Advanced Models of Connectivity – part 1
Hierarchical Unsupervised Generative Embedding (HUGE)

Yu Yao

Translational Neuromodeling Unit

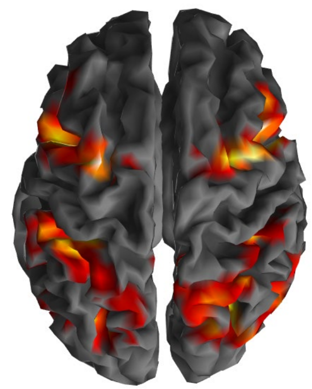
Universität Zürich[UZH]

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Computational Psychiatry Course 2019

Zurich | 4th September 2019

DCM for fMRI

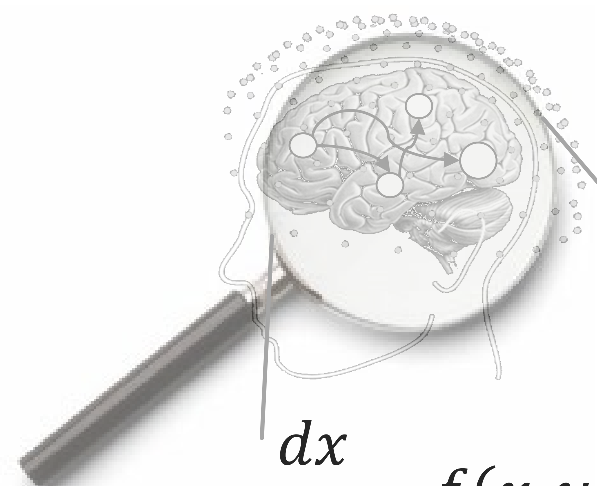


fMRI

Model inversion:
Estimating neuronal mechanisms

Forward model:
Predicting measured activity

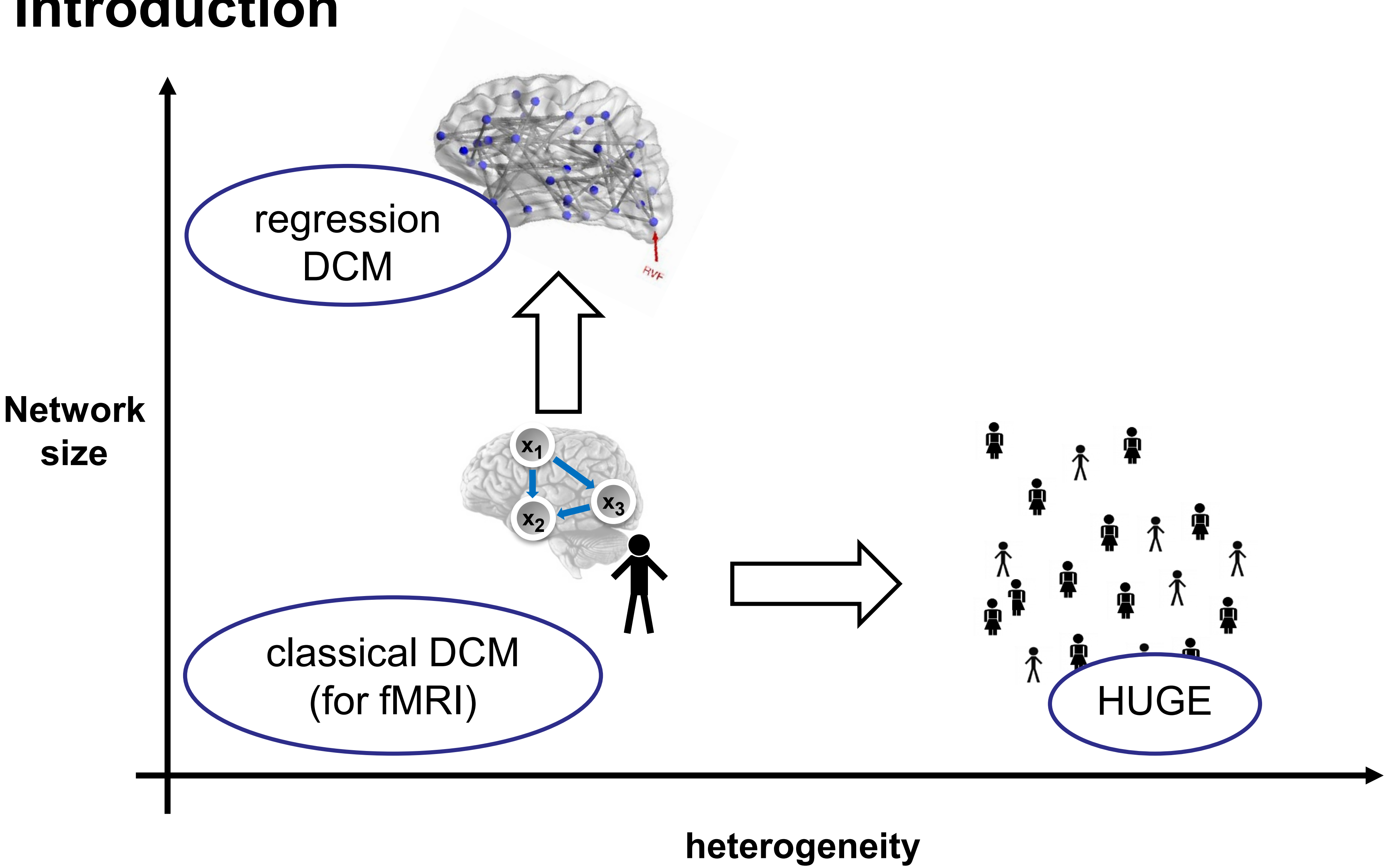
$$y = g(x, \theta) + \varepsilon$$



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

Neural state equation:
Describing neuronal dynamics

Introduction



Introduction

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

1. Empirical Bayes:

Use data to “inform prior distribution”.

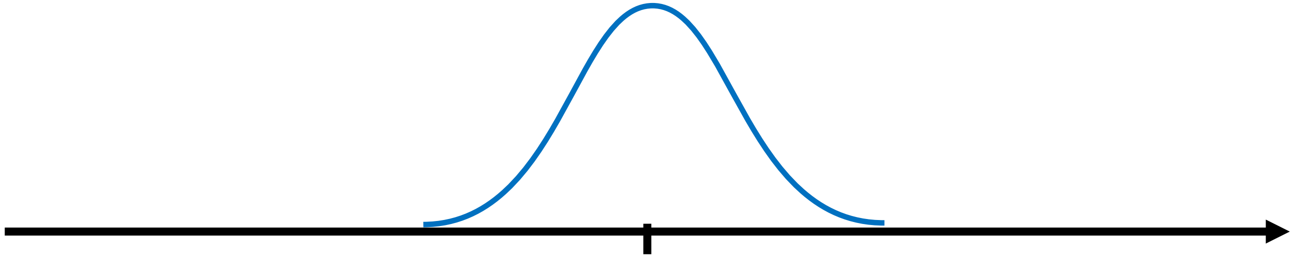
2. Stratification of heterogeneous cohorts:

Find subgroups in heterogeneous cohorts.

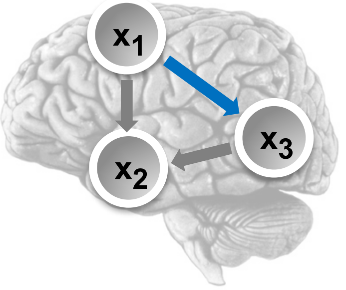
Empirical Bayes

Classical DCM

Prior distribution:
Range of a priori plausible variations in the population



Strength of connection $x_1 \rightarrow x_3$



Empirical Bayes

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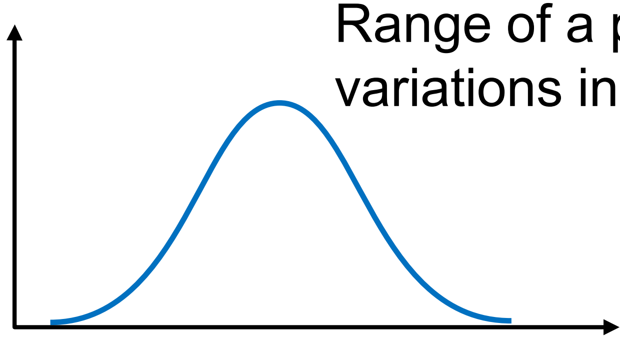

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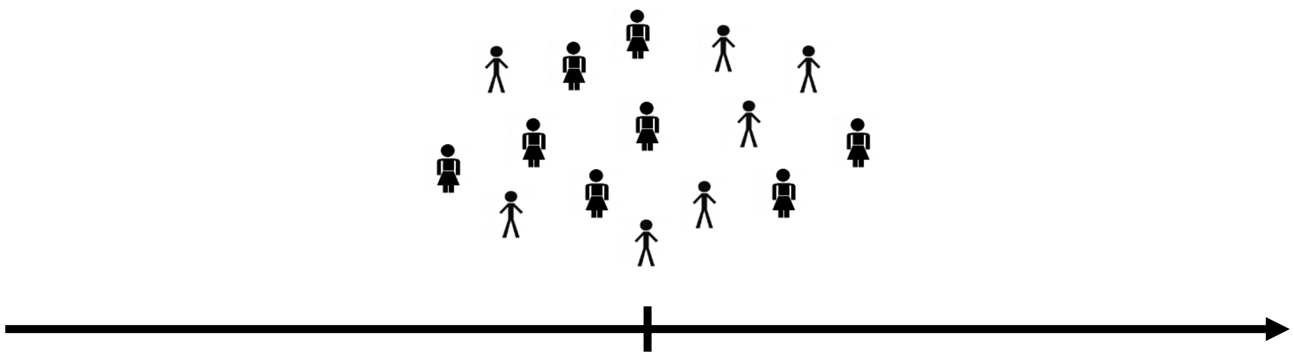

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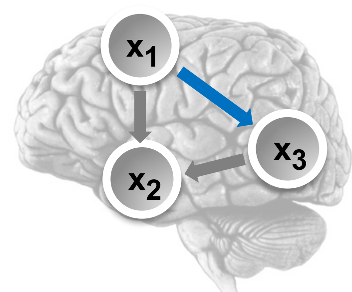

Empirical Bayes

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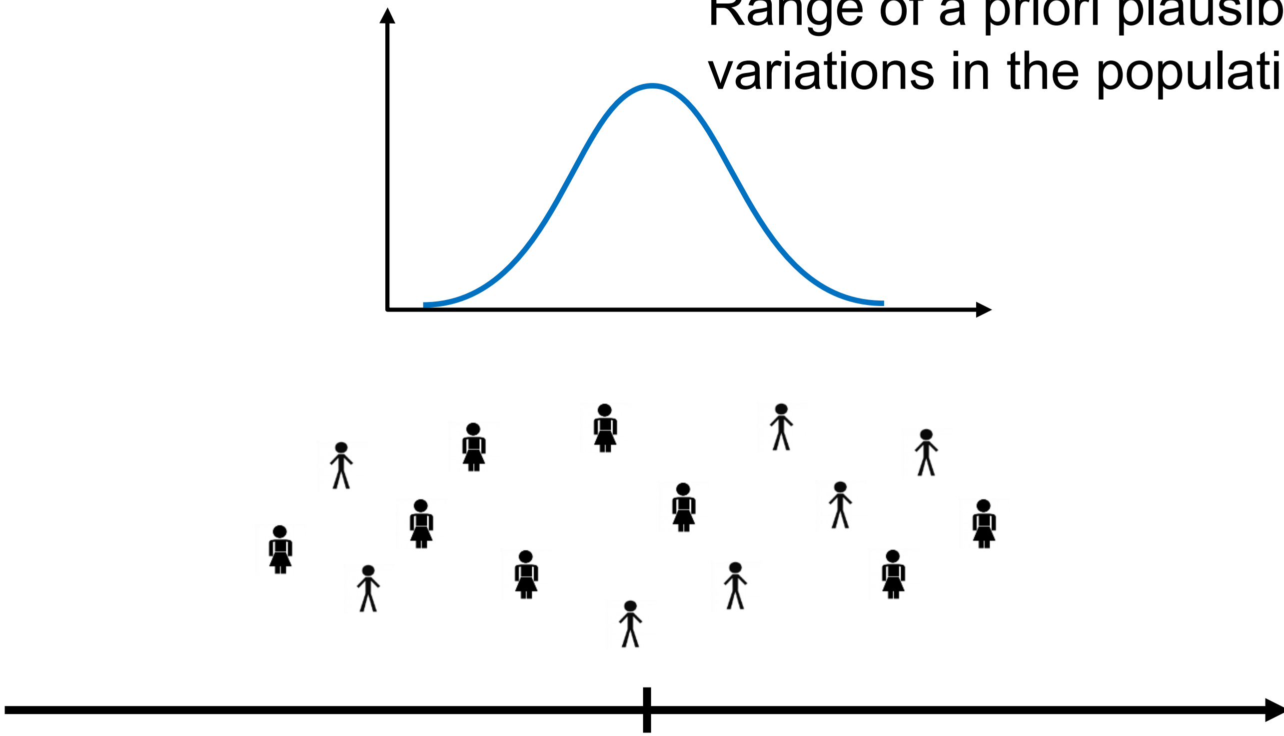
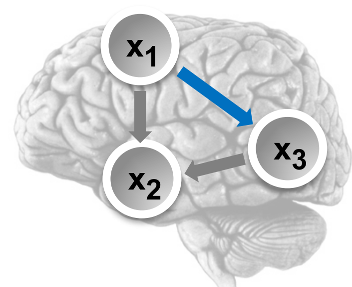
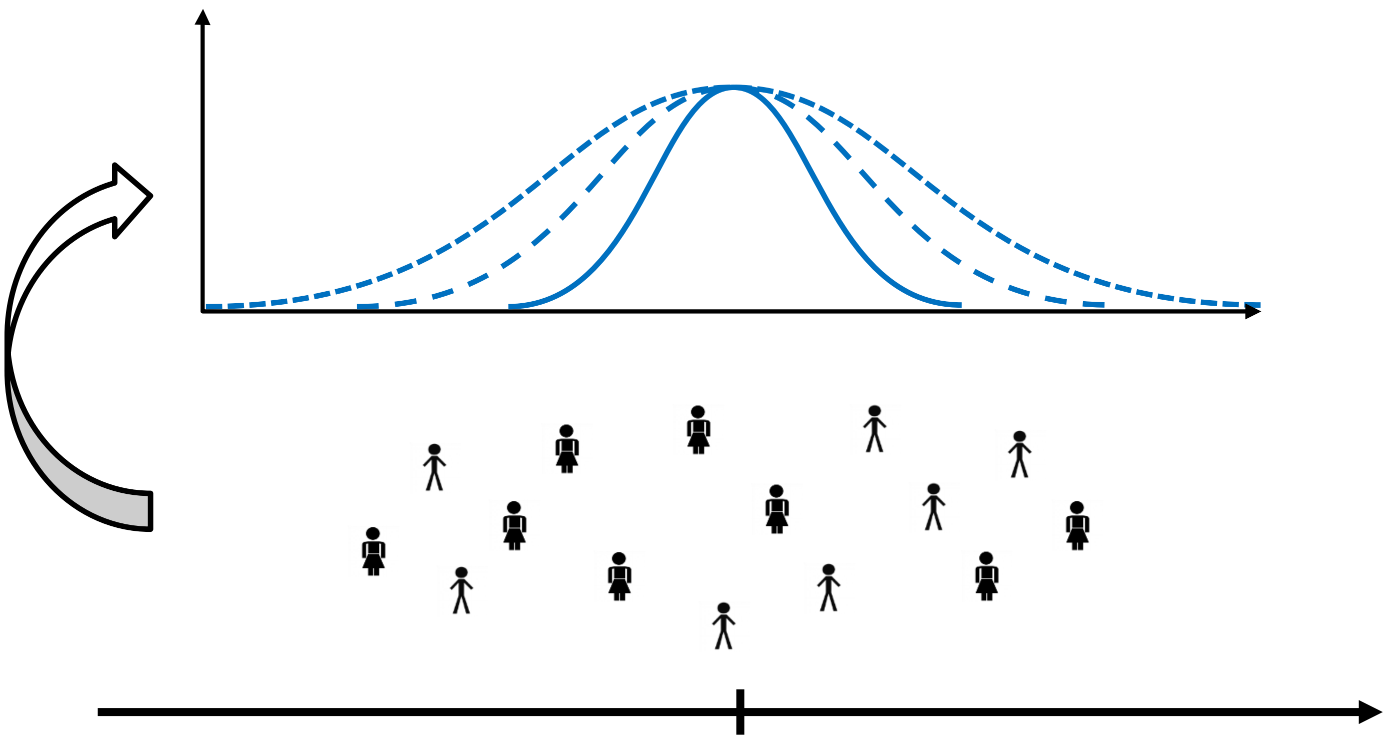


Strength of connection $\mathbf{x_1 \rightarrow x_3}$



Empirical Bayes

Joint estimation of individual and population-level DCM parameters



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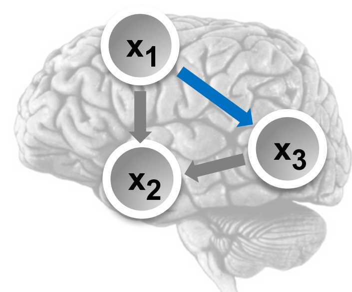
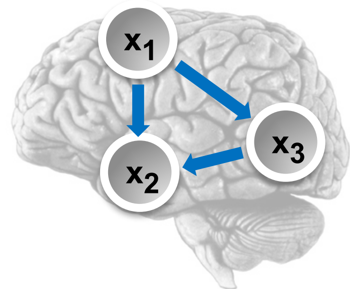
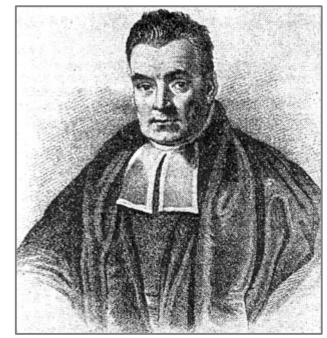


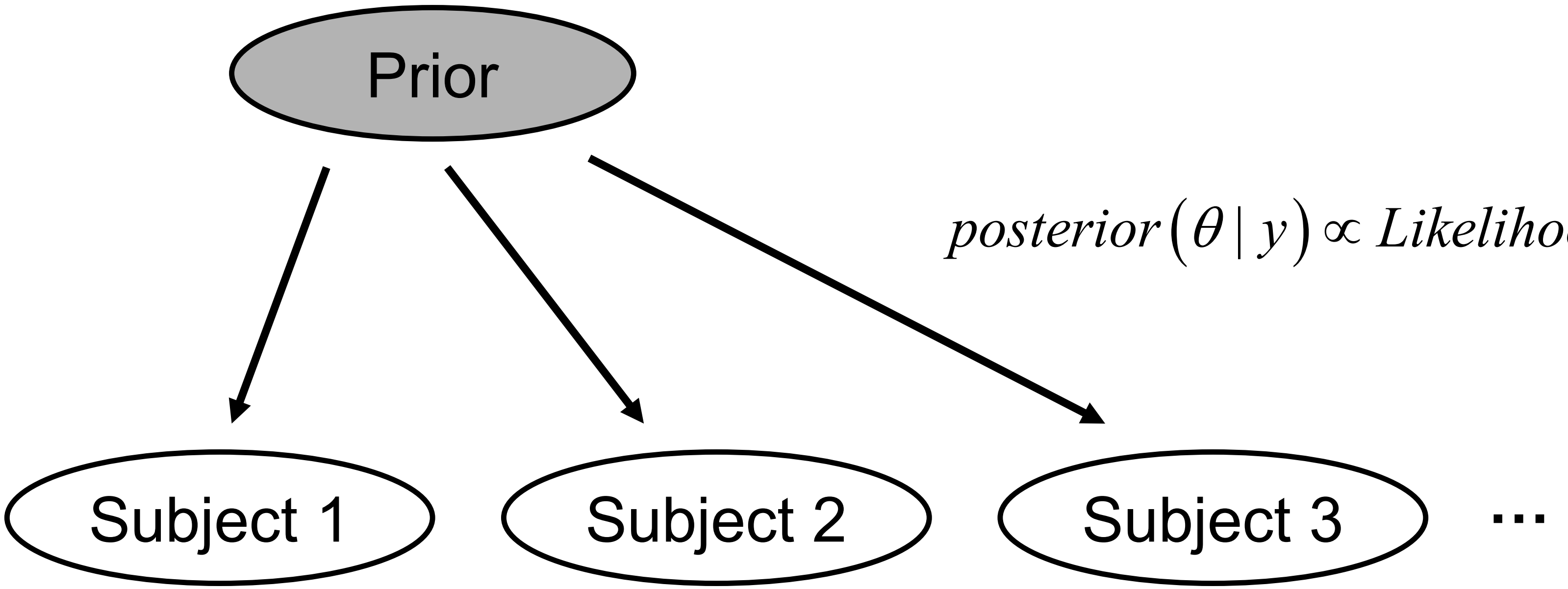
Introducing a Hierarchy

Classical DCM

θ = Subject-specific DCM connection strength (A, B, C, D)







$$posterior(\theta \mid y) \propto Likelihood(y \mid \theta)\, prior(\theta)$$

Introducing a Hierarchy

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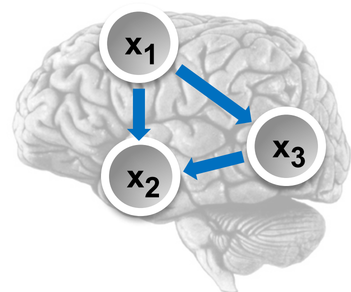
Empirical Bayes

μ = population-level average connection strength



Prior

Population

Subject 1

Subject 2

Subject 3

...

Joint estimation of individual and population-level DCM parameters

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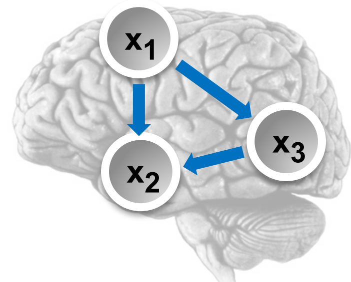

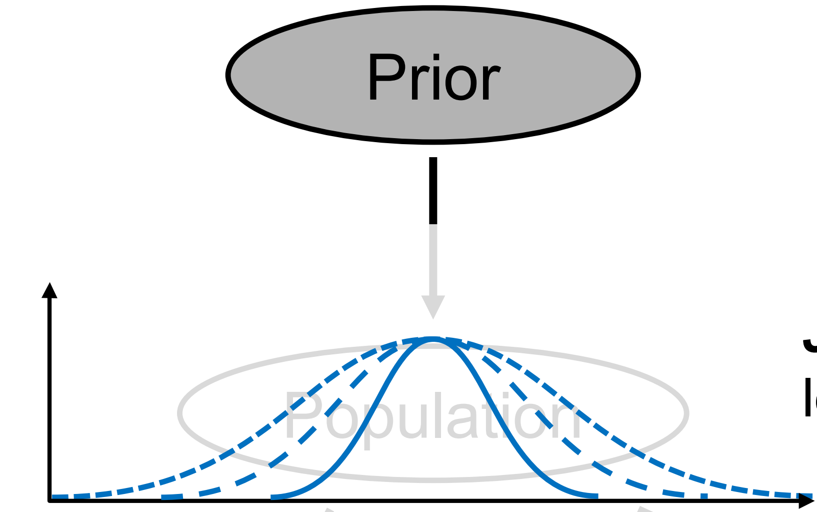

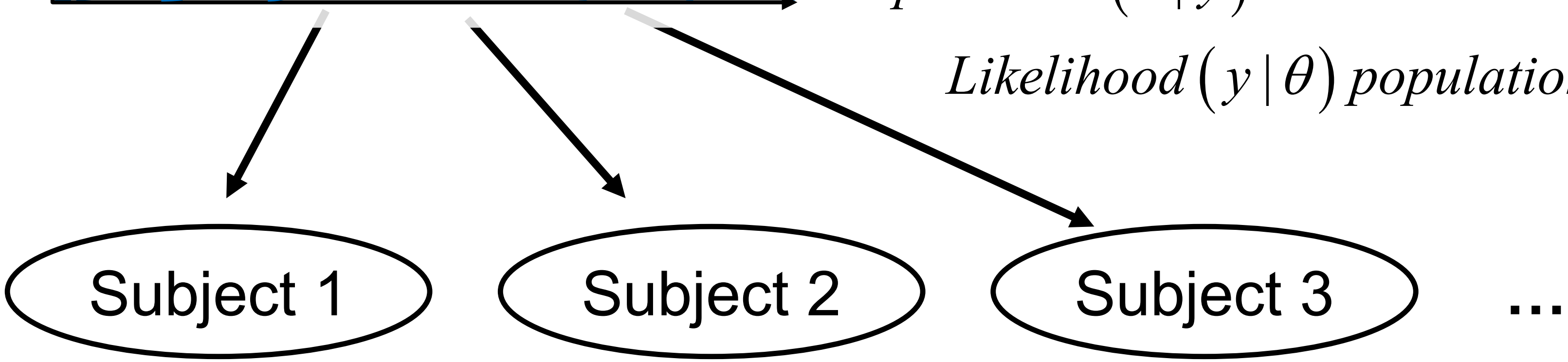

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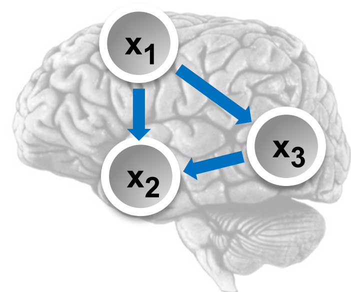

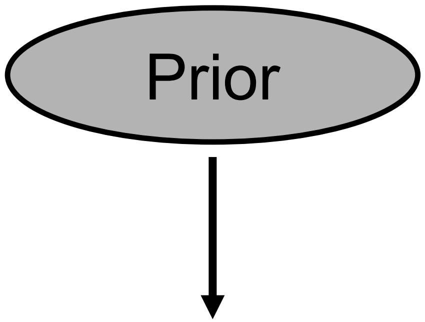

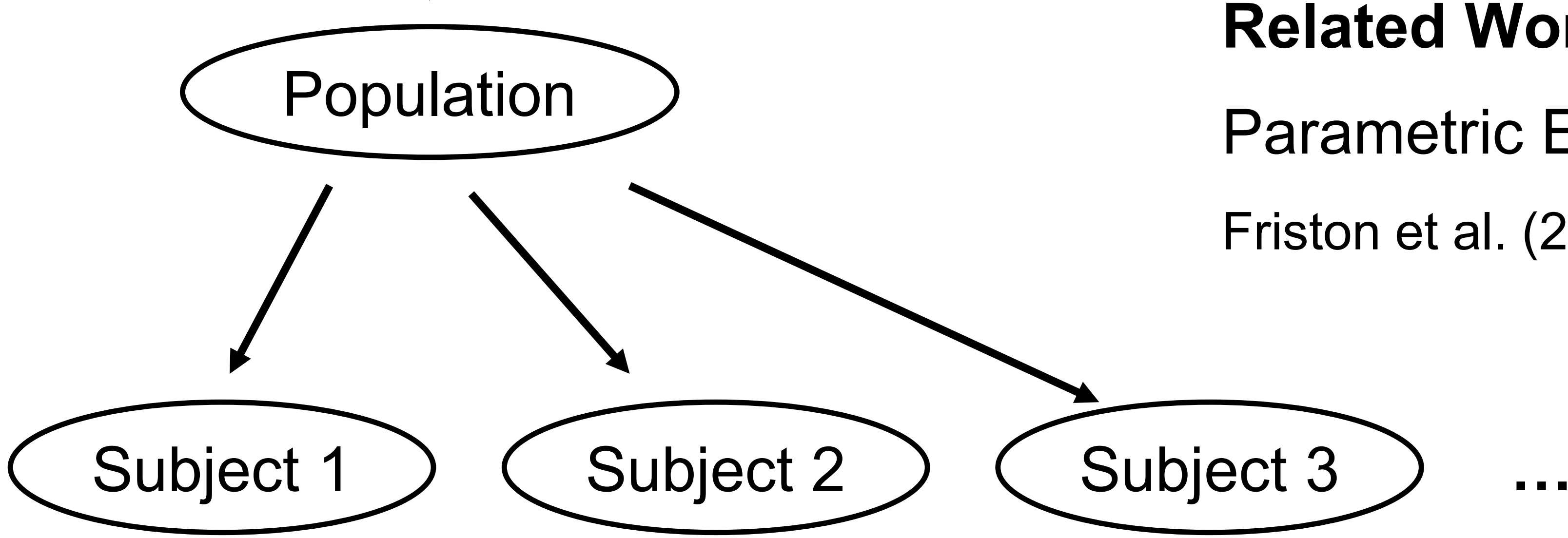

Related Work

Parametric Empirical Bayes

Friston et al. (2016) *NeuroImage*

Beyond Empirical Bayes

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

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Beyond Empirical Bayes

For Example:

- Studies involving patients and healthy controls.
- Studies involving patients with spectrum disorders (schizophrenia, bipolar disorder, etc.).
- Studies involving patients with varying severity of a condition (casual gamblers vs. gambling addicts, acute vs. chronic patients).

Beyond Empirical Bayes

The easy solution:

If assignment known a priori, (e.g. controls vs patients):

- divide cohort
- do empirical Bayesian analysis separately

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What if the assignment is unclear?

(e.g., schizophrenic patients)

From Empirical Bayes to Stratification

We need a **model** that supports:

Joint estimation of individual and
group-level DCM parameters.

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empirical Bayes

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Do the above for multiple (sub)groups
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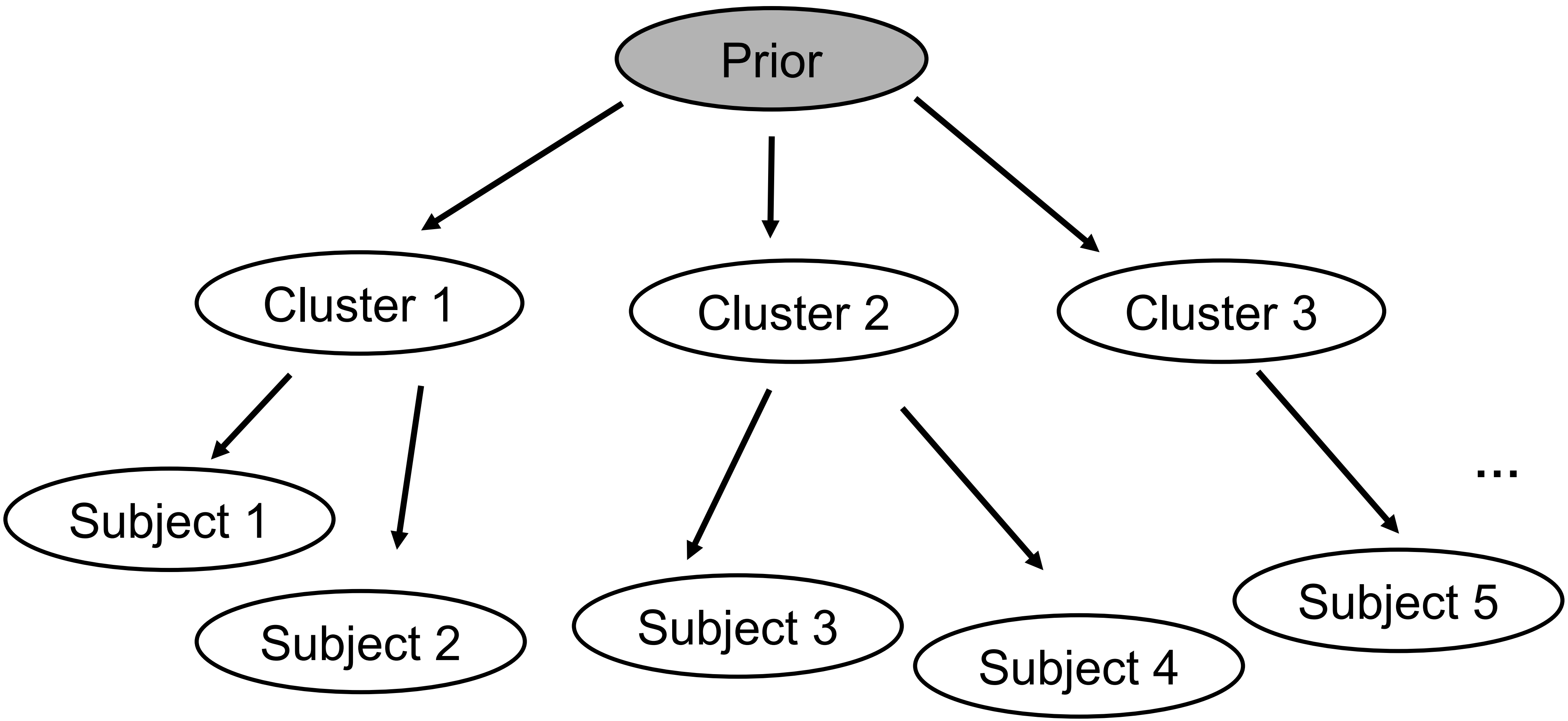
Find out which subject belongs to which group.

A Unified Model for Empirical Bayes and Stratification

A generative, hierarchical model for unsupervised learning

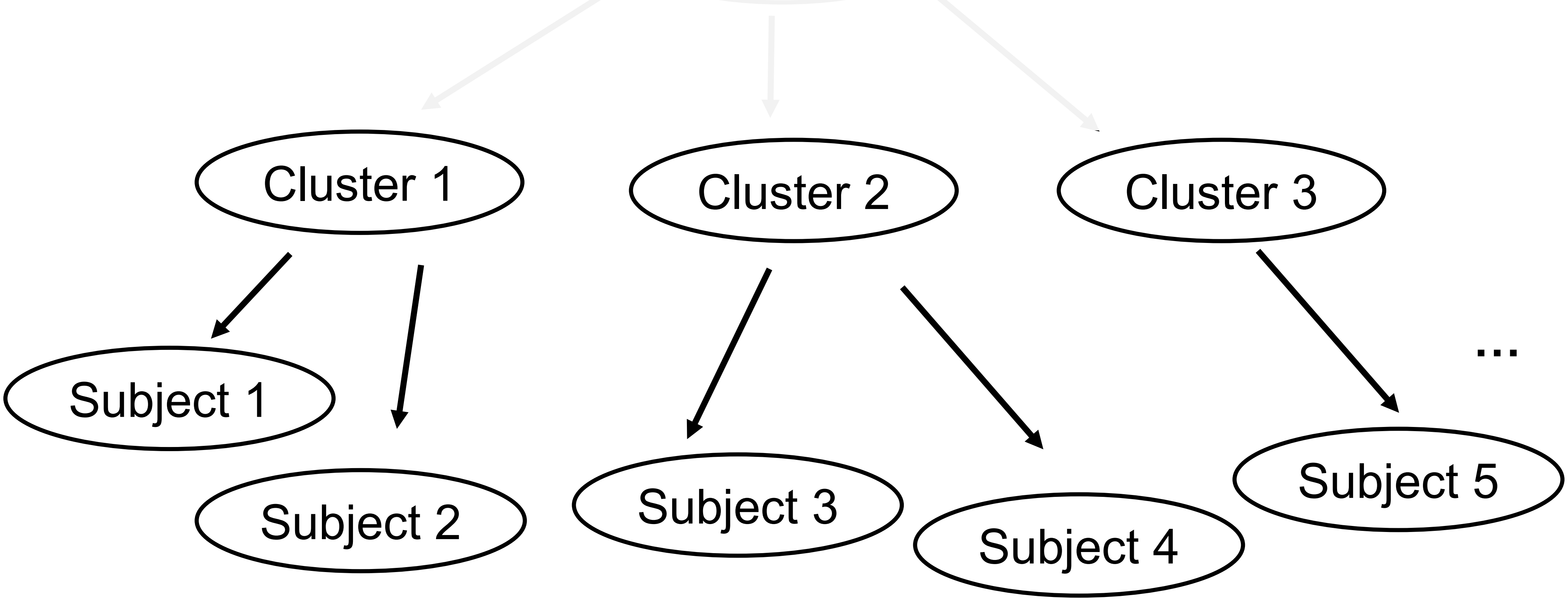


A Unified Model for Empirical Bayes and Stratification

A generative, hierarchical model for unsupervised learning

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

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



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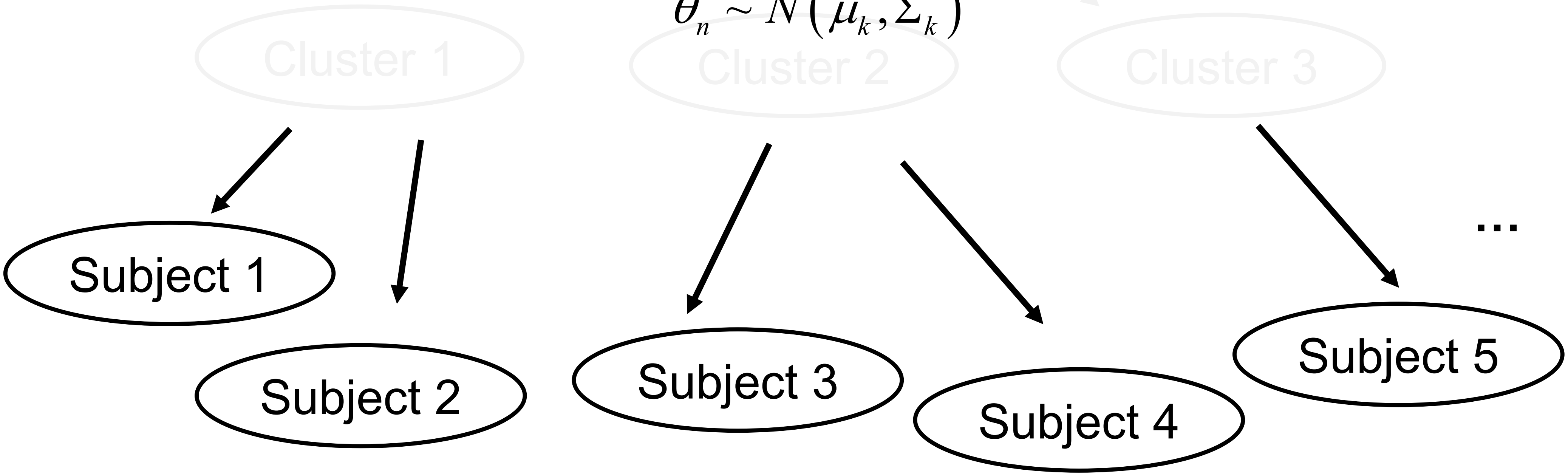
$$\theta_n \sim N\left(\mu_k, \Sigma_k\right)$$



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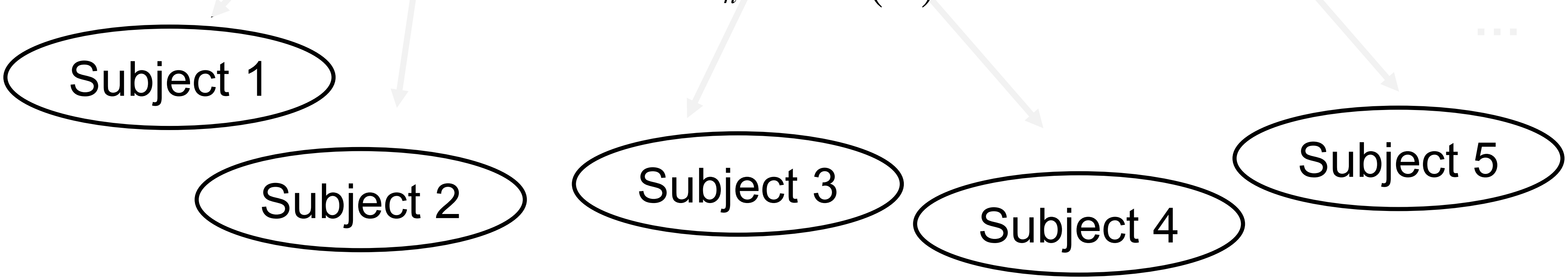
Assignment: Model which subject belongs to which cluster.

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



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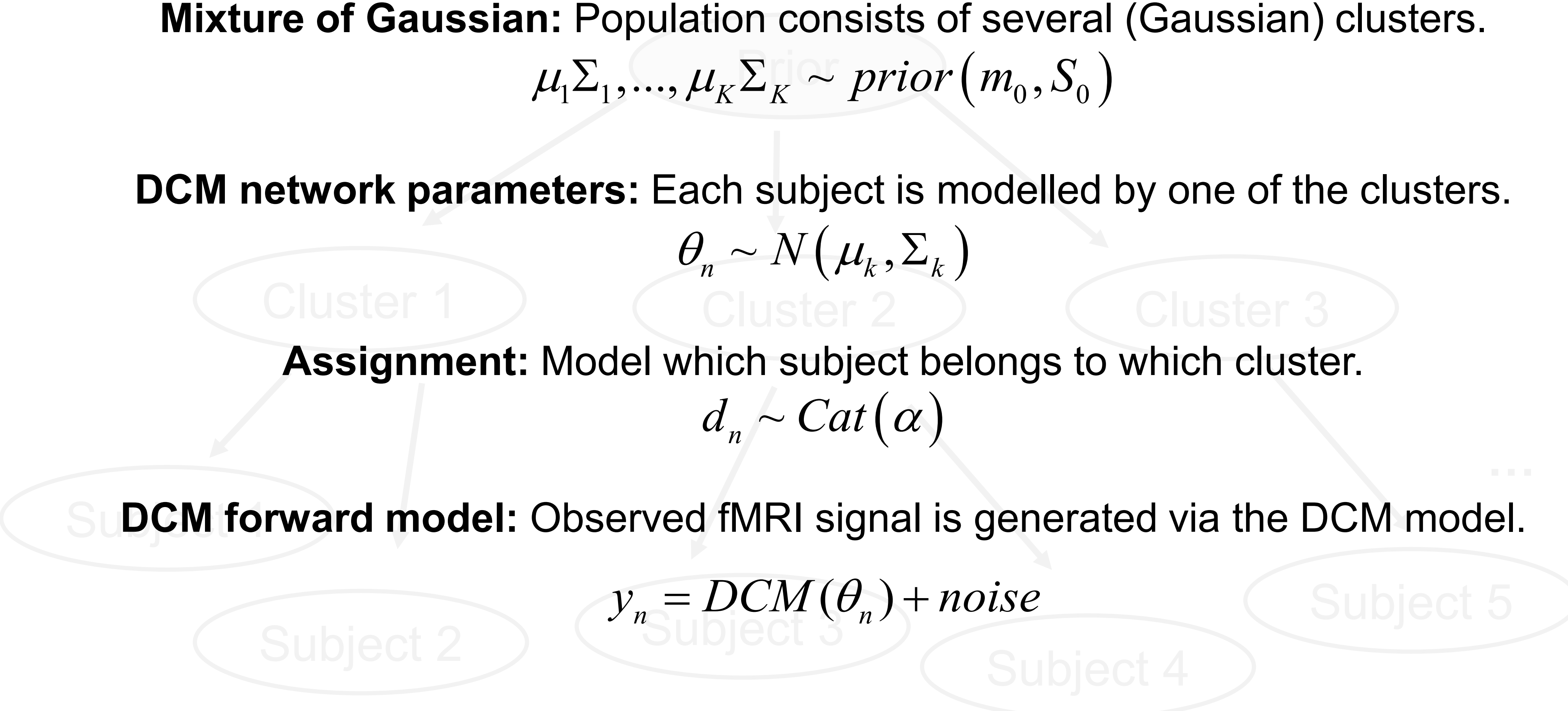
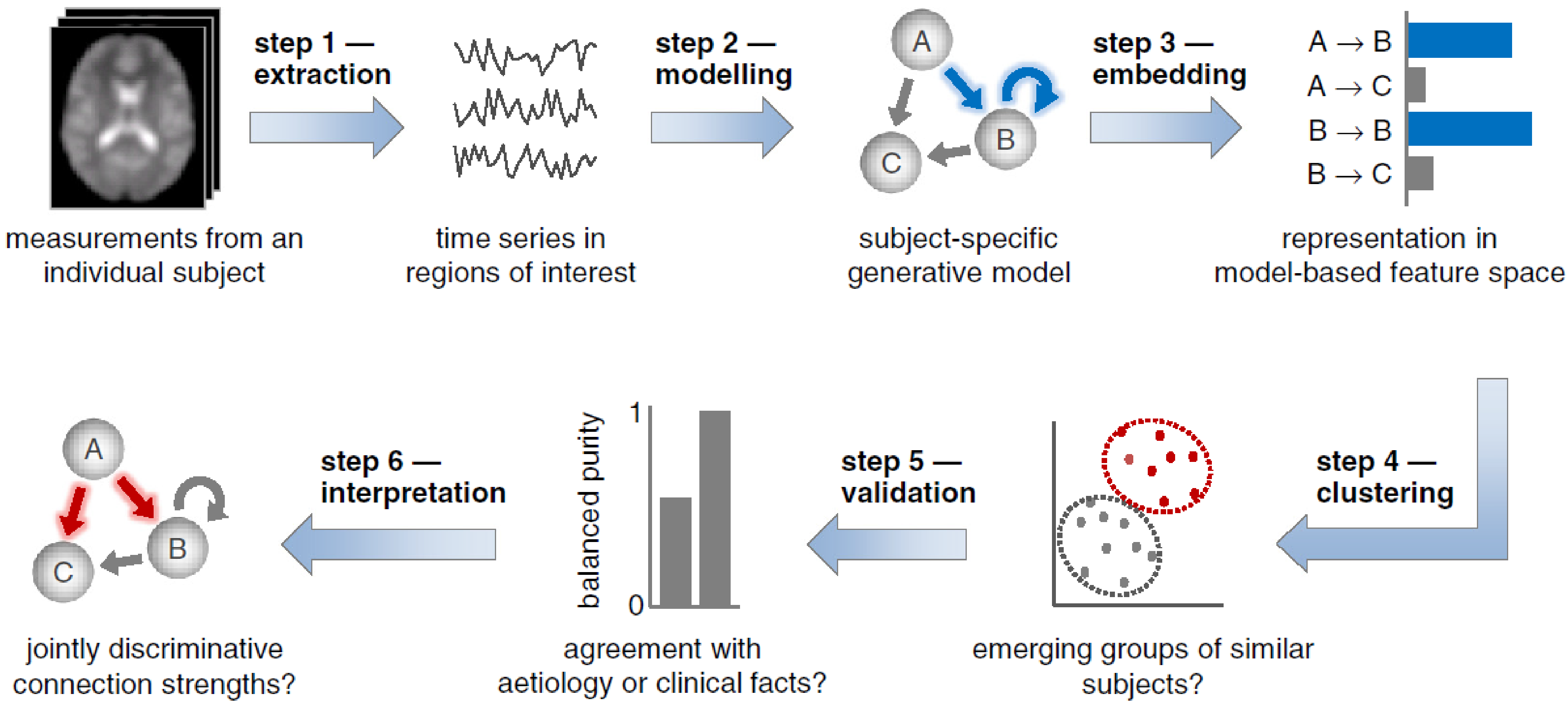
DCM forward model: Observed fMRI signal is generated via the DCM model.

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



Related Work

Generative Embedding Brodersen et al. (2014) *NeuroImage: Clinical*



Related Work

Hierarchical Unsupervised Generative Embedding (HUGE)

Yao et al. (2018) *NeuroImage*

Joint estimation of individual and group-level DCM parameters.

Parametric Empirical Bayes

Friston et al. (2016) *NeuroImage*

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

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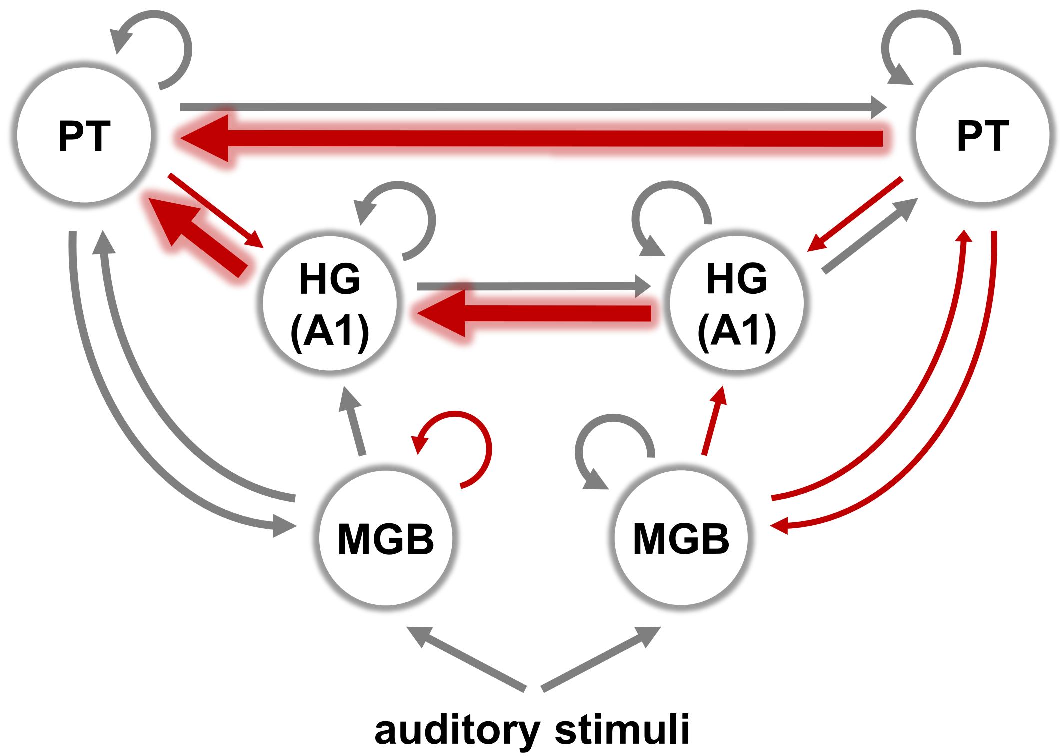
Generative Embedding

Brodersen et al. (2014) *NeuroImage: Clinical*

Example: Aphasia Study

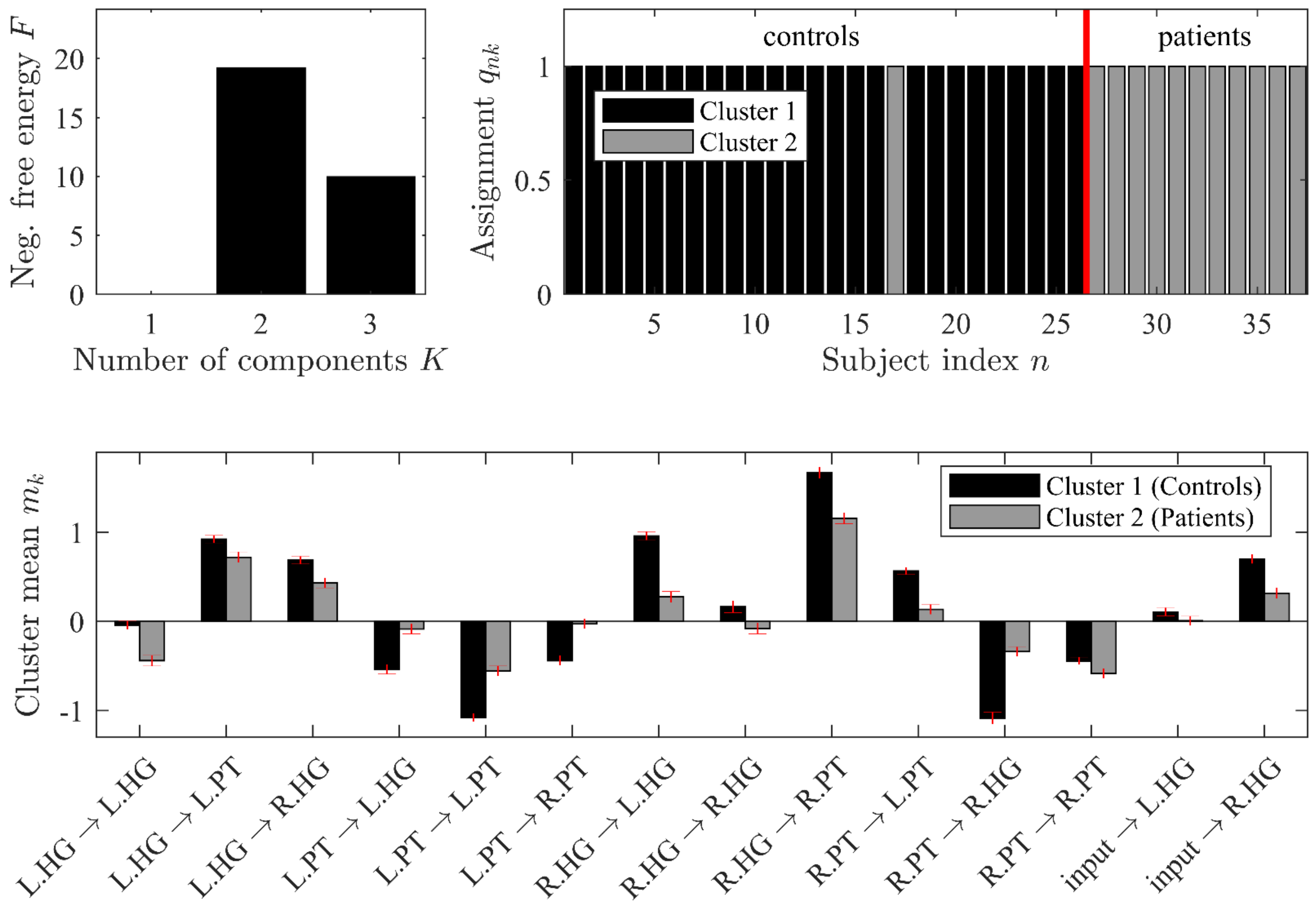
- Aphasic patients (N=11) vs. controls (N=26)
- passive speech listening
- 6-region DCM of auditory areas
- SVM Classification on DCM parameters (supervised learning): Patients vs Control achieved balanced accuracy of 98%



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

Example: Aphasia Study

HUGE (unsupervised) achieved a balanced purity of 96%



Yao et al. (2018)
NeuroImage

Software

Code available as part of TAPAS

www.translationalneuromodeling.org/tapas

CPC Practical Session (Friday)
Tutorial G: Advanced Models of Connectivity

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.

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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.

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.

Thank you

Thanks to Jakob Heinzle for the introduction slide.