Models of Connectivity: Advanced
Hierarchical Unsupervised Generative Embedding (HUGE)

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Translational Neuromodeling Unit

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Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Computational Psychiatry Course 2020

Zurich | 10th September 2020

Introduction

Hierarchical

Unsupervised

Generative

Embedding

Introduction

Hierarchical

Unsupervised

Generative

Embedding

Generative Embedding

- model-based dimensionality reduction
- mechanically interpretable features
- stratification of heterogeneous cohorts

Generative Embedding

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Generative Embedding for Model-Based Classification of fMRI Data

Kay H. Brodersen[1,2]*, Thomas M. Schofield[3], Alexander P. Leff[3], Cheng Soon Ong[1], Ekaterina I. Lomakina[1,2], Joachim M. Buhmann[1], Klaas E. Stephan[2,3]

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Abstract

Decoding models, such as those underlying multivariate classification algorithms, have been increasingly used to infer cognitive or clinical brain states from measures of brain activity obtained by functional magnetic resonance imaging (fMRI). The practicality of current classifiers, however, is restricted by two major challenges. First, due to the high data dimensionality and low sample size, algorithms struggle to separate informative from uninformative features, resulting in poor generalization performance. Second, popular discriminative methods such as support vector machines (SVMs) rarely afford mechanistic interpretability. In this paper, we address these issues by proposing a novel generative-embedding approach that incorporates neurobiologically interpretable generative models into discriminative classifiers. Our approach extends previous work on trial-by-trial classification for electrophysiological recordings to subject-by-subject classification for fMRI and offers two key advantages over conventional methods: it may provide more accurate predictions by exploiting discriminative information encoded in 'hidden' physiological quantities such as synaptic connection strengths; and it affords mechanistic interpretability of clinical classifications. Here, we introduce generative embedding for fMRI using a

Generative Embedding

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- Model: DCM; effective connectivity

Generative Embedding

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Generative Embedding

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- Model: DCM; effective connectivity
- classification: supervised learning
- data: fMRI

Generative Embedding

Dataset:

- patients (N=11) vs. controls (N=26)
  - moderate aphasia due to stroke
- passive speech listening
  - (i) normal speech
  - (ii) time-reversed speech
- 1.5 T, TR 3.15 s

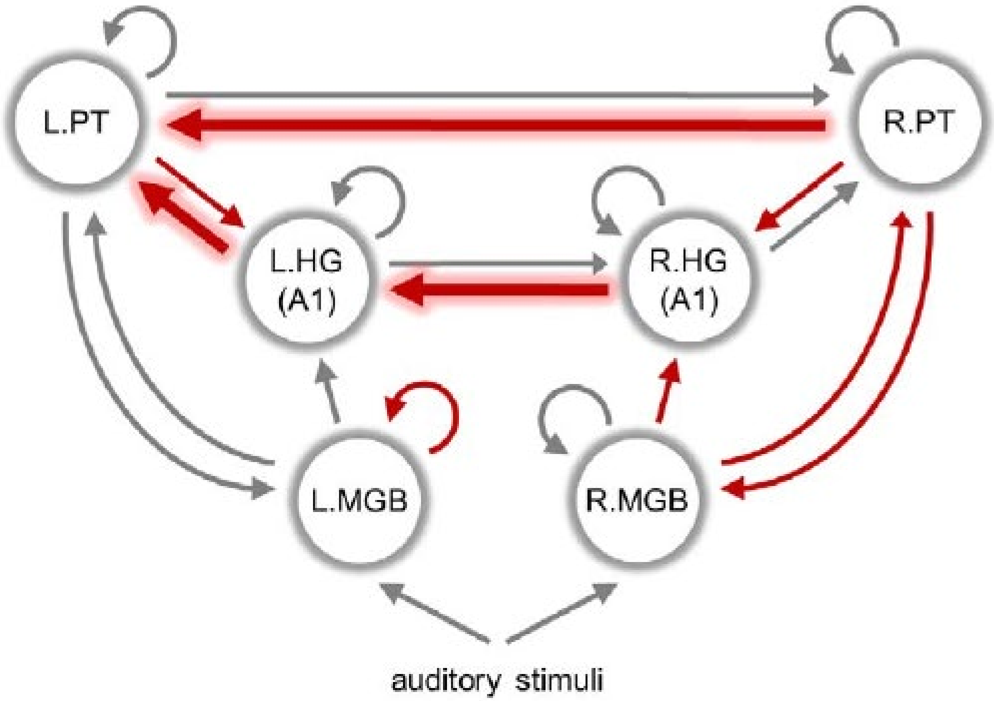
Leff AP, Schofield TM, Stephan KE, Crinion JT, Friston KJ, et al. (2008) The cortical dynamics of intelligible speech. J Neurosci 28: 13209–13215.

Generative Embedding

DCM → model inversion → point estimates → classification → result

model specification

- specify a DCM network structure
- language network
- non-lesioned part of brain



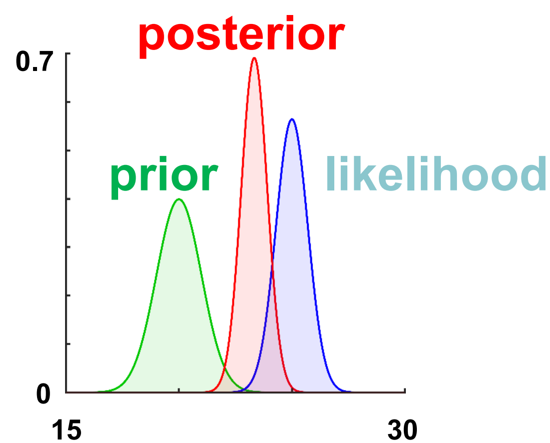
Generative Embedding

DCM → **model inversion** → point estimates → classification → result

model inversion

- VBL (Variational Bayes under Laplace approx.)
- posterior over connectivity

$$\underbrace{p(\theta|y,m)}_{\text{posterior}} = \frac{\overbrace{p(y|\theta,m)}^{\text{likelihood}}\,\overbrace{p(\theta|m)}^{\text{prior}}}{\underbrace{p(y|m)}_{\text{model evidence}}}$$

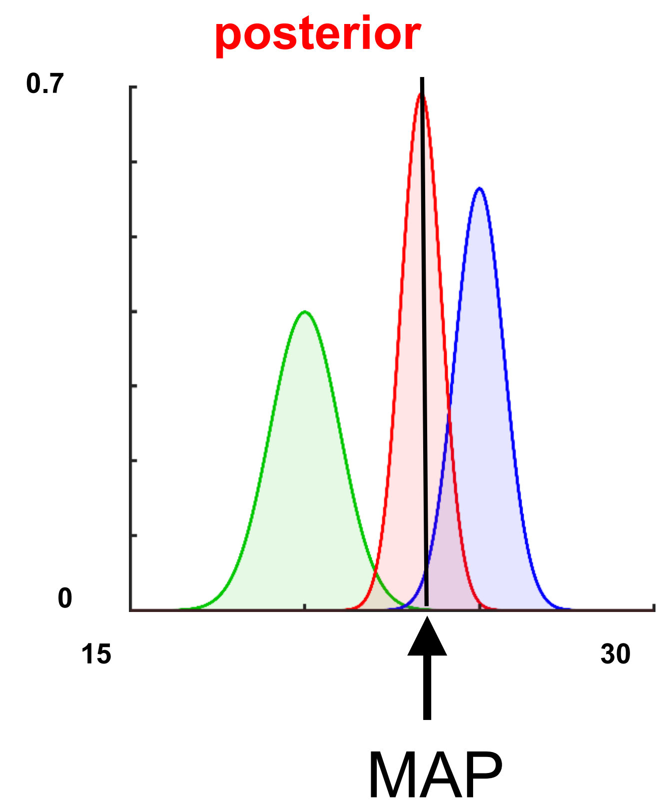


Generative Embedding

DCM → model inversion → point estimates → classification → result

extracting point estimates

- MAP (Maximum a posteriori)

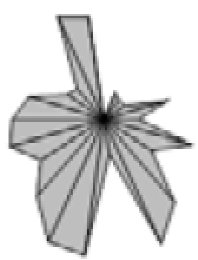


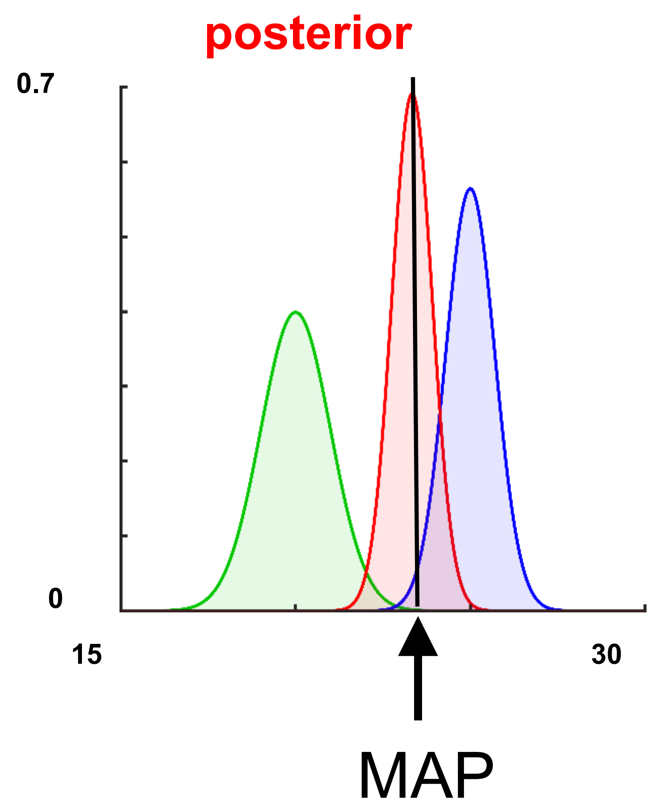
Generative Embedding

DCM → model inversion → point estimates → classification → result

extracting point estimates

- MAP (Maximum a posteriori)
- represent data from a subject as a **single point** in the space of model parameters



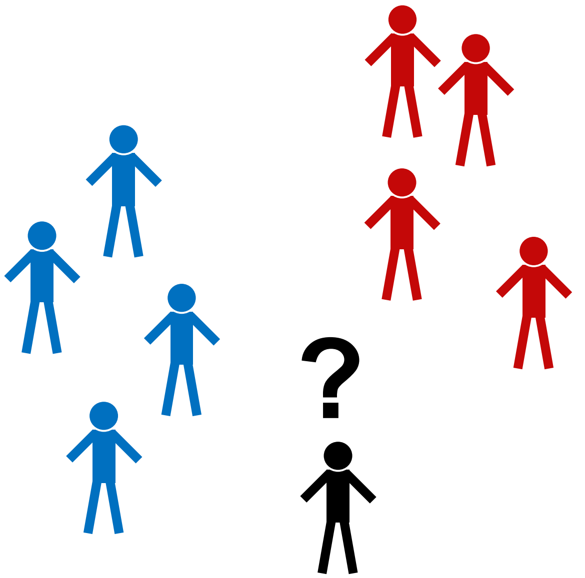


Generative Embedding

DCM → model inversion → point estimates → classification → result

classification

- supervised learning
- SVM (Support Vector Machine)



Generative Embedding

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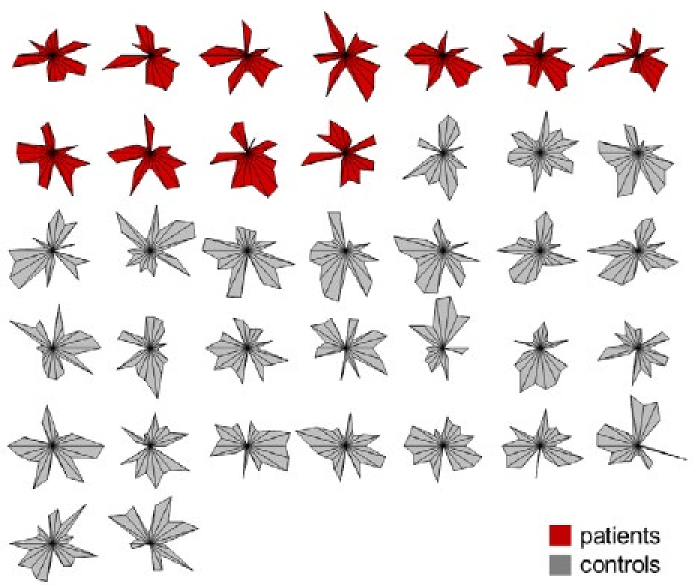
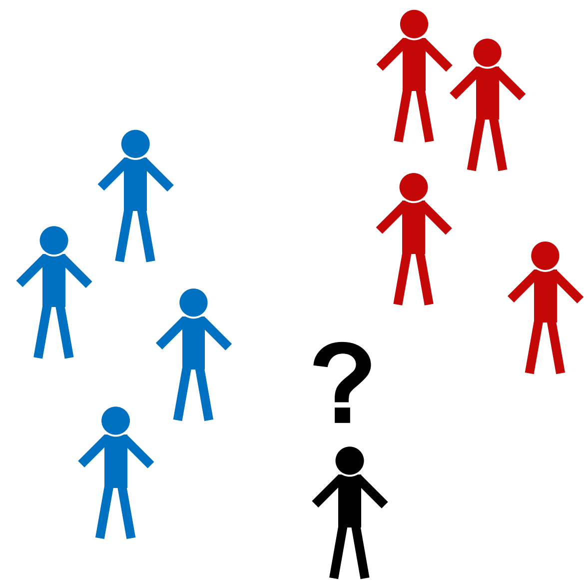
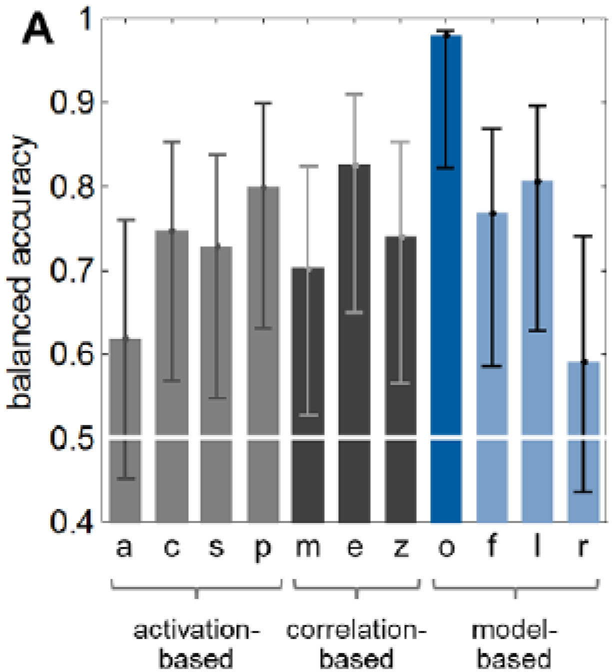
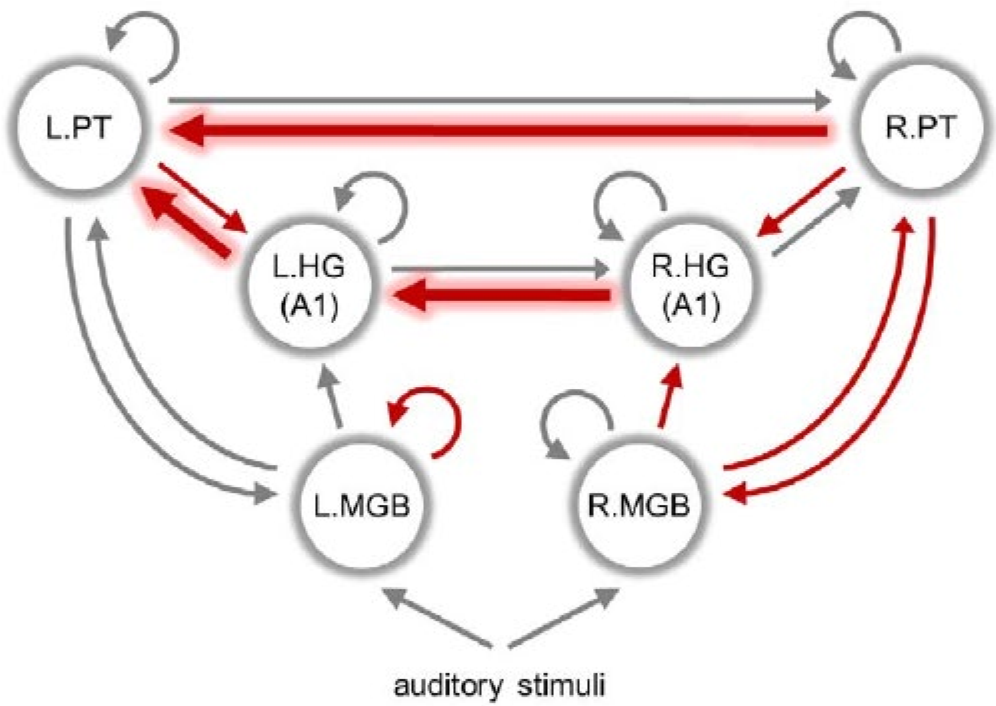




Generative Embedding

DCM → **model inversion** → **point estimates** → **classification** → **result**

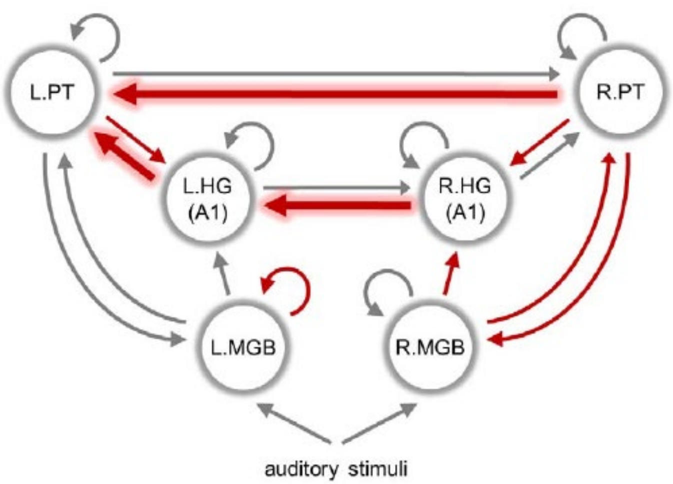


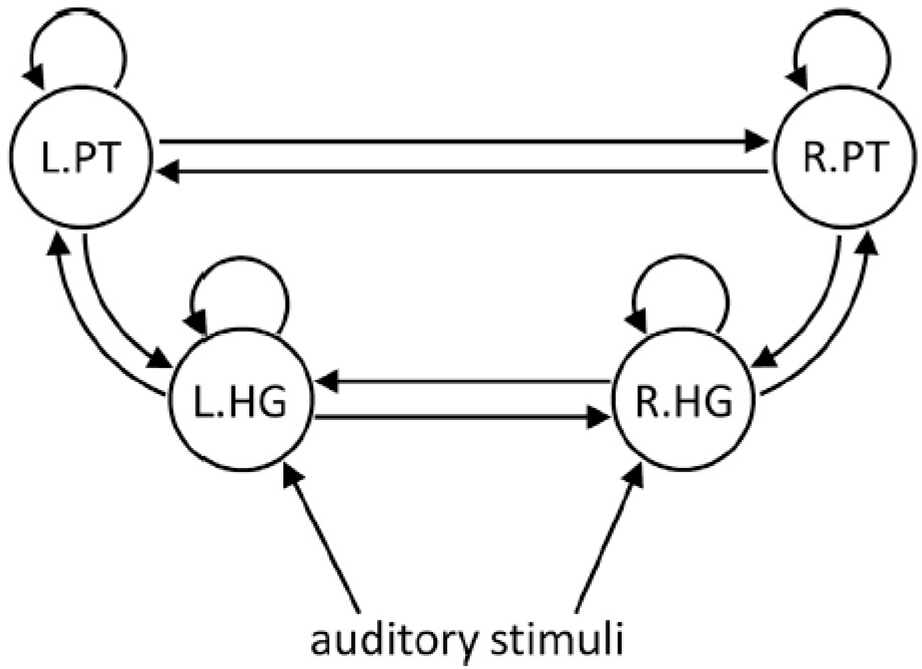


Hierarchical Unsupervised Generative Embedding

DCM → **model inversion** → **point estimates** → **classification** → **result**

model specification





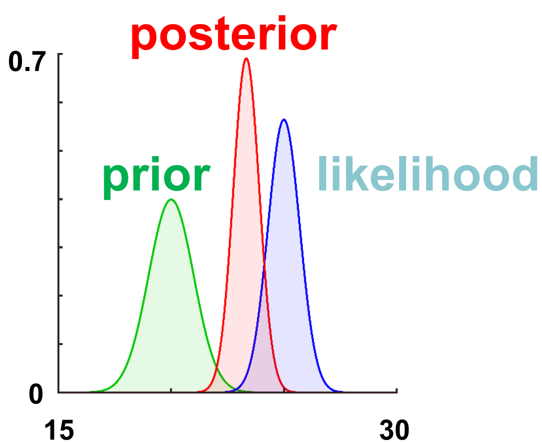
Hierarchical Unsupervised Generative Embedding

DCM → **model inversion** → point estimates → classification → result

model inversion

- Variational Bayes
- conjugate priors

Yao et al. (2018). Variational Bayesian Inversion for Hierarchical Unsupervised Generative Embedding (HUGE). NeuroImage



Hierarchical Unsupervised Generative Embedding

DCM → **model inversion** → ~~point estimates~~ → ~~classification~~ → **result**

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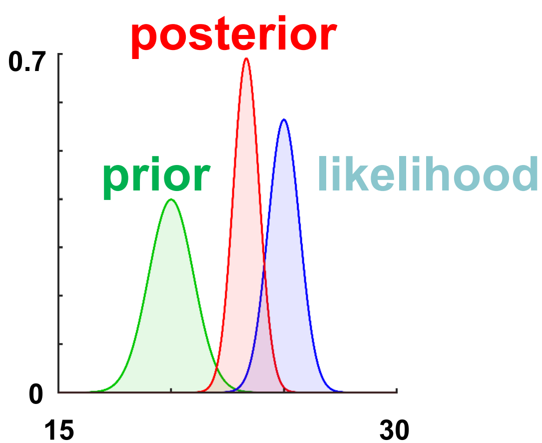
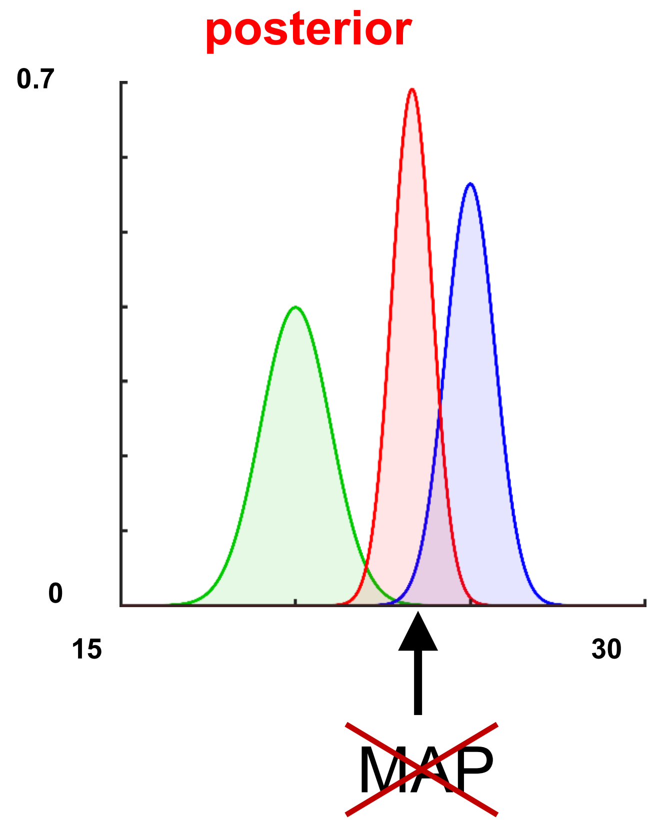


Hierarchical Unsupervised Generative Embedding

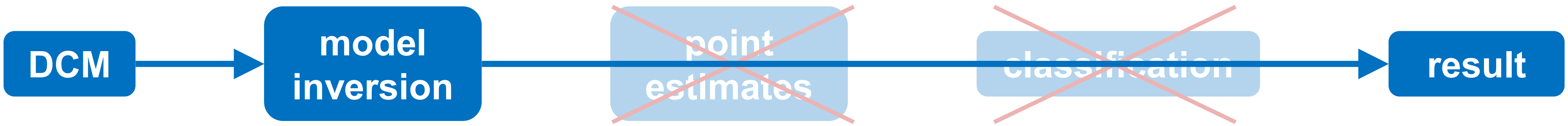
DCM → **model inversion** → ~~point estimates~~ → ~~classification~~ → **result**

extracting point estimates

- HUGE is a **hierarchical** model
- uses information from the entire posterior instead of a point estimate

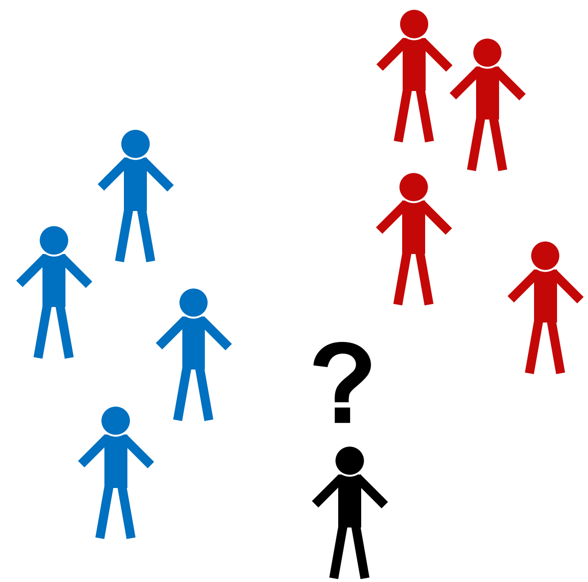


Hierarchical Unsupervised Generative Embedding

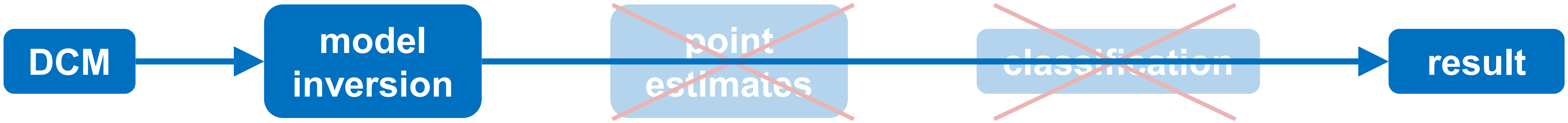


classification

- HUGE is **unsupervised**
- clustering instead of classification



Hierarchical Unsupervised Generative Embedding



classification

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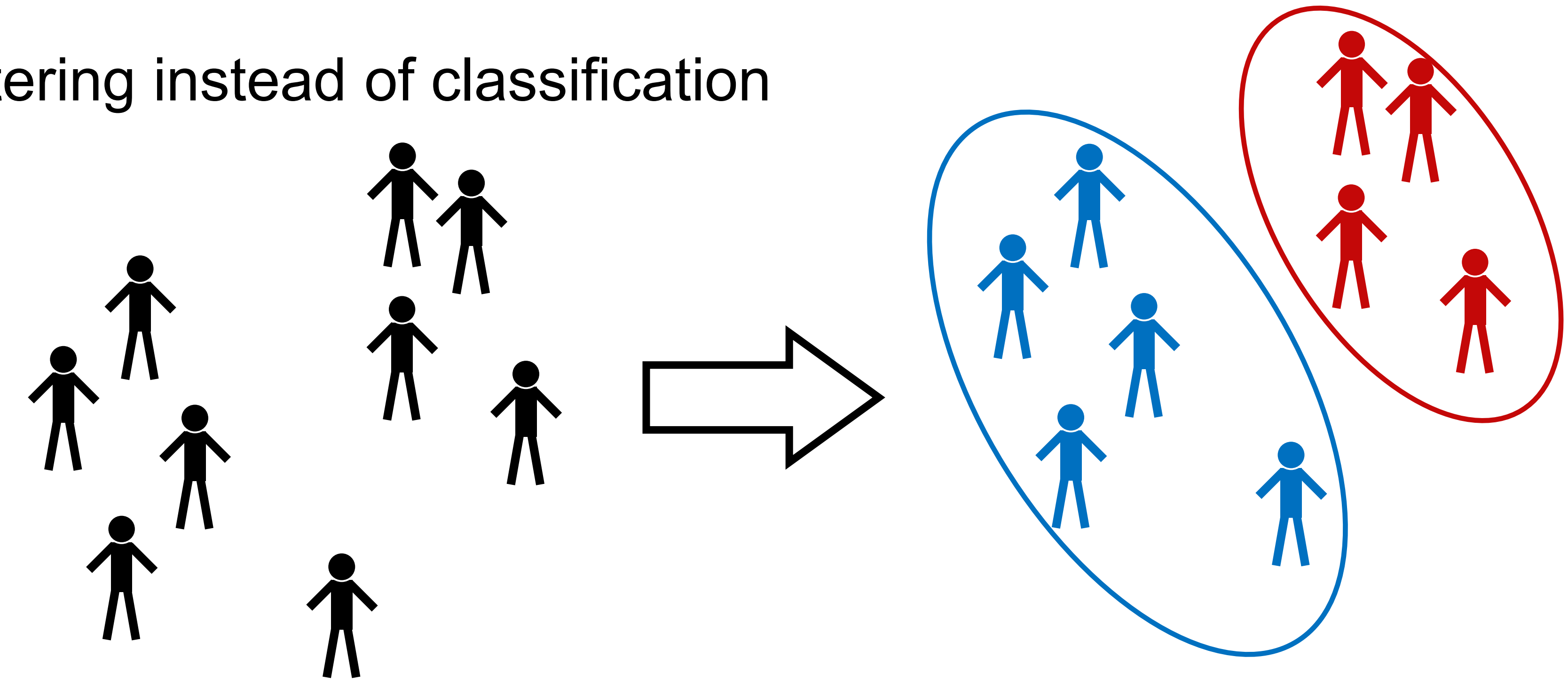
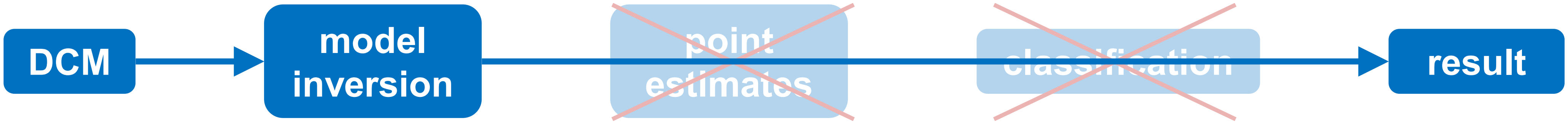


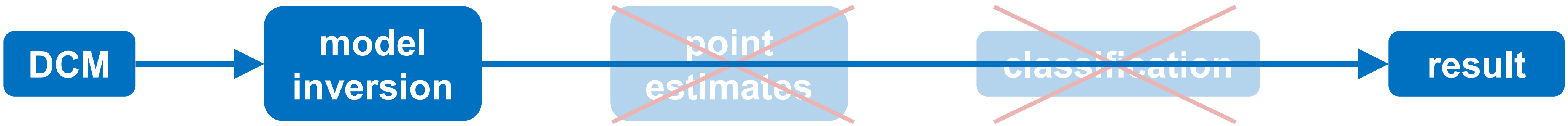
Hierarchical Unsupervised Generative Embedding



MATLAB interface

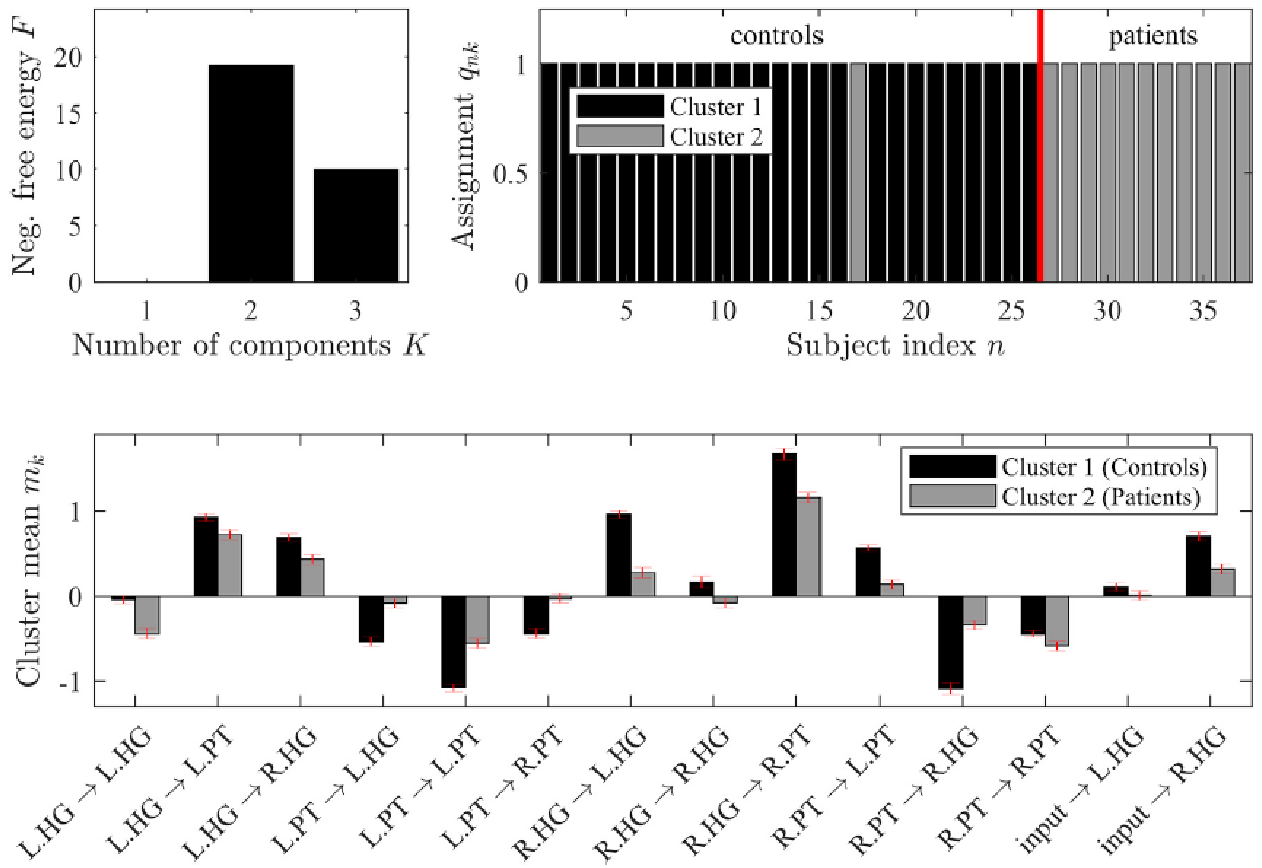
```
model = tapas_Huge('dcm',list_of_dcm); % build HUGE model
model.estimate('K',2); % fit model to data
```

Hierarchical Unsupervised Generative Embedding



result

- HUGE detects existence of two subgroups
- subgroups match onto patients and controls with a balanced purity of 96%

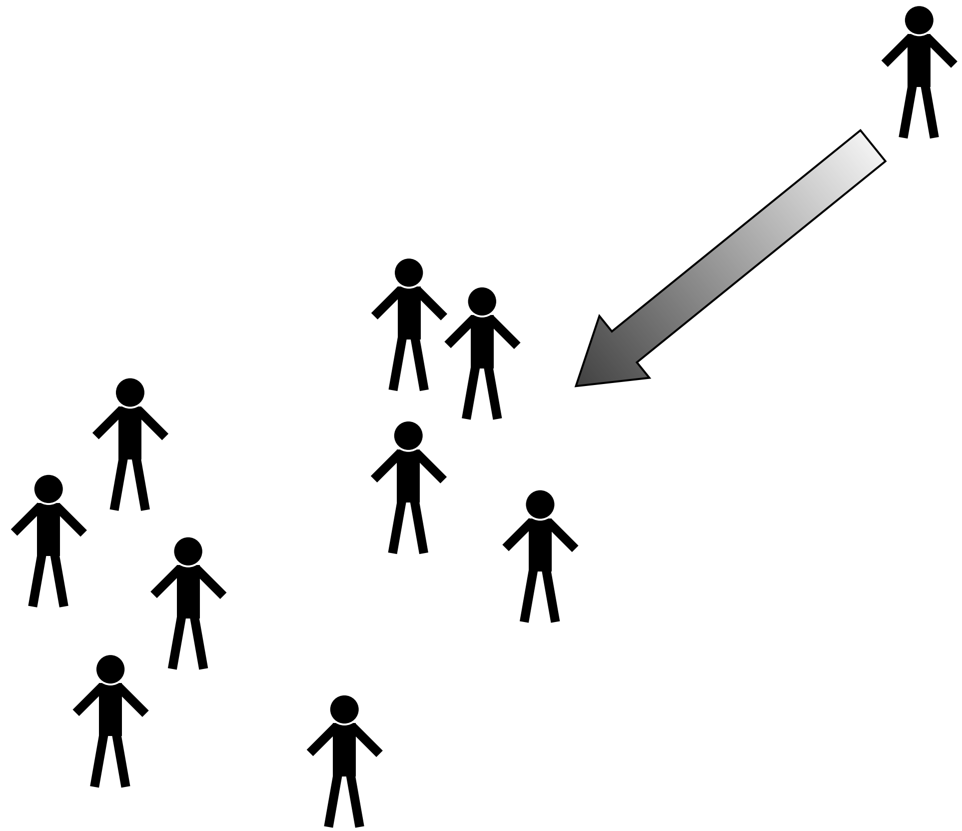


Hierarchical Unsupervised Generative Embedding

DCM → model inversion → ~~point estimates~~ → ~~classification~~ → result

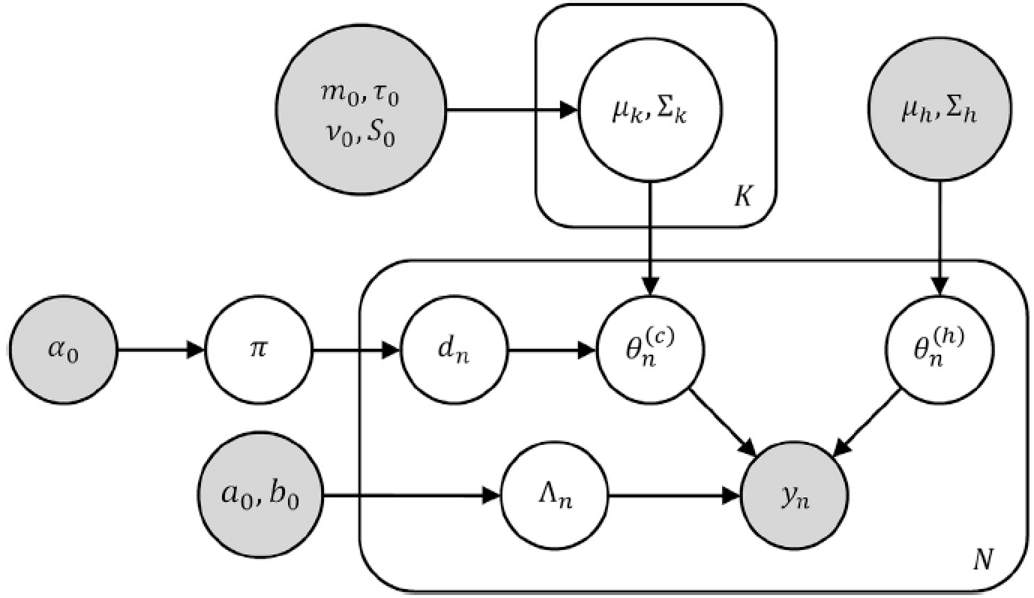
beyond GE

- HUGE can also be used for **Empirical Bayes**
- "estimate" prior from data
- regularize outliers



HUGE Model Equations

graphical model



assignment indicator

$$p(d_n = k|\pi) = \mathrm{Cat}(k|\pi) = \pi_k$$

subject-level

connectivity parameters

$$p\left(\theta_n^{(c)} \middle| d_n = k, \mu_k, \Sigma_k\right) = N\left(\theta_n^{(c)} \middle| \mu_k, \Sigma_k\right)$$

hemodynamic parameters

$$p\left(\theta_n^{(h)} \middle| \mu_h, \Sigma_h\right) = N\left(\theta_n^{(h)} \middle| \mu_h, \Sigma_h\right)$$

observation

$$y_n = g(u, \theta_n) + \eta_n$$

cluster-level

cluster weights

$$\pi \sim \mathrm{D}(\pi|\alpha_0)$$

cluster mean and variance

$$\mu_k, \Sigma_k \sim \mathrm{NW}^{-1}(\mu_k, \Sigma_k | m_0, \tau_0, \nu_0, S_0)$$

HUGE Model Equations

Yao et al. (2018). Variational Bayesian Inversion for Hierarchical Unsupervised Generative Embedding (HUGE). NeuroImage

assignment indicator

$$p(d_n = k|\pi) = \mathrm{Cat}(k|\pi) = \pi$$

Variational Bayesian inversion for hierarchical unsupervised generative embedding (HUGE)

Yu Yao [a,*], Sudhir S. Raman [a], Michael Schiek [b], Alex Leff [c], Stefan Frässle [a], Klaas E. Stephan [a,c]

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[b] Central Institute ZEA-2 Electronic Systems, Research Center Jülich, 52425 Jülich, Germany
[c] Wellcome Trust Centre for Neuroimaging, University College London, London, WC1N 3BG, United Kingdom

subject-level

connectivity parameters

$$p\left(\theta_n^{(c)}\middle|d_n = k, \mu_k, \Sigma_k\right) = N\left(\theta_n\right.$$

ARTICLE INFO

Keywords:

ne

hemodynamic parameters

$$p\left(\theta_n^{(h)}\middle|\mu_h, \Sigma_h\right) = N\left(\theta_n^{(h)}\middle|\mu_h, \Sigma_h\right)$$

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$$y_n = g(u, \theta_n) + \eta_n$$

Raman et al. 2016. “A hierarchical model for integrating unsupervised generative embedding and empirical Bayes.” J. Neurosci. Meth. 269, 6–20.

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HUGE Model Equations

assignment indicator

$$p(d_n = k|\pi) = \mathrm{Cat}(k|\pi) = \pi_k$$

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connectivity parameters

$$p\left(\theta_n^{(c)} \middle| d_n = k, \mu_k, \Sigma_k\right) = N\left(\theta_n^{(c)} \middle| \mu_k, \Sigma_k\right)$$

hemodynamic parameters

$$p\left(\theta_n^{(h)} \middle| \mu_h, \Sigma_h\right) = N\left(\theta_n^{(h)} \middle| \mu_h, \Sigma_h\right)$$

observation

$$y_n = g(u, \theta_n) + \eta_n$$

SATURDAY – 12th September 2020

11:45	**Practical Tutorials: Morning**
Tutorial A:	Bayesian Learning Tore Erdmann, Sandra Iglesias, Lilian Weber
Tutorial B:	Active Inference Thomas Parr, Philipp Schwartenbeck
Tutorial C:	Reinforcement Learning Woo-Young Ahn, Nathaniel Haines, Jaeyeong Yang
Tutorial D:	Model Inversion Eduardo Aponte, Lionel Rigoux
Tutorial E:	Machine Learning Thomas Wolfers, Saige Rutherford
Tutorial F:	Dynamic Causal Modeling Jakob Heinzle, Herman Galioulline
Tutorial G:	rDCM Stefan Frässle, Cao Tri Do
Tutorial H:	HUGE Yu Yao, Matthias Müller-Schrader

cluster-

cluster weights

$$\pi \sim \mathrm{D}(\pi|\alpha_0)$$

cluster mean and variance

$$\mu_k, \Sigma_k \sim \mathrm{NW}^{-1}(\mu_k, \Sigma_k | m_0, \tau_0, \nu_0, S_0)$$

HUGE summary

likelihood: encodes generative process

prior: encodes model assumptions

standard model

joint likelihood prior

$$\underbrace{p(y,\theta|\lambda,m)}_{\text{joint}} = \underbrace{p(y|\theta,\lambda,m)}_{\text{likelihood}}\underbrace{p(\theta|\lambda,m)}_{\text{prior}}$$

y: data

θ: model parameters

λ: prior parameters

m: model

HUGE summary

likelihood: encodes generative process

prior: encodes model assumptions

standard model

joint **likelihood** **prior**

$$p(y,\theta|\lambda,m) = p(y|\theta,\lambda,m)p(\theta|\lambda,m)$$

Remember:

$$p(x,y,z) = p(x|y,z)p(y|z)p(z)$$

y: data

θ: model parameters

λ: prior parameters

m: model

HUGE summary

likelihood: encodes generative process

prior: encodes model assumptions

hierarchical model

$$\underbrace{p(y,\theta,\lambda|\phi,m)}_{\text{joint}} = \underbrace{p(y|\theta,\lambda,\phi,m)}_{\text{likelihood}}\underbrace{p(\theta|\lambda,\phi,m)}_{\text{prior}}\underbrace{p(\lambda|\phi,m)}_{\text{hyperprior}}$$

Remember:

$$p(x,y,z) = p(x|y,z)p(y|z)p(z)$$

y: data

θ: model parameters

λ: prior parameters

ϕ: parameters of hyperprior

m: model

HUGE summary

likelihood: encodes generative process

prior: encodes a clustering model

hierarchical model

joint **likelihood** **prior** **hyperprior**

$$p(y,\theta,\lambda|\phi,m) = p(y|\theta,\lambda,\phi,m)\,p(\theta|\lambda,\phi,m)\,p(\lambda|\phi,m)$$

mixture of Gaussians

$$p(\theta|\lambda,\phi,m) = \sum_k \pi_k N(\theta|\mu_k,\Sigma_k)$$

$$\lambda = \{\pi,\mu,\Sigma\}$$

y: data

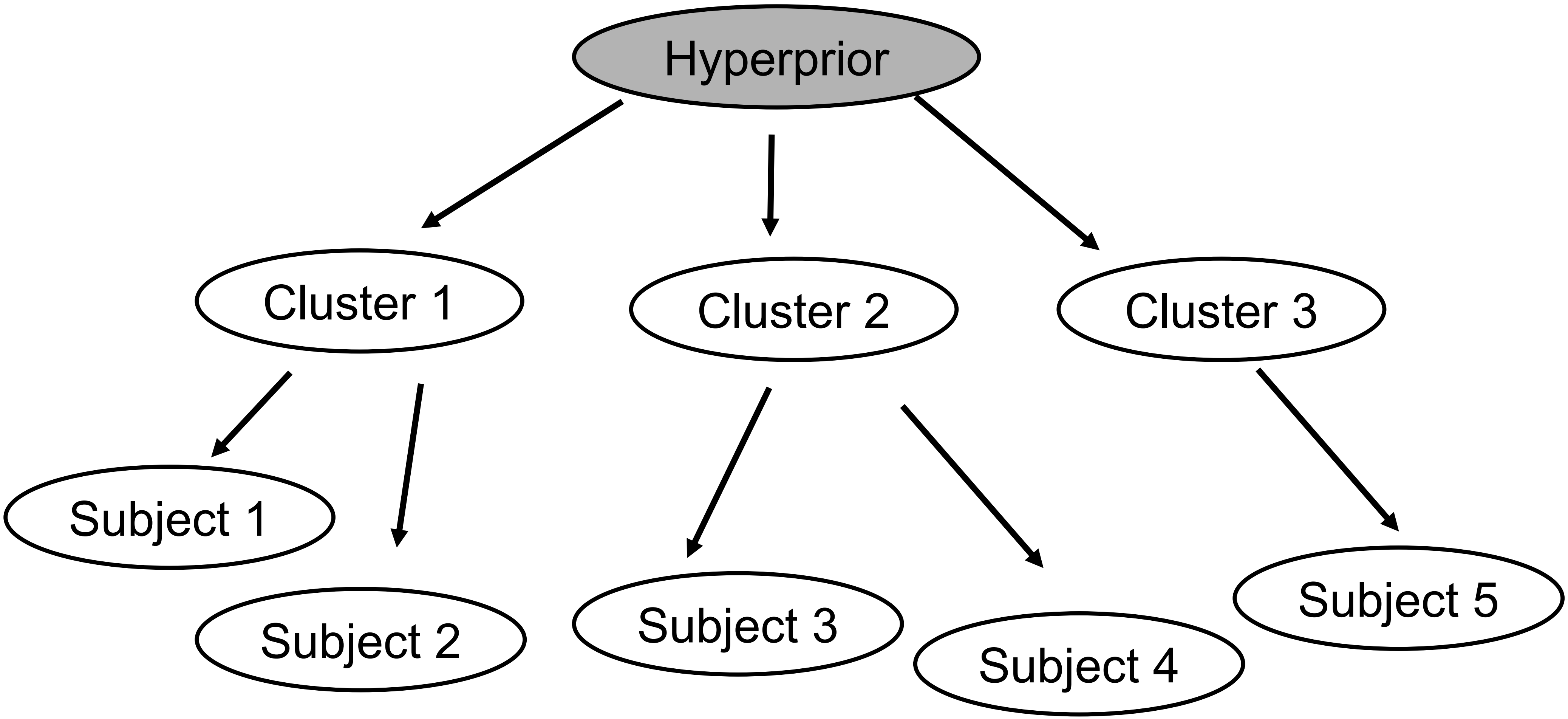
θ: model parameters

λ: prior parameters

ϕ: parameters of hyperprior

m: model

HUGE summary



Software

Code available as part of TAPAS

www.translationalneuromodeling.org/tapas

CPC Practical Session (Saturday)
Tutorial H: HUGE

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.

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