DCM: Advanced topics

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SPM Course Zurich
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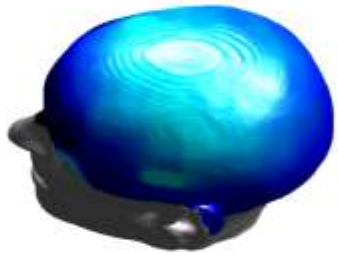
Overview

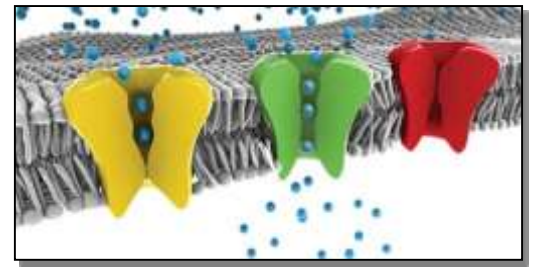
- DCM – a generative model
- Evolution of DCM for fMRI
- Bayesian model selection (BMS)
- Translational Neuromodeling

Generative model



$$p(y \mid \theta, m) \cdot p(\theta \mid m)$$

$$p(\theta \mid y, m)$$



1. enforces mechanistic thinking: how could the data have been caused?
2. generate synthetic data (observations) by sampling from the prior – can model explain certain phenomena at all?
3. inference about model structure: formal approach to disambiguating mechanisms → p(y|m)
4. inference about parameters → p(θ|y)
5. basis for predictions about interventions → control theory

Bayesian system identification

$u(t)$

Neural dynamics

$$dx/dt = f(x,u,\theta)$$

Observer function

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

$$p(y \mid \theta, m) = N(g(\theta), \Sigma(\theta))$$

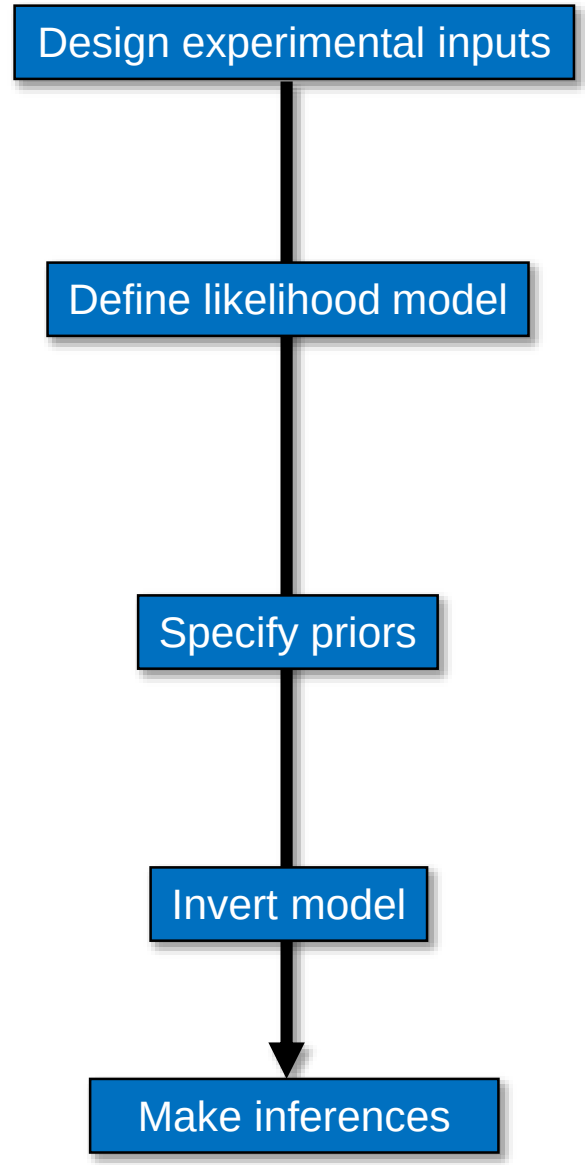
$$p(\theta, m) = N(\mu_\theta, \Sigma_\theta)$$

Inference on model structure

$$p(y \mid m) = \int p(y \mid \theta, m)\, p(\theta) d\theta$$

Inference on parameters

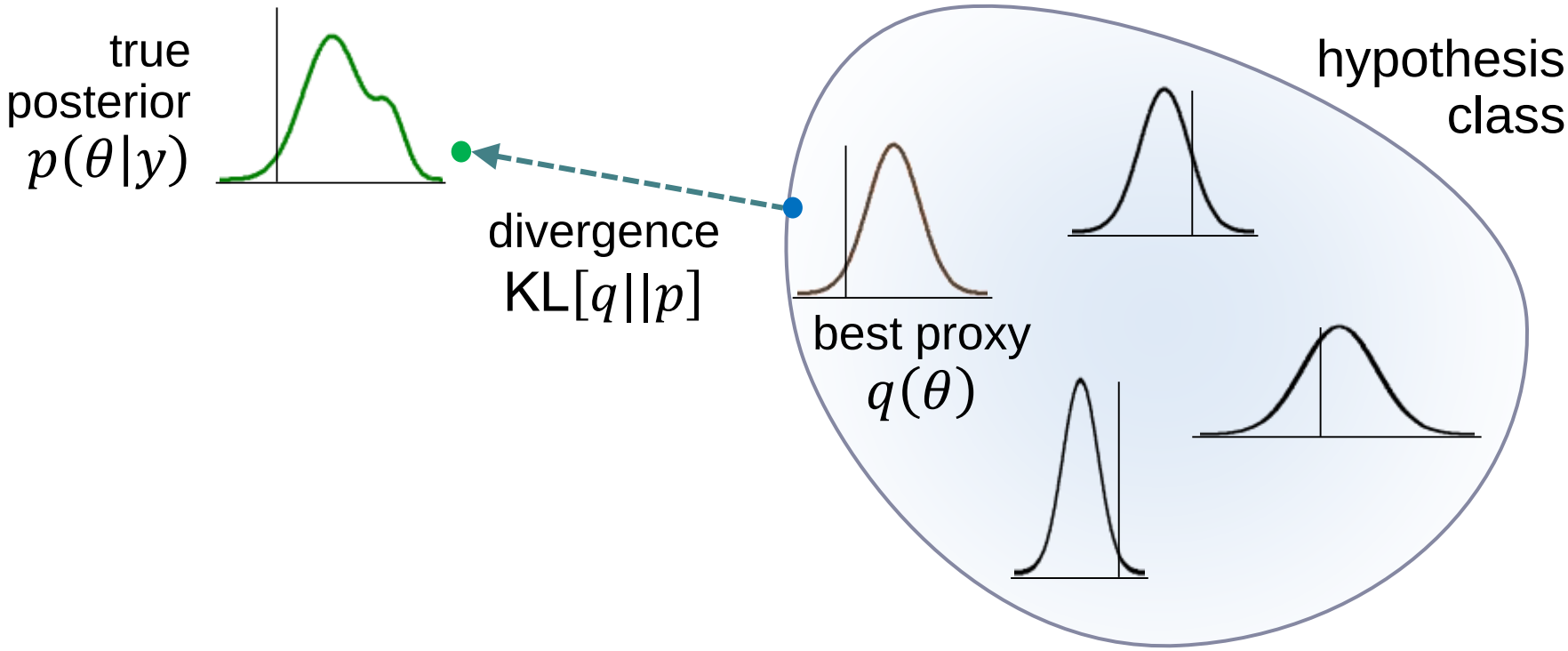
$$p(\theta \mid y, m) = \frac{p(y \mid \theta, m)\, p(\theta, m)}{p(y \mid m)}$$



Variational Bayes (VB)

Idea: find an approximation $q(\theta)$ to the true posterior $p(\theta|y)$.

Often done by assuming a particular form for q and then optimizing its sufficient statistics (fixed form VB).



Variational Bayes

$$\ln p(y) = \underbrace{\mathrm{KL}[q||p]}_{\text{divergence}} + \underbrace{F(q,y)}_{\text{neg. free energy}}$$

divergence ≥ 0 (unknown)

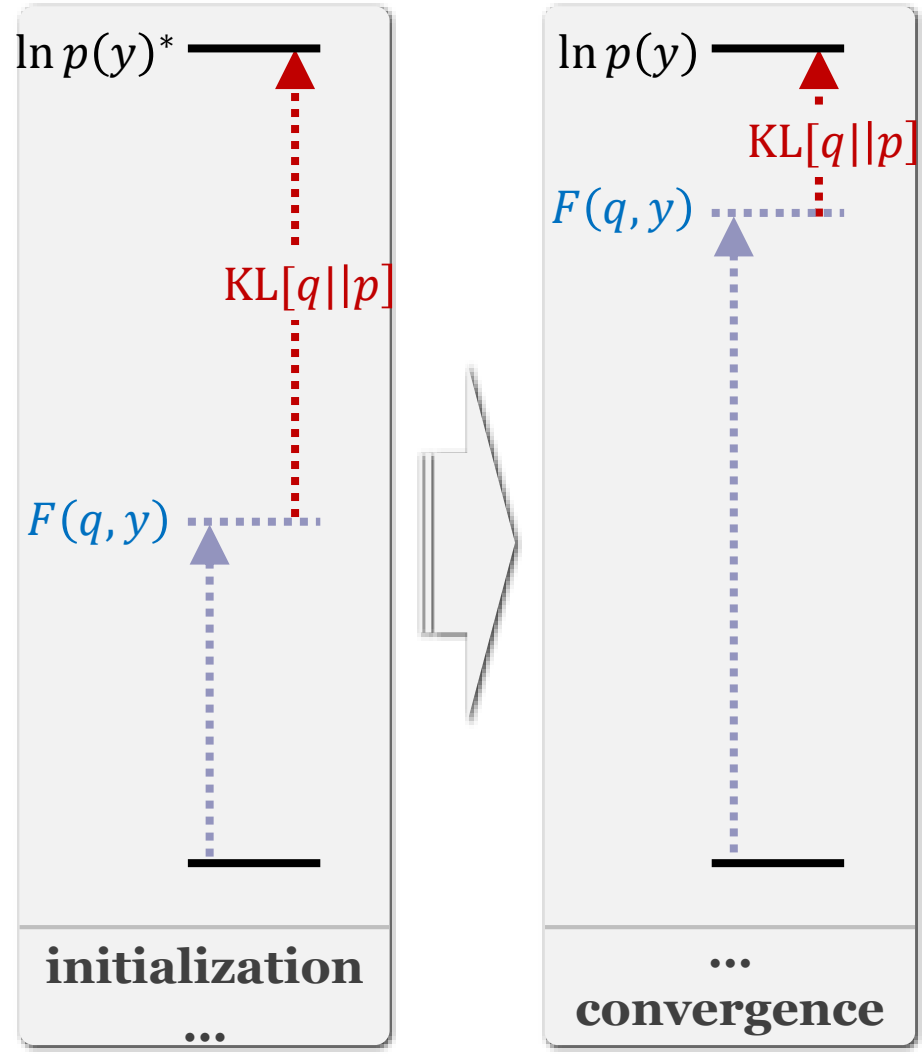
neg. free energy (easy to evaluate for a given q)

$F(q,y)$ is a functional wrt. the approximate posterior $q(\theta)$.

Maximizing $F(q,y)$ is equivalent to:

- minimizing $\mathrm{KL}[q||p]$
- tightening $F(q,y)$ as a lower bound to the log model evidence

When $F(q,y)$ is maximized, $q(\theta)$ is our best estimate of the posterior.



Alternative optimisation schemes

- Global optimisation schemes for DCM:
  - MCMC
  - Gaussian processes
- Papers submitted – in SPM soon

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The evolution of DCM in SPM

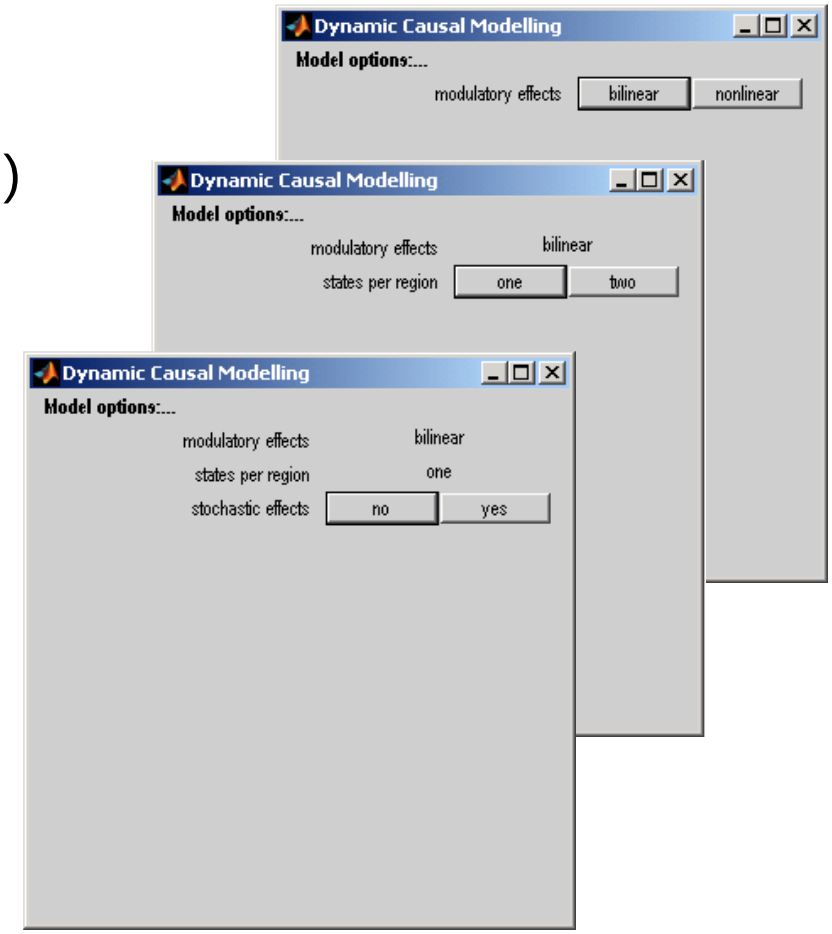
- DCM is not one specific model, but a framework for Bayesian inversion of dynamic system models

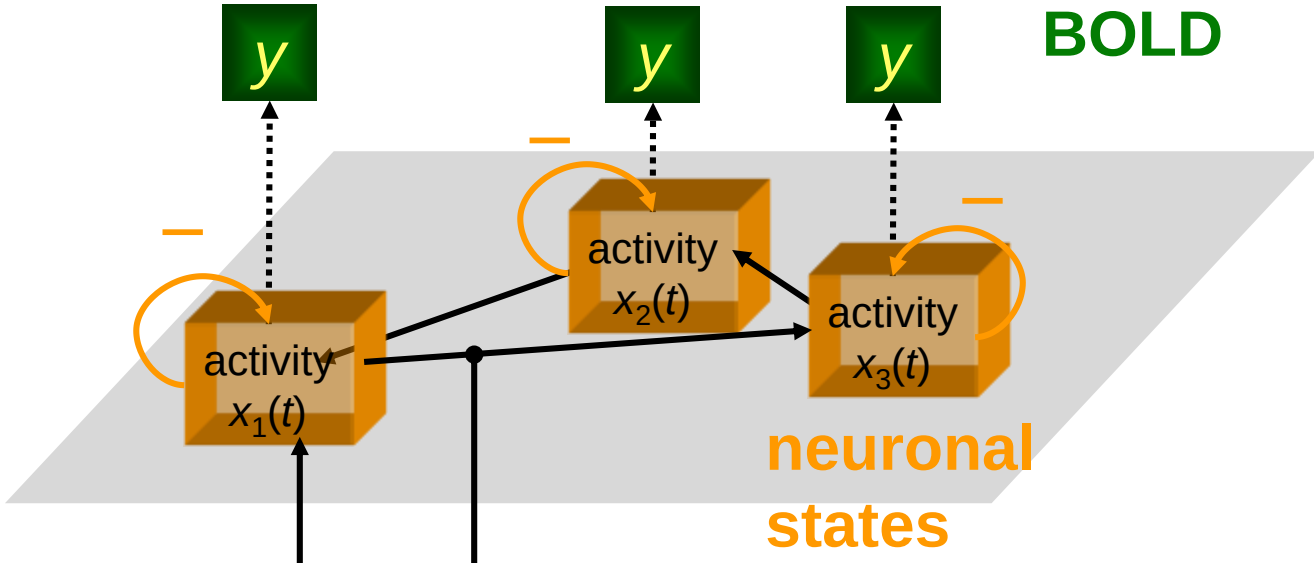
- The implementation in SPM has been evolving over time, e.g.
  - improvements of numerical routines (e.g., optimisation scheme)
  - change in priors to cover new variants (e.g., stochastic DCMs)
  - changes of hemodynamic model

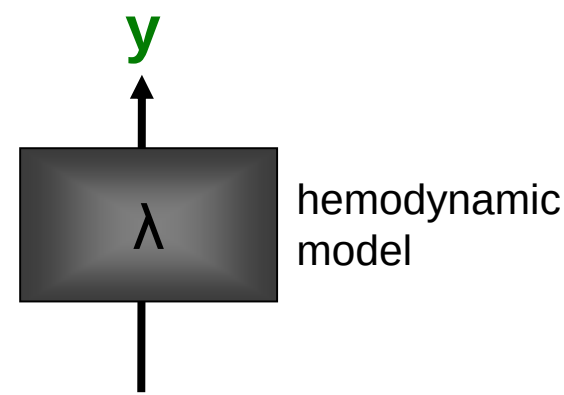
To enable replication of your results, you should ideally state which SPM version (release number) you are using when publishing papers.

Factorial structure of model specification

- Three dimensions of model specification:
  - bilinear vs. nonlinear
  - single-state vs. two-state (per region)
  - deterministic vs. stochastic



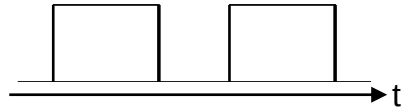




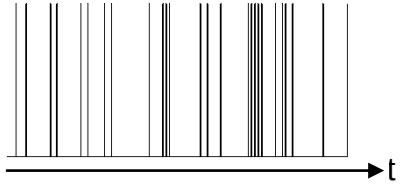
x

integration

modulatory
input $u_2(t)$



driving
input $u_1(t)$



The classical DCM:
a deterministic, one-state, bilinear model

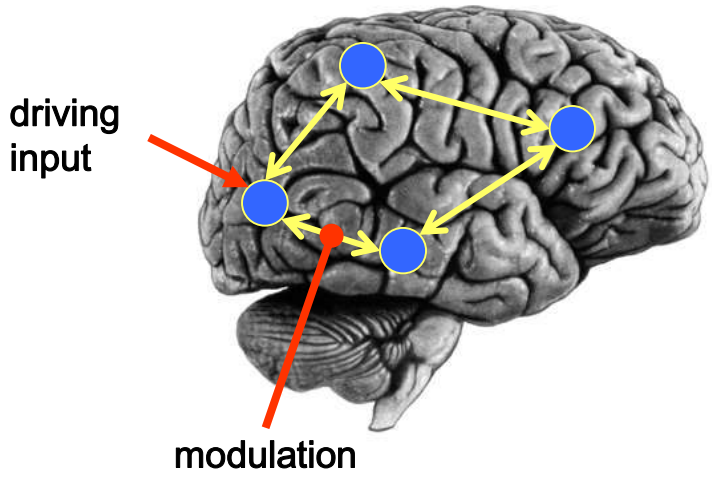
Neural state equation $\dot{x} = (A + \sum u_j B^{(j)})x + Cu$

endogenous connectivity → $A = \frac{\partial \dot{x}}{\partial x}$

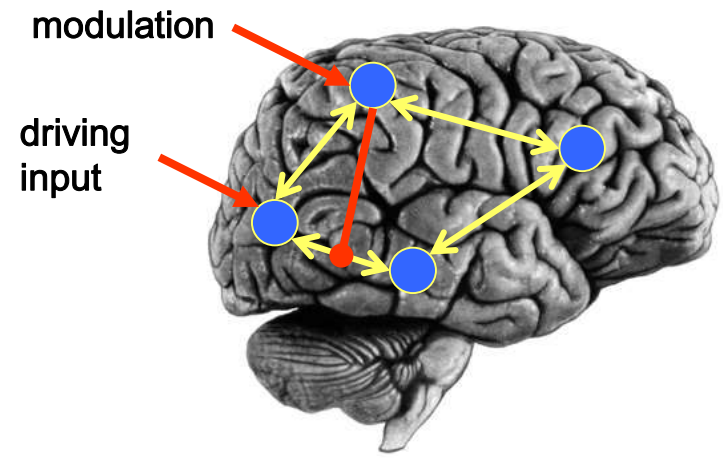
modulation of connectivity → $B^{(j)} = \frac{\partial}{\partial u_j}\frac{\partial \dot{x}}{\partial x}$

direct inputs → $C = \frac{\partial \dot{x}}{\partial u}$

bilinear DCM



non-linear DCM



Two-dimensional Taylor series (around $x_0=0$, $u_0=0$):

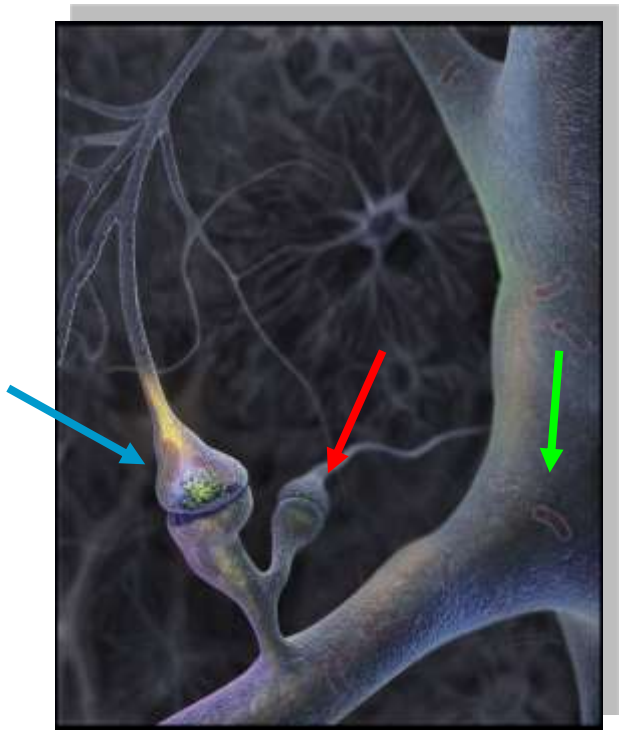
$$\frac{dx}{dt} = f(x,u) \approx f(x_0,0) + \frac{\partial f}{\partial x}x + \frac{\partial f}{\partial u}u + \frac{\partial^2 f}{\partial x \partial u}ux + \frac{\partial^2 f}{\partial x^2}\frac{x^2}{2} + \ldots$$

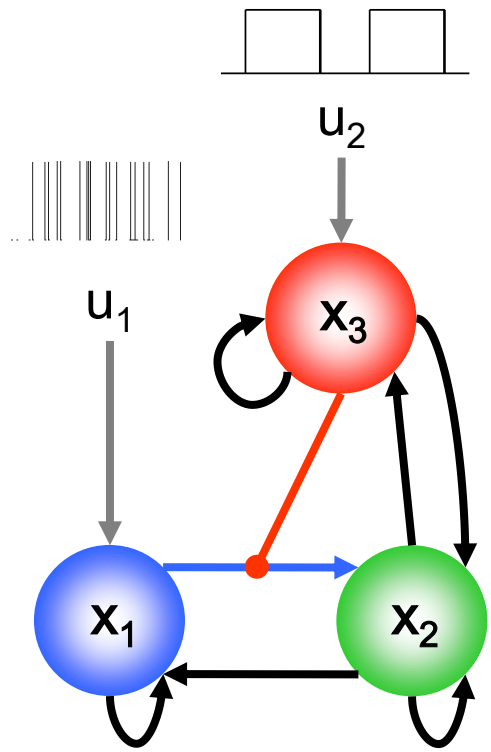
Bilinear state equation:

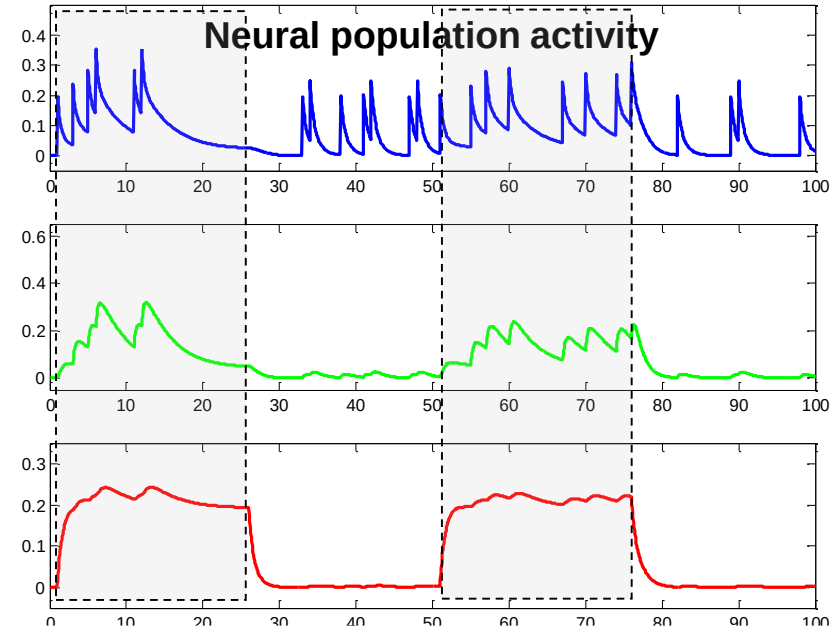
$$\frac{dx}{dt} = \left(A + \sum_{i=1}^{m} u_i B^{(i)}\right)x + Cu$$

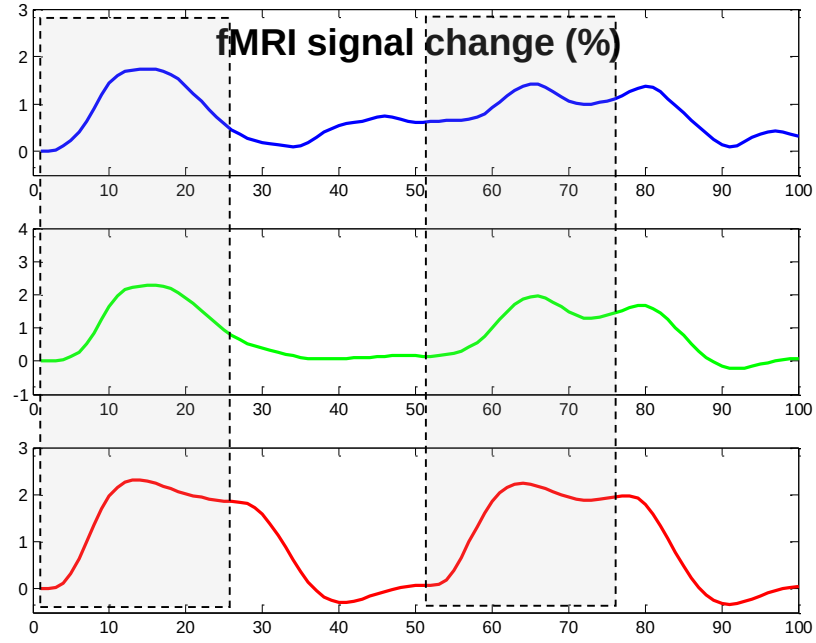
Nonlinear state equation:

$$\frac{dx}{dt} = \left(A + \sum_{i=1}^{m} u_i B^{(i)} + \sum_{j=1}^{n} x_j D^{(j)}\right)x + Cu$$







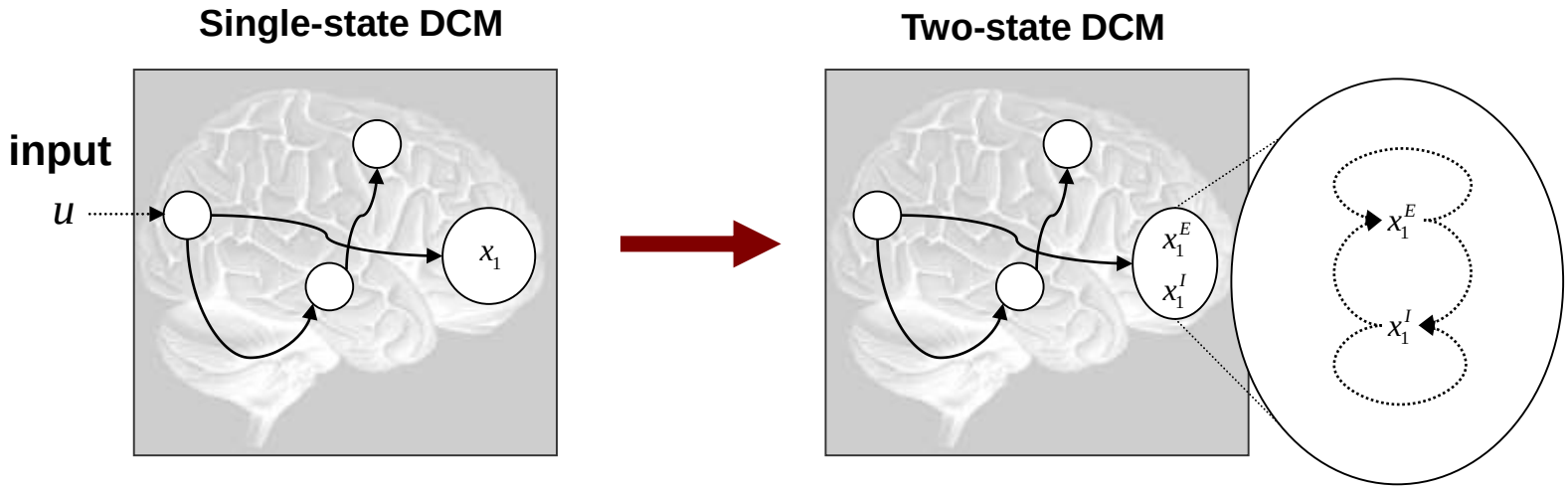


Nonlinear Dynamic Causal Model for fMRI

$$\frac{dx}{dt} = \left(A + \sum_{i=1}^{m} u_i B^{(i)} + \sum_{j=1}^{n} x_j D^{(j)} \right) x + Cu$$

Stephan et al. 2008, *NeuroImage*

Two-state DCM



$$\dot{x} = \Im x + Cu$$

$$\Im_{ij} = A_{ij} + uB_{ij}$$

$$\Im = \begin{bmatrix} \Im_{11} & \cdots & \Im_{1N} \\ \vdots & \ddots & \vdots \\ \Im_{N1} & \cdots & \Im_{NN} \end{bmatrix} \quad x = \begin{bmatrix} x_1 \\ \vdots \\ x_N \end{bmatrix}$$

$$\dot{x} = \Im x + Cu$$

$$\Im_{ij}^{\bullet\bullet} = \mu_{ij}^{\bullet\bullet} \exp(A_{ij}^{\bullet\bullet} + uB_{ij}^{\bullet\bullet})$$

$$\Im = \begin{bmatrix} \Im_{11}^{EE} & \Im_{11}^{EI} & \cdots & \Im_{1N}^{EE} & 0 \\ \Im_{11}^{IE} & \Im_{11}^{II} & & 0 & 0 \\ \vdots & & \ddots & & \vdots \\ \Im_{N1}^{EE} & 0 & & \Im_{NN}^{EE} & \Im_{NN}^{EE} \\ 0 & 0 & \cdots & \Im_{NN}^{IE} & \Im_{NN}^{II} \end{bmatrix} \quad x = \begin{bmatrix} x_1^E \\ x_1^I \\ \vdots \\ x_N^E \\ x_N^I \end{bmatrix}$$

Extrinsic (between-region) coupling

Intrinsic (within-region) coupling

Marreiros et al. 2008, *NeuroImage*

Stochastic DCM

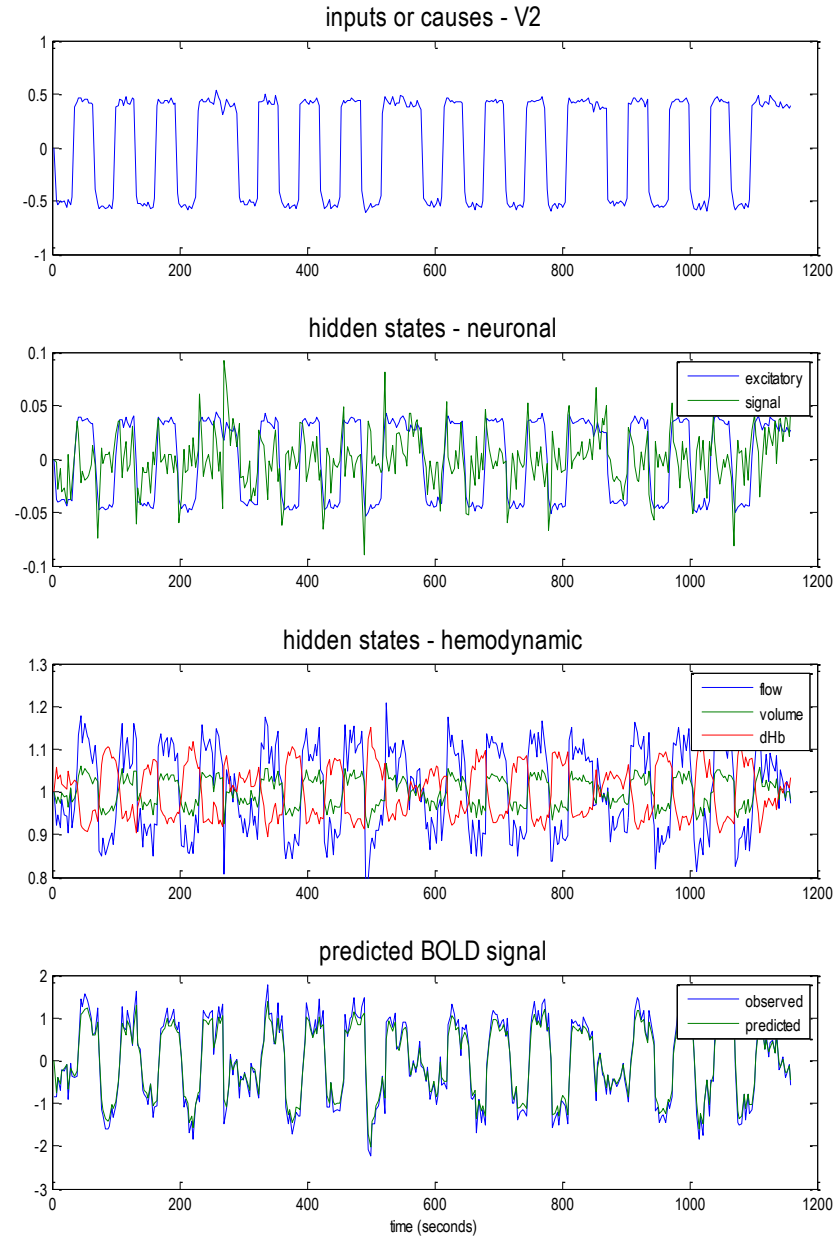
$$\frac{dx}{dt} = (A + \sum_j u_j B^{(j)})x + Cv + \omega^{(x)}$$

$$v = u + \omega^{(v)}$$

- all states are represented in generalised coordinates of motion
- random state fluctuations $w^{(x)}$ account for endogenous fluctuations,
  have unknown precision and smoothness
  $\rightarrow$ two hyperparameters
- fluctuations $w^{(v)}$ induce uncertainty about how inputs influence neuronal activity
- can be fitted to "resting state" data

Li et al. 2011, *NeuroImage*

Estimates of hidden causes and states (Generalised filtering)



Spectral DCM

- deterministic model that generates predicted crossed spectra in a distributed neuronal network or graph

- finds the effective connectivity among hidden neuronal states that best explains the observed functional connectivity among hemodynamic responses

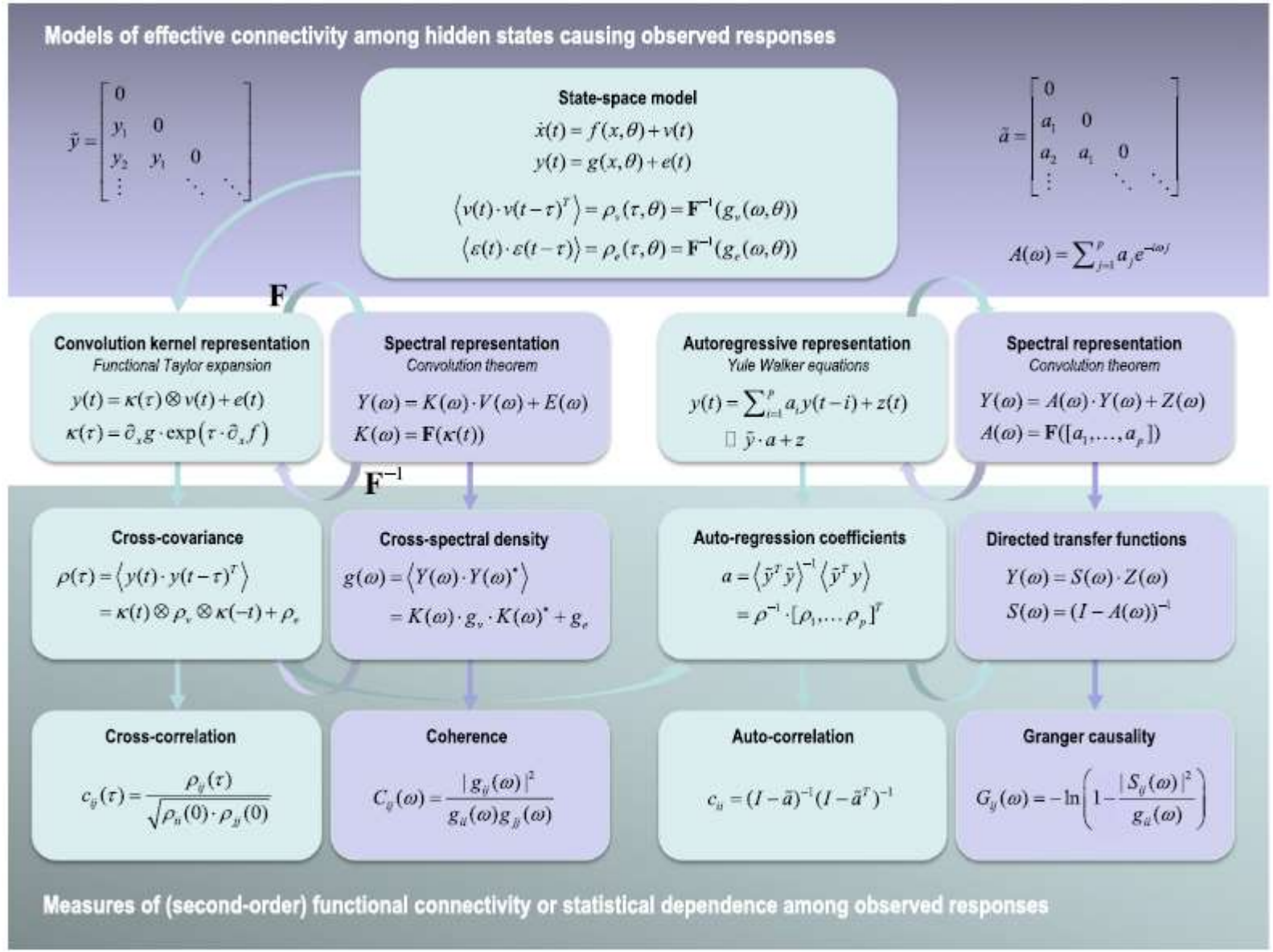
- advantage:
  - replaces an optimisation problem wrt. stochastic differential equations with a deterministic approach from linear systems theory → computationally very efficient

- disadvantages:
  - assumes stationarity

Friston et al. 2014, *NeuroImage*

cross-spectra
= inverse Fourier transform of cross-correlation

cross-correlation
= generalized form of correlation (at zero lag, this is the conventional measure of functional connectivity)



Friston et al. 2014, *NeuroImage*

Overview

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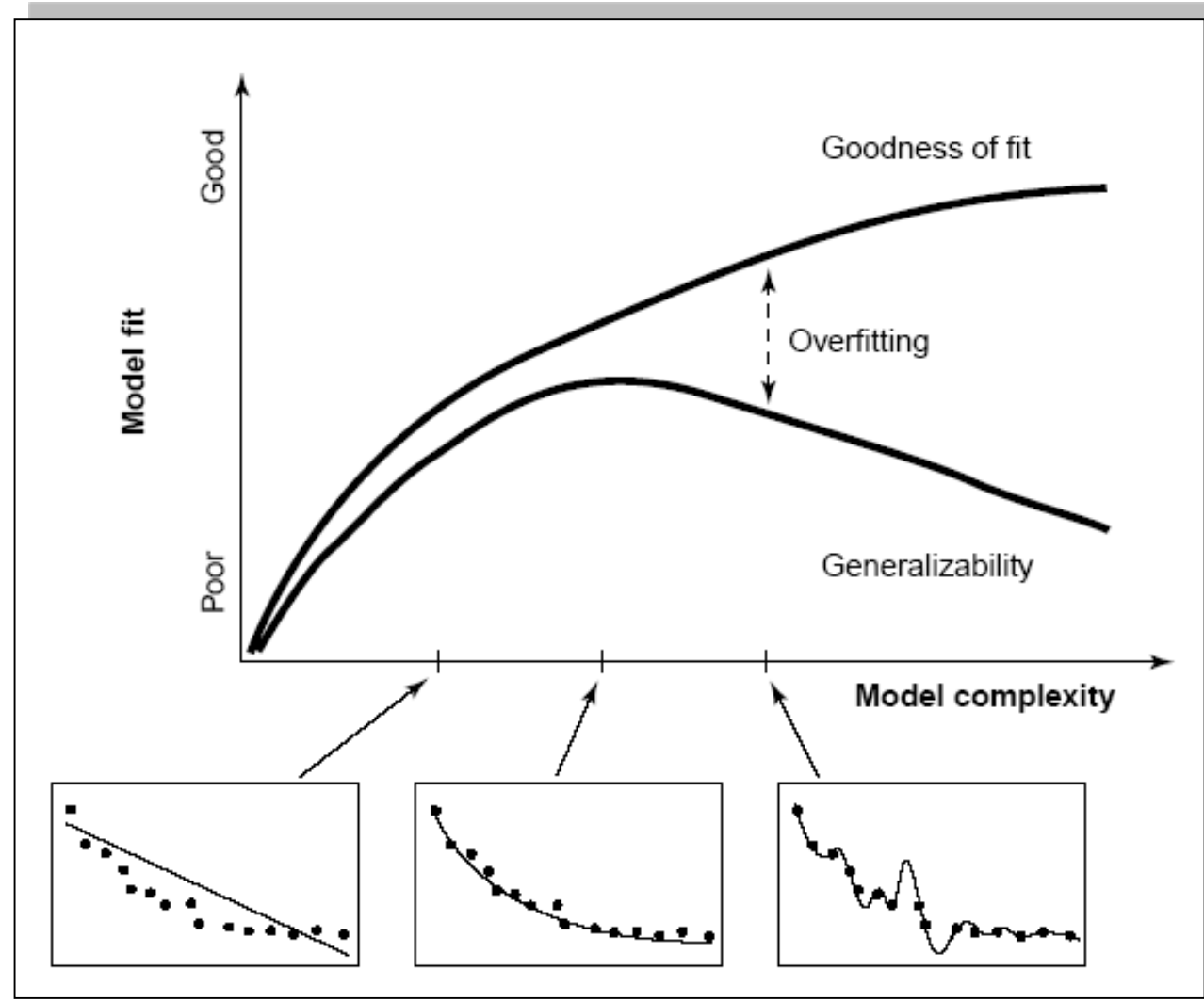
Model comparison and selection

Given competing hypotheses on structure & functional mechanisms of a system, which model is the best?

Which model represents the best balance between model fit and model complexity?

For which model m does $p(y|m)$ become maximal?



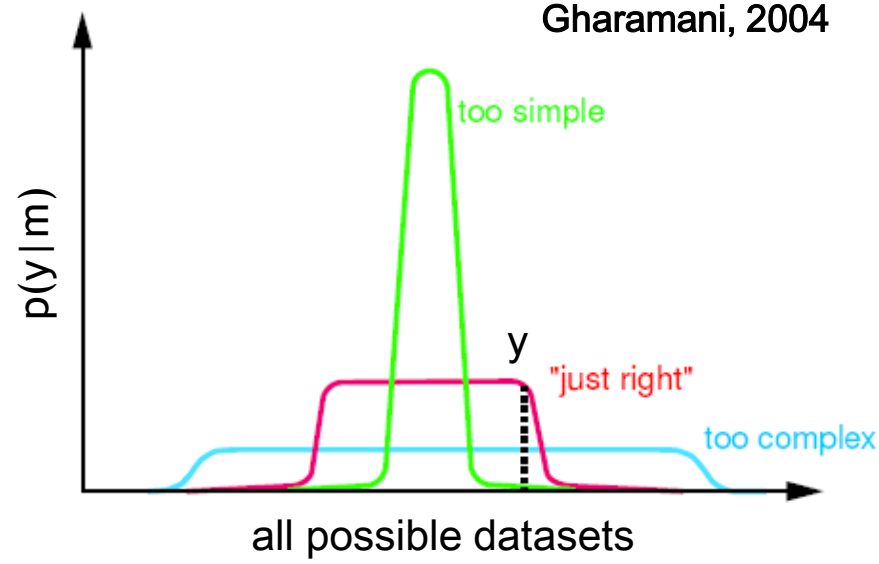
Pitt & Miyung (2002) *TICS*

Bayesian model selection (BMS)

Model evidence:

$$p(y \mid m) = \int p(y \mid \theta, m)\, p(\theta \mid m)\, d\theta$$

Gharamani, 2004



accounts for both accuracy and complexity of the model

allows for inference about model structure

Various approximations, e.g.:

- negative free energy, AIC, BIC

McKay 1992, *Neural Comput.*
Penny et al. 2004a, *NeuroImage*

Approximations to the model evidence in DCM

Logarithm is a monotonic function

Maximizing log model evidence
= Maximizing model evidence

Log model evidence = balance between fit and complexity

$$\log p(y \mid m) = accuracy(m) - complexity(m)$$
$$= \log p(y \mid \theta, m) - complexity(m)$$

Akaike Information Criterion: $AIC = \log p(y \mid \theta, m) - p$

Bayesian Information Criterion: $BIC = \log p(y \mid \theta, m) - \frac{p}{2} \log N$

No. of parameters

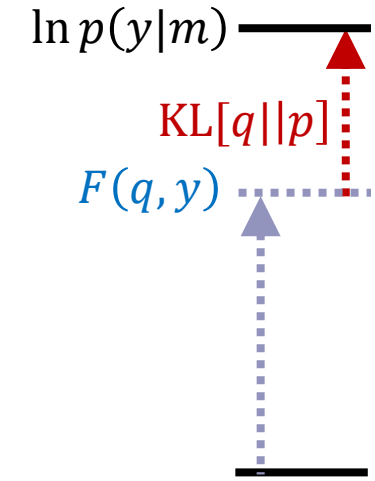
No. of data points

Penny et al. 2004a, *NeuroImage*

The (negative) free energy approximation F

Neg. free energy is a lower bound on log model evidence:

$$\log p(y \mid m) = F + KL\left[q(\theta), p(\theta \mid y, m)\right]$$



Like AIC/BIC, F is an accuracy/complexity tradeoff:

$$F = \underbrace{\left\langle \log p(y \mid \theta, m) \right\rangle}_{accuracy} - \underbrace{KL\left[q(\theta), p(\theta \mid m)\right]}_{complexity}$$

The complexity term in *F*

- In contrast to AIC & BIC, the complexity term of the negative free energy *F* accounts for parameter interdependencies.

$$KL\left[q(\theta), p(\theta \mid m)\right]$$
$$= \frac{1}{2}\ln\left|C_\theta\right| - \frac{1}{2}\ln\left|C_{\theta|y}\right| + \frac{1}{2}\left(\mu_{\theta|y} - \mu_\theta\right)^T C_\theta^{-1}\left(\mu_{\theta|y} - \mu_\theta\right)$$

- The complexity term of *F* is higher
  - the more independent the prior parameters (↑ effective DFs)
  - the more dependent the posterior parameters
  - the more the posterior mean deviates from the prior mean

Bayes factors

To compare two models, we could just compare their log evidences.

But: the log evidence is just some number – not very intuitive!

A more intuitive interpretation of model comparisons is made possible by Bayes factors:

positive value, [0; ∞[

$$B_{12} = \frac{p(y \mid m_1)}{p(y \mid m_2)}$$

Kass & Raftery classification:

B_{12}	$p(m_1 \mid y)$	Evidence
1 to 3	50-75%	weak
3 to 20	75-95%	positive
20 to 150	95-99%	strong
≥ 150	≥ 99%	Very strong

Kass & Raftery 1995, *J. Am. Stat. Assoc.*

Fixed effects BMS at group level

Group Bayes factor (GBF) for 1...*K* subjects:

$$GBF_{ij} = \prod_k BF_{ij}^{(k)}$$

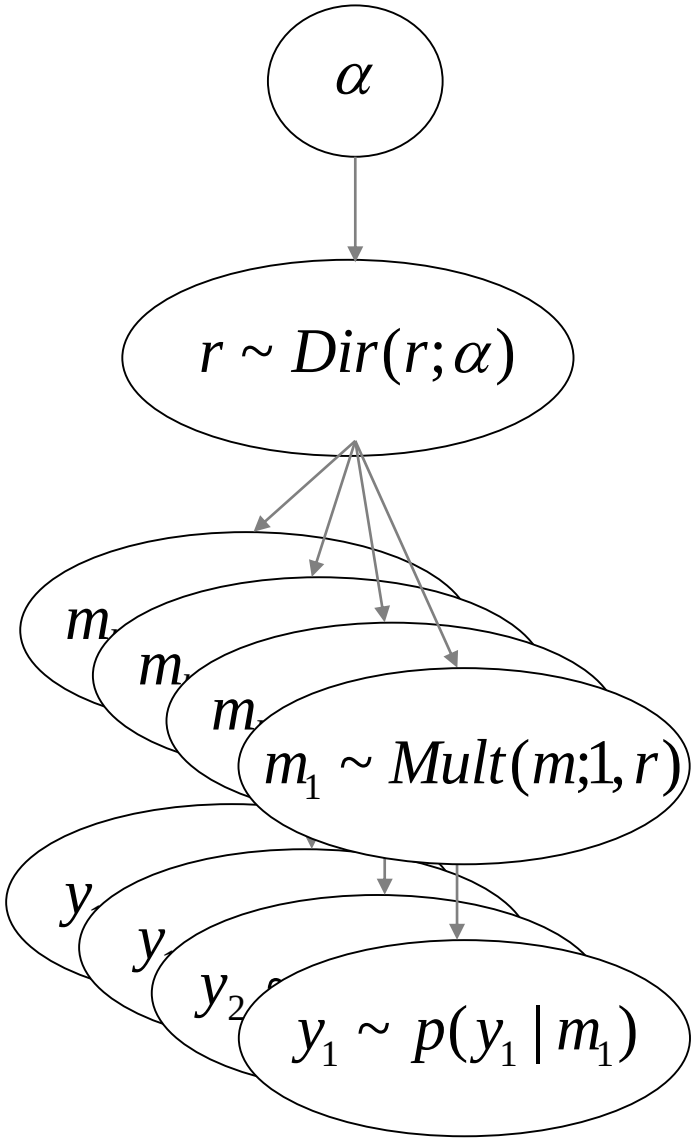
Average Bayes factor (ABF):

$$ABF_{ij} = \sqrt[K]{\prod_k BF_{ij}^{(k)}}$$

Problems:

- blind with regard to group heterogeneity
- sensitive to outliers

Random effects BMS for heterogeneous groups



Dirichlet parameters α
= "occurrences" of models in the population

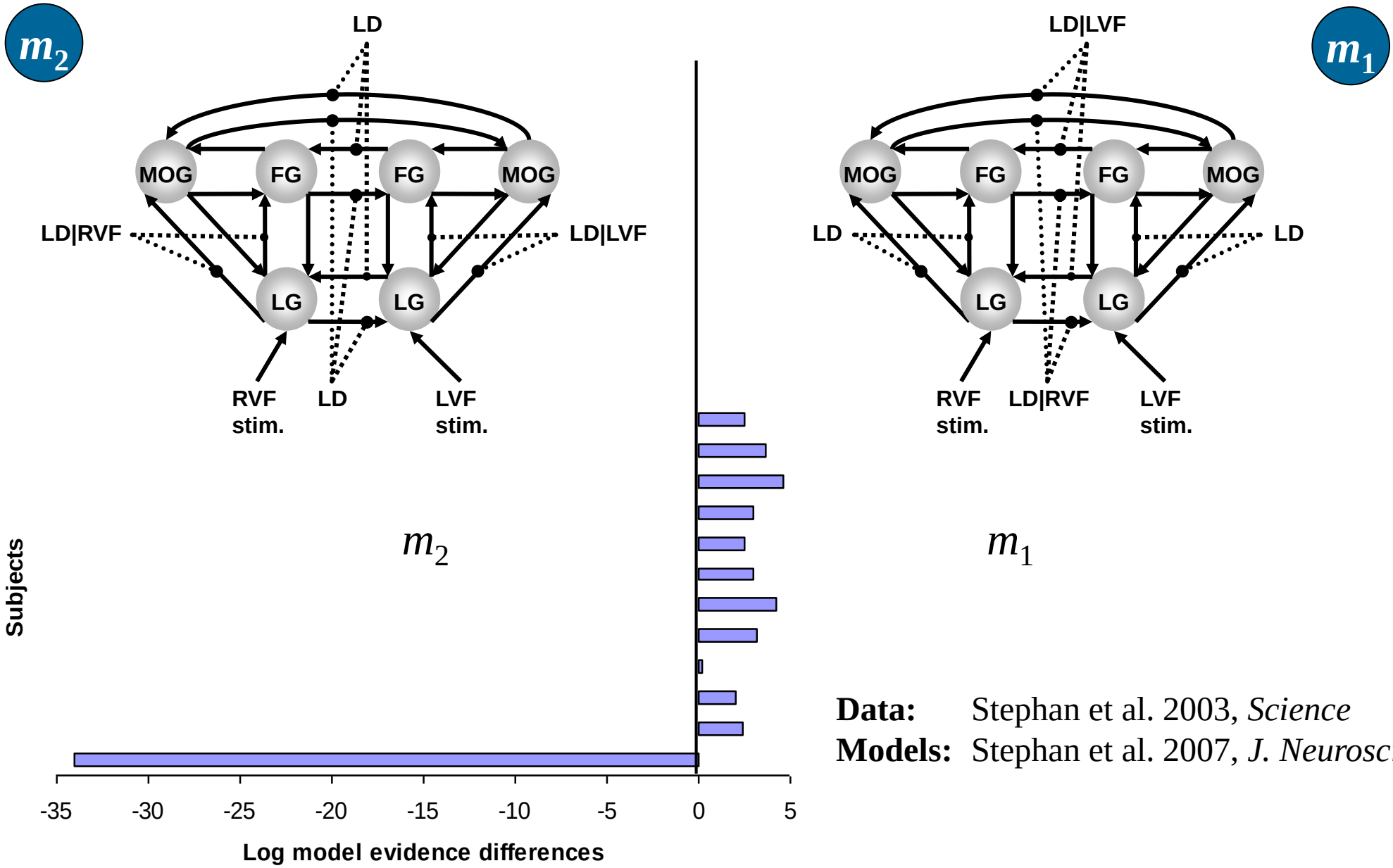
Dirichlet distribution of model probabilities r

Multinomial distribution of model labels m

Measured data y

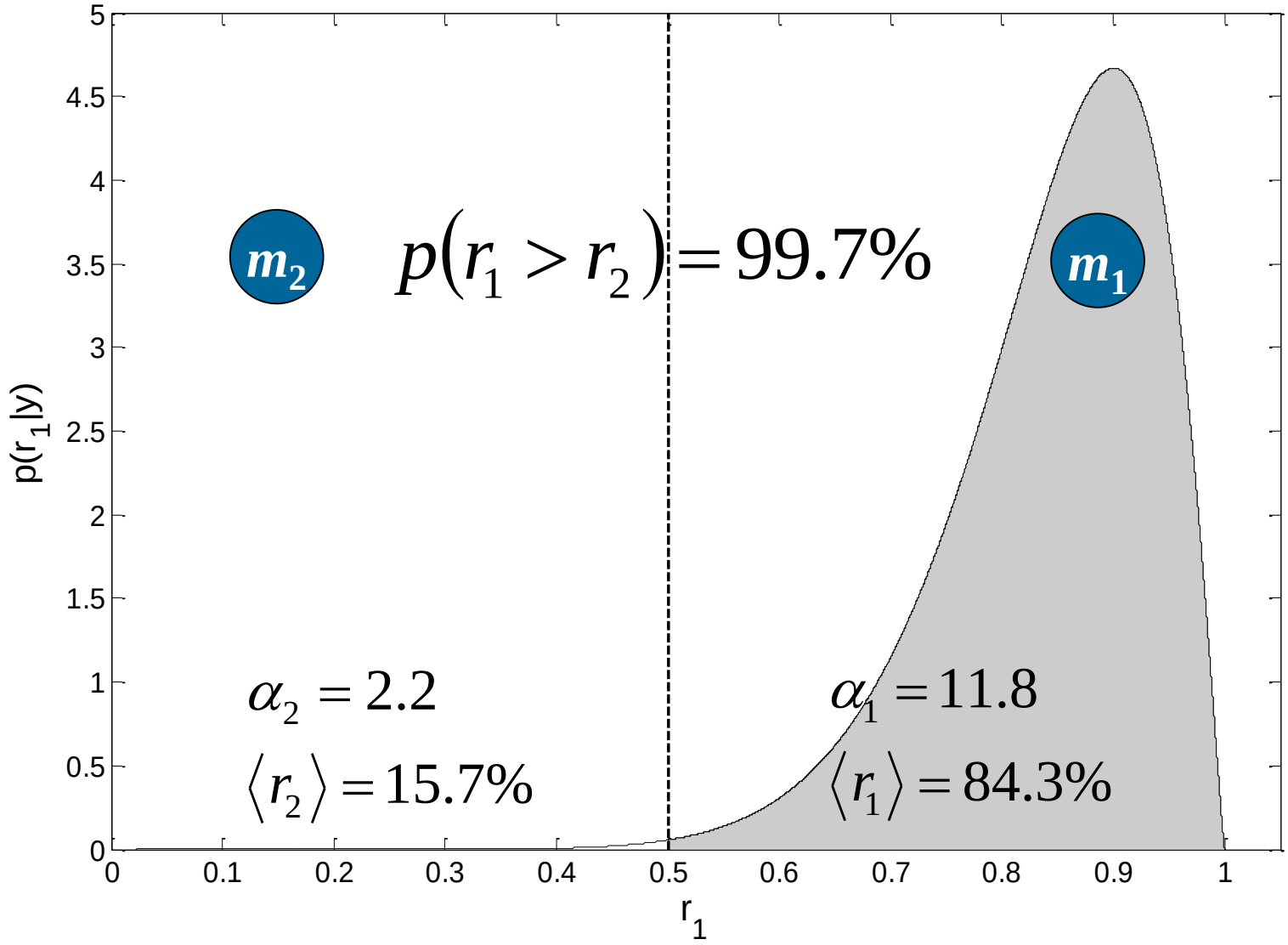
Model inversion by Variational Bayes (VB) or MCMC

Stephan et al. 2009a, *NeuroImage*
Penny et al. 2010, *PLoS Comp. Biol.*



Data: Stephan et al. 2003, *Science*

Models: Stephan et al. 2007, *J. Neurosci.*



Stephan et al. 2009a, *NeuroImage*

When does an EP signal deviation from chance?

- EPs express our confidence that the posterior probabilities of models are different – under the hypothesis H_1 that models differ in probability: $r_k \neq 1/K$
- does not account for possibility "null hypothesis" H_0: $r_k = 1/K$
- **Bayesian omnibus risk (BOR)** of wrongly accepting H_1 over H_0:

$$P_o = \frac{1}{1 + \frac{p(m|H_1)}{p(m|H_0).}}$$

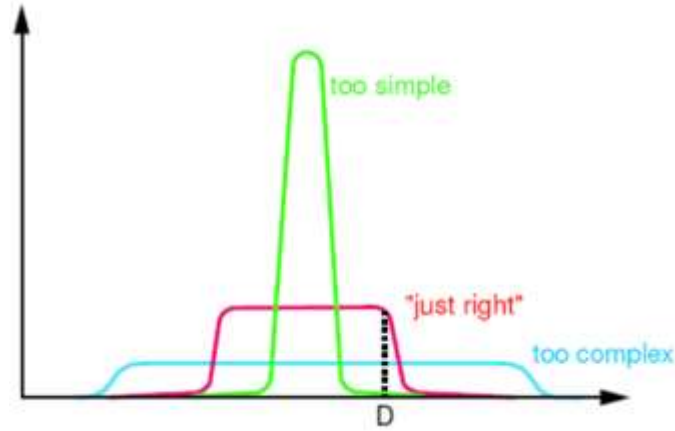
- **protected EP**: Bayesian model averaging over H_0 and H_1:

$$\begin{aligned}\widetilde{\varphi}_k &= P(r_k \geq r_{k' \neq k}|y) \\ &= P(r_k \geq r_{k' \neq k}|y, H_1)P(H_1|y) + P(r_k \geq r_{k' \neq k}|y, H_0)P(H_0|y) \\ &= \varphi_k(1-P_0) + \frac{1}{K}P_0\end{aligned}$$

Rigoux et al. 2014, *NeuroImage*

Overfitting at the level of models

- ↑ #models ⇒ ↑ risk of overfitting
- solutions:
  - regularisation: definition of model space = setting p(m)
  - family-level BMS
  - Bayesian model averaging (BMA)



posterior model probability:

$$p(m \mid y)$$

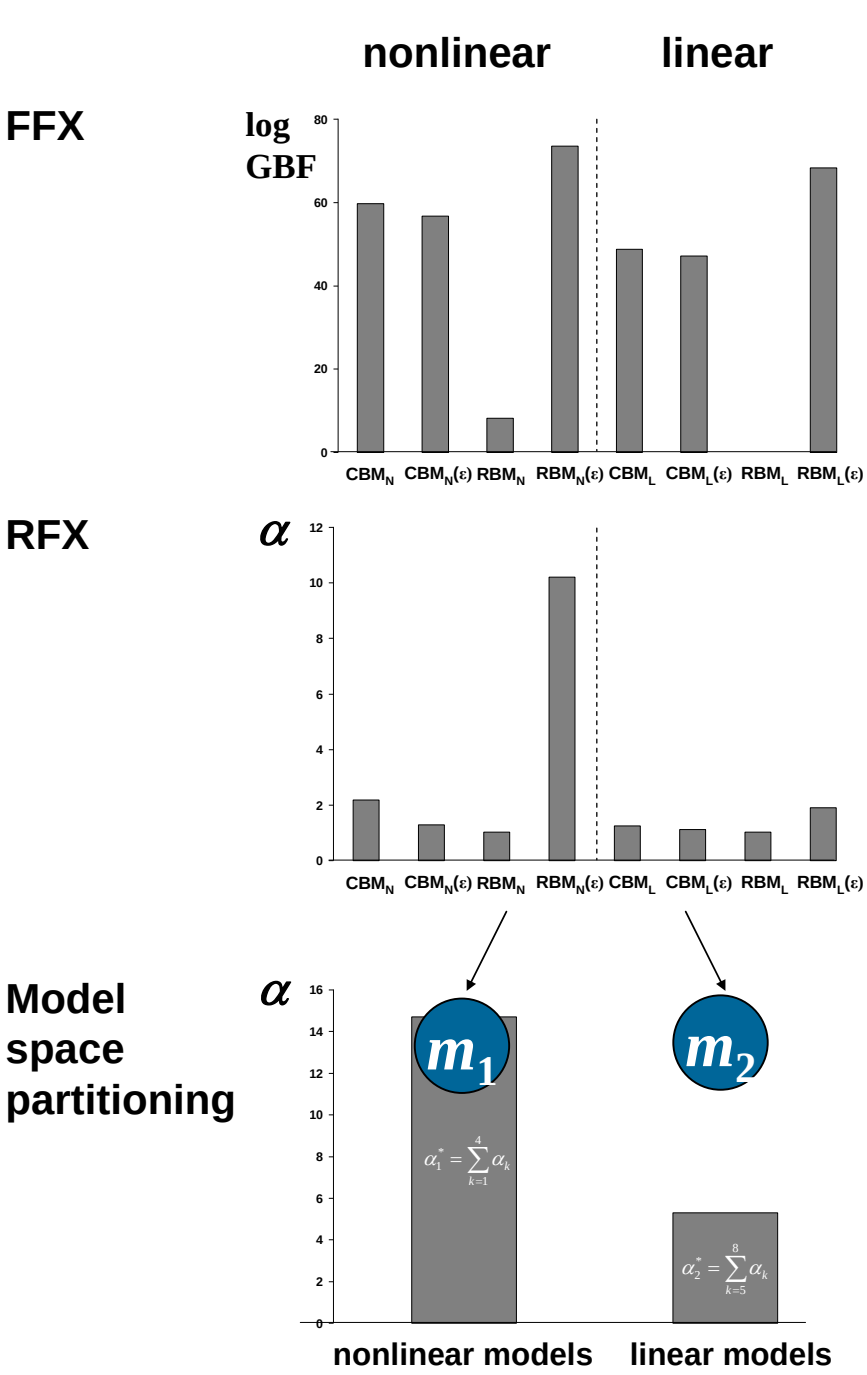
$$= \frac{p(y \mid m)\, p(m)}{\sum_m p(y \mid m)\, p(m)}$$

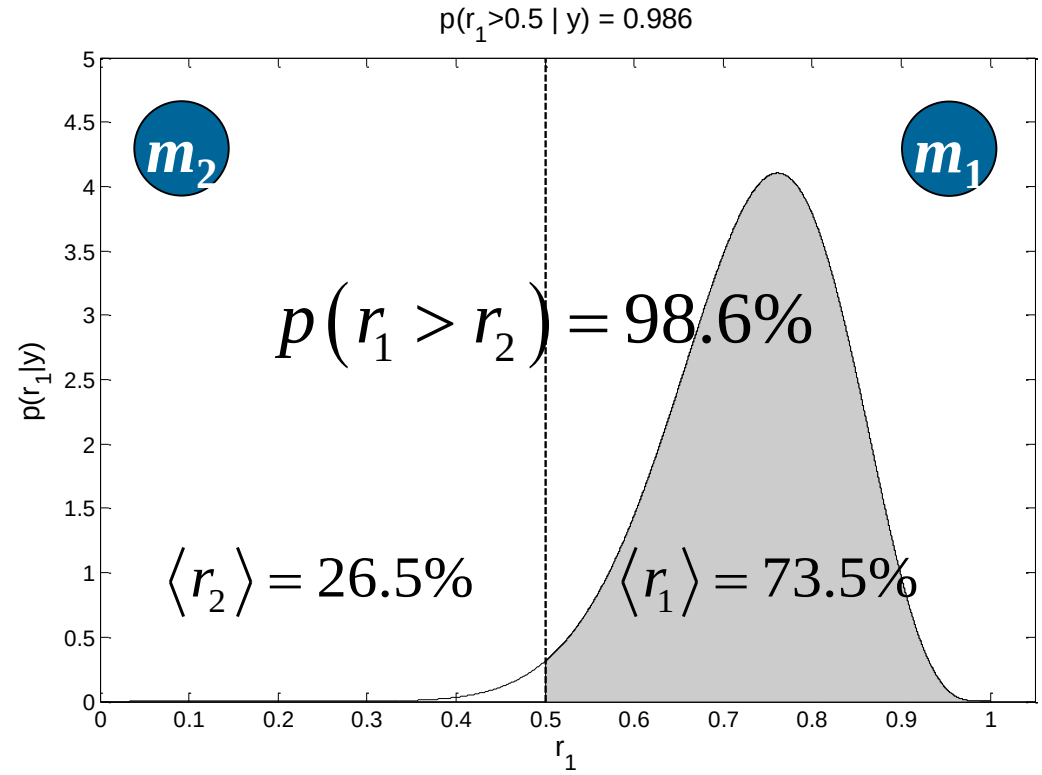
BMA:

$$p(\theta \mid y)$$

$$= \sum_m p(\theta \mid y, m) p(m \mid y)$$

Model space partitioning: comparing model families





Stephan et al. 2009, *NeuroImage*

Bayesian Model Averaging (BMA)

- abandons dependence of parameter inference on a single model and takes into account model uncertainty
- represents a particularly useful alternative
  - when none of the models (or model subspaces) considered clearly outperforms all others
  - when comparing groups for which the optimal model differs

single-subject BMA:

$$p(\theta \mid y)$$

$$= \sum_m p(\theta \mid y, m) p(m \mid y)$$

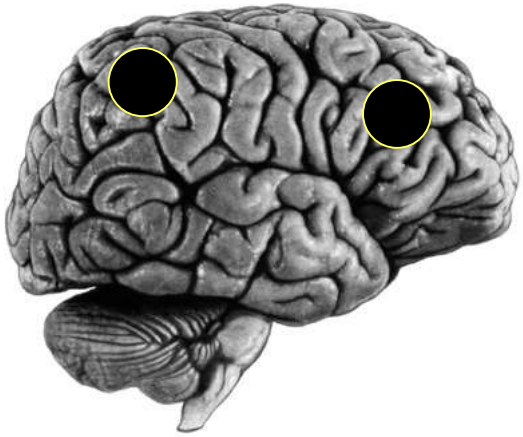
group-level BMA:

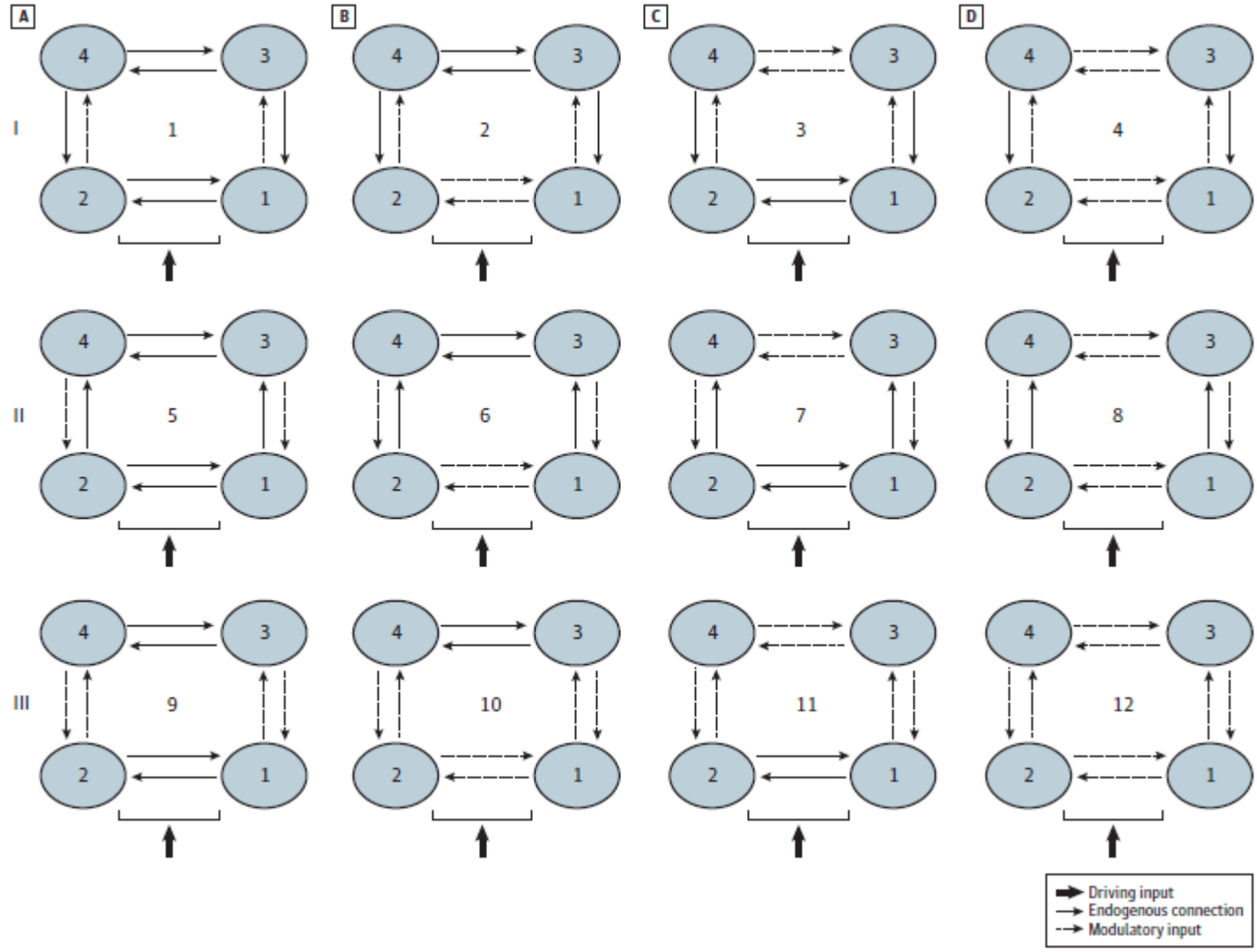
$$p(\theta_n \mid y_{1..N})$$

$$= \sum_m p(\theta_n \mid y_n, m) p(m \mid y_{1..N})$$

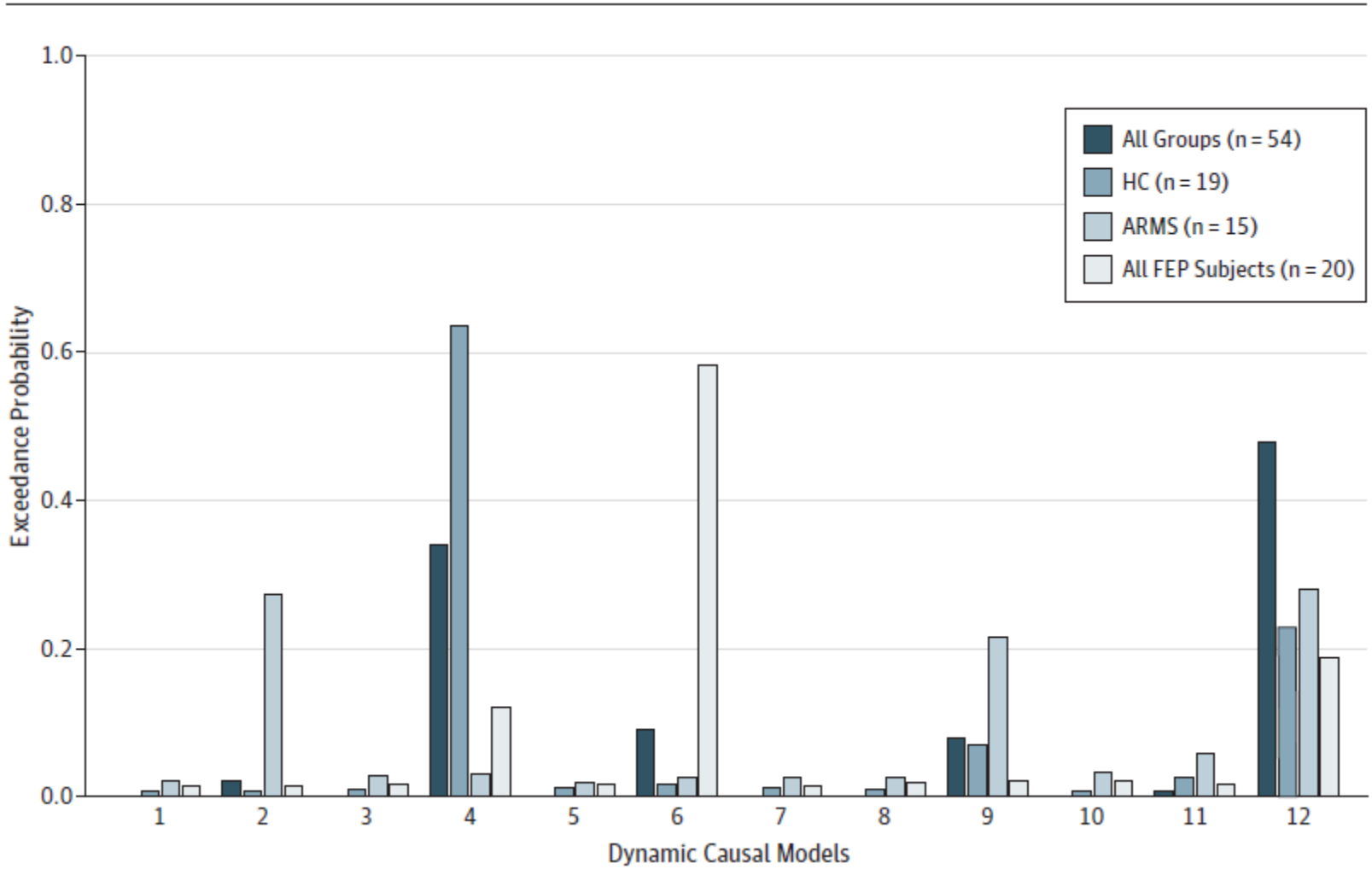
NB: $p(m|y_{1..N})$ can be obtained by either FFX or RFX BMS

Penny et al. 2010, *PLoS Comput. Biol.*



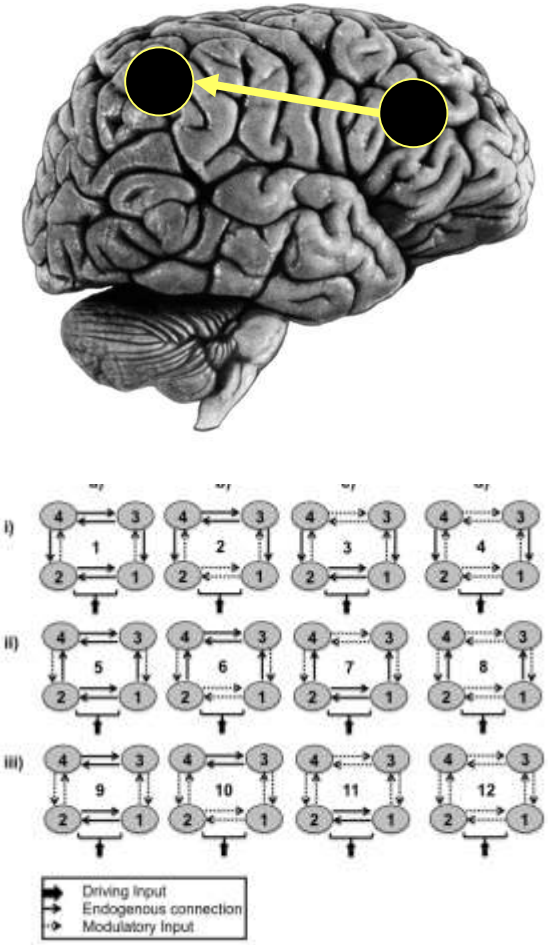


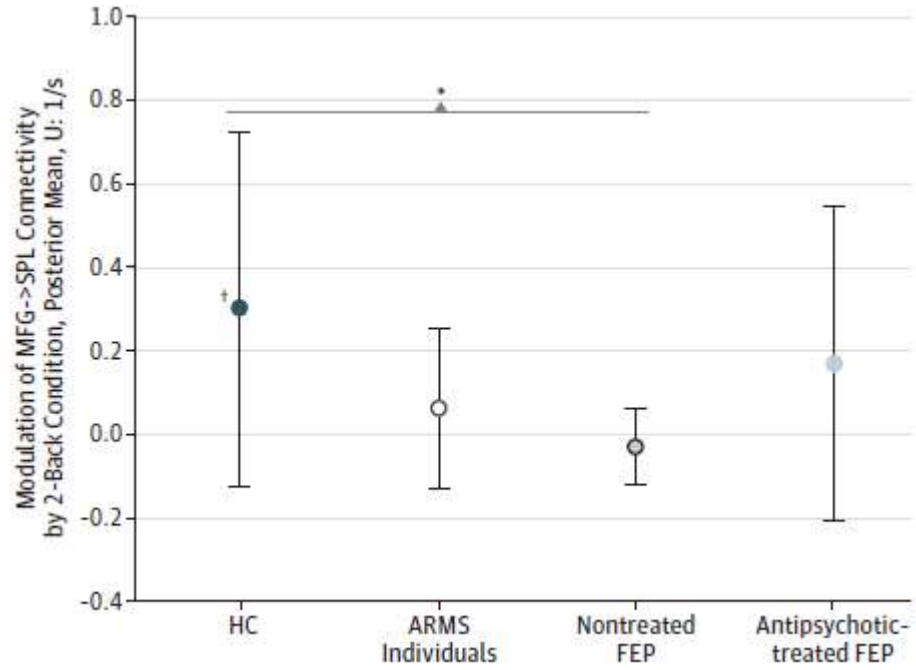
Schmidt et al. 2013, *JAMA Psychiatry*



Schmidt et al. 2013, *JAMA Psychiatry*

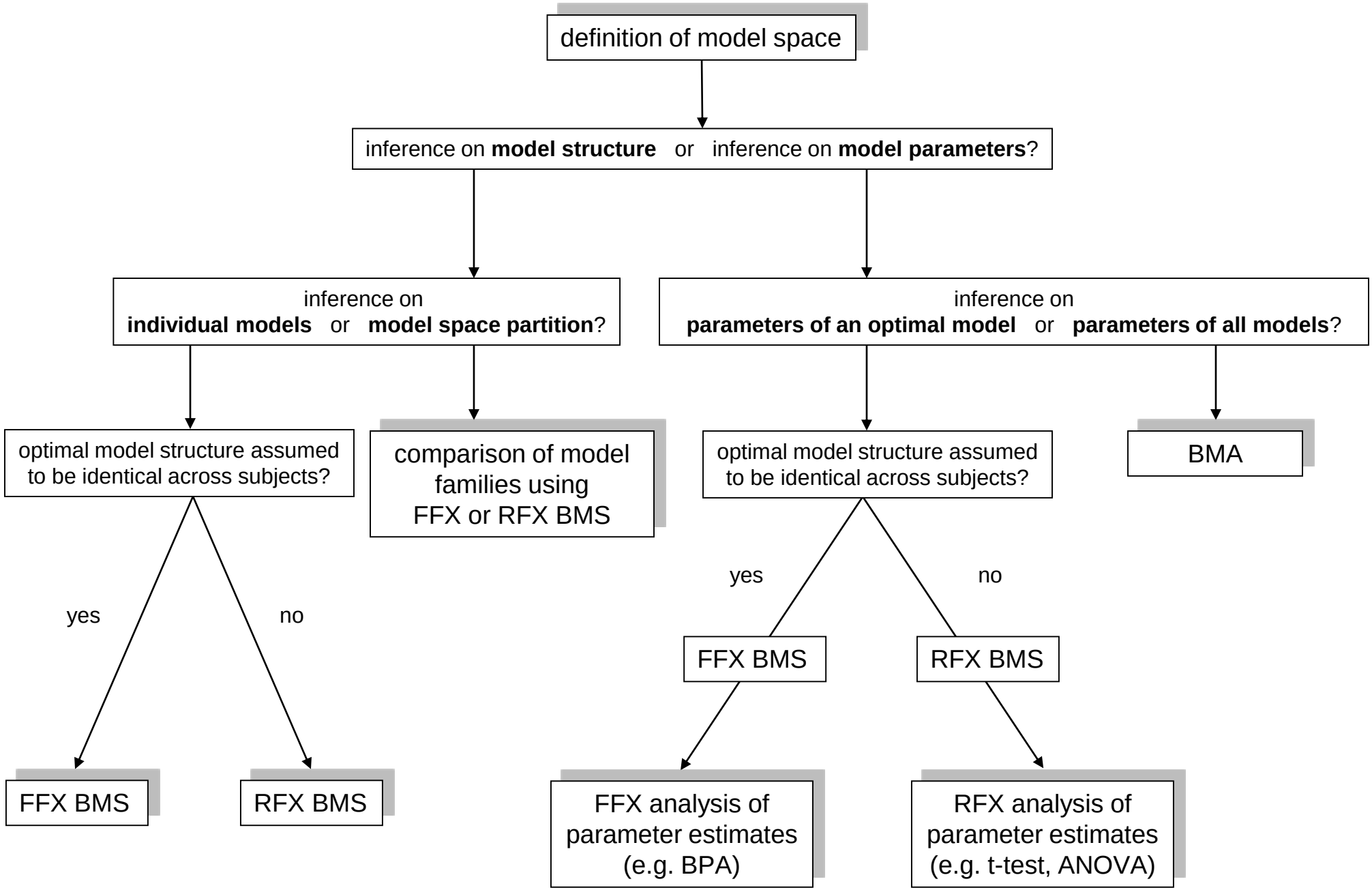
Prefrontal-parietal connectivity during working memory in schizophrenia





17 ARMS, 21 first-episode (13 non-treated), 20 controls

Schmidt et al. 2013, *JAMA Psychiatry*



Stephan et al. 2010, *NeuroImage*

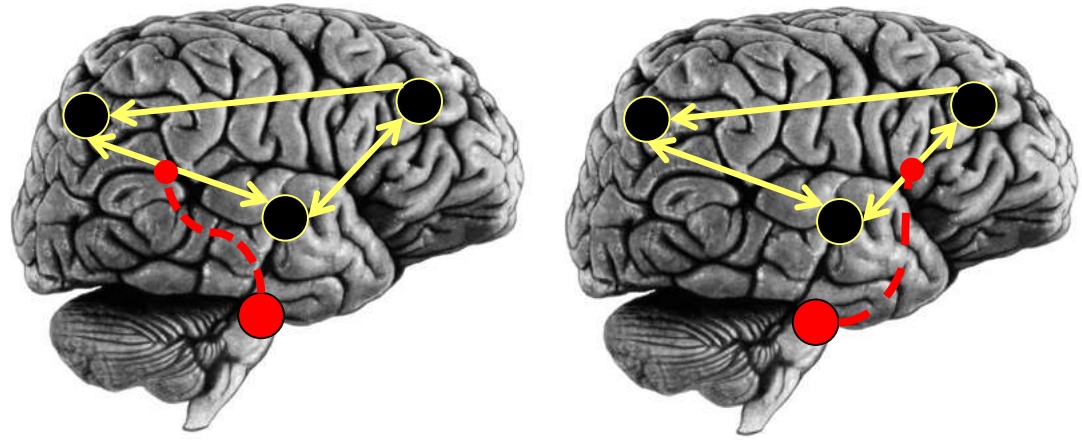
Overview

- DCM – a generative model
- Evolution of DCM for fMRI
- Bayesian model selection (BMS)
- Translational Neuromodeling

Model-based predictions for single patients

model structure

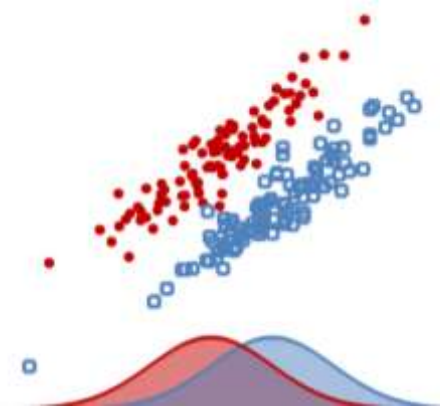
→ ***BMS***



DA

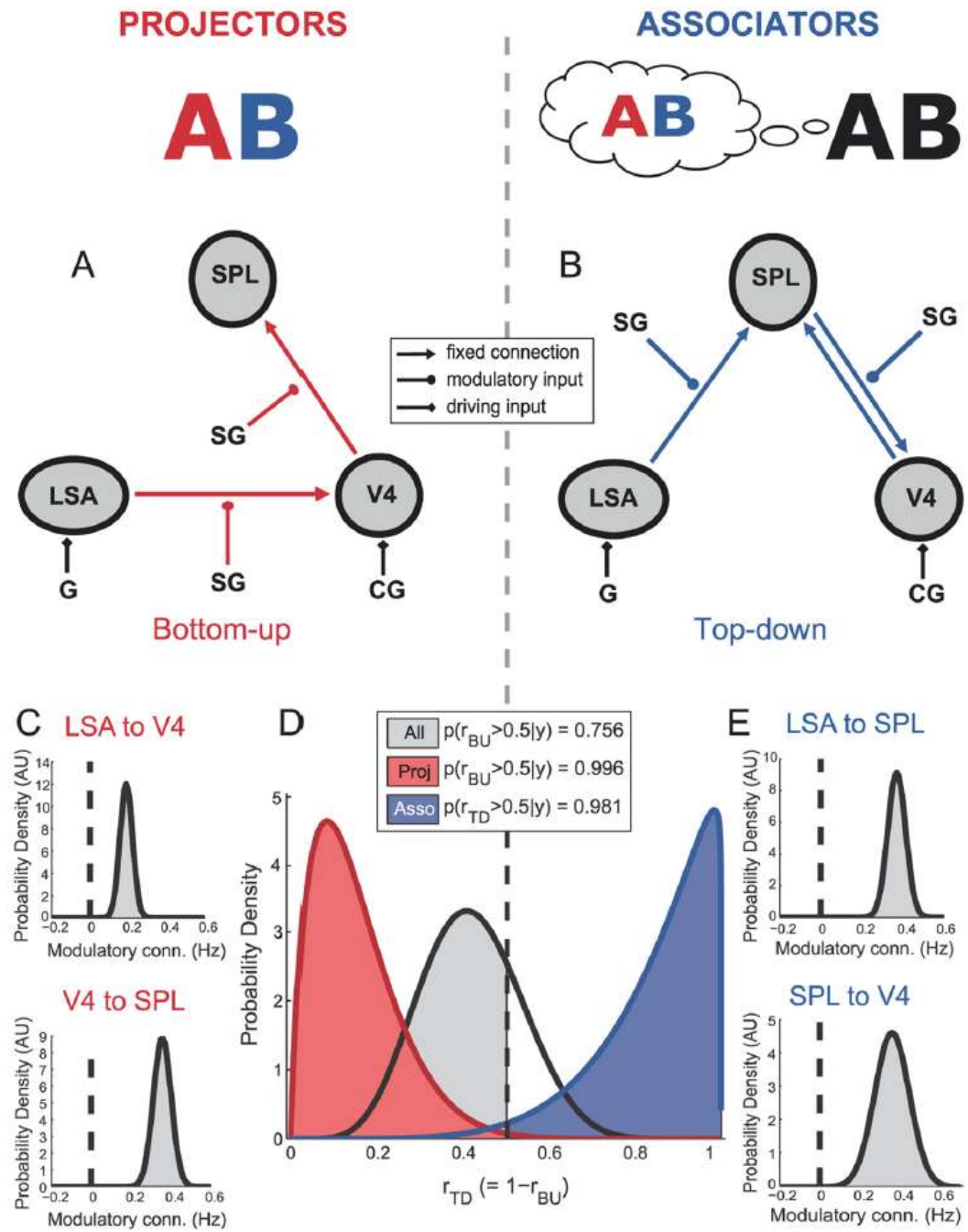
parameter estimates

→ ***generative embedding***



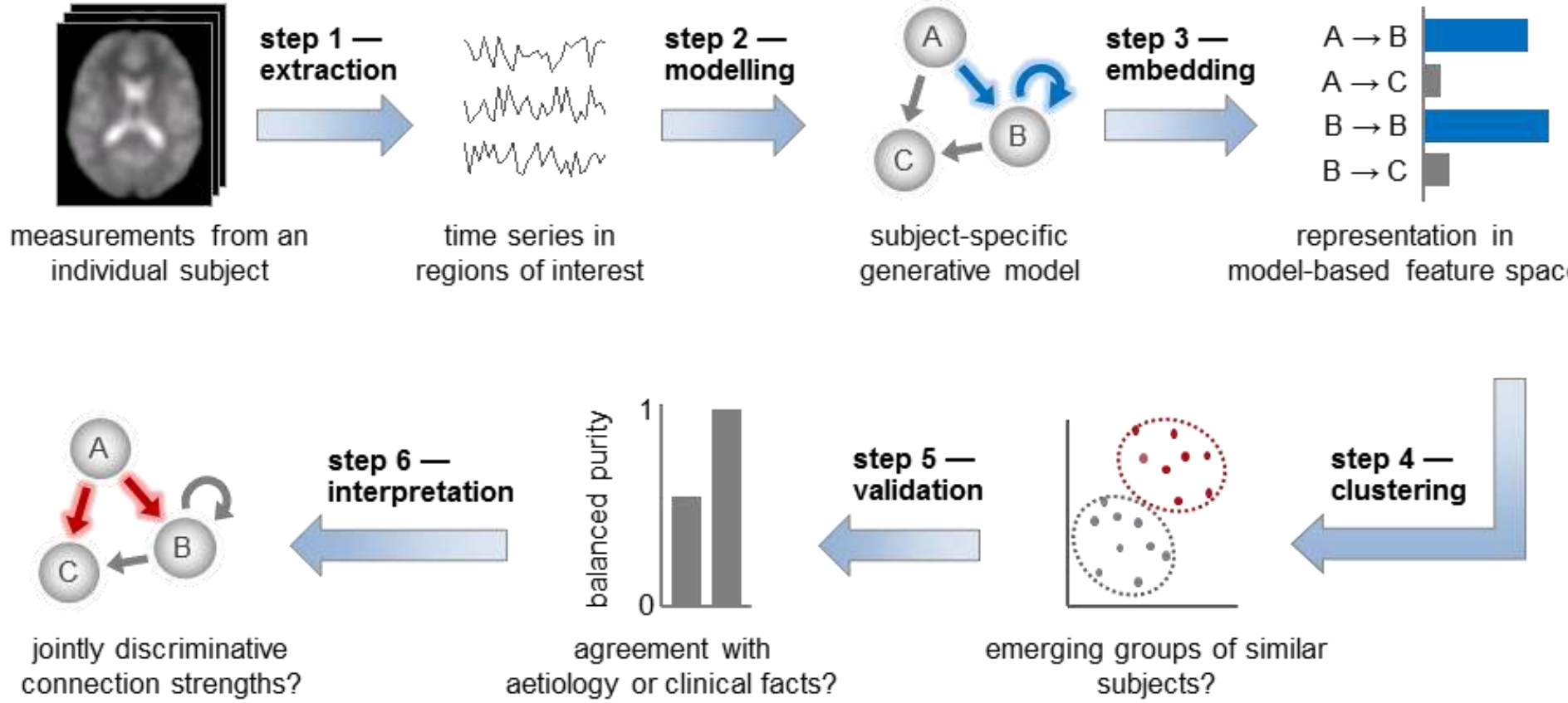
Synaesthesia

- “projectors” experience color externally colocalized with a presented grapheme
- “associators” report an internally evoked association
- across all subjects: no evidence for either model
- but BMS results map precisely onto projectors (bottom-up mechanisms) and associators (top-down)



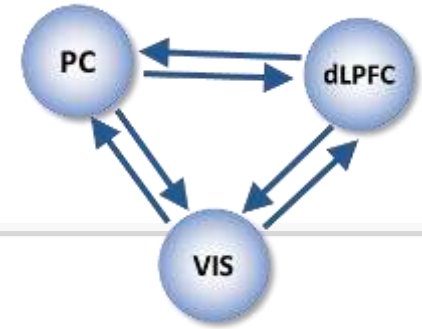
van Leeuwen et al. 2011, *J. Neurosci.*

Generative embedding (unsupervised): detecting patient subgroups

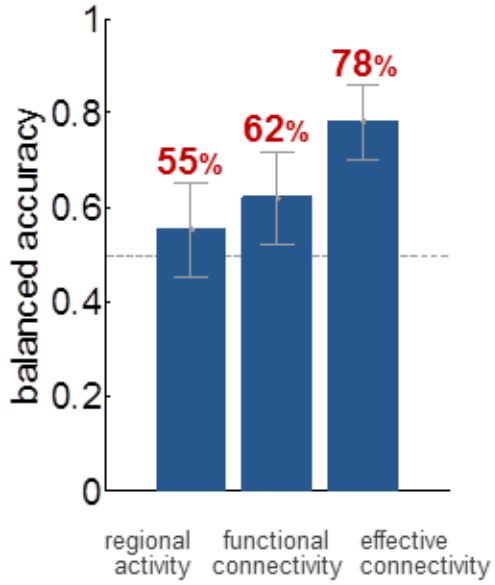


Brodersen et al. 2014, *NeuroImage: Clinical*

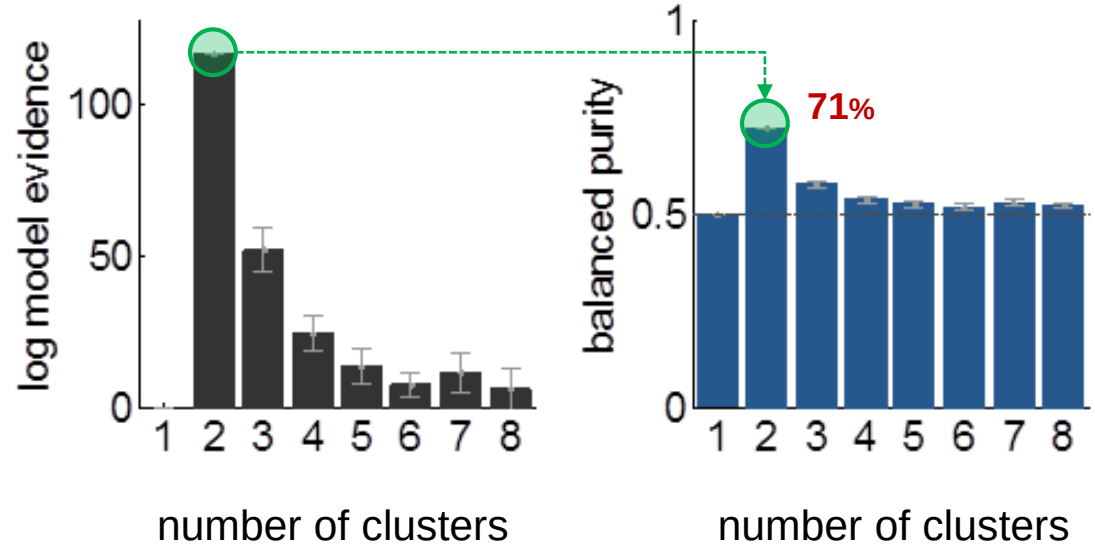
Generative embedding: DCM and variational Gaussian Mixture Models



Supervised:
SVM classification



Unsupervised:
GMM clustering

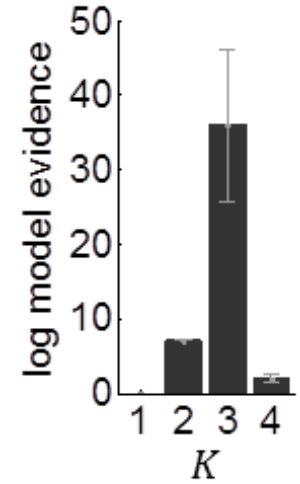


- 42 controls vs. 41 schizophrenic patients
- fMRI data from working memory task (Deserno et al. 2012, J. Neurosci)

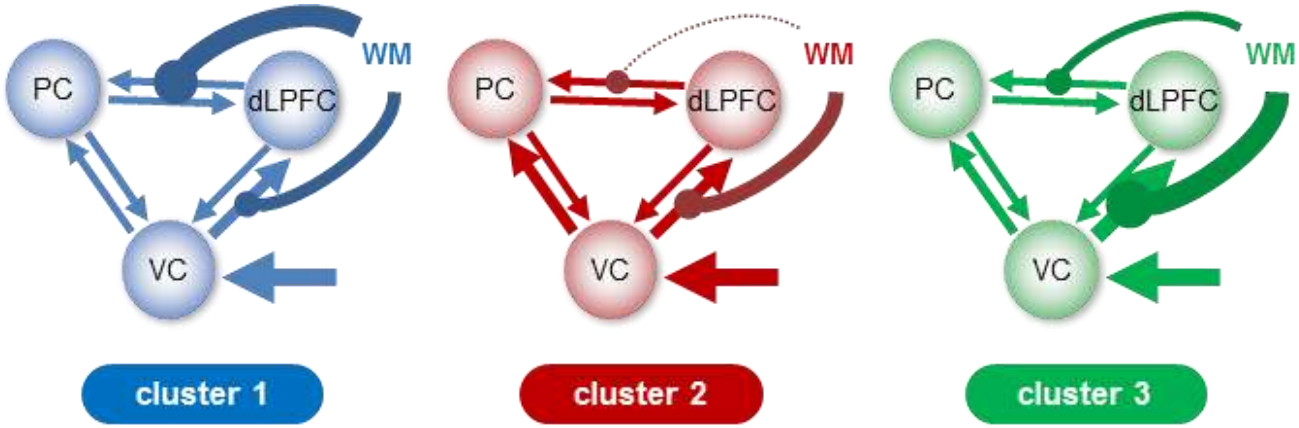
Brodersen et al. (2014) *NeuroImage: Clinical*

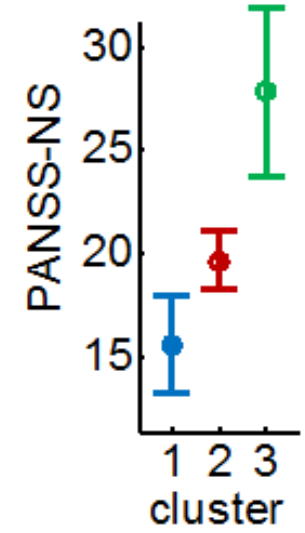
Detecting subgroups of patients in schizophrenia

Optimal cluster solution



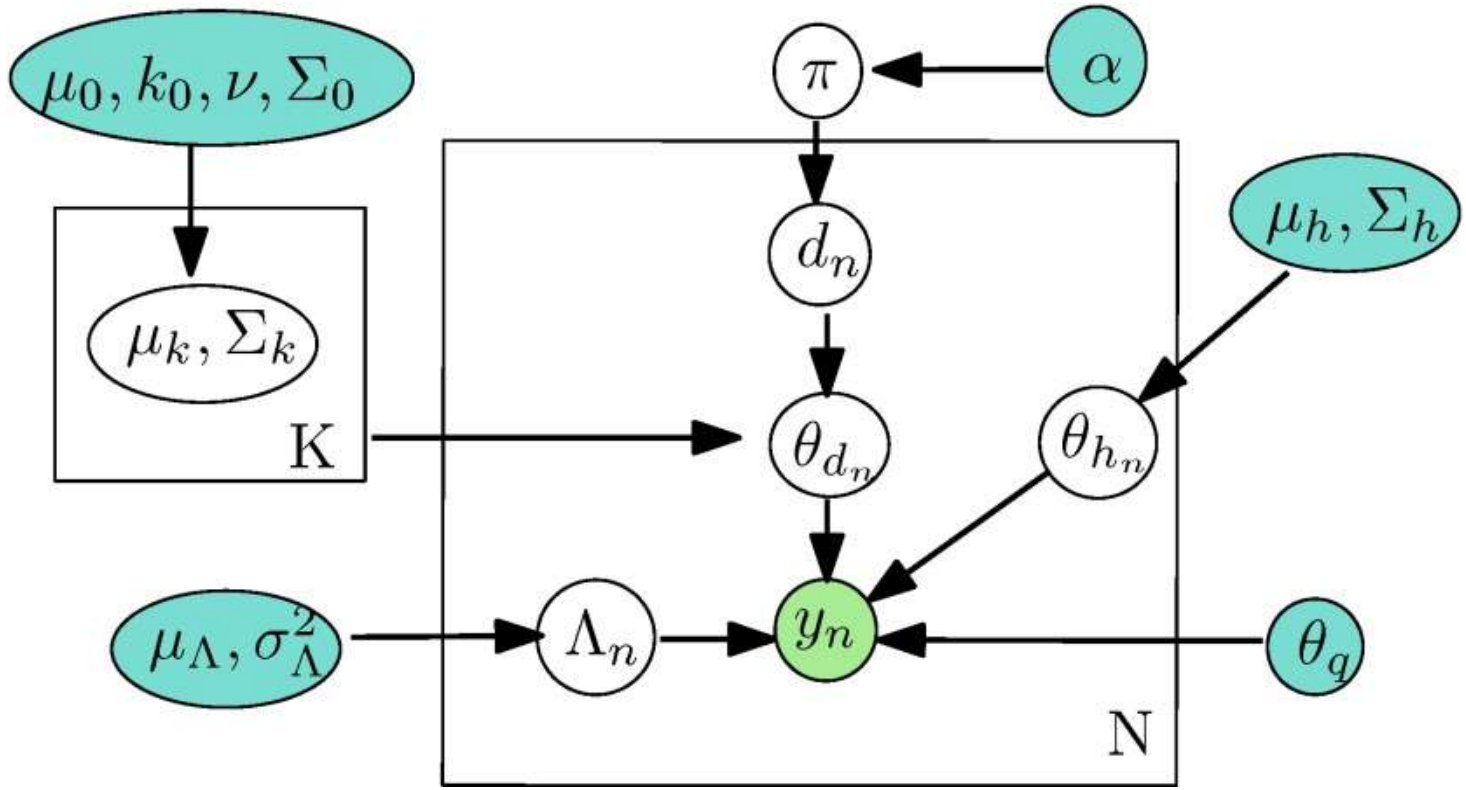
- three distinct subgroups (total N=41)
- subgroups differ ($p < 0.05$) wrt. negative symptoms on the *positive and negative symptom scale* (PANSS)



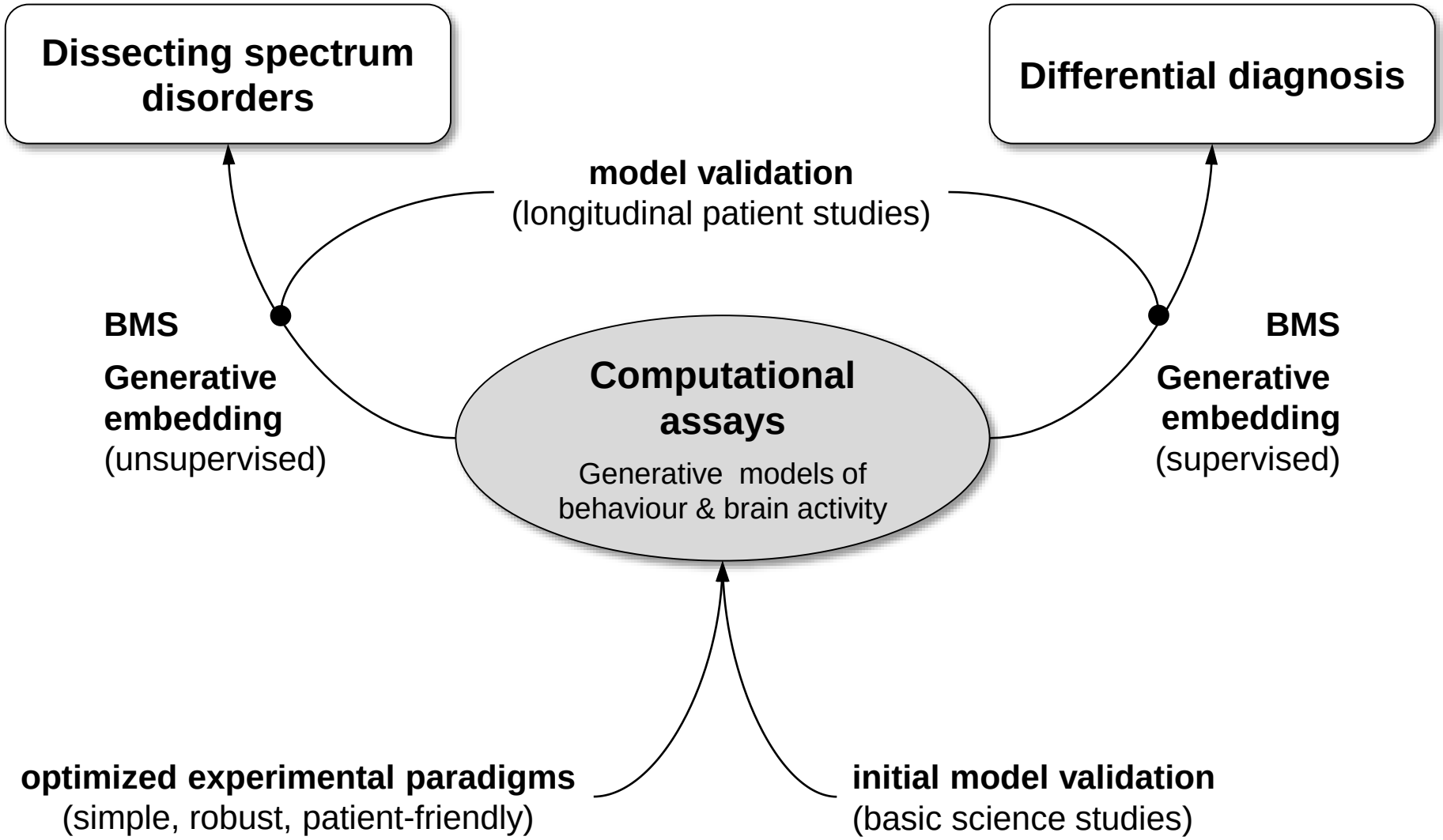


Brodersen et al. (2014) *NeuroImage: Clinical*

A hierarchical model for unifying unsupervised generative embedding and empirical Bayes



Raman et al., *submitted*



Stephan & Mathys 2014, *Curr. Opin. Neurobiol.*

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Thank you