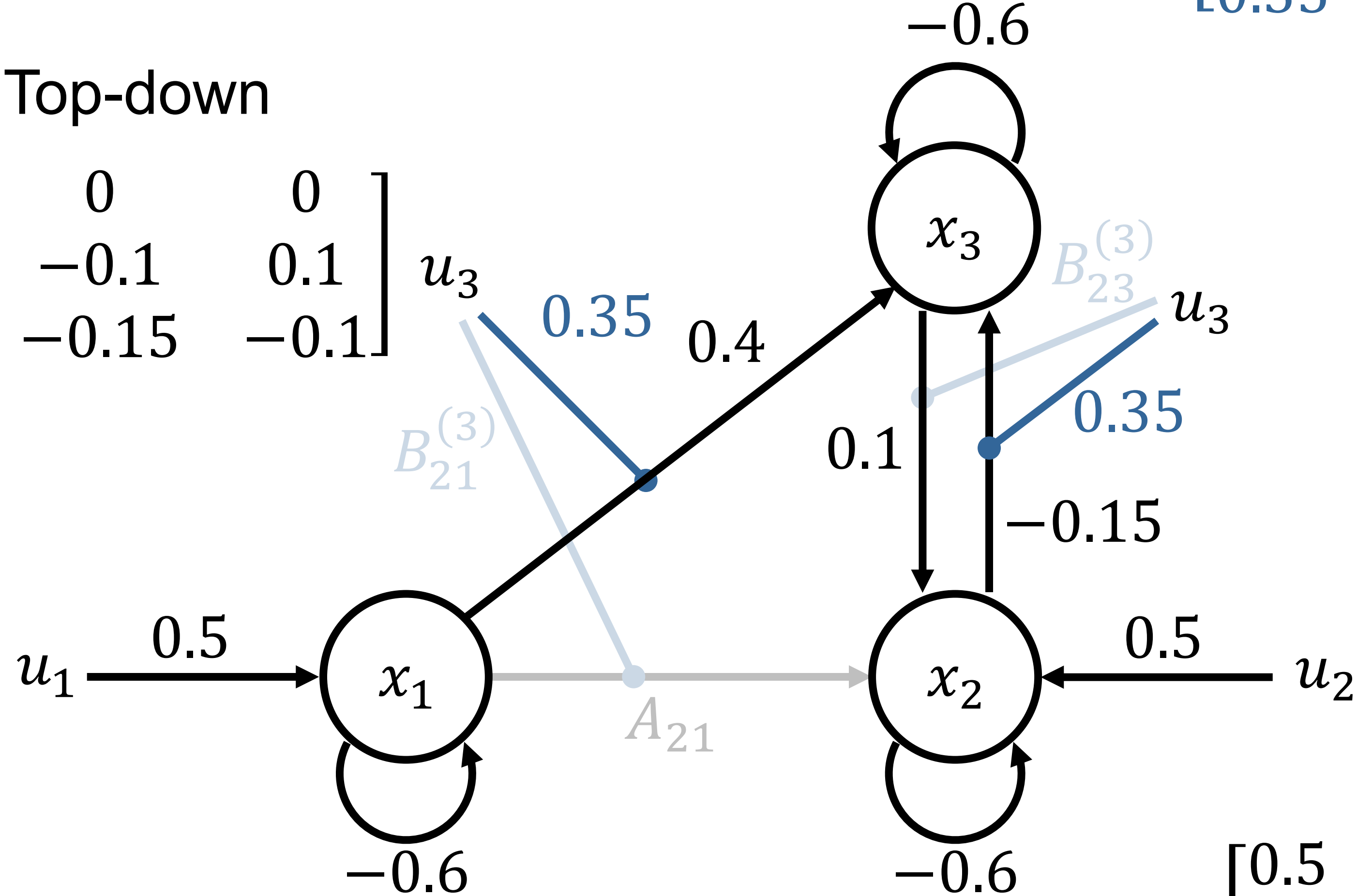
Leeuwen et al. (2011) *J. Neurosci*

DCM Network Structure

$$B(:,:,3) = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0.35 & 0.35 & 0 \end{bmatrix}$$

Group 2: Top-down

$$A = \begin{bmatrix} -0.1 & 0 & 0 \\ 0 & -0.1 & 0.1 \\ 0.4 & -0.15 & -0.1 \end{bmatrix}$$



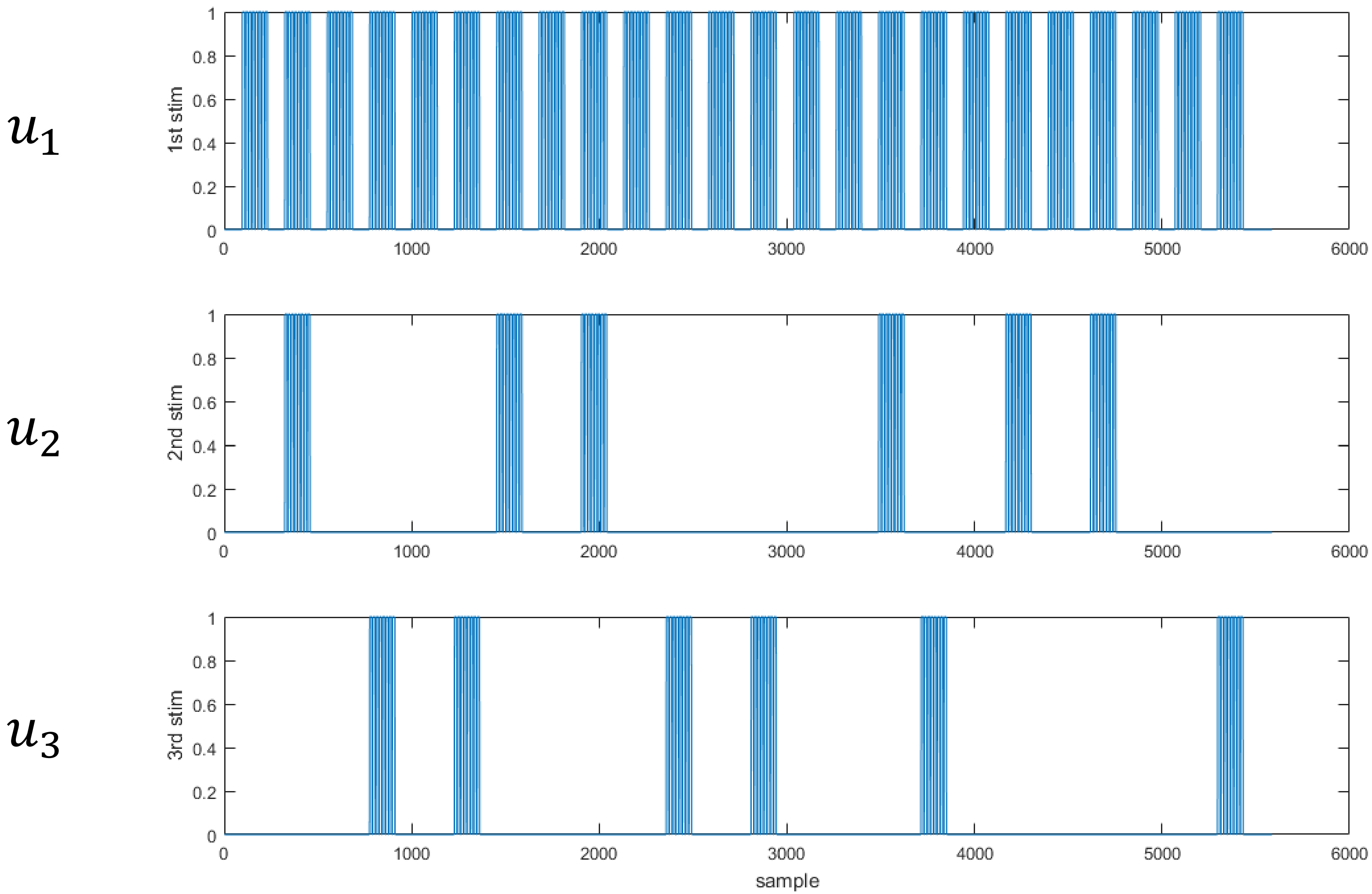
$$C = \begin{bmatrix} 0.5 & 0 & 0 \\ 0 & 0.5 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

Leeuwen et al. (2011) *J. Neurosci*

DCM Network Structure

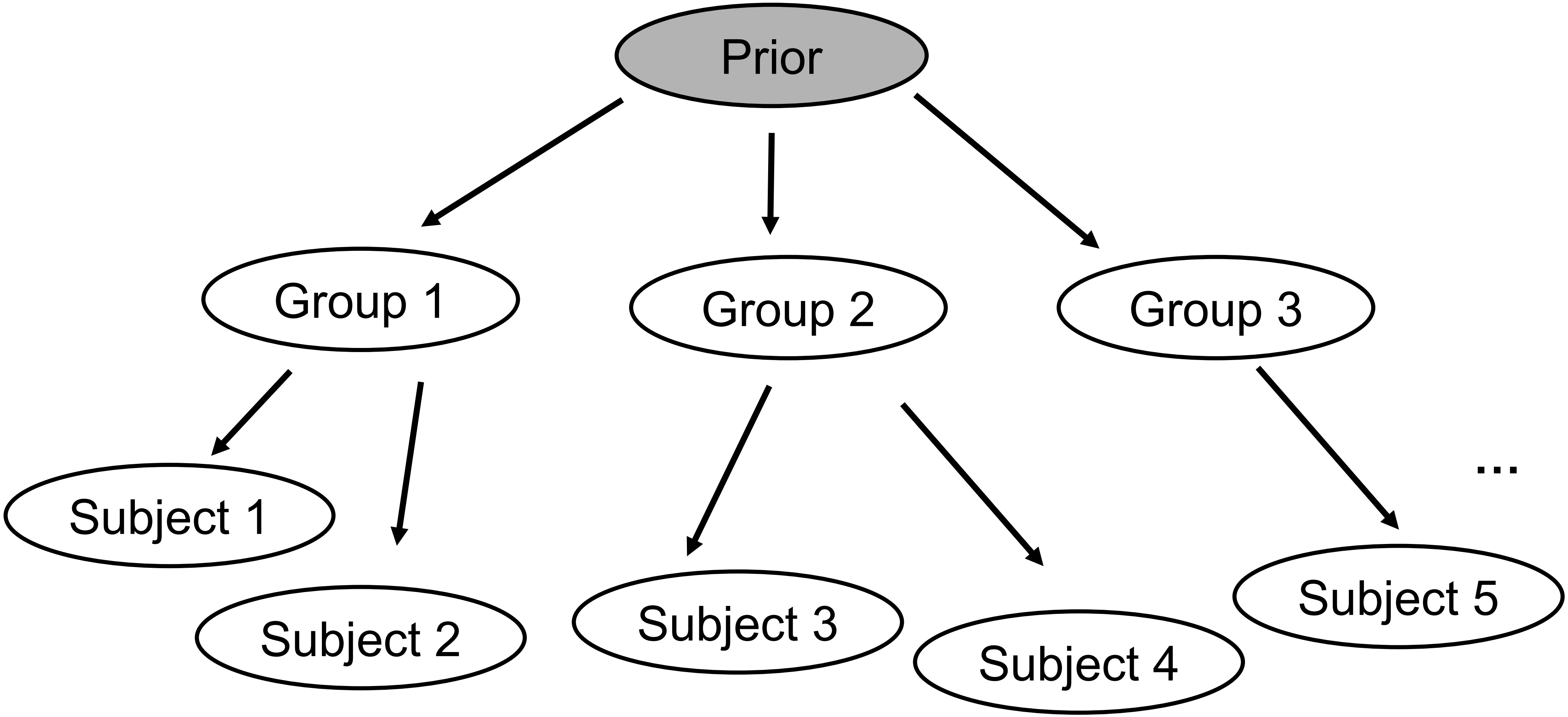
Leeuwen et al. (2011) *J. Neurosci*

Experimental Stimuli

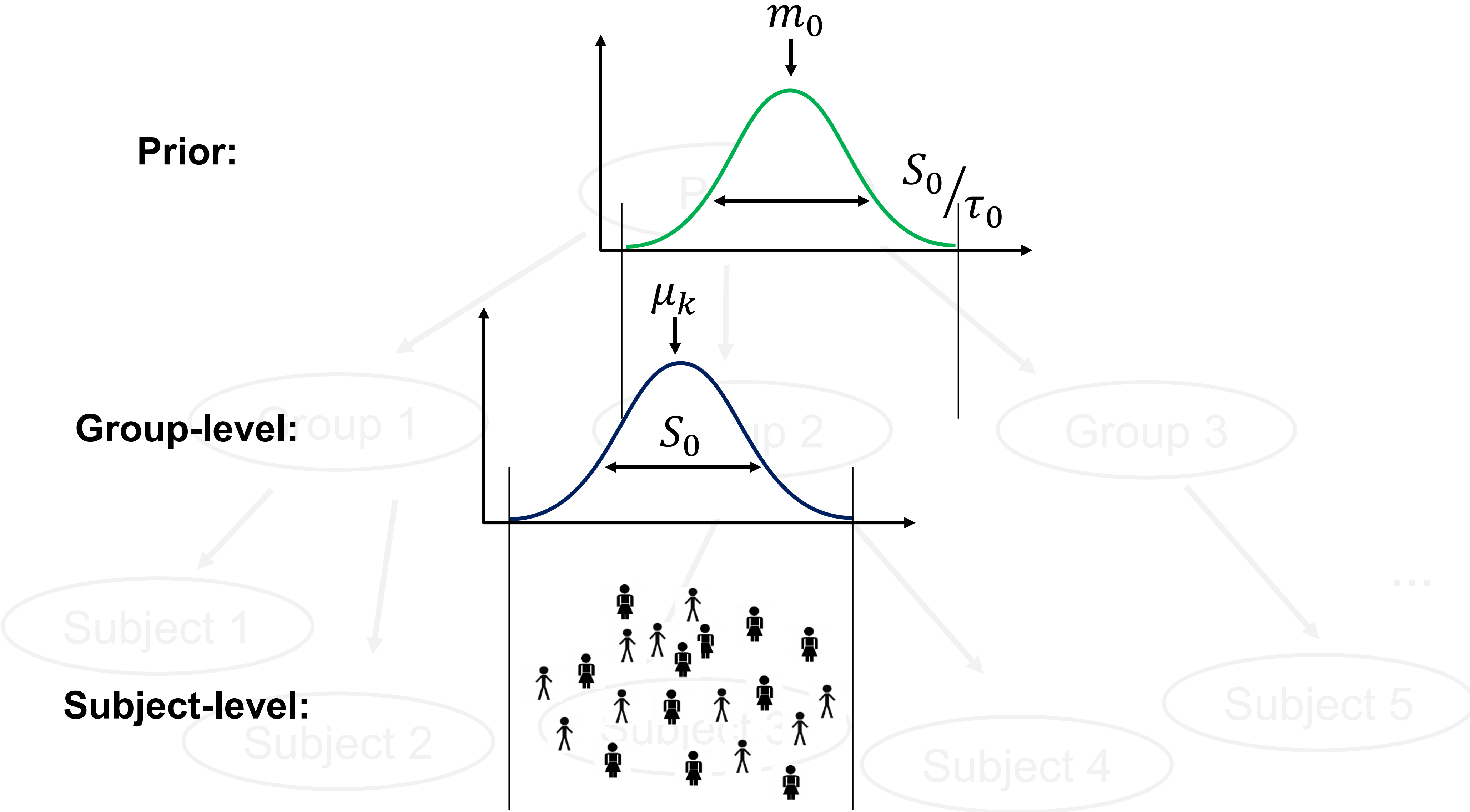


Advanced Topics

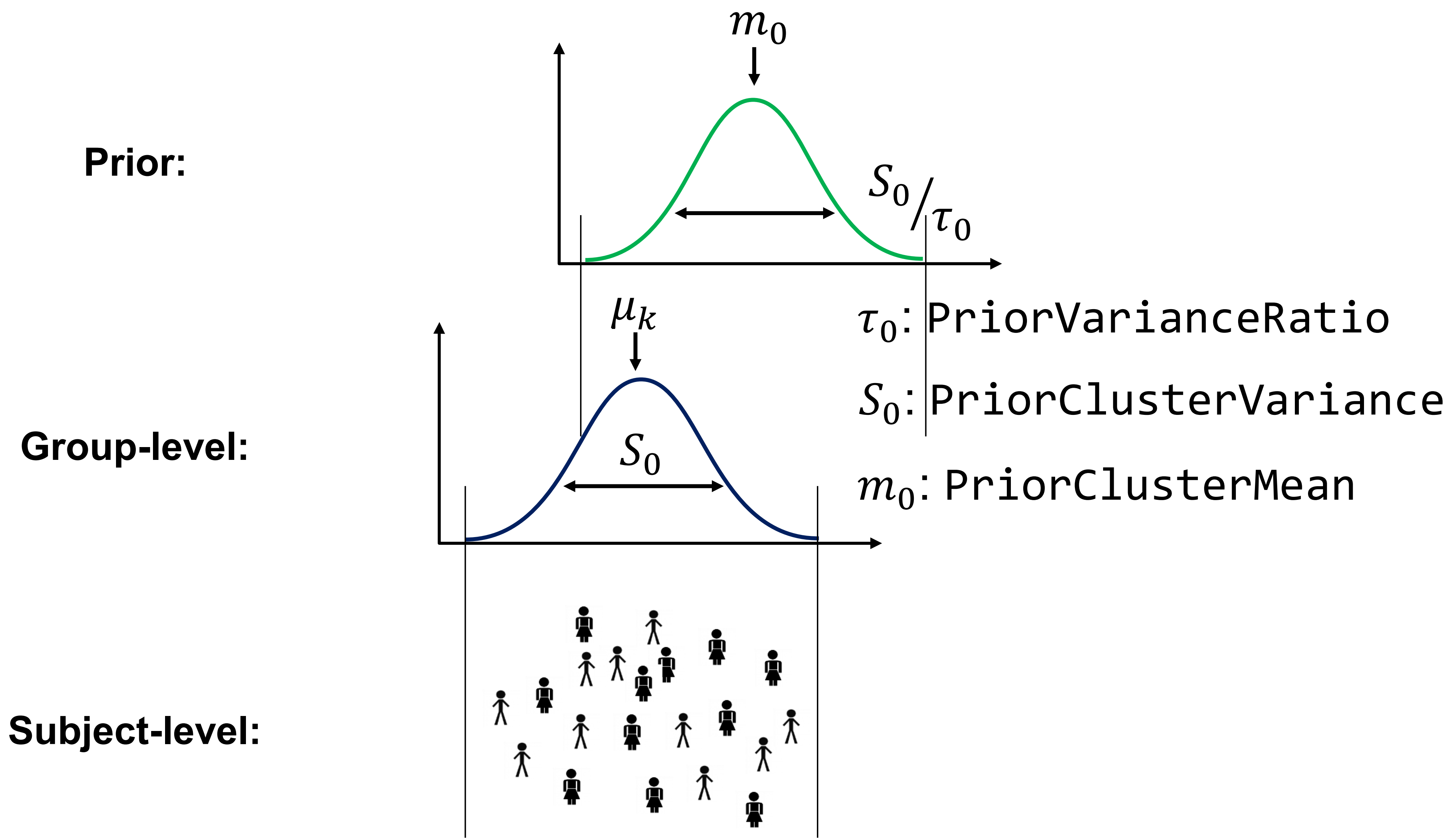
A Word on Priors



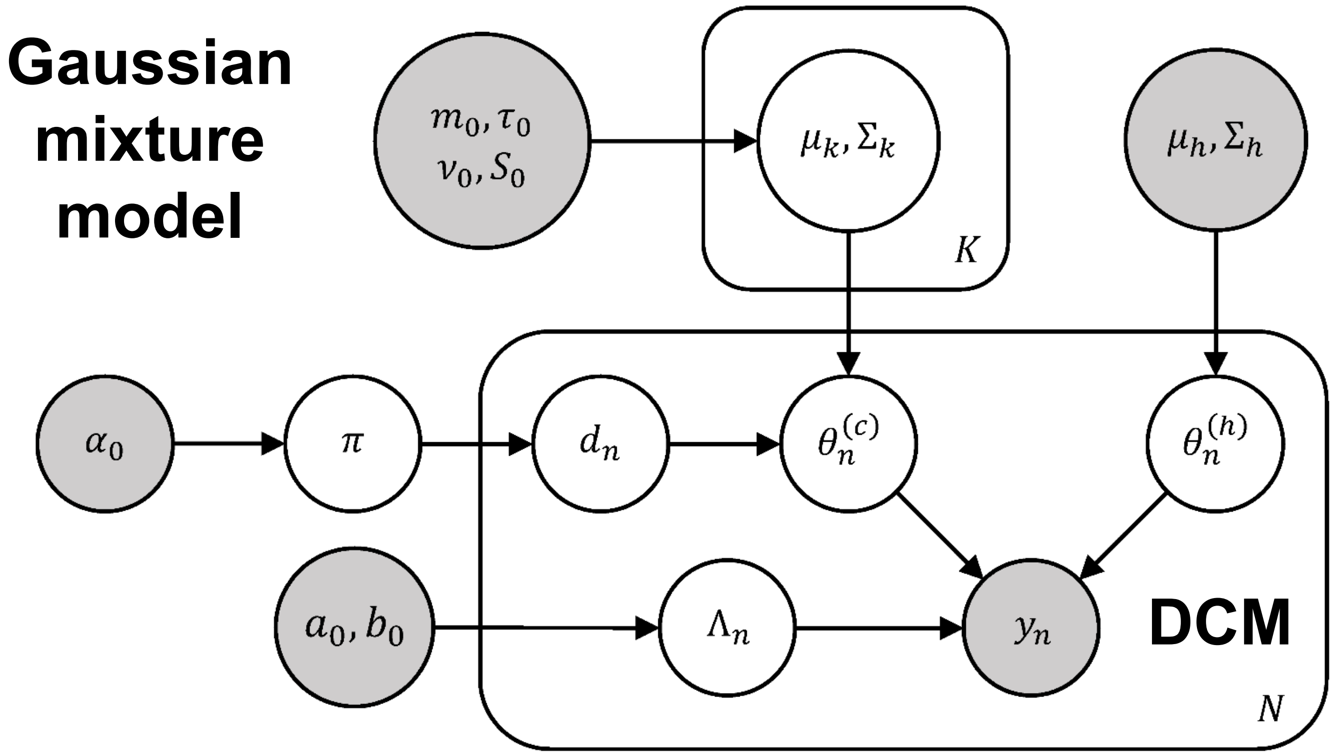
A Word on Priors



A Word on Priors



A Word on Priors



Excluding DCM Parameters

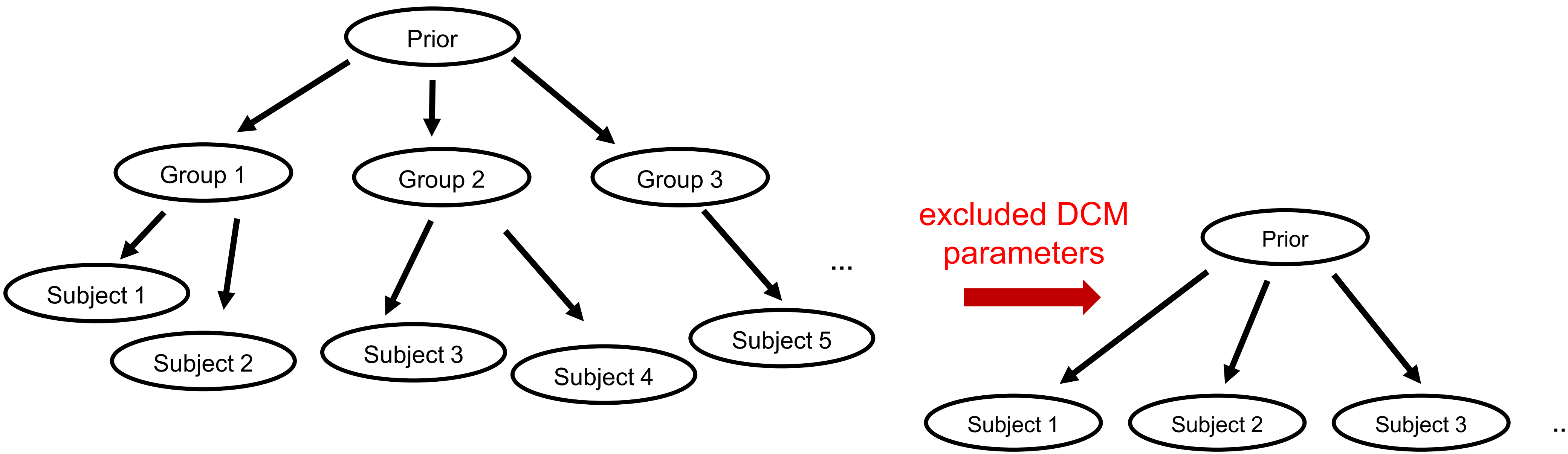
DCM parameters can be **excluded** from clustering if they are …

- not relevant for research question.
  - e.g.: self-connections, input strength, …
- strongly correlated with other parameter.
  - e.g.: A and C matrix
- difficult to estimate.
- strong prior knowledge.
  - e.g.: results from previous studies

Excluding DCM Parameters

Excluded parameters are still being estimated (on a per-subject basis), …

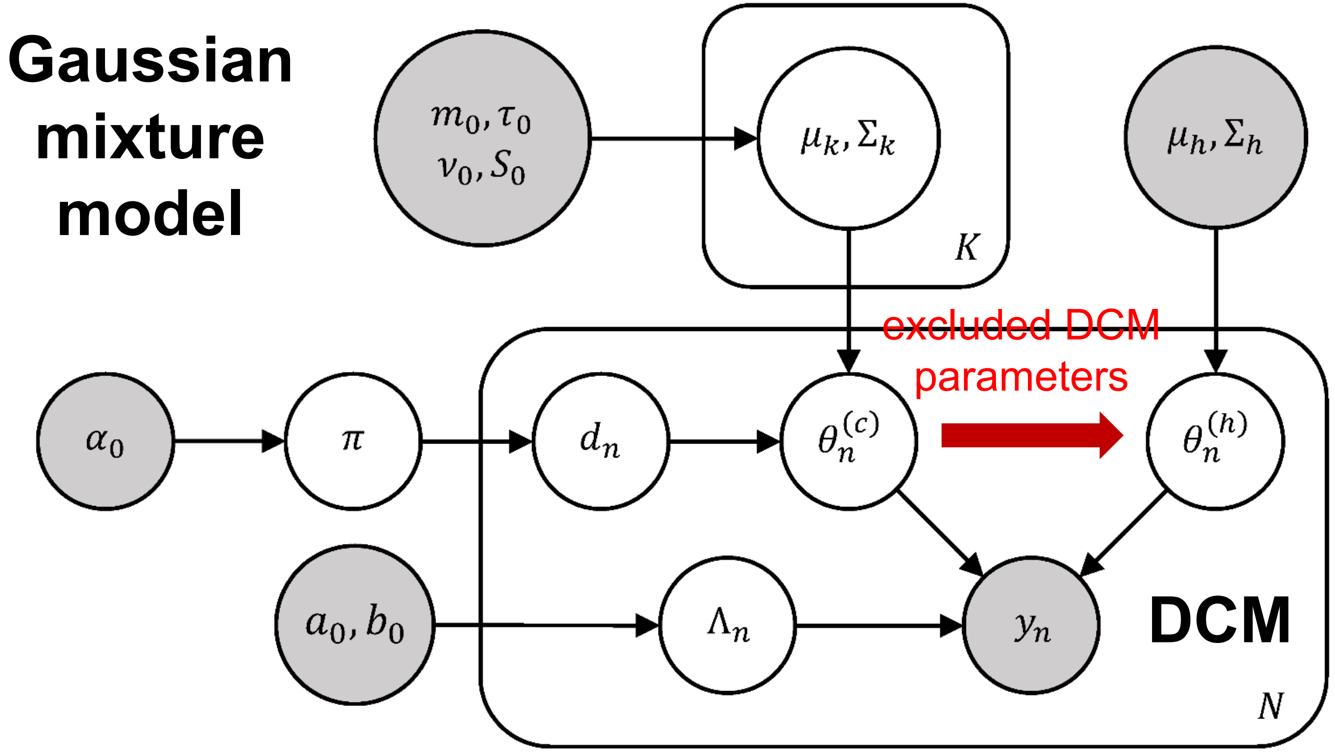
… but they do not contribute to the **clustering** model.



Excluding DCM Parameters

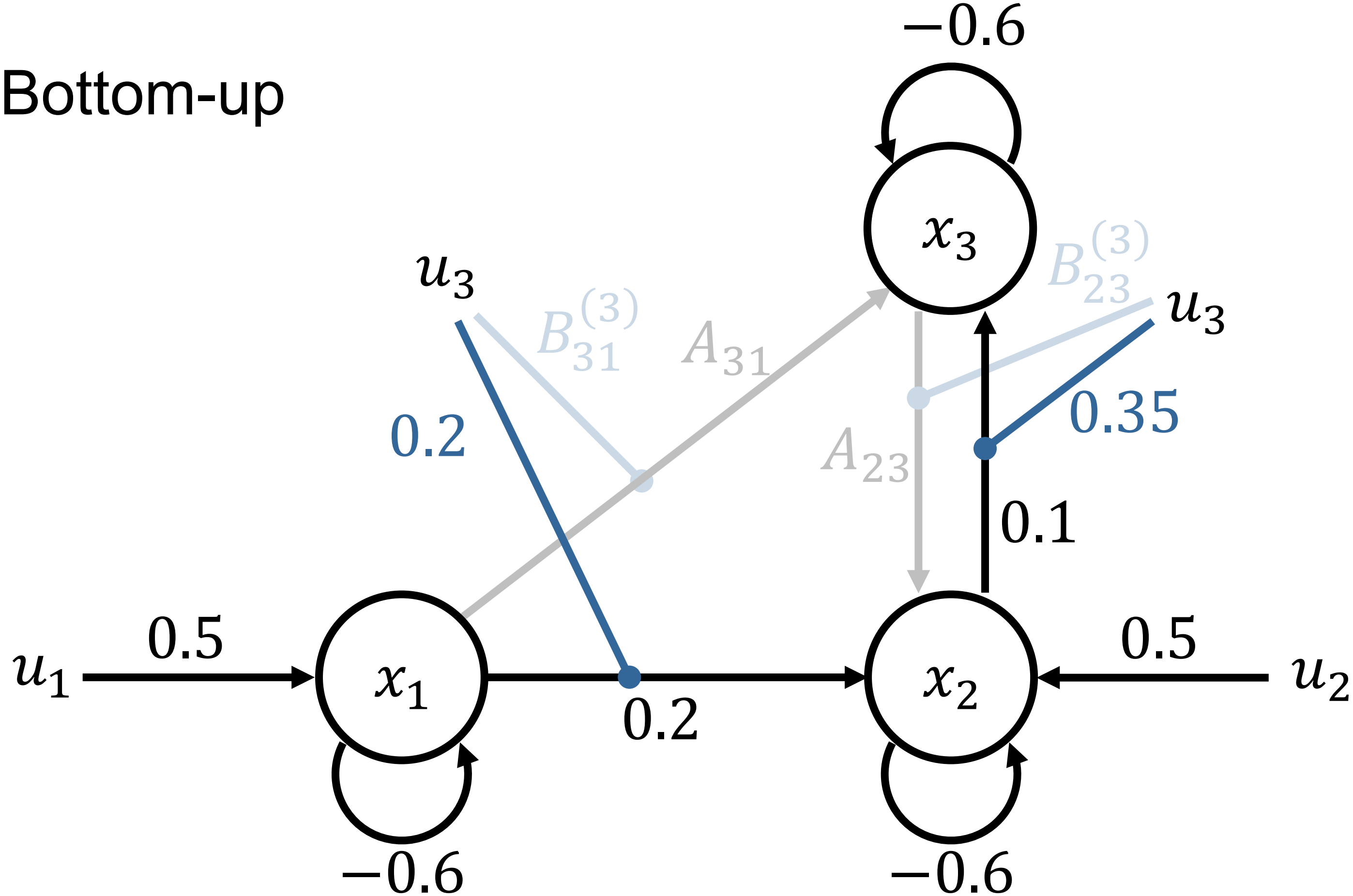
Excluded parameters are still being estimated (on a per-subject basis), …

… but they do not contribute to the **clustering** model.



Excluding DCM Parameters

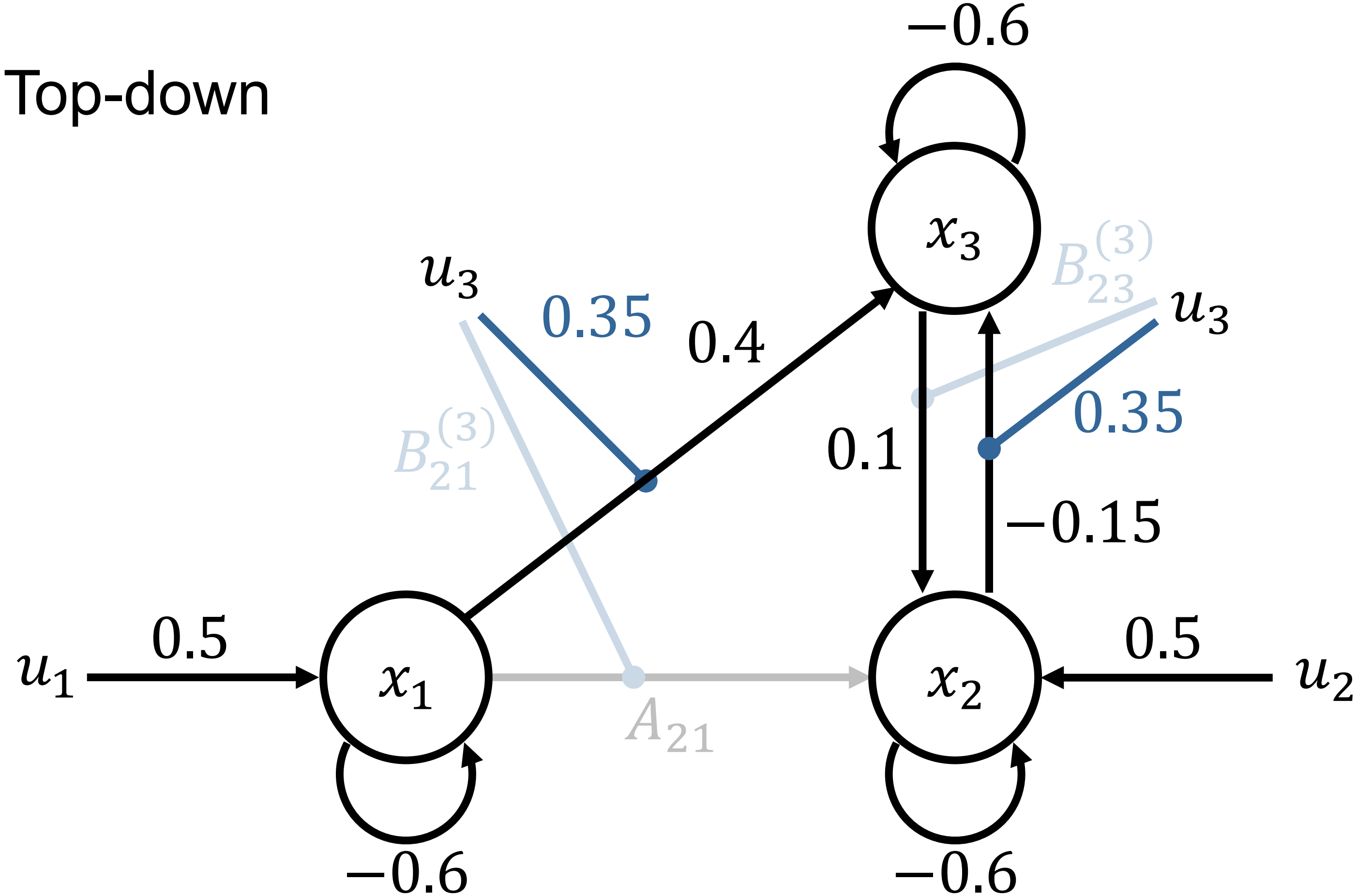
Group 1: Bottom-up



Leeuwen et al. (2011) *J. Neurosci*

Excluding DCM Parameters

Group 2: Top-down



Leeuwen et al. (2011) *J. Neurosci*

Excluding DCM Parameters

To **exclude** parameters, use name-value pair argument

`OmitFromClustering`

in combination with argument **`Dcm`**

Excluding DCM Parameters

To **exclude** parameters, use name-value pair argument

`OmitFromClustering`

in combination with argument **`Dcm`**

Note:

- By excluding certain parameters, you are changing the model.
- Negative free energy might change (BMS).
- Consider compatibility with research question.

General Suggestions

- Keep networks simple
- Choice of priors
  - Are priors sensible for data at hand?
- Experiment design
  - Choice of paradigm
  - Research question

General Suggestions

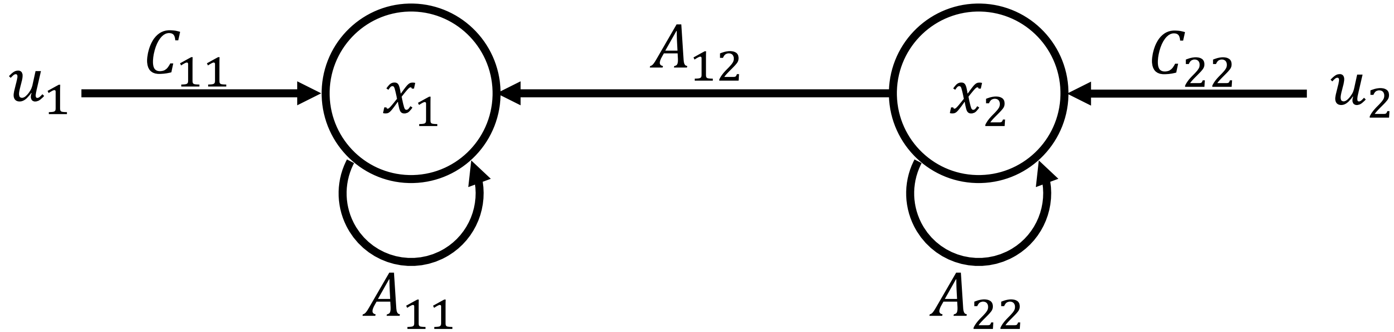
- Keep networks simple
- Choice of priors
  - Are priors sensible for data at hand?
- Experiment design
  - Choice of paradigm
  - Research question

Find a suitable experiment for a given research question, not the most significant model for a given dataset.

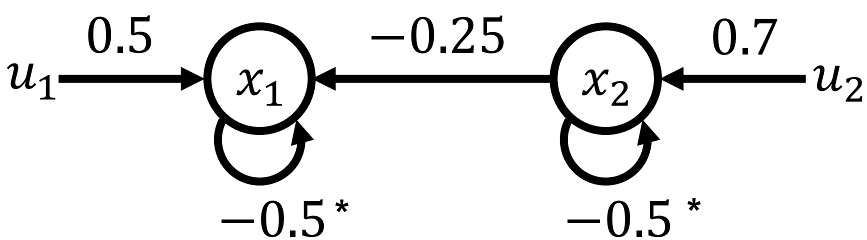
Matlab Exercise

open **cpc_practical_exercise_huge.m**

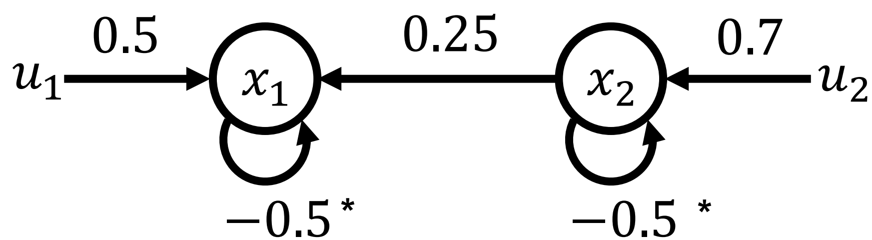
Exercise



Group 1



Group 2



* self-connections are -0.5 by default

References

Brodersen, K.H., Schofield, T.M., Leff, A.P., Ong, C.S., Lomakina, E.I., Buhmann, J.M., Stephan, K.E., 2011. Generative embedding for model-based classification of fMRI data. PLoS Comput. Biol. 7.

Brodersen, K.H., Deserno, L., Schlagenhauf, F., Lin, Z., Penny, W.D., Buhmann, J.M., Stephan, K.E., 2014. Dissecting psychiatric spectrum disorders by generative embedding. Neuroimage: Clinica 4, 98–111.

Friston, K.J., Litvak, V., Oswal, A., Razi, A., Stephan, K.E., van Wijk, B.C.M., Ziegler, G., Zeidman, P., 2016. Bayesian model reduction and empirical Bayes for group (DCM) studies. Neuroimage 128, 413–431.

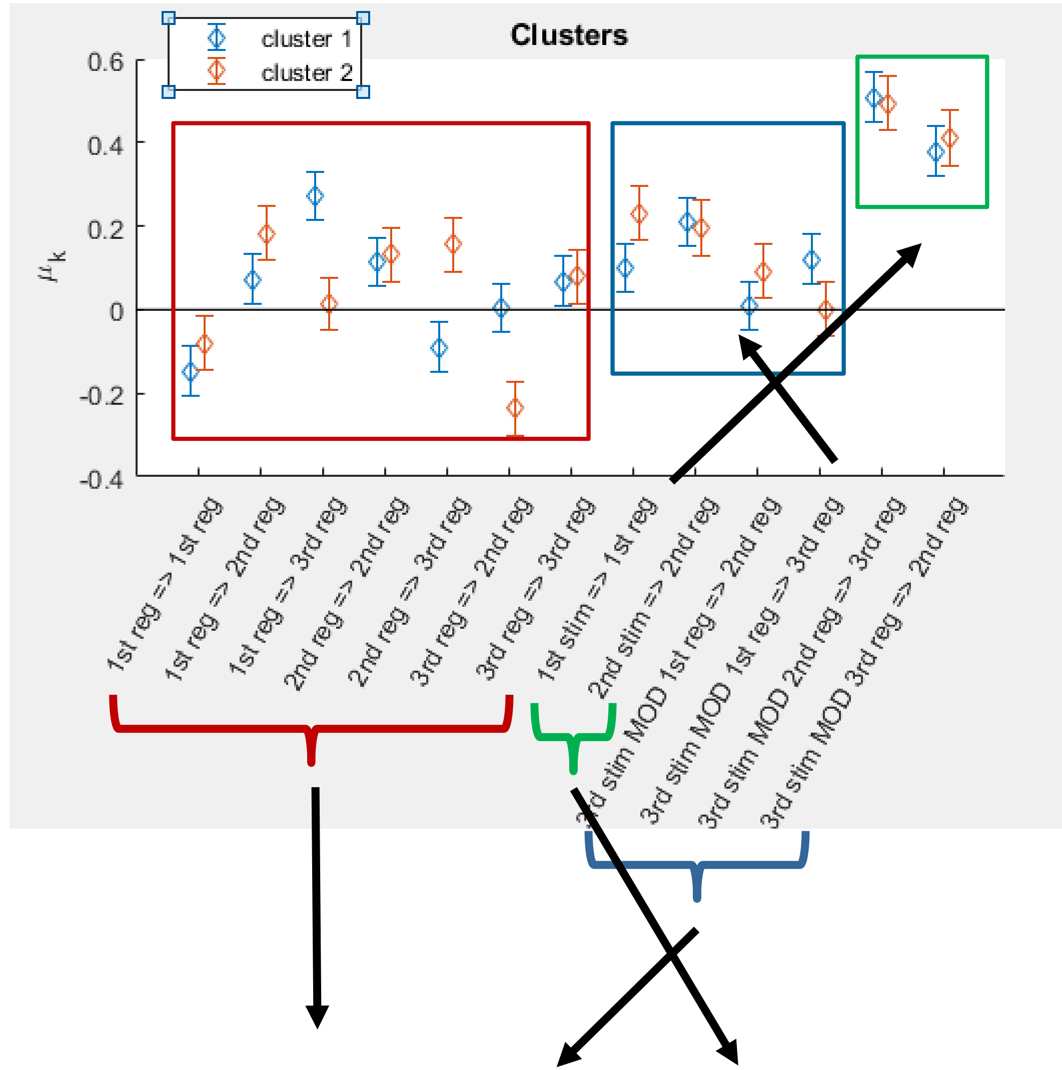
van Leeuwen, T.M., den Ouden, H.E.M., Hagoort, P., 2011. Effective Connectivity Determines the Nature of Subjective Experience in Grapheme-Color Synesthesia. The Journal of Neuroscience 31, 9879-9884.

Raman, S., Deserno, L., Schlagenhauf, F., Stephan, K.E., 2016. A hierarchical model for integrating unsupervised generative embedding and empirical Bayes. J. Neurosci. Meth. 269, 6–20.

Yao Y, Raman SS, Schiek M, Leff A, Frässle S, Stephan KE. Variational Bayesian Inversion for Hierarchical Unsupervised Generative Embedding (HUGE);179:604–619.

Correction

Tick labels for input strength and modulations are switched in current version



Correct order: **A matrix elements** **B matrix elements** **C matrix elements**