Dynamic Causal Modelling

SPM for MRI Course, October 2017

Peter Zeidman
Wellcome Trust Centre for Neuroimaging,
University College London

Learning Objectives

By the end of today, you should be able to:

1. Place DCM in the fMRI analysis pipeline
2. State the difference between structural, functional and effective connectivity
3. Explain how a generative model helps to separate the BOLD signal into neuronal activity (effective connectivity), haemodynamics and noise.
4. Explain the interpretation of the parameters in the neuronal formula in DCM for fMRI
5. Explain how parameter estimates and the log model evidence are used to test hypotheses

Contents

- Overview of DCM
  - Effective connectivity, DCM framework, generative models
- Specific models for fMRI
  - Neural model, haemodynamic model
- Bayesian inference
  - Model inversion, parameter inference

Contents

- **Overview of DCM**
  - Effective connectivity, DCM framework, generative models
- Specific models for fMRI
  - Neural model, haemodynamic model
- Bayesian inference
  - Model inversion, parameter inference

Dynamic Causal Modelling

is a framework

for inferring systems / effective connectivity

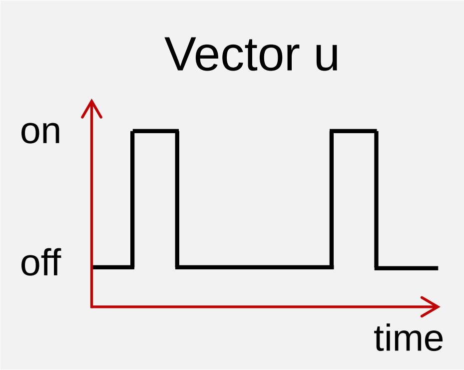
in the brain

The system of interest

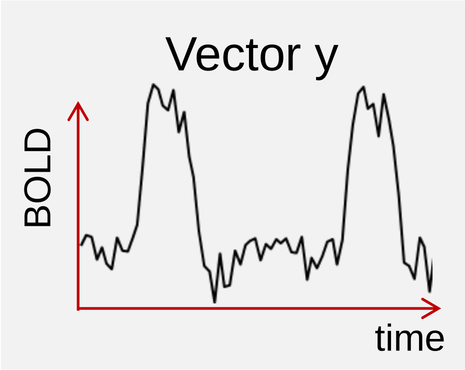
Experimental Stimulus

(Hidden) Neural Activity

Observations (BOLD)



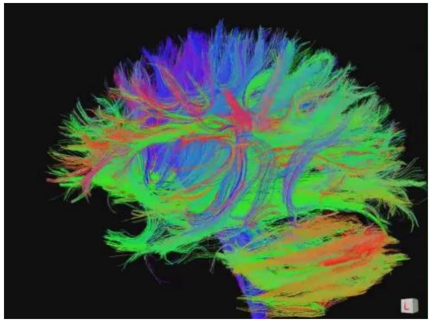
?



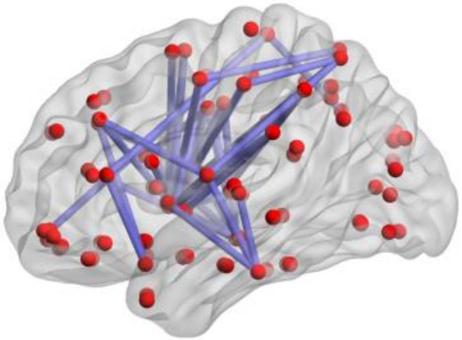
Stimulus from Buchel and Friston, 1997
Brain by Dierk Schaefer, Flickr, CC 2.0

Connectivity

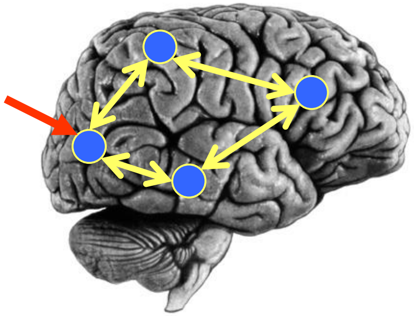
- Structural Connectivity
  Physical connections of the brain



- Functional Connectivity
  Dependencies between BOLD observations



- Effectivity Connectivity
  Causal relationships between brain regions



"Connectome" by jgmarcelino. CC 2.0 via Wikimedia Commons
Figure 1, Hong et al. 2013 PLOS ONE.
KE Stefan, SPM Course 2011

Where DCM sits in the pipeline

Functional MRI acquisition and image reconstruction

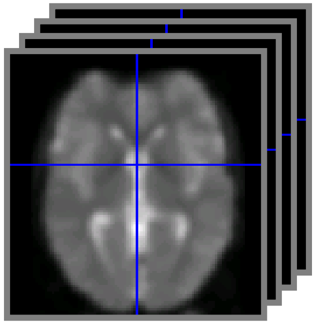
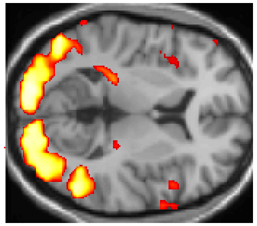
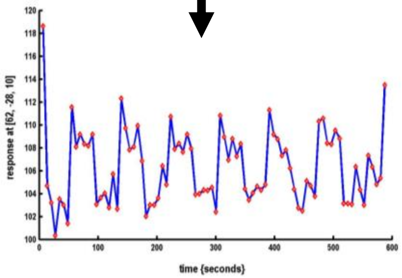


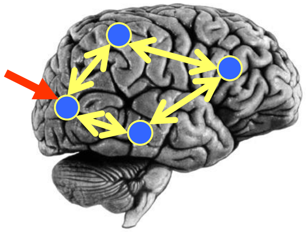
Image preprocessing (realignment, coregistration, normalisation, smoothing)



Statistical Parameter Mapping (SPM) / General Linear Model



Timeseries extraction from Regions of Interest (ROIs)

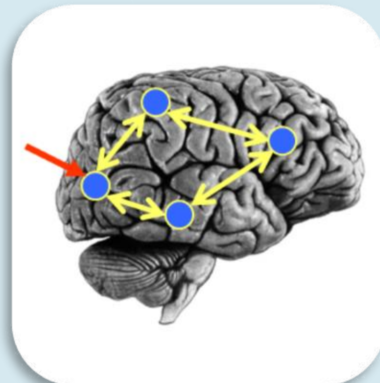


Dynamic Causal Modelling (DCM)

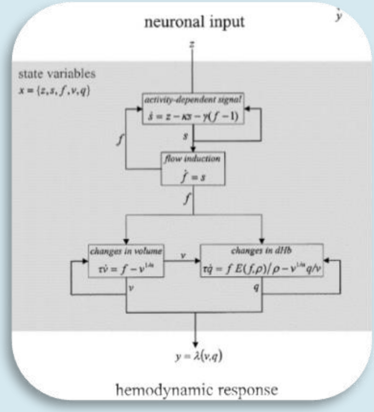
DCM Framework

Experimental Stimulus (u)

Neural Model



Observation Model



Observations (y)

How brain activity **z** changes over time

$$\dot{z} = f(z,u,\theta^n)$$

What we would see in the scanner, y, given the neural model?

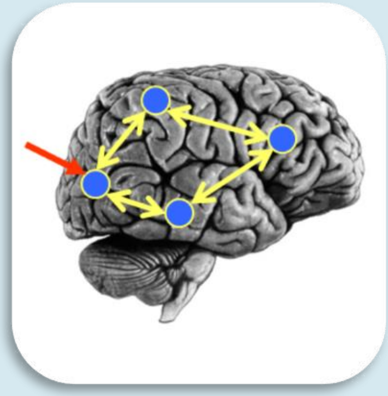
$$y = g(z, \theta^h)$$

Stimulus from Buchel and Friston, 1997
Figure 3 from Friston et al., Neuroimage, 2003

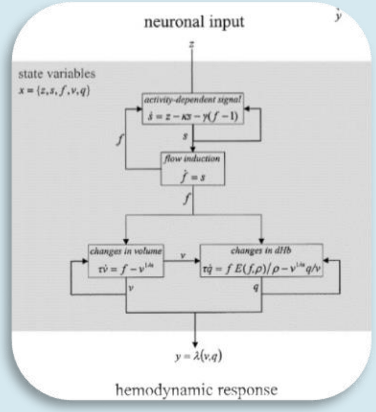
DCM Framework

Experimental Stimulus (u)

Neural Model



Observation Model



Observations (y)

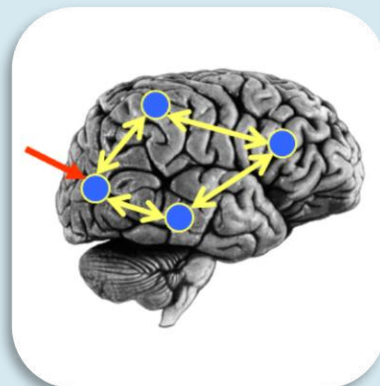
Generative model
p(u,y)

Stimulus from Buchel and Friston, 1997
Figure 3 from Friston et al., Neuroimage, 2003
Brain by Dierk Schaefer, Flickr, CC 2.0

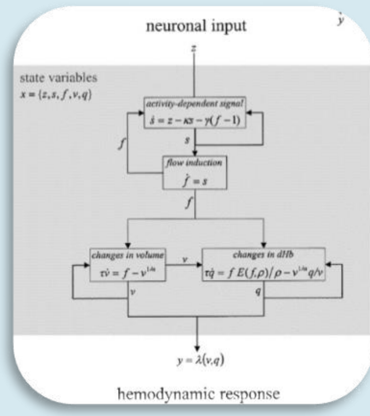
DCM Framework

Experimental Stimulus (u)

Neural Model



Observation Model



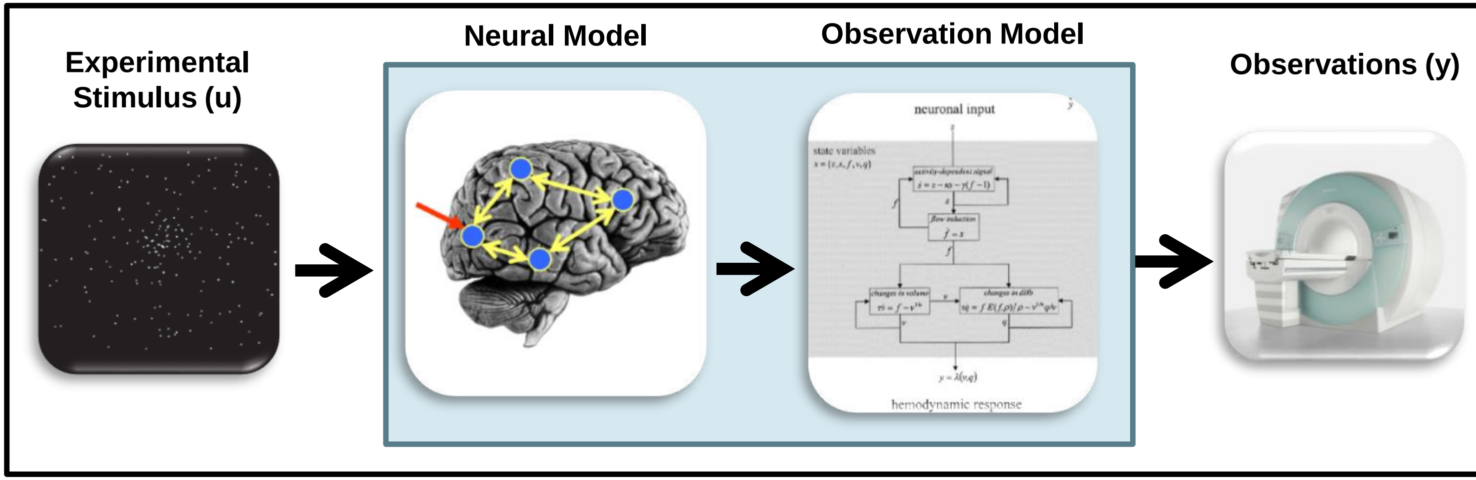
Observations (y)

Model Inversion
(Variational EM)

Given our observations y, and stimuli u, what parameters **θ** make the model best fit the data?

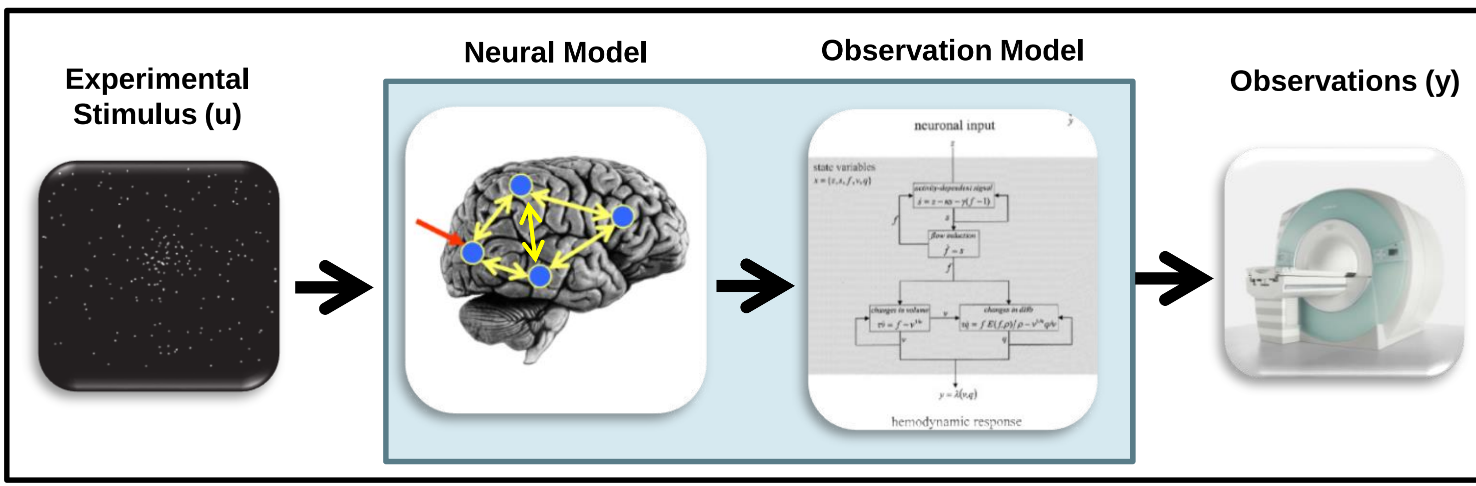
DCM Framework

Model 1:



Model comparison: Which model best explains my observed data?

Model 2:



DCM Framework

1. We embody each of our hypotheses in a generative model.

   The generative model separates neural activity from haemodynamics

2. We perform model estimation (inversion)

   This identifies parameters $\theta = \{\theta^n, \theta^h\}$ which make the model best fit the data. (Variational EM.)

3. We inspect the estimated parameters and / or we compare models to see which best explains the data.

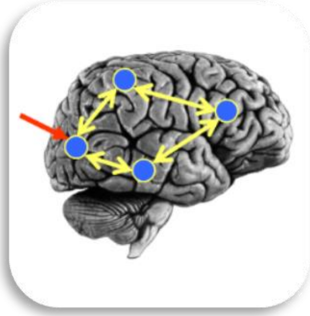
Contents

- Overview of DCM
  - Effective connectivity, DCM framework, generative models
- **Specific models for fMRI**
  - Neural model, haemodynamic model
- Bayesian inference
  - Model inversion, parameter inference

The Neural Model

The brain activity in each of n regions:

$$z = \begin{bmatrix} z_1 \\ \vdots \\ z_n \end{bmatrix}$$



The “response” of these regions is their change over time:

$$\dot{z} = \begin{bmatrix} \dot{z}_1 \\ \vdots \\ \dot{z}_n \end{bmatrix} = f(z, u, \theta)$$

Neural response function

Experimental input

Parameters (e.g. connection strengths)

The Neural Model

$$\dot{z} = \begin{bmatrix} \dot{z}_1 \\ \vdots \\ \dot{z}_n \end{bmatrix} = f(z, u, \theta)$$

Deterministic DCM for fMRI

Task

$$\dot{z} = (A + \sum_{j=1}^{m} u_j B^j)z + Cu$$

(Taylor approximation)

Friston et al., Neuroimage, 2003

DCM for CSD

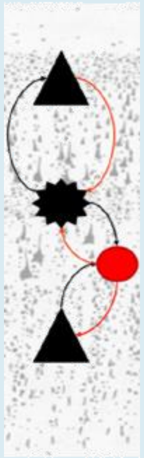
Resting State

$$\dot{z} = Az + v$$

Friston et al., Neuroimage, 2014

Canonical Microcircuit

Multi-modal data



Friston et al., Neuroimage, 2017

The Neural Model

$$\dot{z} = (A + \sum_{j=1}^{m} u_j B^j)z + Cu$$

Where does this come from?

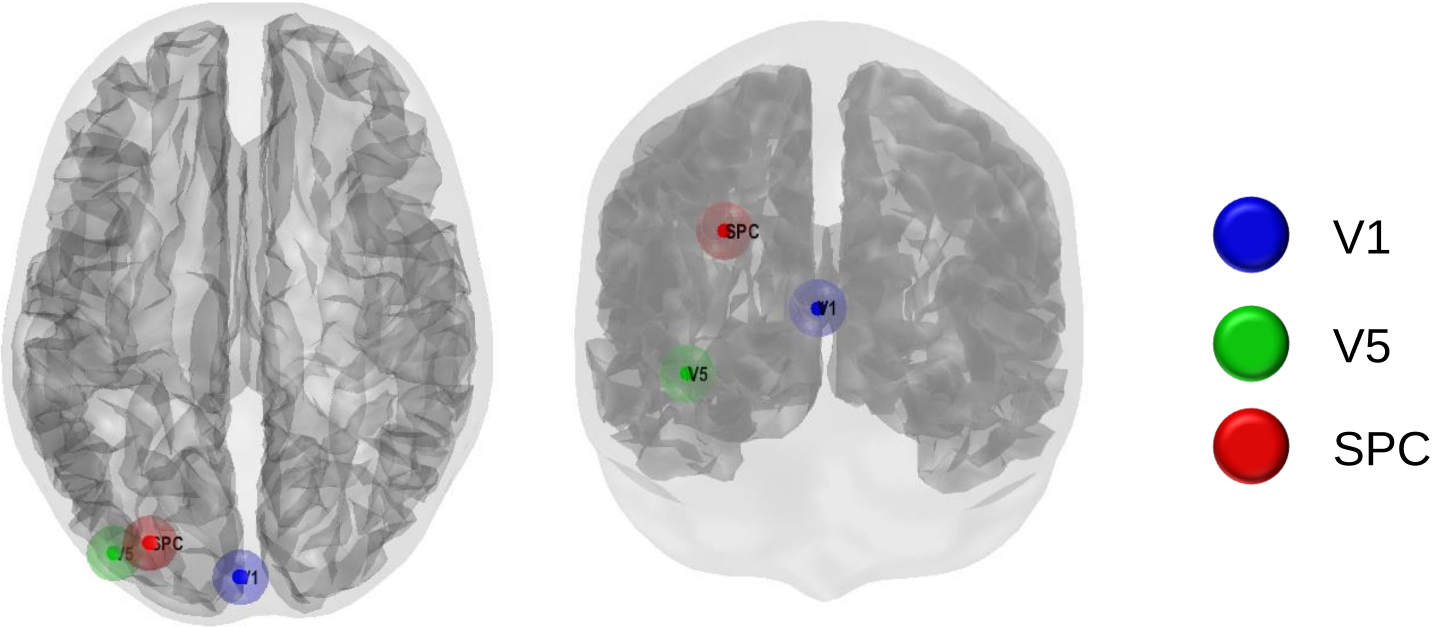
$$\begin{aligned}\dot{z} &= f(z,u) \\ &= f(z_0,u) + \frac{\delta f}{\delta z} z + \frac{\delta f}{\delta u} u + \frac{\delta^2 f}{\delta z \delta u} uz + \cdots \\ &\approx \left(A + \sum_j B^j u_j\right) + Cu\end{aligned}$$

Taylor series

The Neural Model

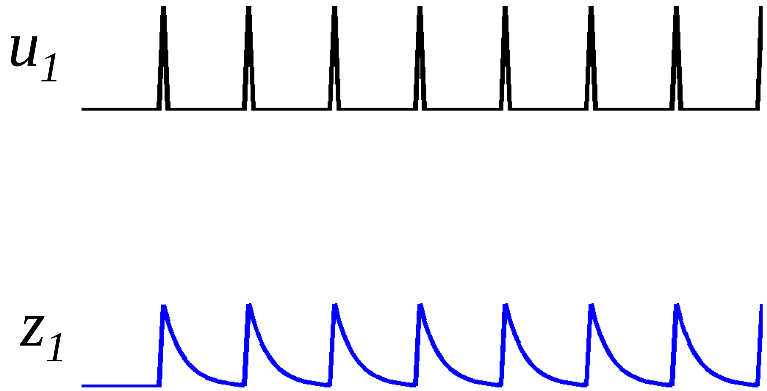
"How does brain activity, z, change over time?"

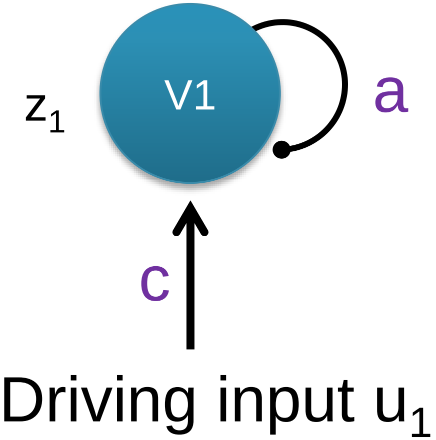
- Subjects viewed moving dots during fMRI
- On some trials, subjects were instructed to pay attention to the speed of the dots' motion
- Question: How does attention to motion change the strength of the connections between V1, V5 and Superior Parietal Cortex?



The Neural Model

"How does brain activity, z, change over time?"





$$\dot{z}_1 = az + cu_1$$

Inhibitory self-connection (Hz).
Rate constant: controls rate of decay in region 1. More negative = faster decay.

The Neural Model

"How does brain activity, z, change over time?"

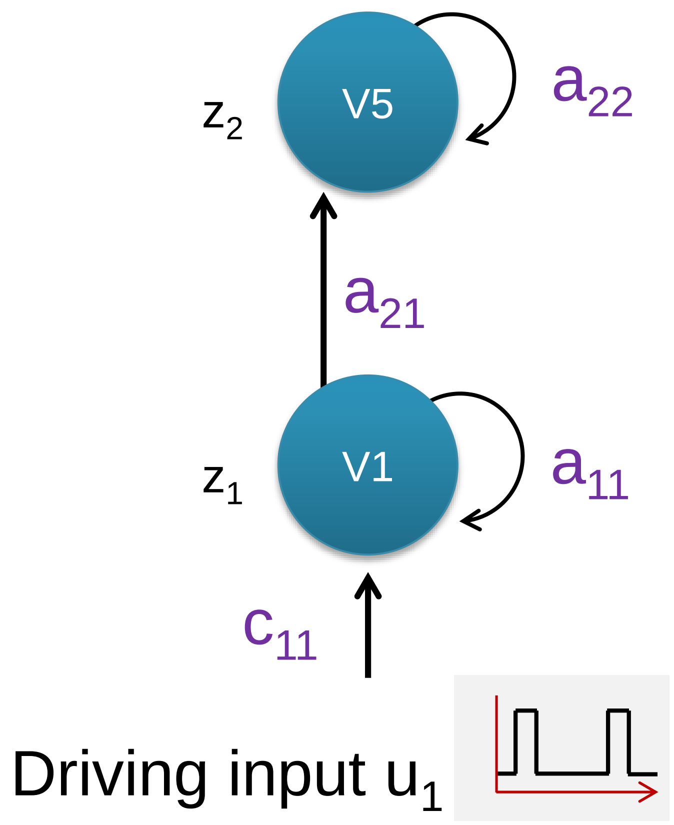
Change of activity in V1:

$$\dot{z}_1 = a_{11} z_1 + c_{11} u_1$$

Change of activity in V5:

$$\dot{z}_2 = a_{22} z_2 + a_{21} z_1$$

Self decay V1 input



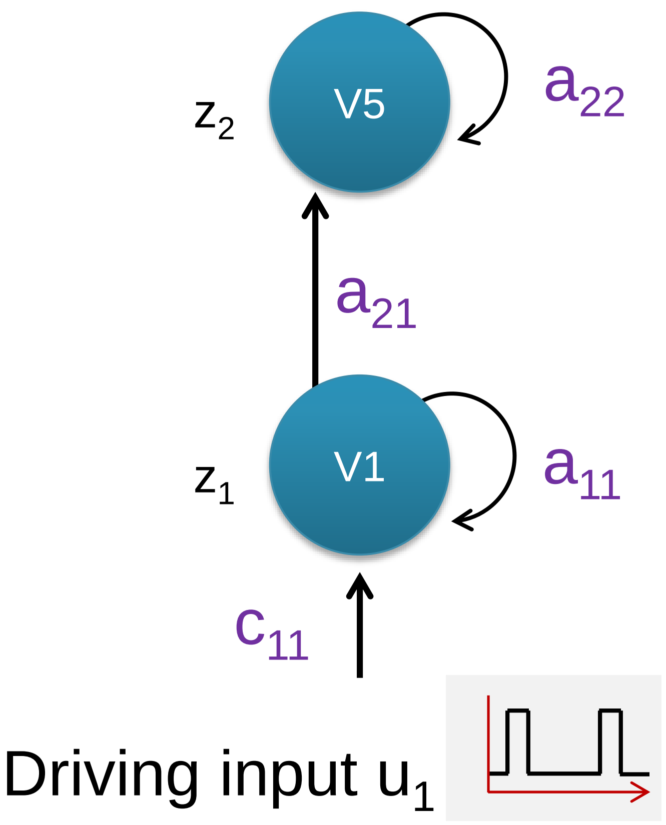
The Neural Model

"How does brain activity, z, change over time?"

$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = \begin{bmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} c_{11} \\ 0 \end{bmatrix} u_1$$

Columns are outgoing connections
Rows are incoming connections

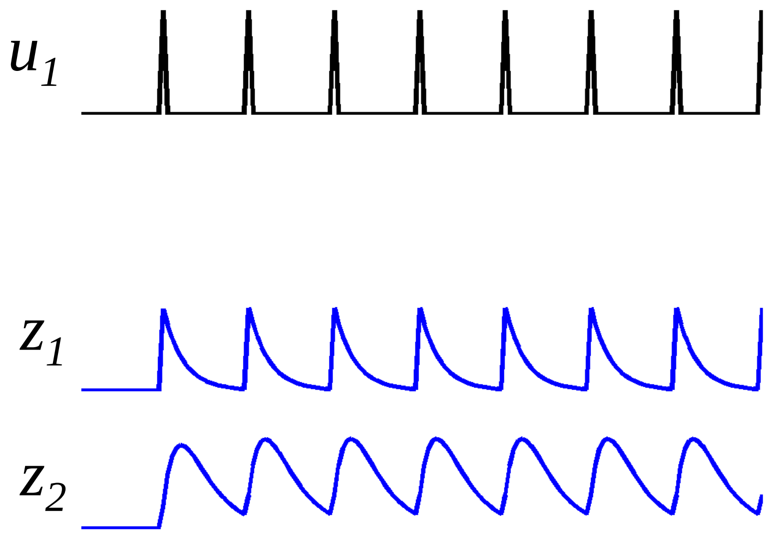
$$\dot{z} = Az + Cu_1$$

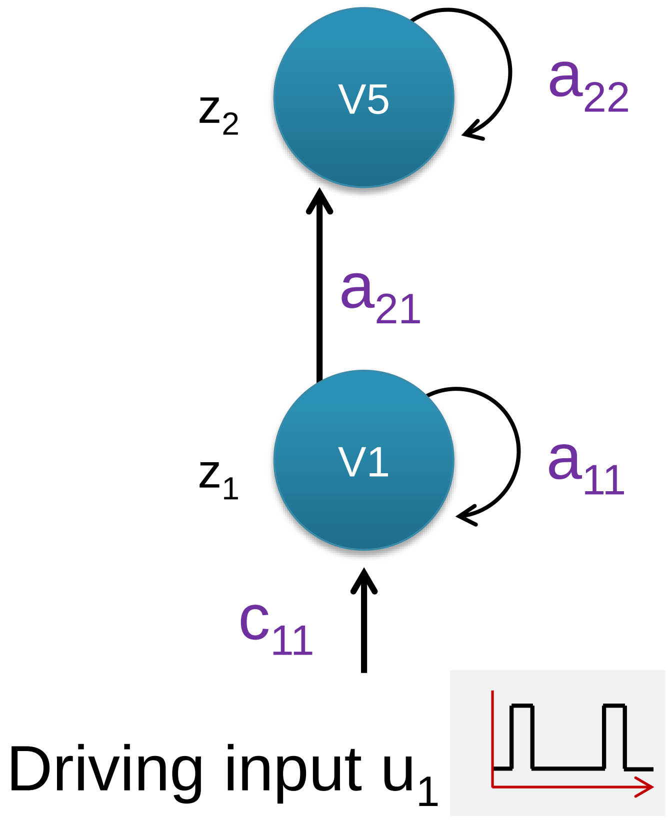


The Neural Model

"How does brain activity, z, change over time?"

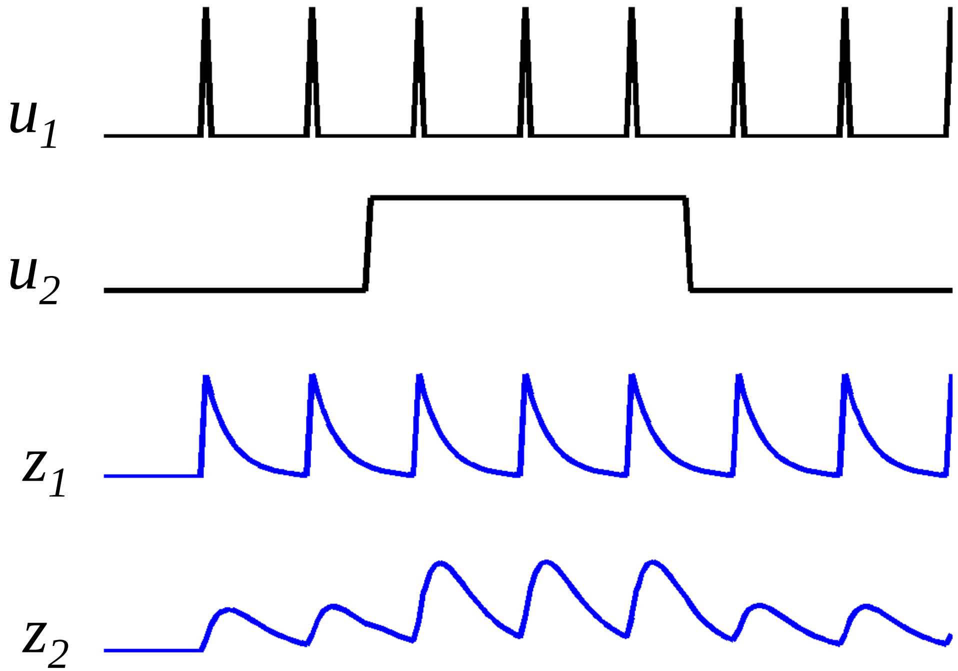
$$\dot{z} = Az + Cu_1$$

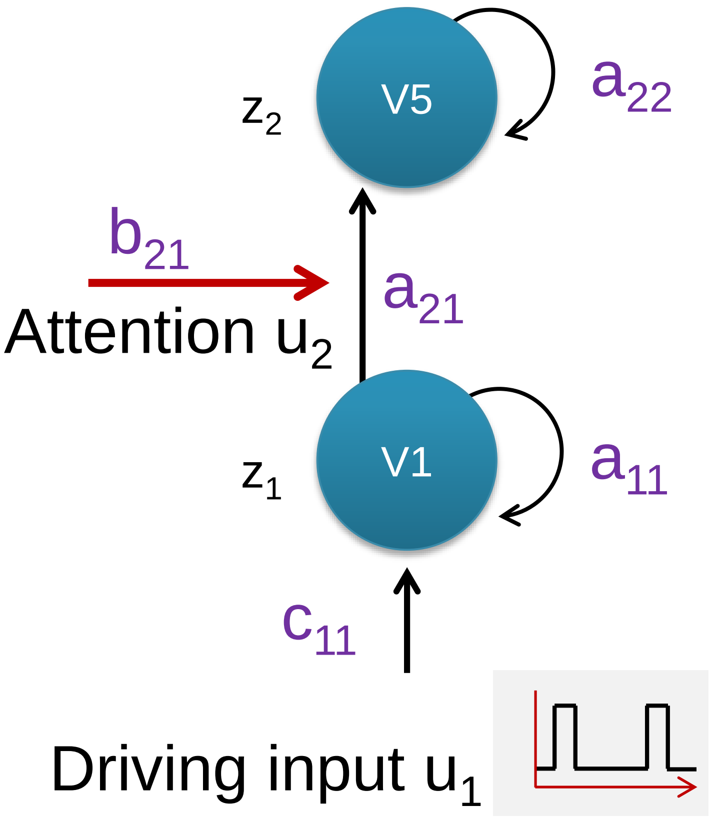




The Neural Model

"How does brain activity, z, change over time?"





Could model be used to model a main effect and interaction

The Neural Model

"How does brain activity, z, change over time?"

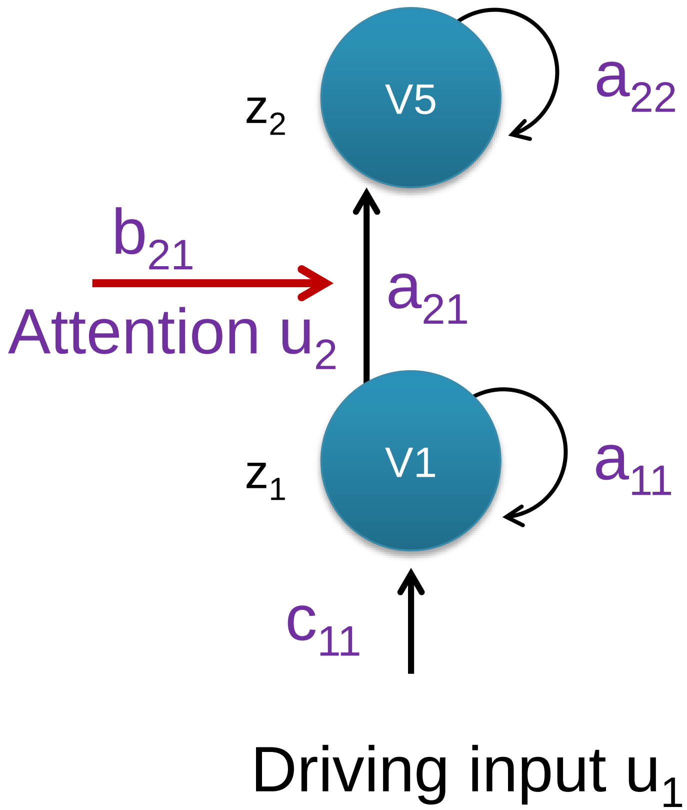
Change of activity in V1:

$$\dot{z}_1 = a_{11} z_1 + c_{11} u_1$$

Change of activity in V5:

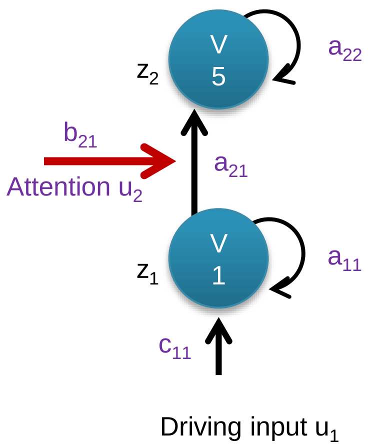
$$\dot{z}_2 = a_{22} z_2 + a_{21} z_1 + (b_{21} u_2) z_1$$

Self decay — V1 input — Modulatory input



The Neural Model

"How does brain activity, z, change over time?"



For m inputs:

$$\dot{z} = (A + \sum_{j=1}^{m} u_j B^j)z + Cu$$

Columns: outgoing connections
Rows: incoming connections

A: Structure — B: Modulatory Input — C: Driving Input

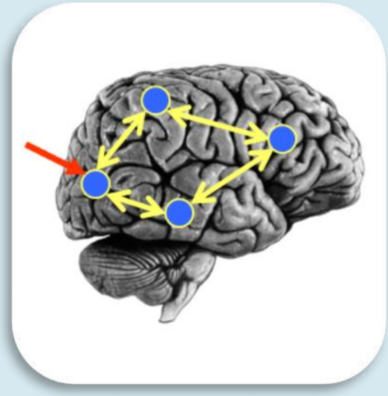
$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = \left(\begin{bmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ b_{21} & 0 \end{bmatrix} \right) \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

Change in activity per region — External input 2 (attention) — Current activity per region — All external input

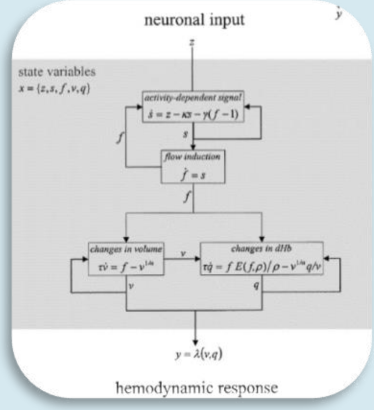
DCM Framework

Experimental Stimulus (u)

Neural Model



Observation Model



Observations (y)

How brain activity **z** changes over time

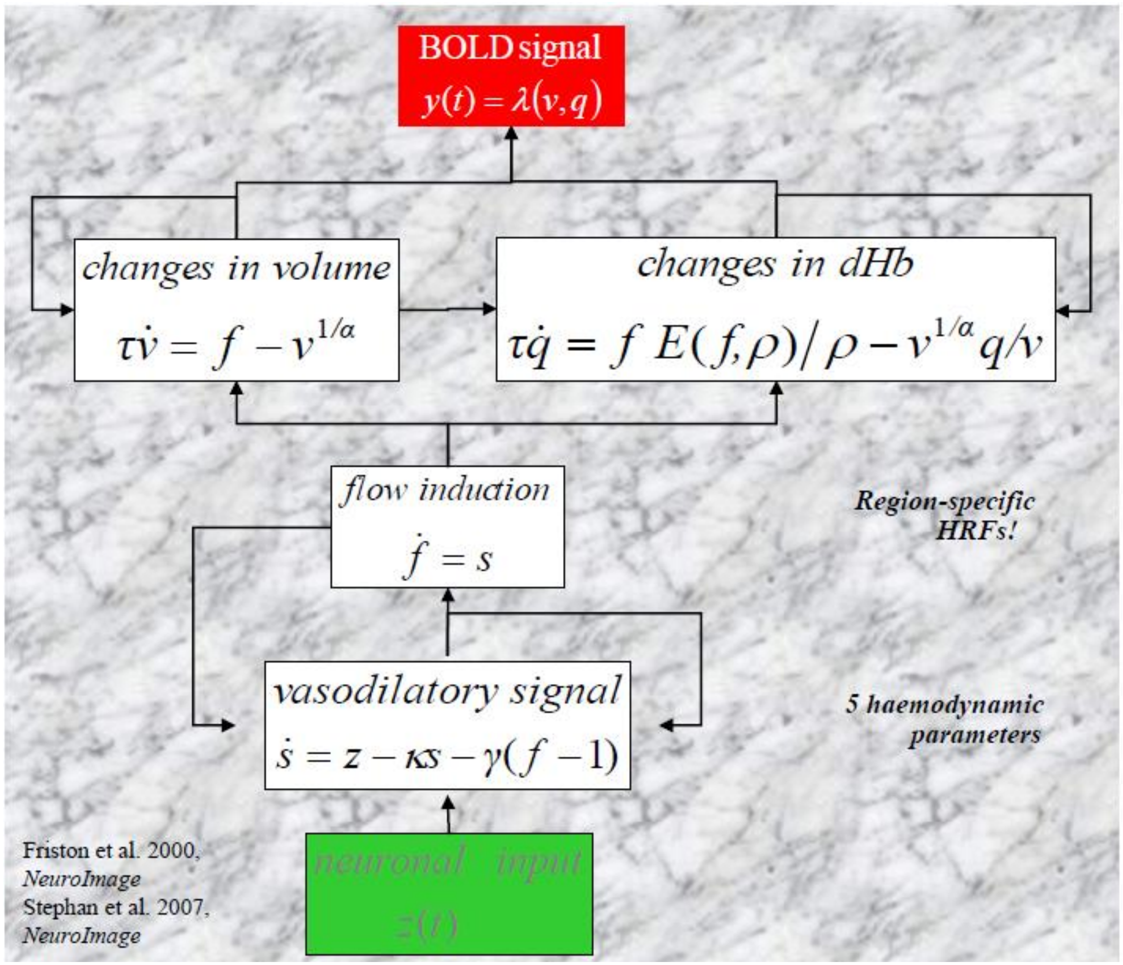
$$\dot{z} = f(z,u,\theta^n)$$

What we would see in the scanner, y, given the neural model?

$$y = g(z, \theta^h)$$

Stimulus from Buchel and Friston, 1997
Figure 3 from Friston et al., Neuroimage, 2003
Brain by Dierk Schaefer, Flickr, CC 2.0

The Haemodynamic Model



Contents

- Overview of DCM
  - Effective connectivity, DCM framework, generative models
- Specific models for fMRI
  - Neural model, haemodynamic model
- **Bayesian inference**
  - Model inversion, parameter inference

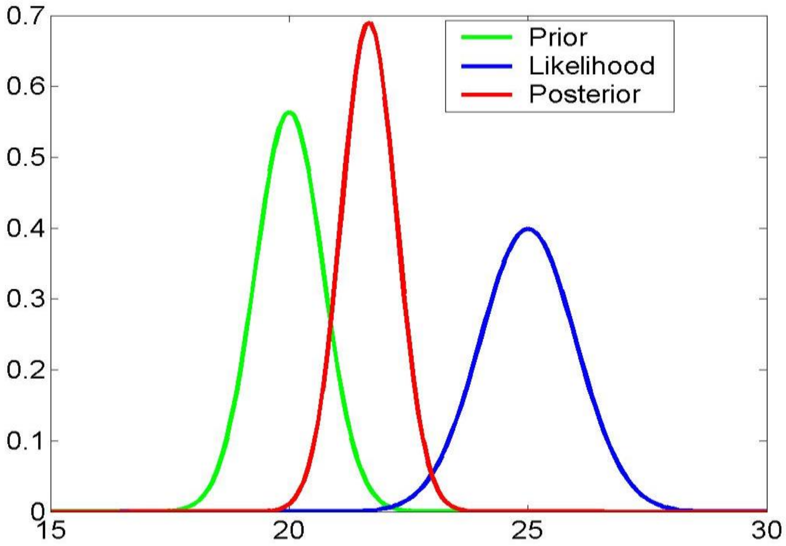
Bayesian Models

new data prior knowledge

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

posterior $\propto$ likelihood · prior

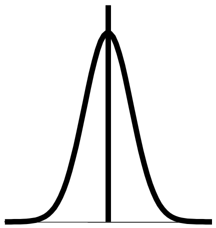
parameter estimates



Model estimation

Inverting or estimating the model gives:

1. Posterior probability distribution for each parameter $p(\theta|y,m)$



2. Estimation of the model evidence $p(y|m)$

$$F \cong \log p(y|m) = \text{accuracy} - \text{complexity}$$

Free energy

Bayes Factors

Assuming the prior probability on each model is equal, two models (i and j) can easily be compared using the Bayes factor B:

Ratio of model evidence

$$B_{ji} = \frac{p(y|m=j)}{p(y|m=i)}$$

Evidence for model j relative to i

$$B_{ij} = \frac{1}{B_{ji}}$$

Evidence for model i relative to j

Table 1
Interpretation of Bayes factors

B_{ij}	$p(m=i\|y)$ (%)	Evidence in favor of model i
1–3	50–75	Weak
3–20	75–95	Positive
20–150	95–99	Strong
≥150	≥99	Very strong

Bayes factors can be interpreted as follows. Given candidate hypotheses i and j, a Bayes factor of 20 corresponds to a belief of 95% in the statement 'hypothesis i is true'. This corresponds to strong evidence in favor of i.

From Raftery et al. (1995)

Note: The free energy approximates the log of the model evidence. So the log Bayes factor is:

$$\log \mathrm{B_{ji}} = \log p(y|m=j) - \log p(y|m=i) \approx F_j - F_i$$

Bayes Factors cont.

We might like to transform our Bayes factor into a posterior probability for each of models i and j . This is done using Bayes rule (assuming equal priors per model):

$$p(m=i|y) = \frac{p(y|m=i)}{p(y)}$$

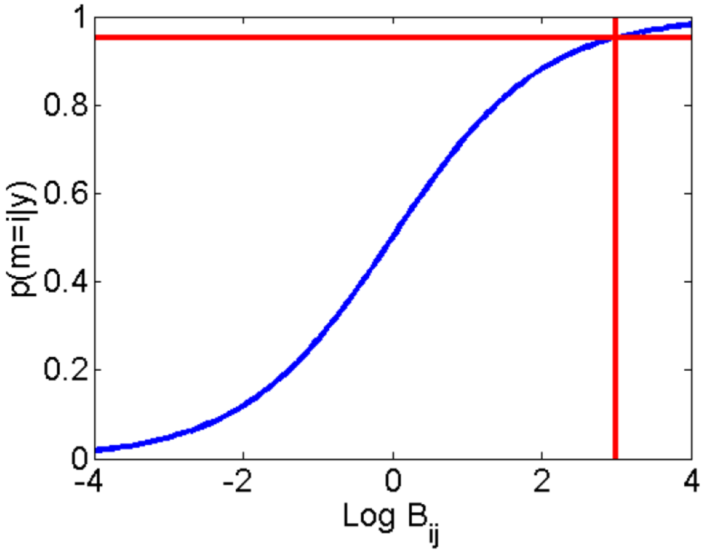
$$= \frac{p(y|m=i)}{p(y|m=i)+p(y|m=j)}$$

$$= \frac{1}{1+\frac{p(y|m=j)}{p(y|m=i)}}$$

$$= \frac{1}{1+B_{ji}}$$

$$= \frac{1}{1+\exp(\log(B_{ji}))}$$

$$= \frac{1}{1+\exp(-\log(B_{ij}))}$$

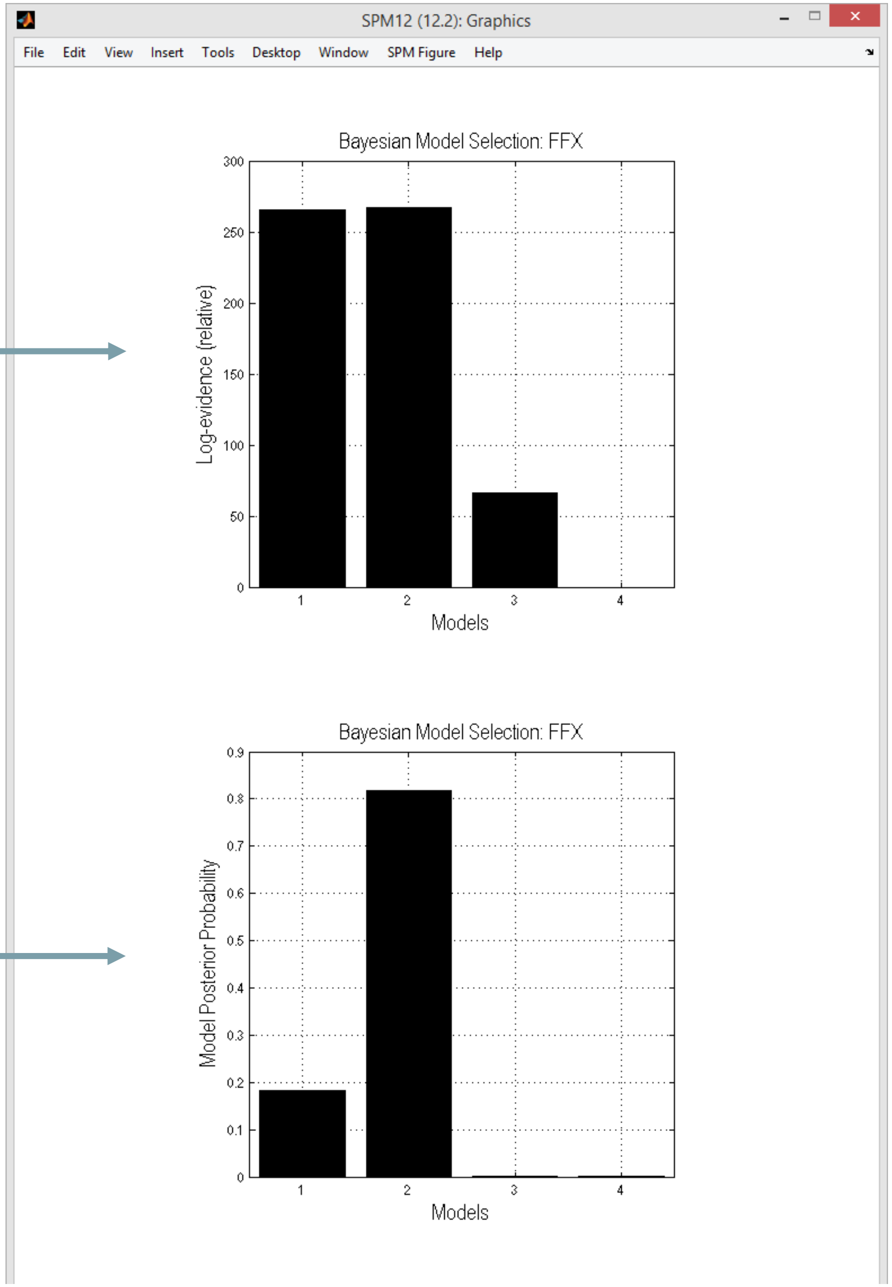


Posterior probability of a model is
the sigmoid function of the log Bayes factor

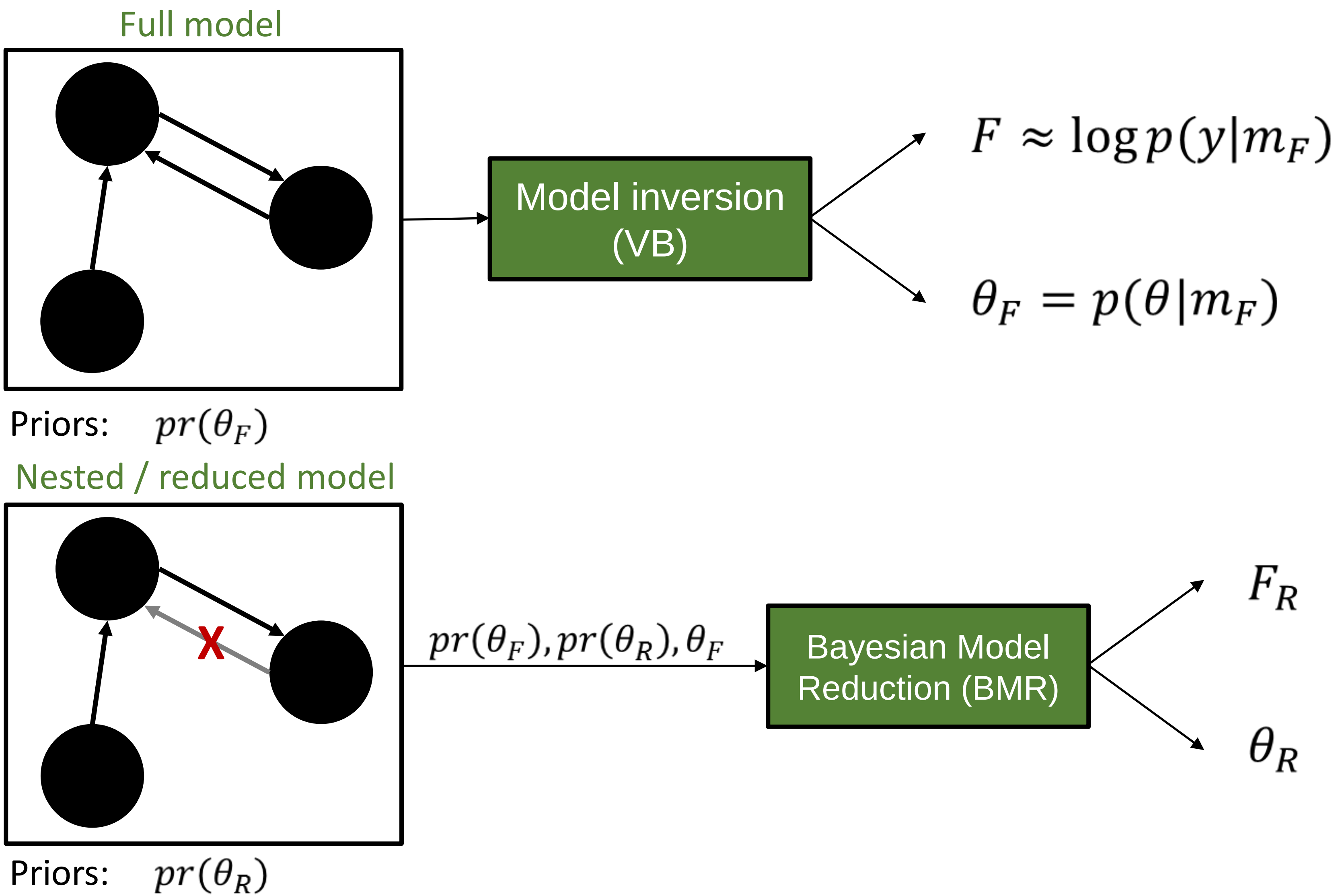
Log BF relative to worst model

$$F^{(1)} - F^{(4)}$$
$$F^{(2)} - F^{(4)}$$
$$F^{(3)} - F^{(4)}$$
$$F^{(4)} - F^{(4)}$$

Posterior probabilities



Bayesian Model Reduction



Summary

- DCM is a framework which enables us to make inferences about the effective connectivity of brain regions, which we can’t directly observe

- We create one or more generative models, each expressing a hypothesis

- We invert the model(s), using Bayesian inference to estimate coupling parameters and the model evidence

- We compare models using Bayesian Model Selection

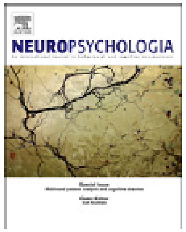
EXAMPLE

Neuropsychologia 50 (2012) 3621–3635

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

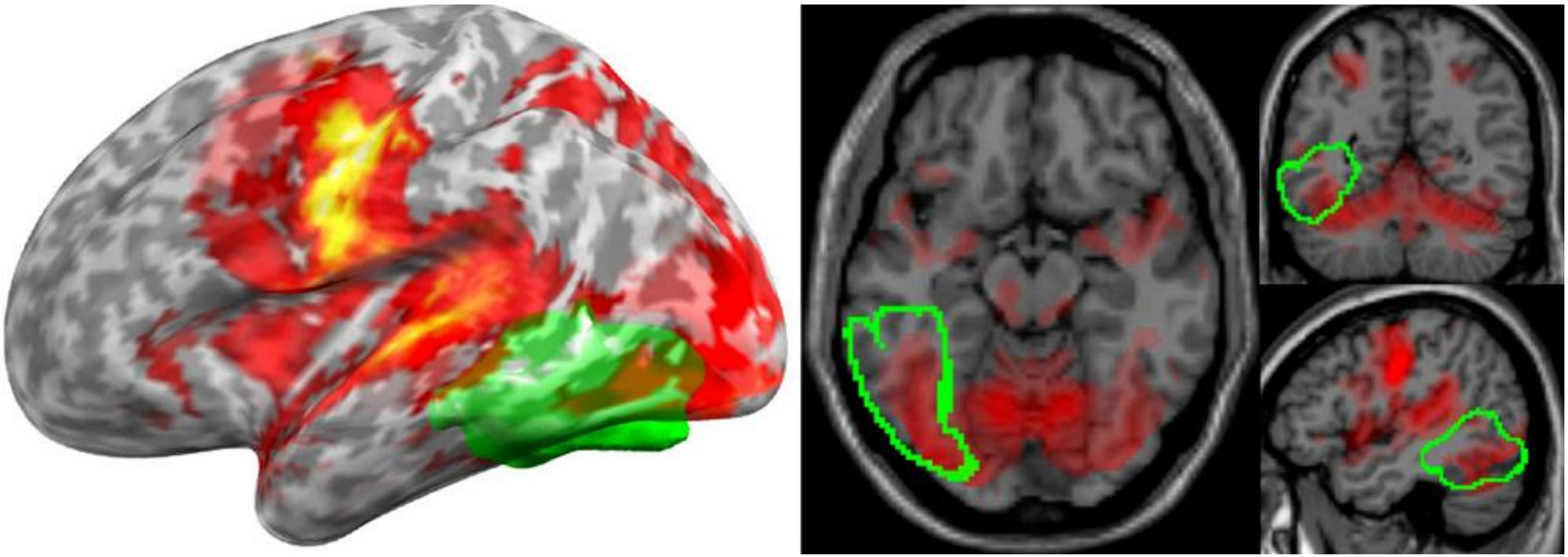


Research Report

Reading without the left ventral occipito-temporal cortex

Mohamed L. Seghier [a,*], Nicholas H. Neufeld [a,b], Peter Zeidman [a], Alex P. Leff [a], Andrea Mechelli [c], Arjuna Nagendran [a], Jane M. Riddoch [d], Glyn W. Humphreys [d,e], Cathy J. Price [a]

[a] Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, London WC1N 3BG, UK
[b] University of Toronto, Toronto, ON, Canada M5S 1A8
[c] Institute of Psychiatry, King's College London, London SE5 8AF, UK
[d] School of Psychology, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK
[e] Department of Experimental Psychology, Oxford University, Oxford OX3 9DU, UK



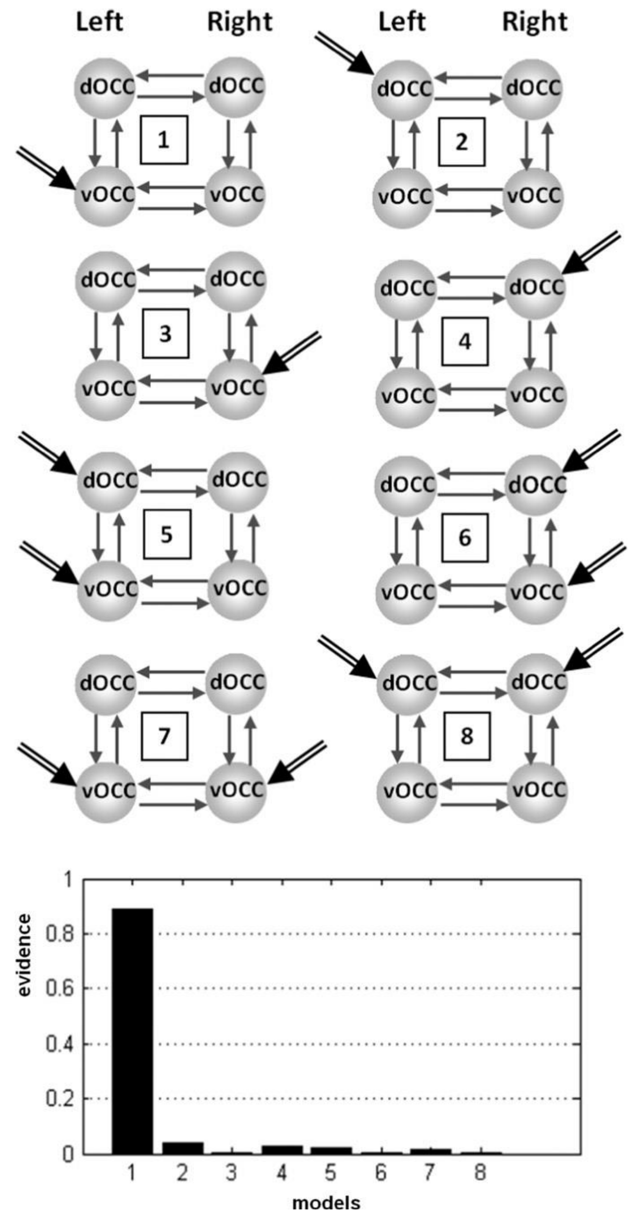
Reading > fixation (29 controls)

Lesion (Patient AH)

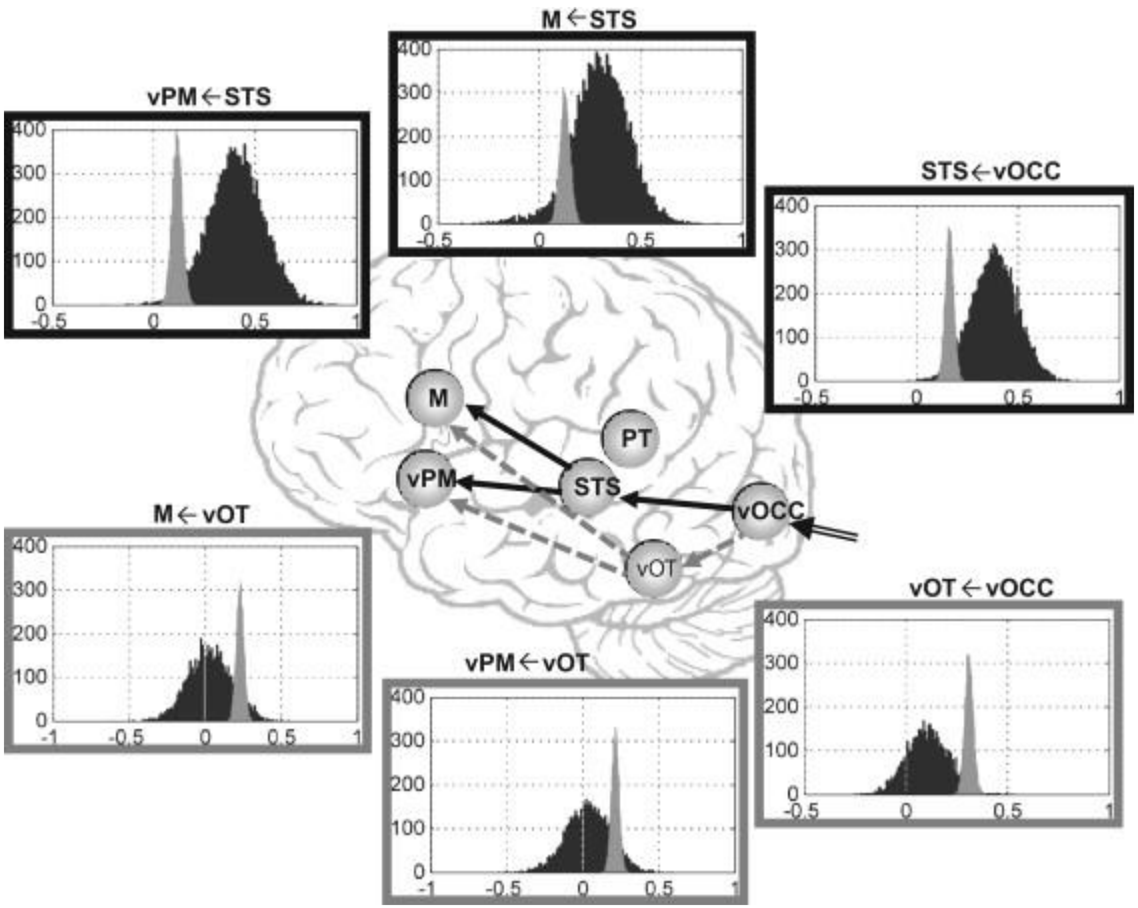
1. Extracted regions of interest. Spheres placed at the peak SPM coordinates from two contrasts:

A. Reading in patient > controls
B. Reading in controls

2. Asked which region should receive the driving input



Bayesian Model Averaging



Key:
Controls
Patient

Seghier et al., Neuropsychologia, 2012

Learning Objectives

By the end of today, you should be able to:

1. Place DCM in the fMRI analysis pipeline
2. State the difference between structural, functional and effective connectivity
3. Explain how a generative model helps to separate the BOLD signal into neuronal activity (effective connectivity), haemodynamics and noise.
4. Explain the interpretation of the parameters in the neuronal formula in DCM for fMRI
5. Explain how parameter estimates and the log model evidence are used to test hypotheses

Further Reading

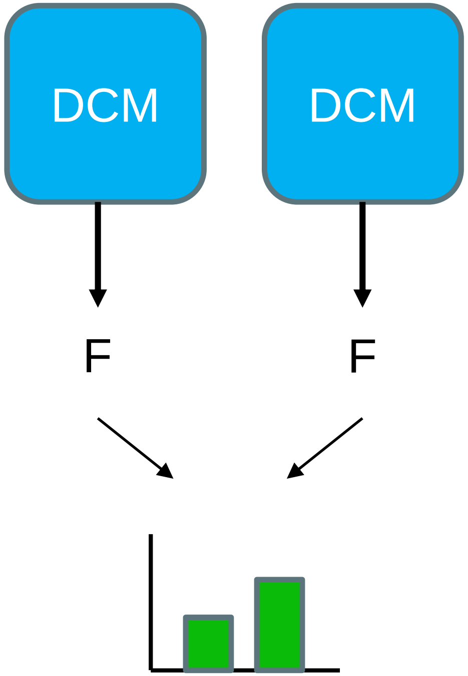
The original DCM paper	Friston et al. 2003, *NeuroImage*
Descriptive / tutorial papers	
Role of General Systems Theory	Stephan 2004, *J Anatomy*
DCM: Ten simple rules for the clinician	Kahan et al. 2013, *NeuroImage*
Ten Simple Rules for DCM	Stephan et al. 2010, *NeuroImage*
DCM Extensions	
Two-state DCM	Marreiros et al. 2008, *NeuroImage*
Non-linear DCM	Stephan et al. 2008, *NeuroImage*
Stochastic DCM	Li et al. 2011, *NeuroImage* Friston et al. 2011, *NeuroImage* Daunizeau et al. 2012, *Front Comput Neurosci*
Post-hoc DCM	Friston and Penny, 2011, *NeuroImage* Rosa and Friston, 2012, *J Neuro Methods*
A DCM for Resting State fMRI	Friston et al., 2014, *NeuroImage*

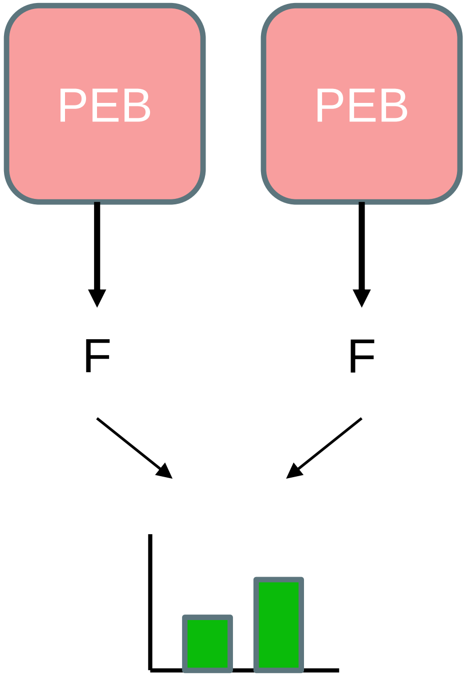
Extras

Inference on Models

We can compare models of single-subject data (DCM)

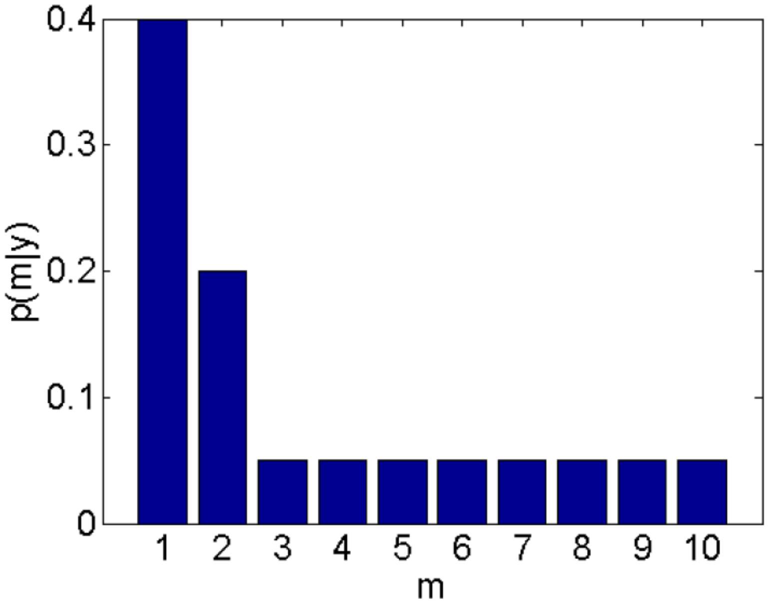
Or we can compare models of group-level data (Parametric Empirical Bayes, PEB)





Bayesian Model Averaging (BMA)

Having compared models, we can look at the parameters (connection strengths). We average over models, weighted by the posterior probability of each model. This can be limited to models within the winning family.



We marginalise over models m:

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

SPM does this using sampling