Dynamic Causal Modelling

SPM for MRI Course, May 2018

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Dynamic Causal Modelling

is a framework

for inferring neural responses / effective connectivity

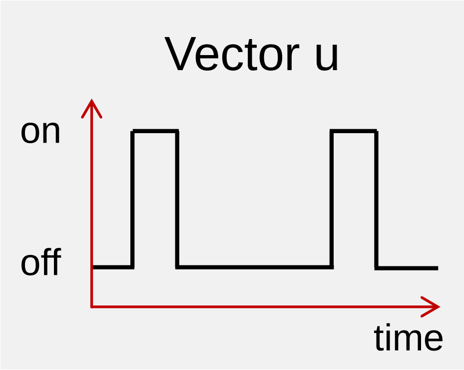
in the brain

The system of interest

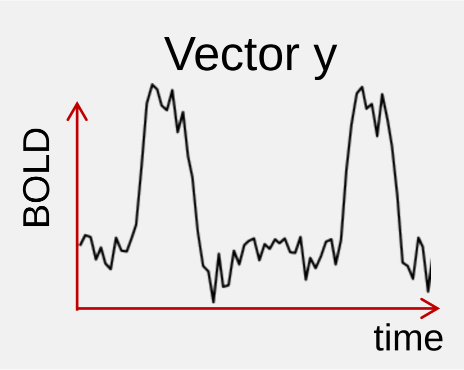
Experimental Stimulus

(Hidden) Neural Activity

Observations (BOLD)



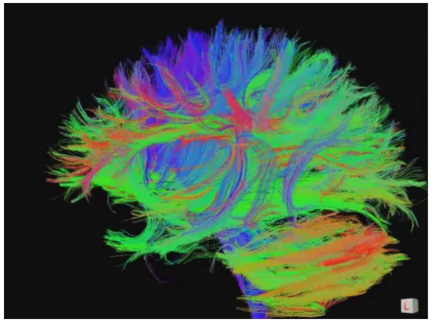
?



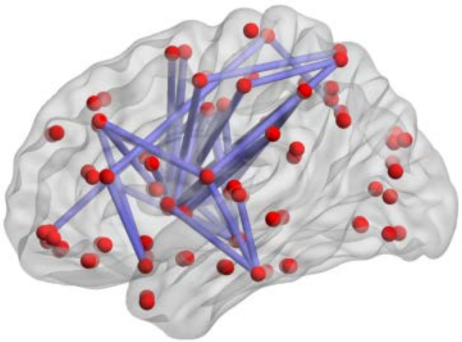
Stimulus from Buchel and Friston, 1997
Brain by Dierk Schaefer, Flickr, [CC 2.0]

Connectivity

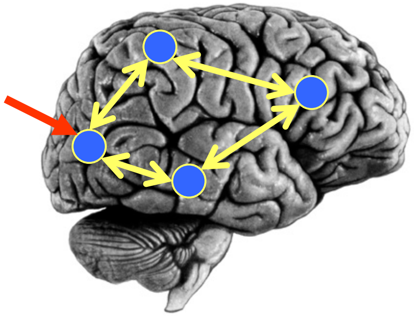
- Structural Connectivity
  Physical connections of the brain



- 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

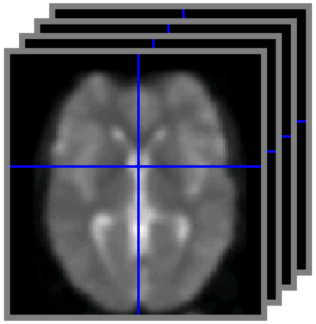
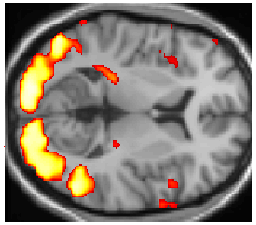
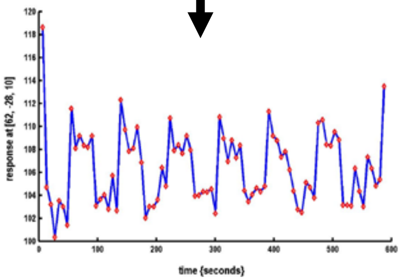


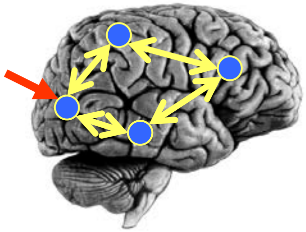
Image preprocessing (realignment, coregistration, normalisation, smoothing)



Statistical Parameter Mapping (SPM) / General Linear Model



Timeseries extraction from Regions of Interest (ROIs)



Dynamic Causal Modelling (DCM)

Recipe

1. **Specify a DCM for each subject**
2. Estimate the DCMs
3. Specify a group level model (PEB)
4. Test hypotheses at the group level
5. (Optional: Perform cross-validation)

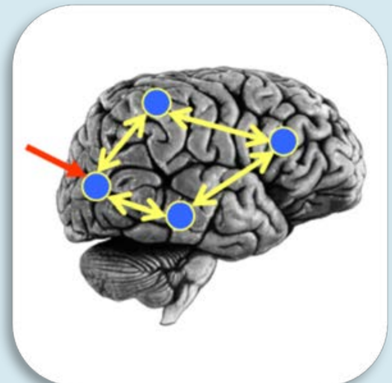
FIRST LEVEL ANALYSIS

MODEL SPECIFICATION

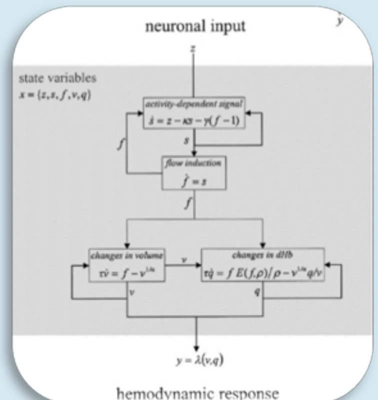
DCM Framework

Experimental Stimulus (u)

Neural Model



Observation Model



Observations (y)

How brain activity **z** changes over time

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

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

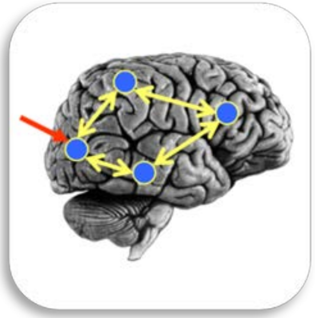
$\mathbf{y = g(z, \theta^h)}$

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

The 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

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

Friston et al., Neuroimage, 2003

DCM for CSD

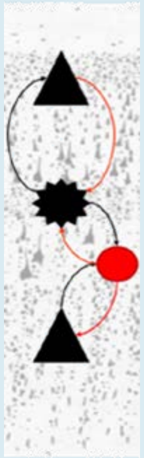
Resting State

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

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?

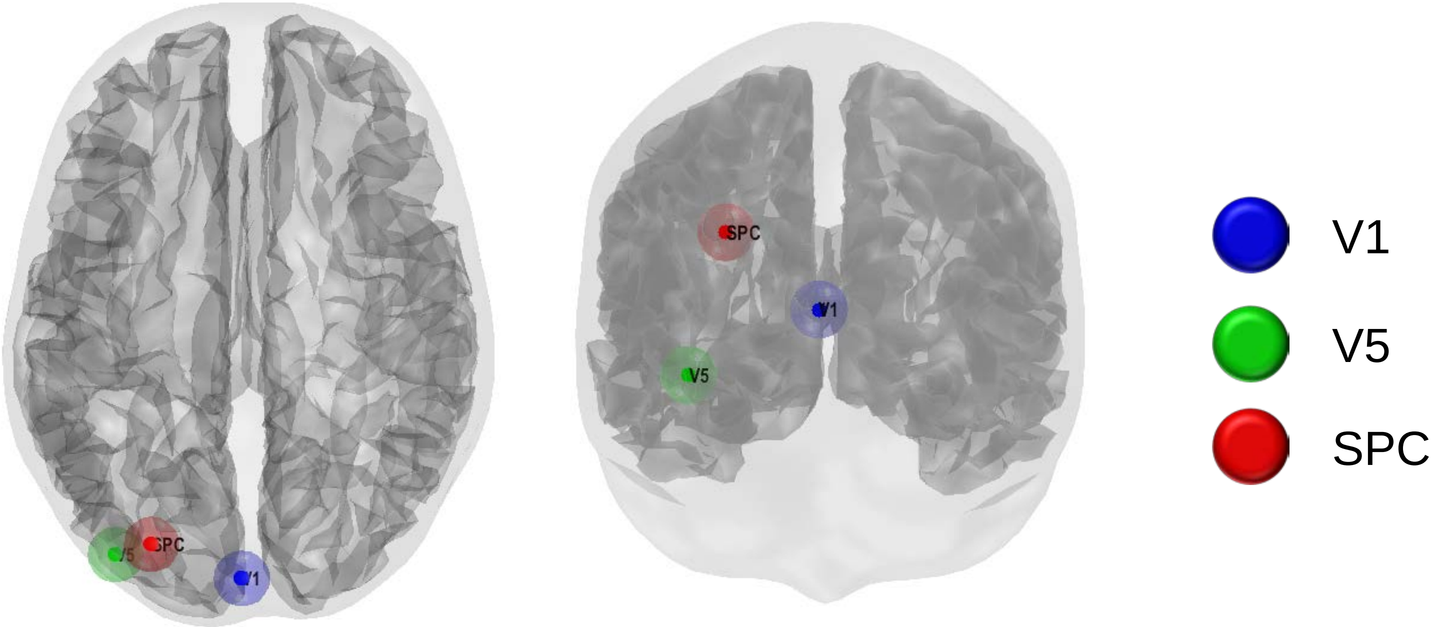
$$\begin{aligned}\dot{z} &= f(z,u) \\ &= f(z_0,u) + \frac{\delta f}{\delta z} z + \frac{\delta f}{\delta u} u + \frac{\delta^2 f}{\delta z \delta u} uz + \cdots \\ &\approx \left(A + \sum_j B^j\, u_j\right) + Cu\end{aligned}$$

Taylor series

The Neural Model

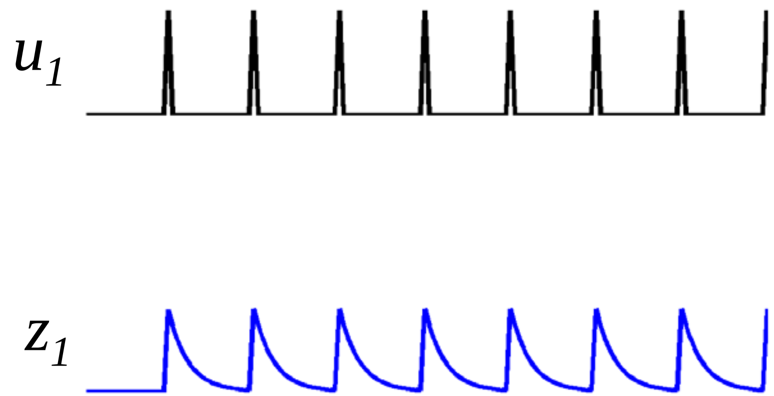
“How does brain activity, z, change over time?”

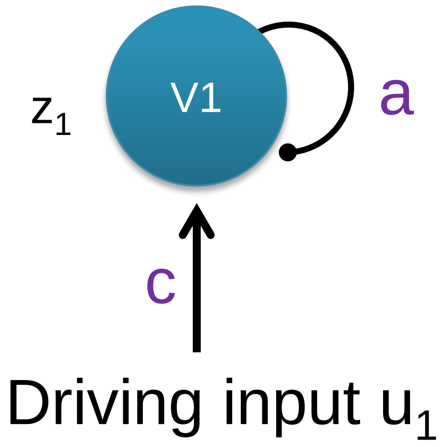
- Subjects viewed moving dots during fMRI
- On some trials, subjects were instructed to pay attention to the speed of the dots’ motion
- Question: How does attention to motion change the strength of the connections between V1, V5 and Superior Parietal Cortex?



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?"

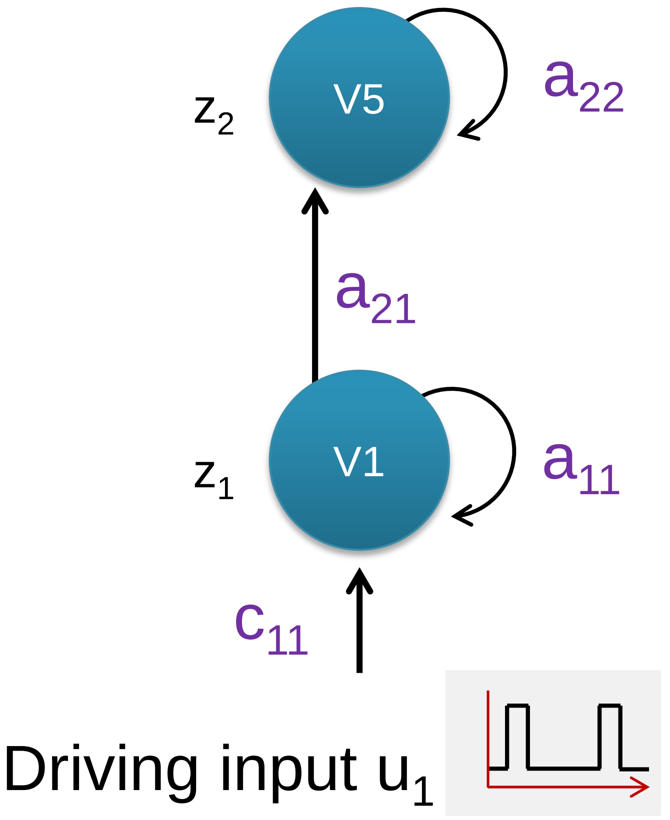
Change of activity in V1:

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

Change of activity in V5:

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

Self decay V1 input



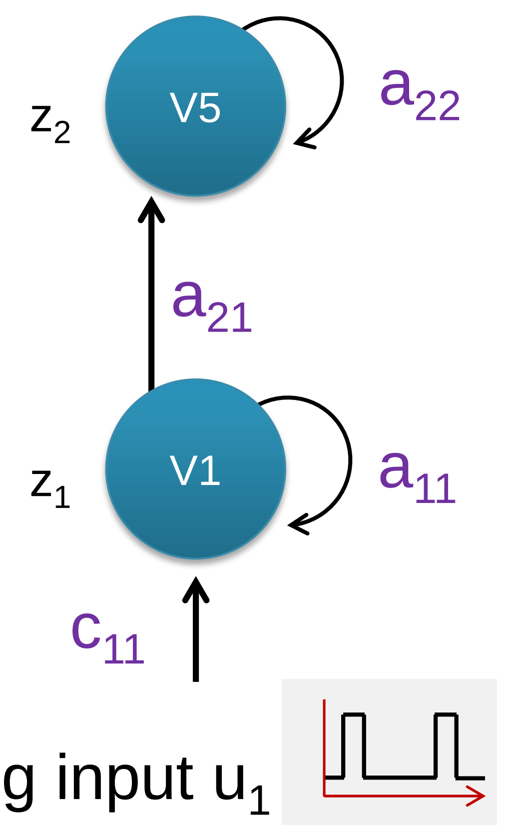
The Neural Model

"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

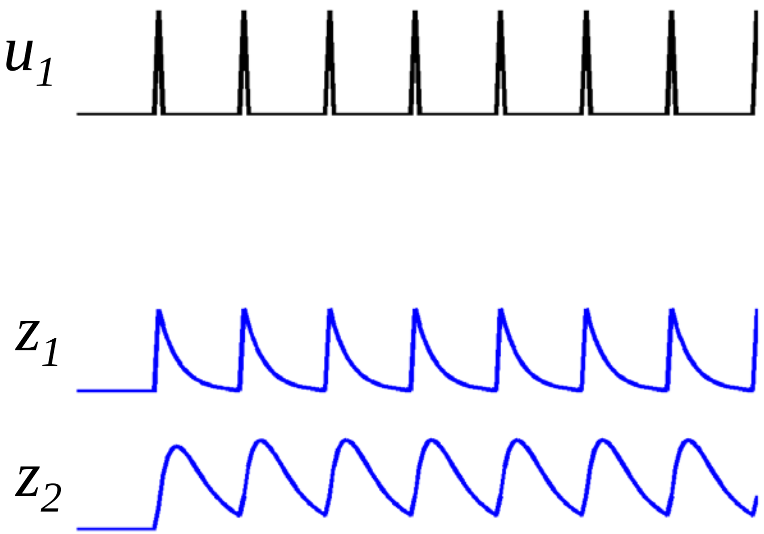
$$\dot{z} = Az + Cu_1$$

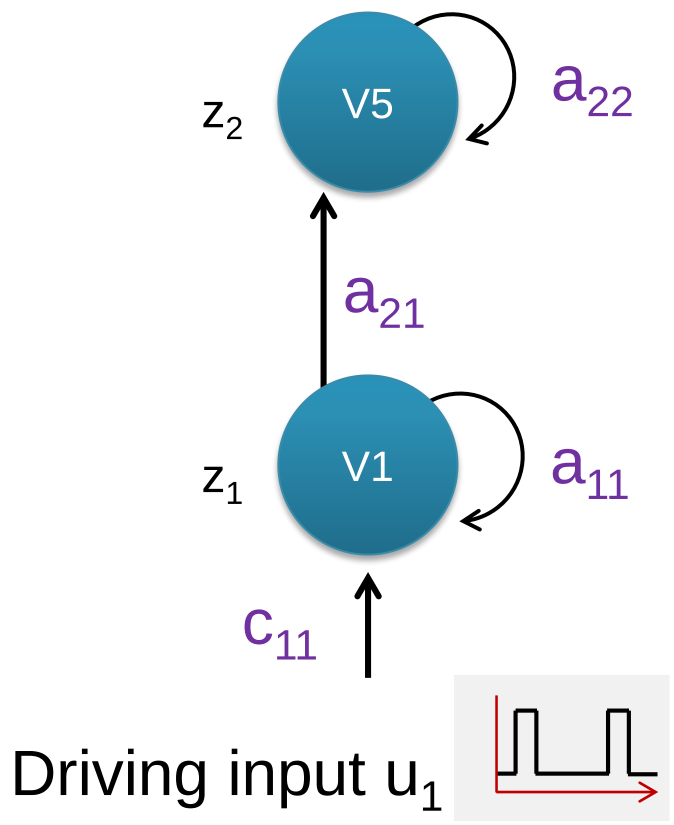


The Neural Model

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

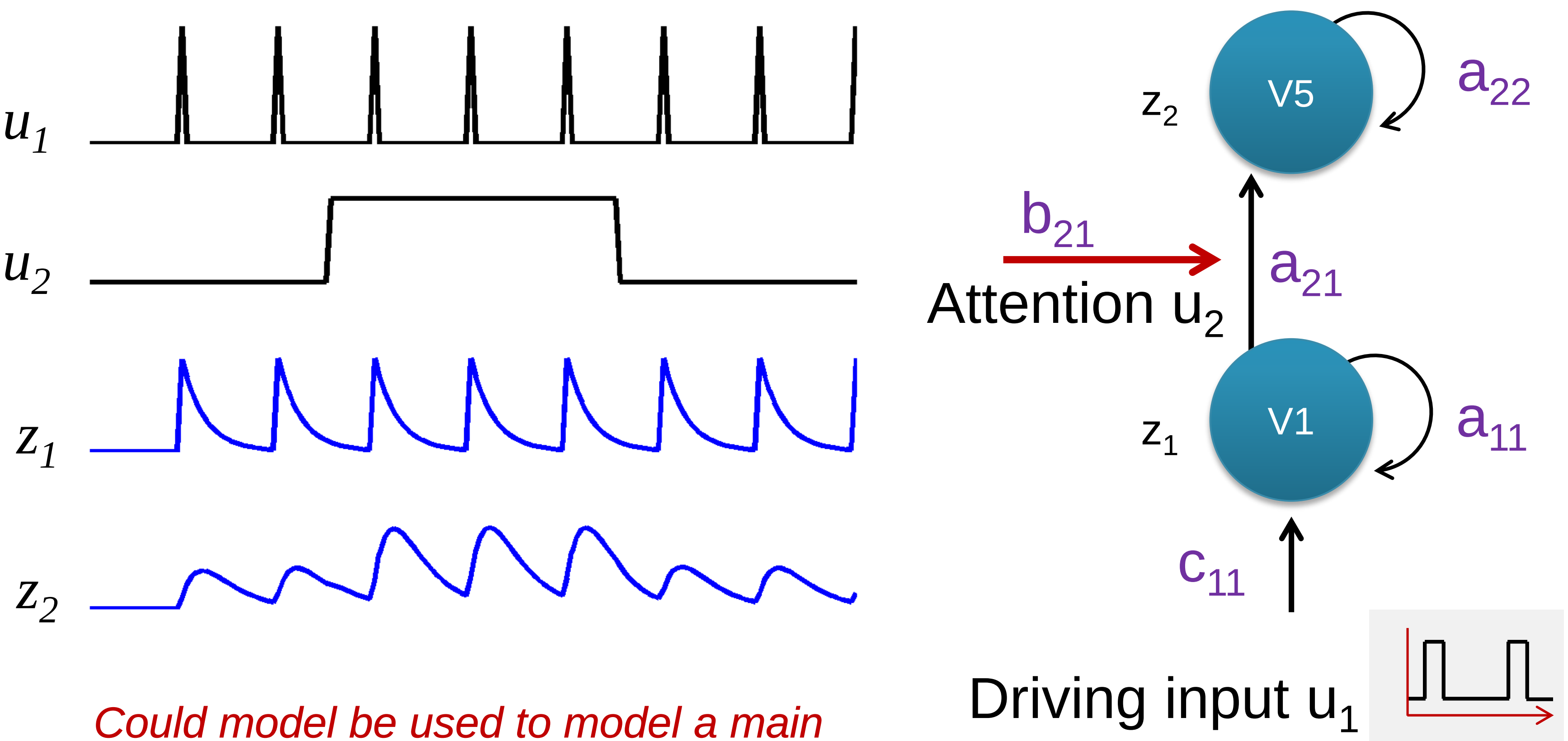
$$\dot{z} = Az + Cu_1$$





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?"

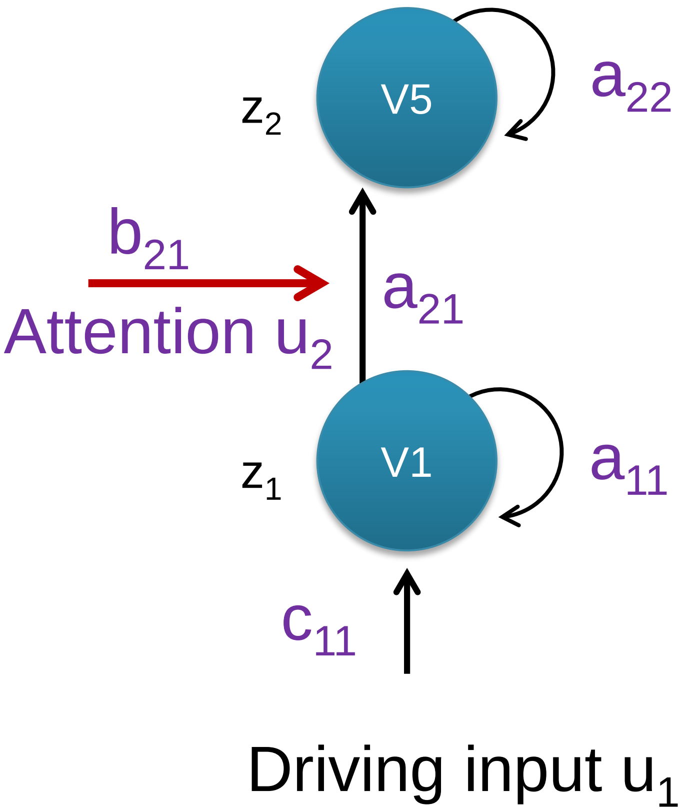
Change of activity in V1:

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

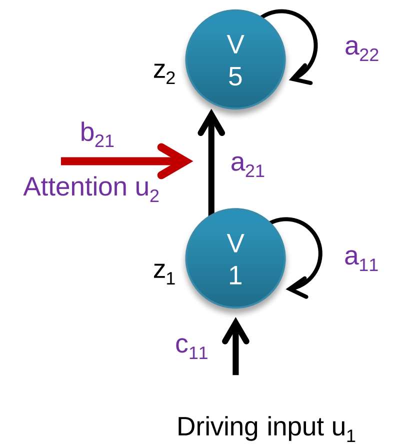
Change of activity in V5:

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

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

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

Change in activity per region

External input 2 (attention)

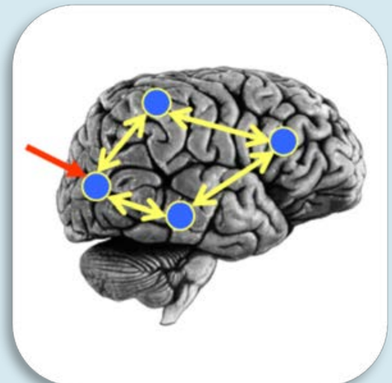
Current activity per region

All external input

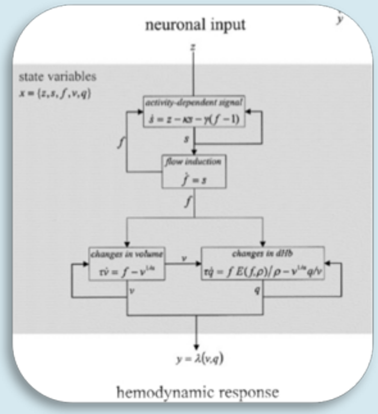
DCM Framework

Experimental Stimulus (u)

Neural Model



Observation Model



Observations (y)

How brain activity **z** changes over time

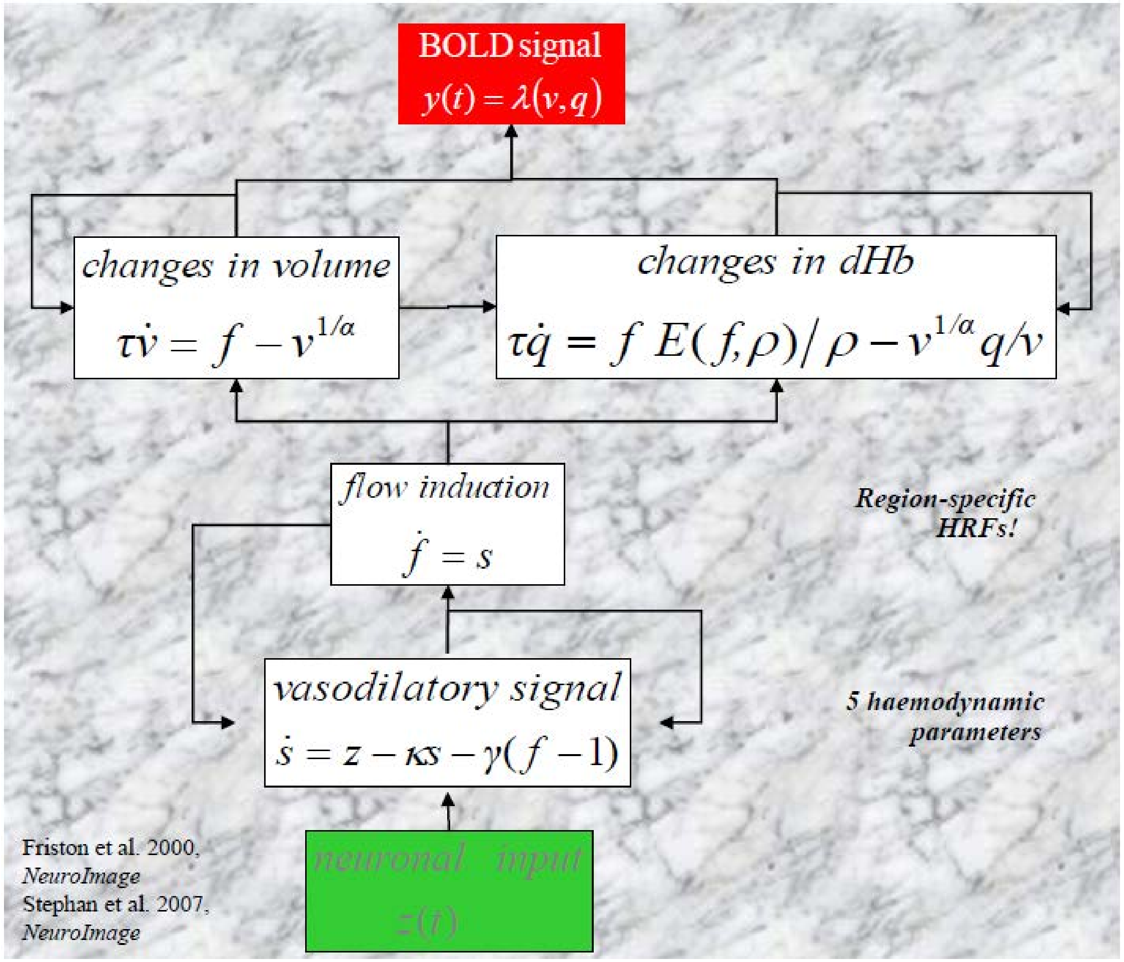
$$\dot{\mathbf{z}} = \mathbf{f}(\mathbf{z},\mathbf{u},\boldsymbol{\theta}^{\mathbf{n}})$$

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

$$\mathbf{y} = \mathbf{g}(\mathbf{z}, \boldsymbol{\theta}^{\mathbf{h}})$$

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



Recipe

1. Specify a DCM for each subject
2. **Estimate the DCMs**
3. Specify a group level model (PEB)
4. Test hypotheses at the group level
5. (Optional: Perform cross-validation)

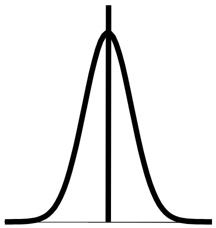
FIRST LEVEL ANALYSIS

MODEL ESTIMATION

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

Recipe

1. Specify a DCM for each subject
2. Estimate the DCMs
3. **Specify a group level model (PEB)**
4. Test hypotheses at the group level
5. (Optional: Perform cross-validation)

SECOND LEVEL ANALYSIS

SPECIFY A PEB MODEL

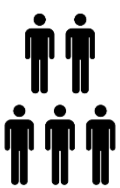
Hierarchical model of parameters

Parametric Empirical Bayes

$$\theta^{(2)} = \eta + \varepsilon^{(3)}$$

Priors on second level parameters

Second level



$$\theta^{(1)} = X\theta^{(2)} + \epsilon^{(2)}$$

Between-subject error

Second level general linear model

First level

$$y = \Gamma_i^{(1)}(\theta^{(1)}) + \varepsilon^{(1)}$$

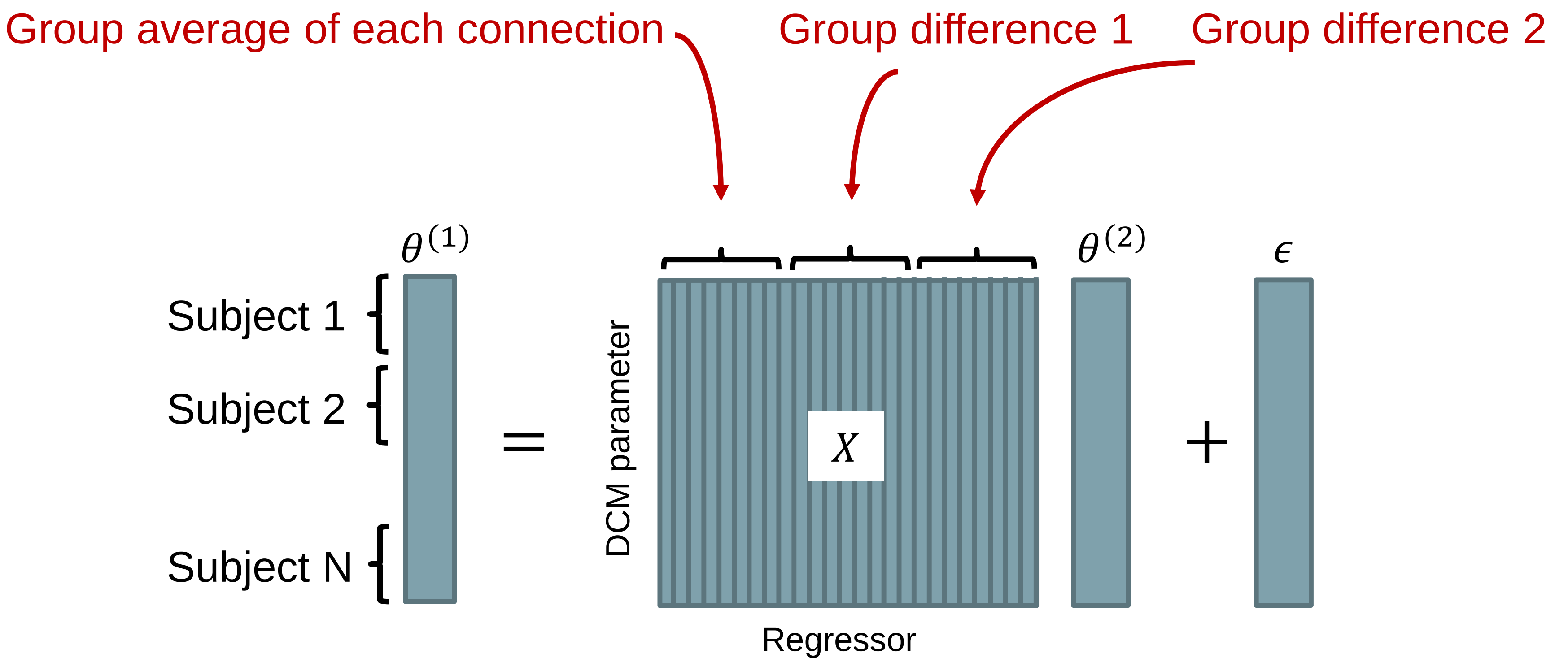
Measurement noise

DCM for subject i

Image credit: Wilson Joseph from Noun Project

Second level model (Bayesian GLM)

$$\theta^{(1)} = X\theta^{(2)} + \epsilon^{(2)}$$

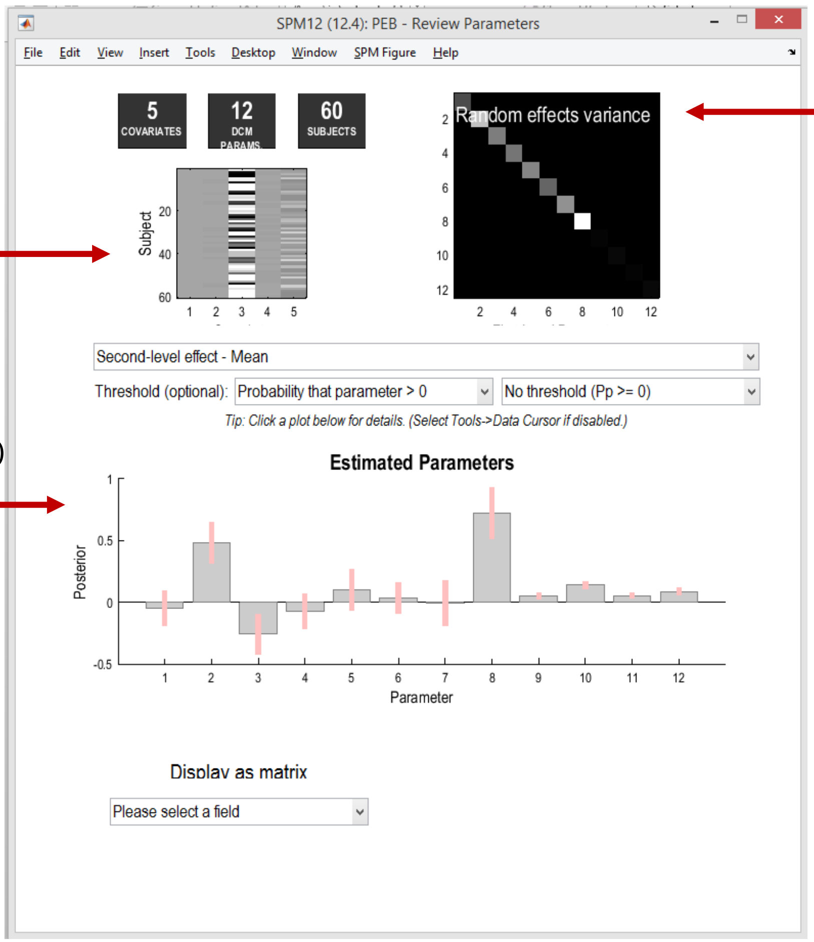


We estimate $\theta^{(2)}$ which contains the commonalities and differences across subjects

PEB results

Covariates

Group-level parameters $\theta^{(2)}$



Estimated between-subject variability $\epsilon^{(2)}$

Recipe

1. Specify a DCM for each subject
2. Estimate the DCMs
3. Specify a group level model (PEB)
4. **Test hypotheses at the group level**
5. (Optional: Perform cross-validation)

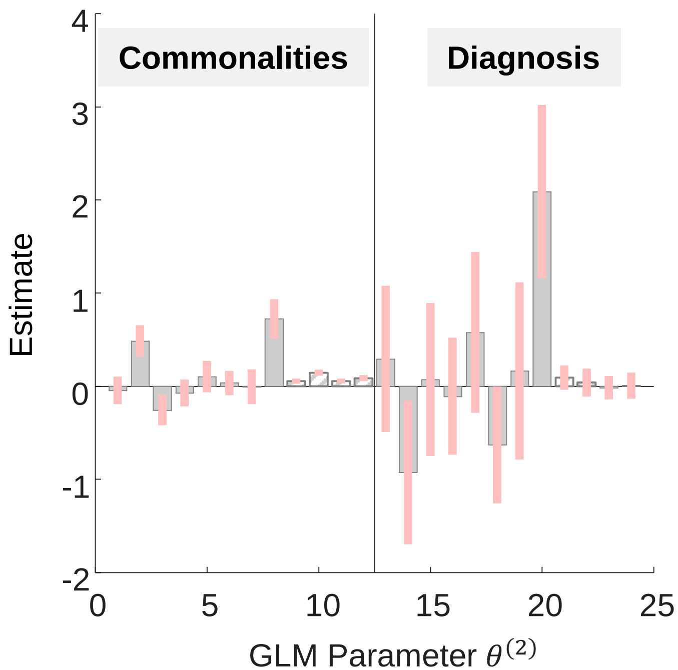
SECOND LEVEL ANALYSIS

TEST HYPOTHESES

Question: Is there an effect of diagnosis on connectivity?

‘Full’ GLM

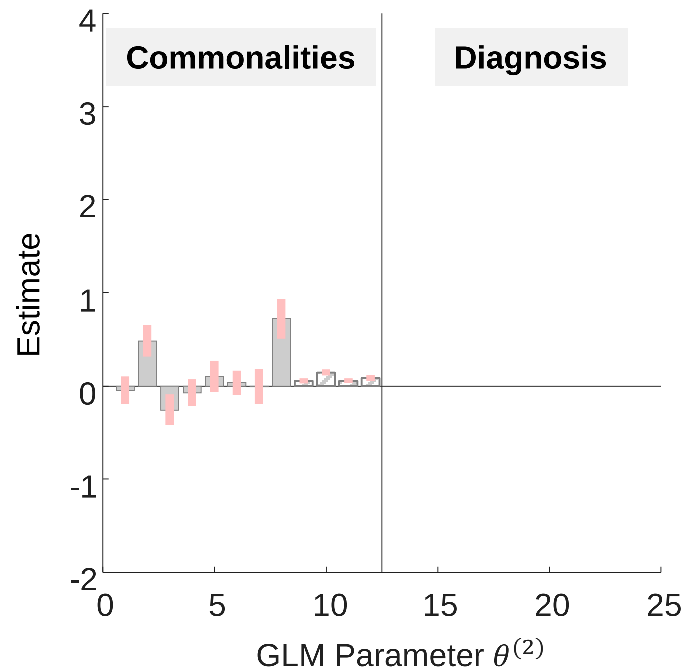
Group level GLM parameters $\theta^{(2)}$



Get the evidence (free energy) F_1

‘Reduced’ GLM

Group level GLM parameters $\theta^{(2)}$



Get the evidence (free energy) F_2

Compare models using Log Bayes Factor: $LBF = \mathrm{F}_1 - \mathrm{F}_2$

Hypothesis testing using PEB

'Bayesian model reduction' enables alternative models to be assessed in milliseconds.

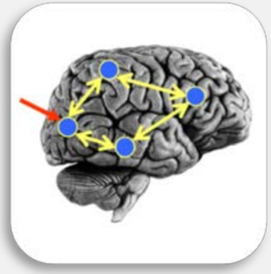
Applications:

- Compare GLMs with / without particular connections (spm_dcm_peb_bmc.m)
- Compare GLMs with / without particular covariates (spm_dcm_bmc_peb.m)
- Automatically search over reduced models to find the best combination of parameters (spm_dcm_peb_bmc.m)

Summary

First level analysis

1. **Specify** a DCM to model effective connectivity



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

2. **Estimate** the DCM for each subject to get:

- Connectivity parameters $\theta^{(1)} = (A, B, C)$
- Evidence (free energy) $F \approx \ln p(y|m)$

Second level analysis

3. Estimate a group-level **Bayesian GLM**

$$\theta^{(1)} = X\theta^{(2)} + \epsilon^{(2)}$$

4. **Test hypotheses** by switching on and off combinations of parameters $\theta^{(2)}$ to see how that changes the evidence

5. Optionally, perform **cross-validation** to see if effect sizes are large enough to be useful.

Further Reading

The original DCM paper	Friston et al. 2003, *NeuroImage*
The original PEB paper	Friston et al. 2016, *NeuroImage*
Descriptive / tutorial DCM 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*
Extensions to DCM for fMRI	
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*
A DCM for Resting State fMRI	Friston et al., 2014, *NeuroImage*
Multi-modal canonical microcircuit	Friston et al., 2017, *NeuroImage*

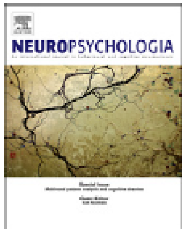
EXAMPLE

Neuropsychologia 50 (2012) 3621–3635

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

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

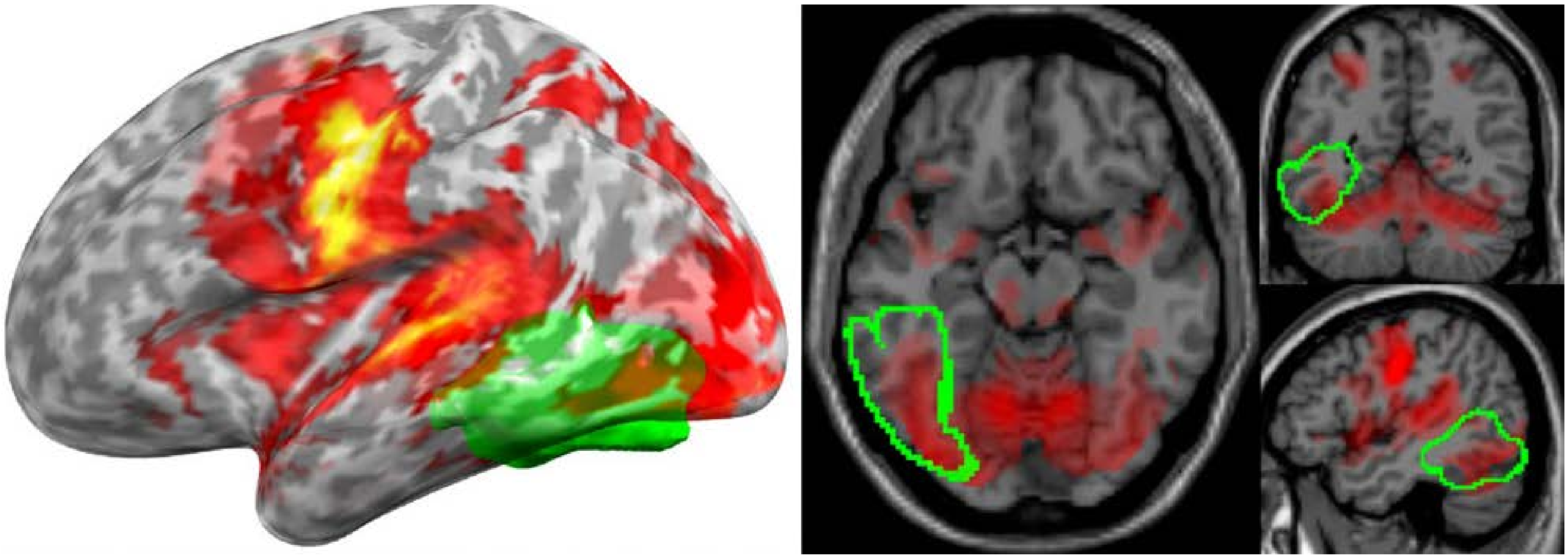


Research Report

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*

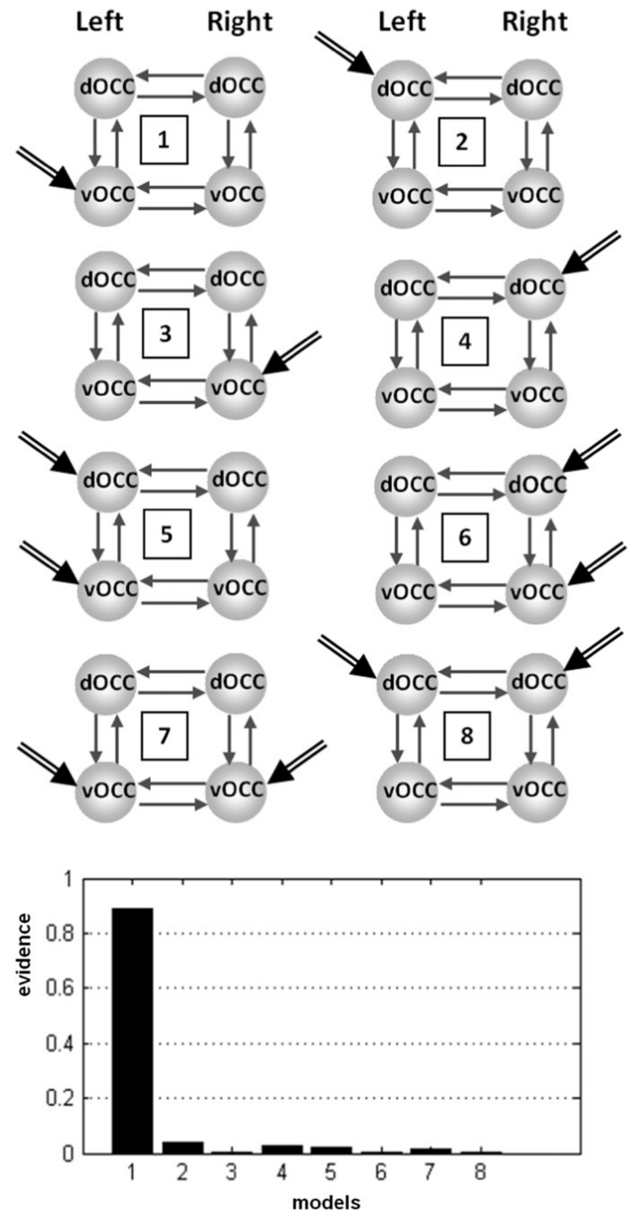


Reading > fixation (29 controls)
Lesion (Patient AH)

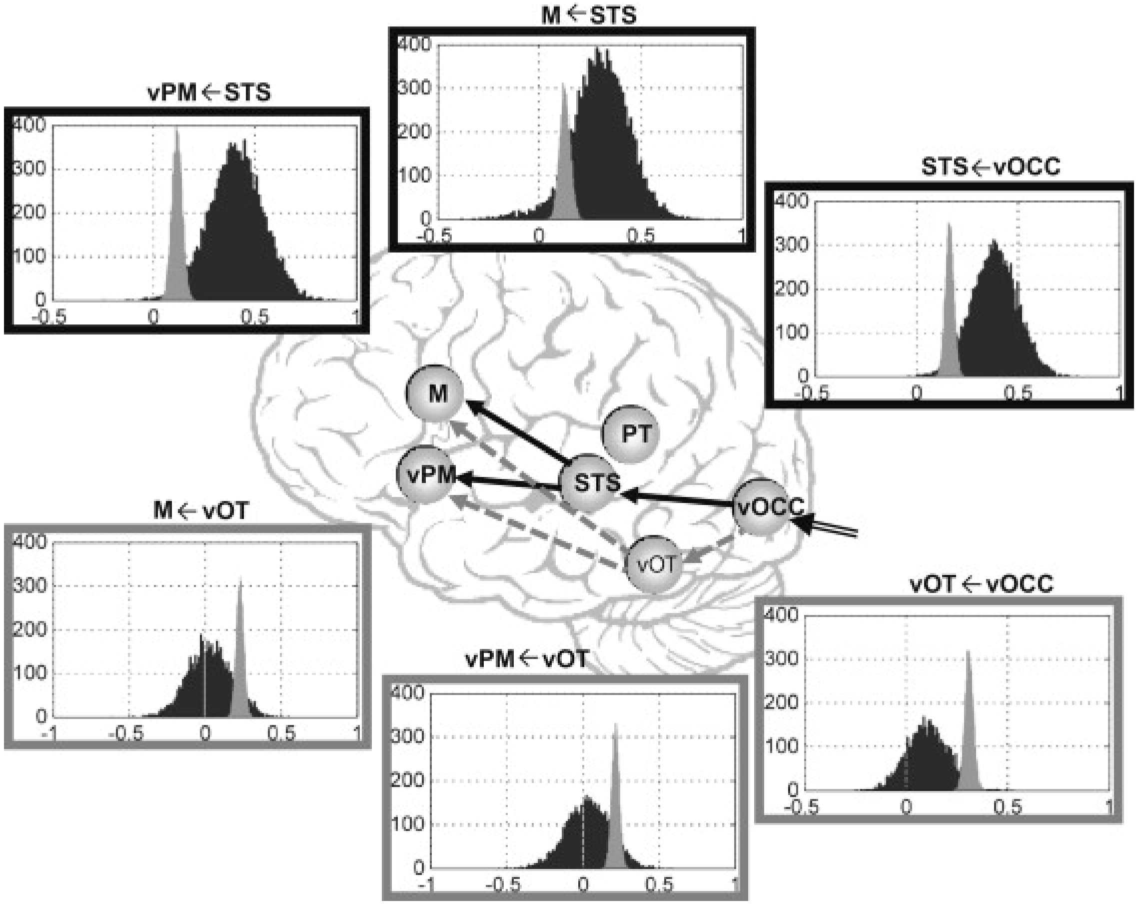
1. Extracted regions of interest. Spheres placed at the peak SPM coordinates from two contrasts:

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

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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*