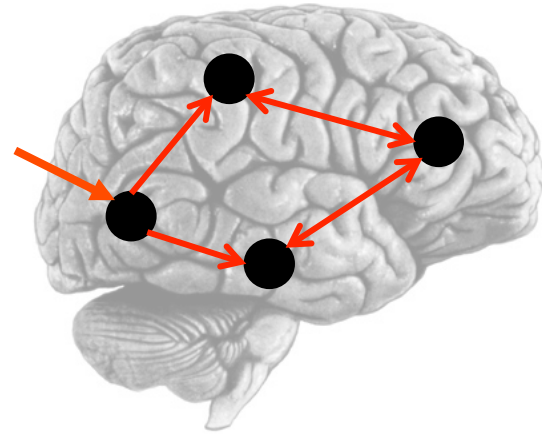
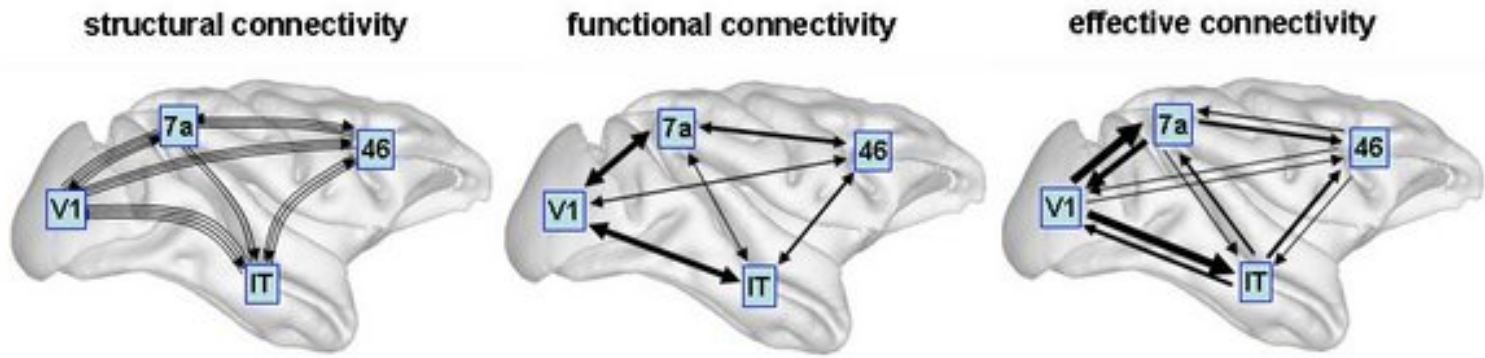
Dynamic Causal Modelling: Tutorial



Rosalyn Moran, Wellcome Trust Centre for Neuroimaging
University College London

MPS-UCL Symposium on Computational Psychiatry
September 16 – 22, 2012, Ringberg Castle

Structural, functional & effective connectivity



Sporns 2007, *Scholarpedia*

- **anatomical/structural connectivity**
  = presence of axonal connections
- **functional connectivity**
  = statistical dependencies between regional time series
- **effective connectivity**
  = causal (directed) influences between neurons or neuronal populations

Methods for effective connectivity analysis

- Regression models
  (e.g. psycho-physiological interactions, PPIs)
  Friston et al. 1997

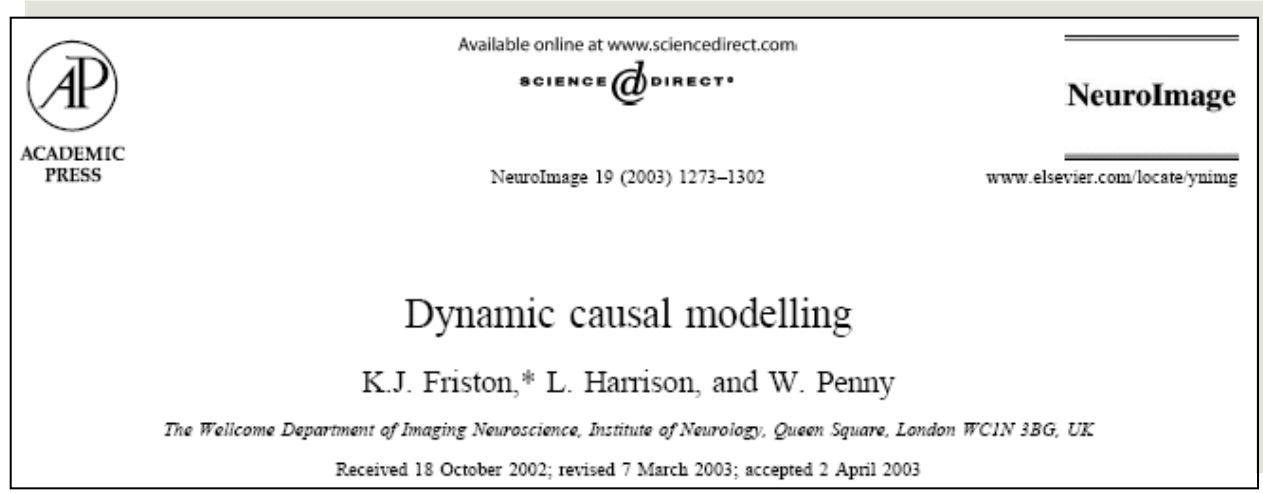
- Structural Equation Models (SEM)
  McIntosh et al. 1991, 1994; Büchel & Friston 1997; Bullmore et al. 2000

- Volterra kernels
  Friston & Büchel 2000

- Time series models (e.g. MAR, Granger causality)
  Harrison et al. 2003, Goebel et al. 2003

- Dynamic Causal Models (DCM)
  bilinear: Friston et al. 2003; *nonlinear:* Stephan et al. 2008; *ERPs* David et al 2006; *LFPs,* Moran et al 2009

Dynamic causal modelling (DCM)



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Dynamic causal modelling

K.J. Friston,* L. Harrison, and W. Penny

The Wellcome Department of Imaging Neuroscience, Institute of Neurology, Queen Square, London WC1N 3BG, UK

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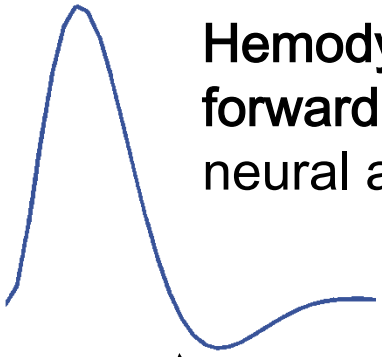
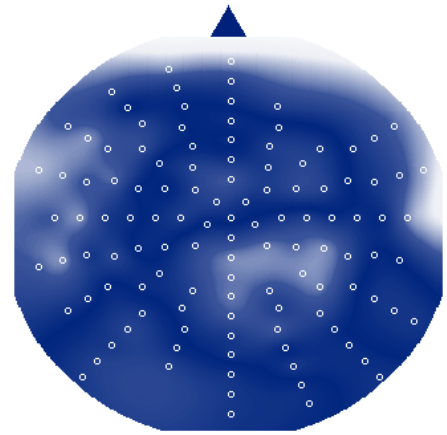
DCMs are generative models of brain responses, which provide posterior estimates of neurobiologically interpretable parameters such as the effective strength of connections among neuronal populations and their context dependent modulation

A Generic Framework



Hemodynamic forward model:
neural activity→BOLD

Electromagnetic forward model:
neural activity→EEG
MEG
LFP



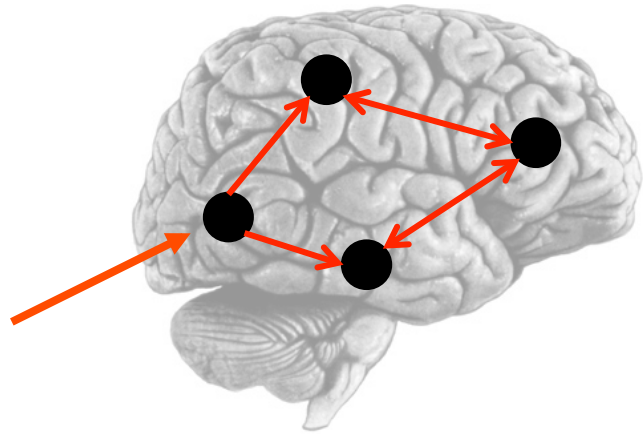
Neural state equation:

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

fMRI

EEG/MEG

1 and 2 state models



13 state model

Its Key Components

Dynamic:

Dynamic (differential) equations describe hidden neuronal dynamics at a level of detail constrained by the measurement

Causal:

In a control theory sense, input perturbations disturb equilibrium neuronal dynamics and propagate through connected networks to other brain regions

Biophysical Observer:

Realistic neuronal to measurement model accounts for regional HRF differences and captures key electrophysiological features eg. Power spectra

Bayesian Inversion:

Priors on biological parameters to constrain them within physiologically plausible ranges
Model evidence objective function maximised during parameter estimation
Mean and covariance estimates for a parameter set

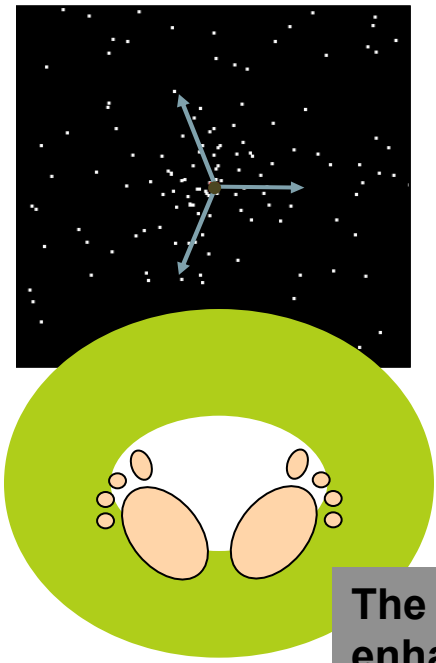
Overview

- Dynamic causal models for fMRI
  - Work through example: Attention to Motion
  - Neural level & Hemodynamic level
  - Parameter estimation, priors & inference

- Dynamic causal models for Steady State Responses (rat LFPs
  - Work through example: Isoflurane effects on connectivity
  - Neural mass model

Attention to Motion

Paradigm

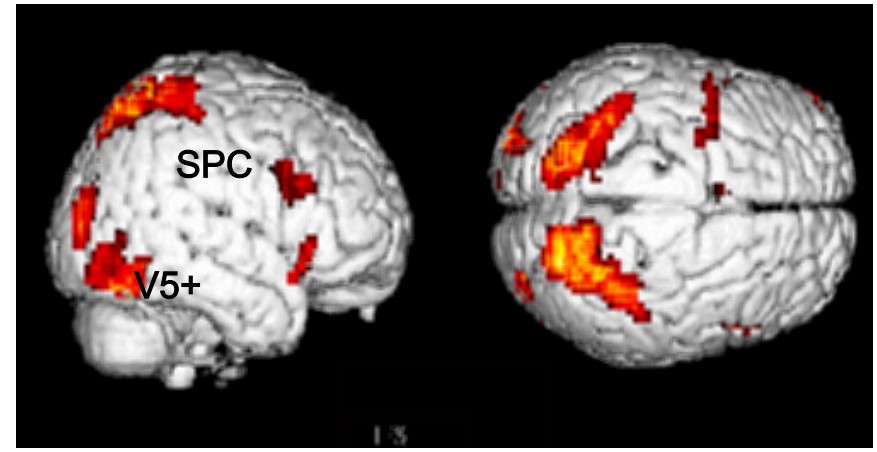


4 conditions

- **fixation only**
- **observe static dots**
- **observe moving dots**
- **attend to moving dots**

GLM Results

Attention – No attention

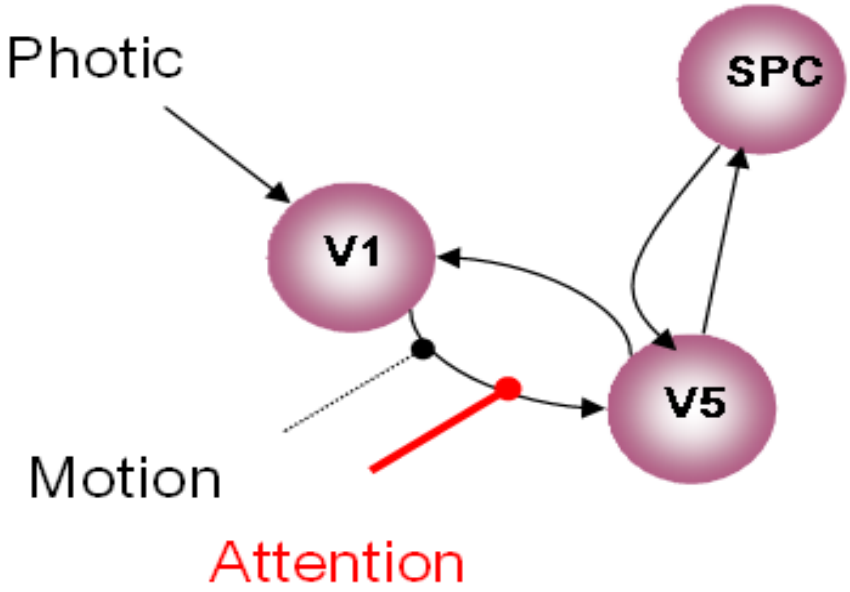


Büchel & Friston 1997, Cereb. Cortex
Büchel et al. 1998, Brain

The GLM analysis showed that activity in area V5 was not only enhanced by moving stimuli, but also by attention to motion.

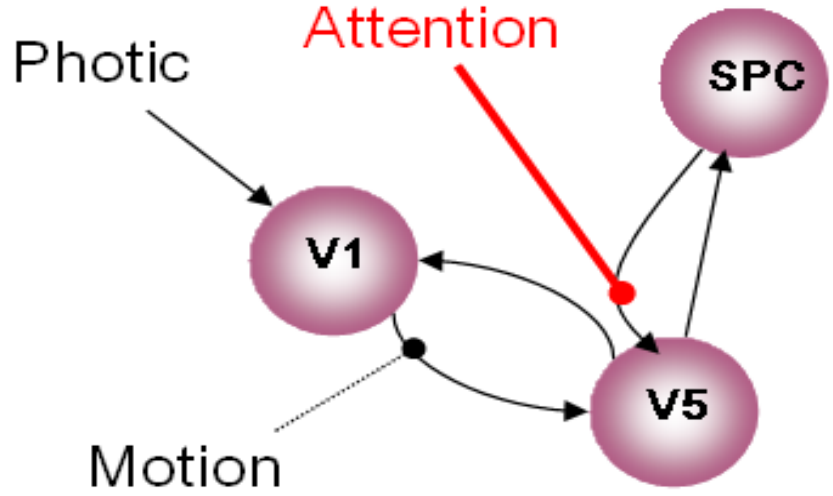
In the following we will model this effect in V5 using DCM, testing competing hypotheses regarding context-dependent modulation or "enabling" of V5 afferents.

Effects of attention on motion responses in V5



Model 1/Hypothesis 1
Bottom-up Model

Model 2/ Hypothesis 2
Top-down Model



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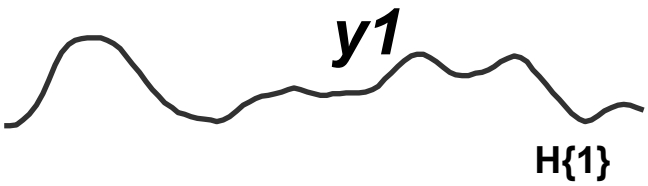
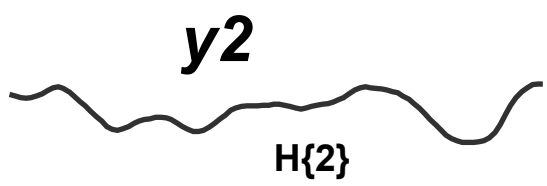
Neural Dynamics and Static Observer

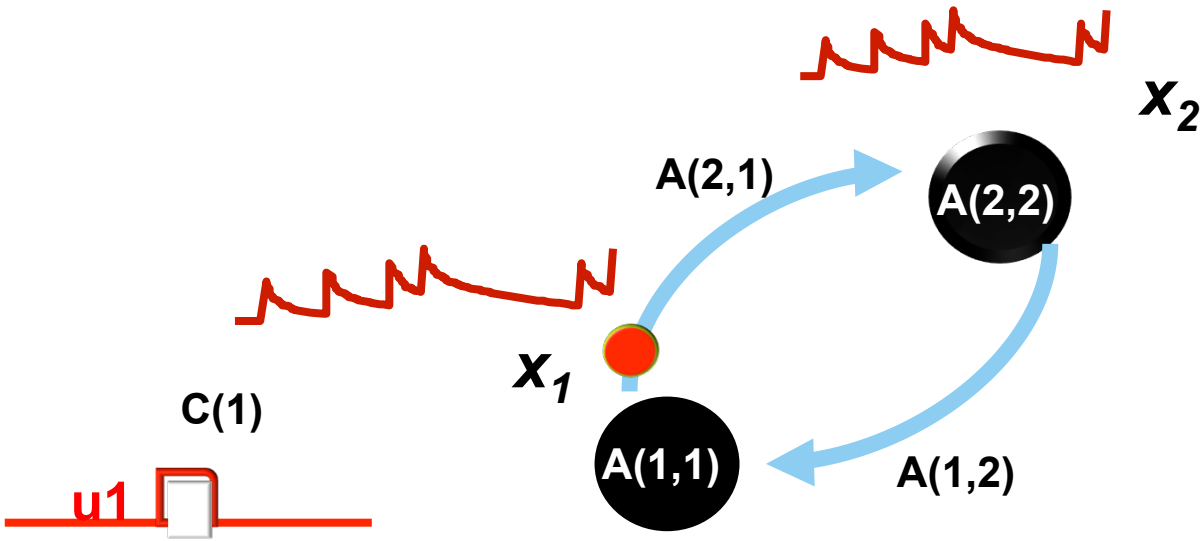




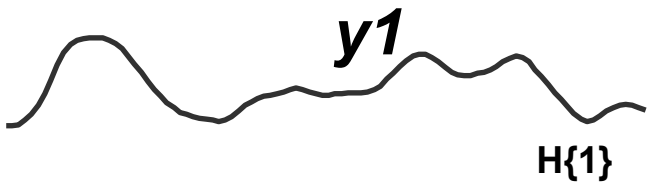
$$\dot{x} = A\,x + Cu$$

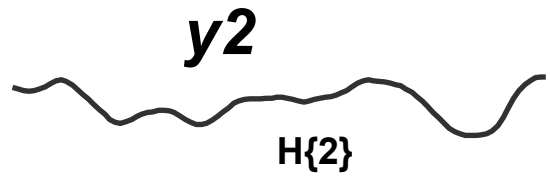
$$y = g(x, H) + \varepsilon$$

$$\varepsilon \sim N(0, \sigma)$$



Neural Dynamics and Static Observer

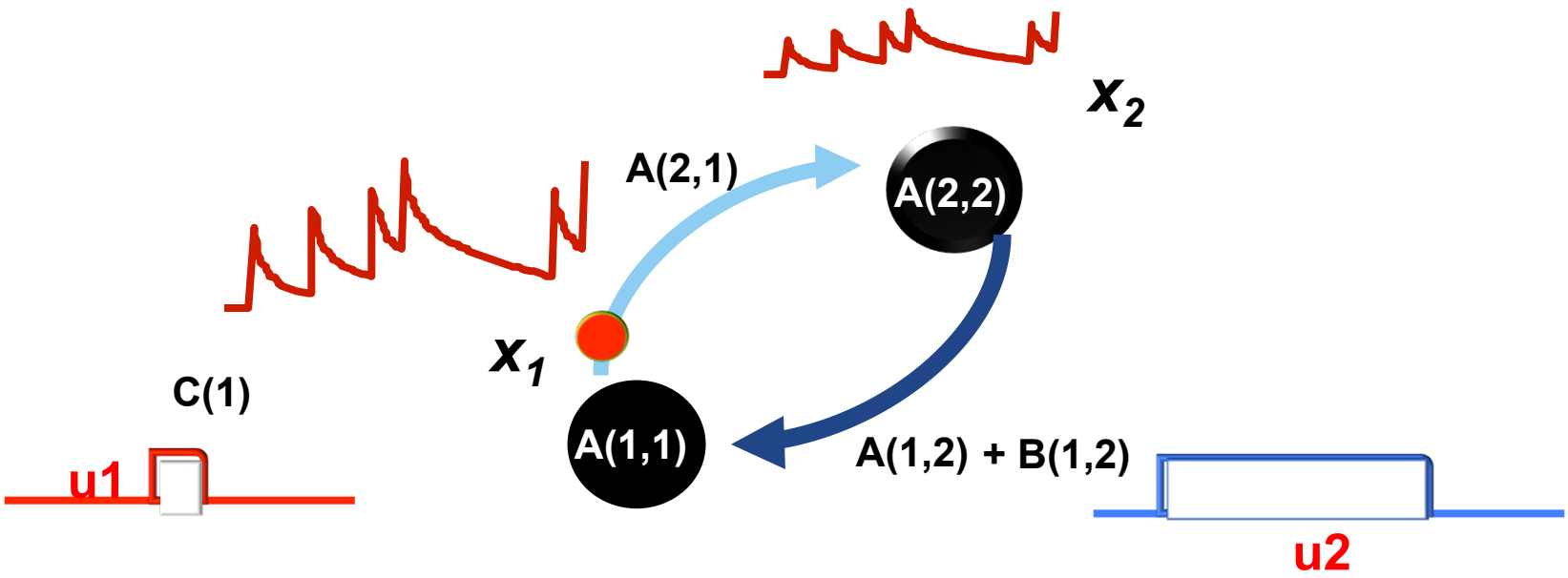




$$\dot{x} = (A + uB)x + Cu$$

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

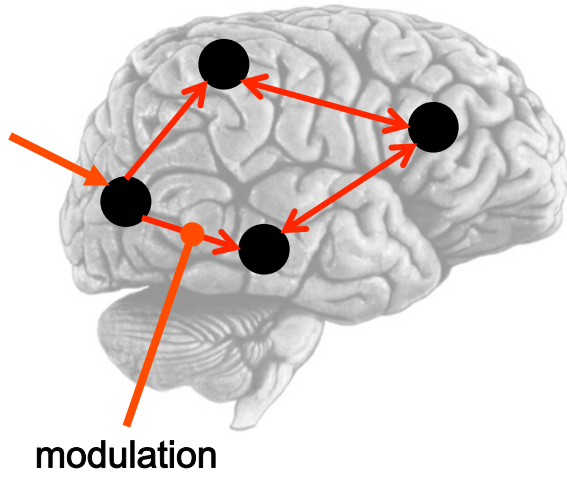
$$\varepsilon \sim N(0, \sigma)$$



Vanilla DCM:
Neural Dynamics : a bilinear approximation

Simply a two-dimensional taylor expansion (around x_0=0, u_0=0):

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



$$A = \left.\frac{\partial f}{\partial x}\right|_{u=0}$$

$$C = \left.\frac{\partial f}{\partial u}\right|_{x=0}$$

$$B = \frac{\partial^2 f}{\partial x \partial u}$$

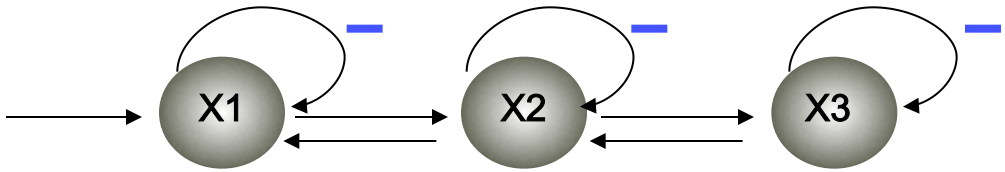
Bilinear state equation:

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

Connectivity Parameters: Rate Constants

Integration of a first-order linear differential equation gives an exponential function:

$$\frac{dx}{dt} = ax \longrightarrow x(t) = x_0 \exp(at)$$



The coupling parameter a thus describes the speed of the exponential change

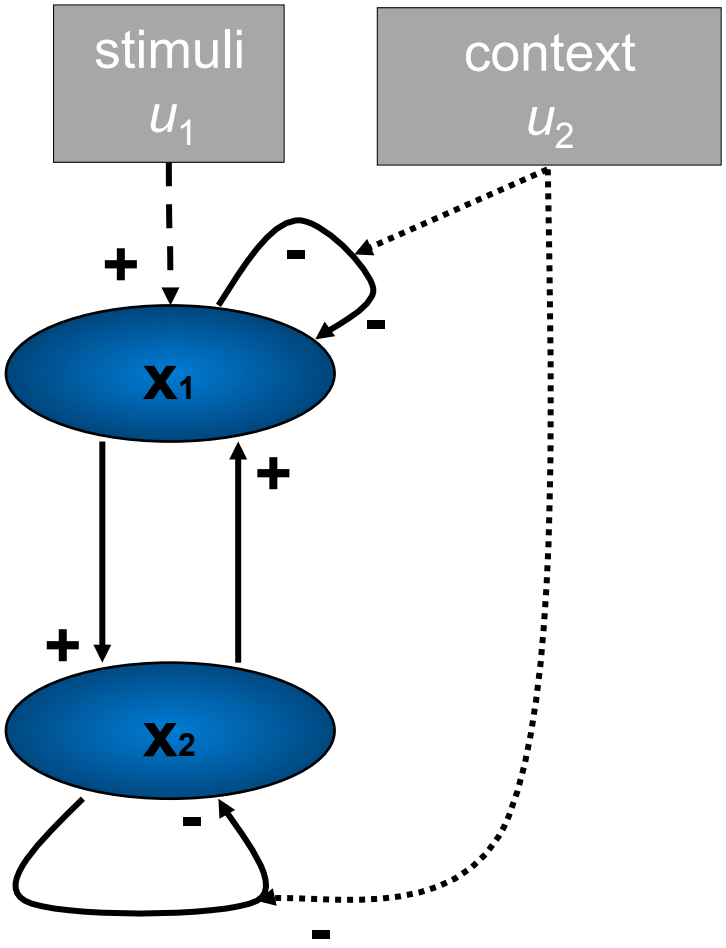
If A→B is 0.10 s^{-1} this means that, per unit time, the increase in activity in B corresponds to 10% of the activity in A

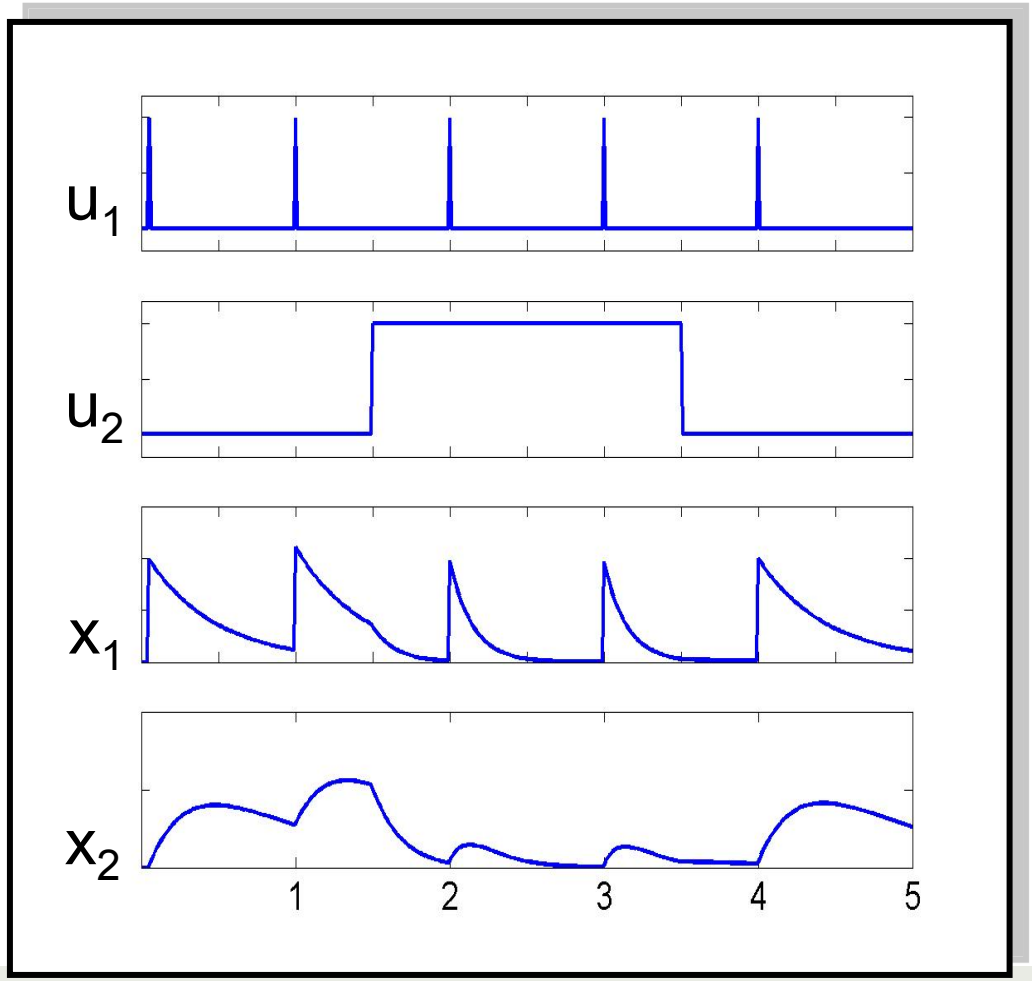
If A→B is -0.10 s^{-1} this means that, per unit time, the decrease in activity in B corresponds to 10% of the activity in A

Context Dependent Decay

$$\dot{x} = Ax + u_2 B^{(2)} x + Cu_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \begin{bmatrix} -1 & a_{12} \\ a_{21} & -1 \end{bmatrix} x + u_2 \begin{bmatrix} b_{11}^2 & 0 \\ 0 & b_{22}^2 \end{bmatrix} x + \begin{bmatrix} c_1 & 0 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

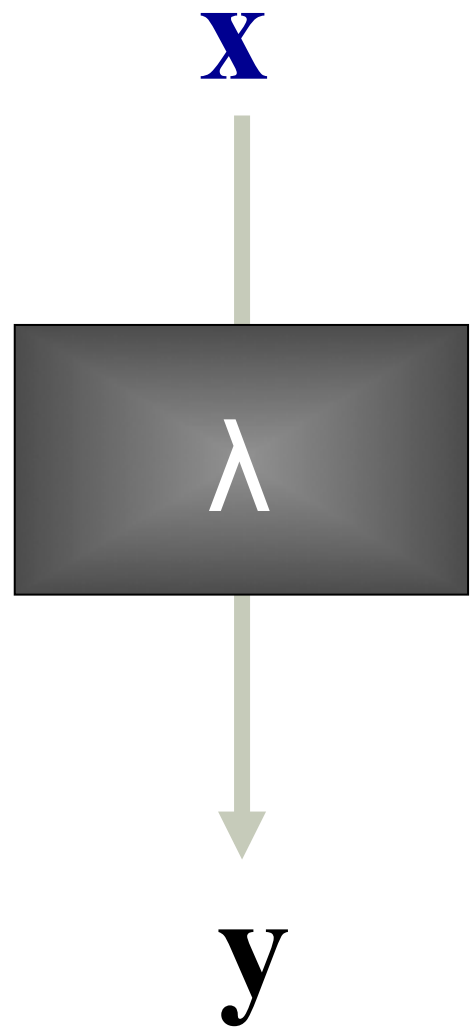




Penny et al. 2004, *NeuroImage*

Neuronal activity to BOLD

- Cognitive system is modelled at its underlying neuronal level (not directly accessible for fMRI).
- The modelled neuronal dynamics (x) are transformed into area-specific BOLD signals (y) by a hemodynamic model (λ).



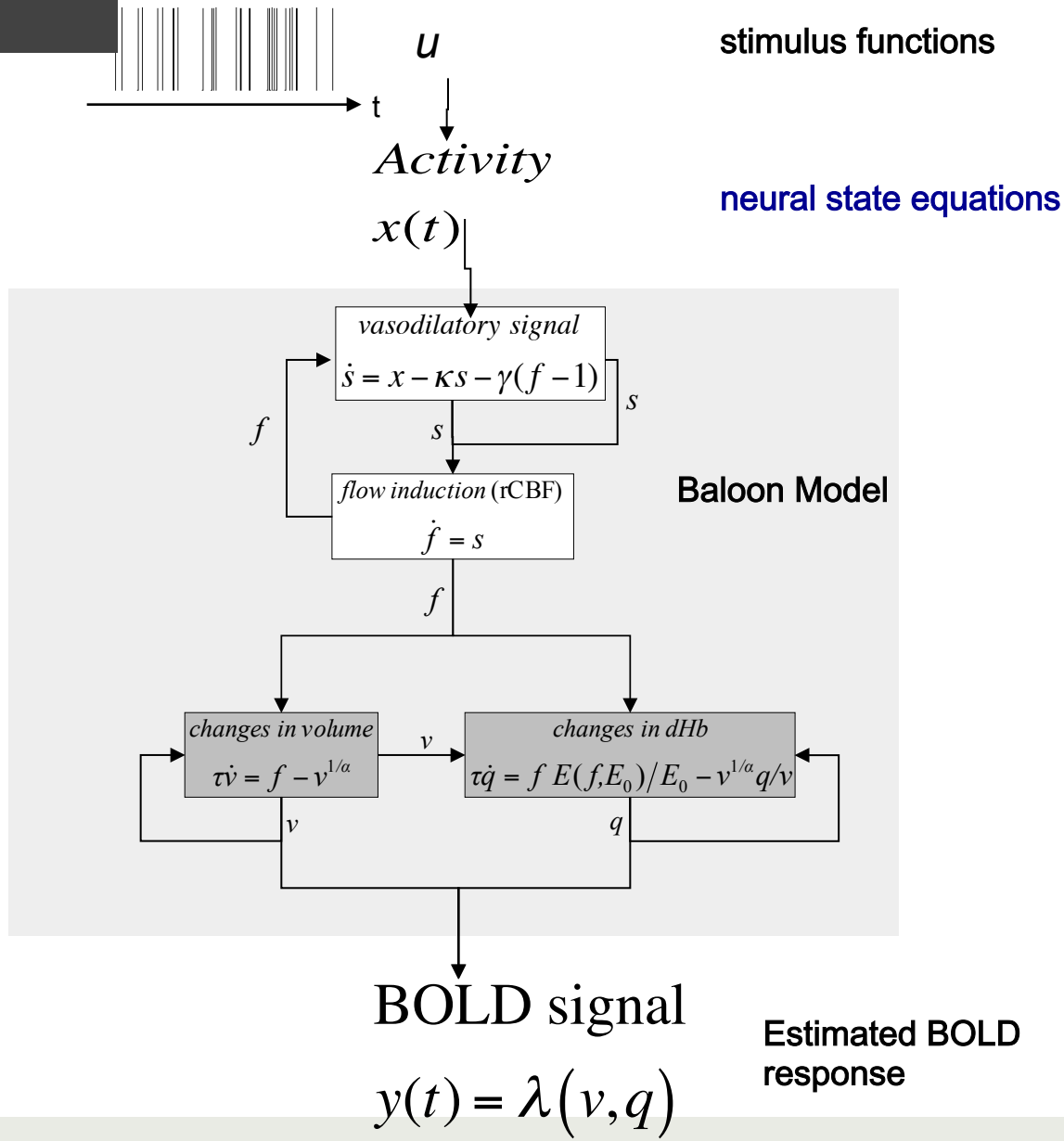
Hemodynamic Model

- 6 parameters:

$$\theta^h = \{\kappa, \gamma, \tau, \alpha, \rho, \varepsilon\}$$

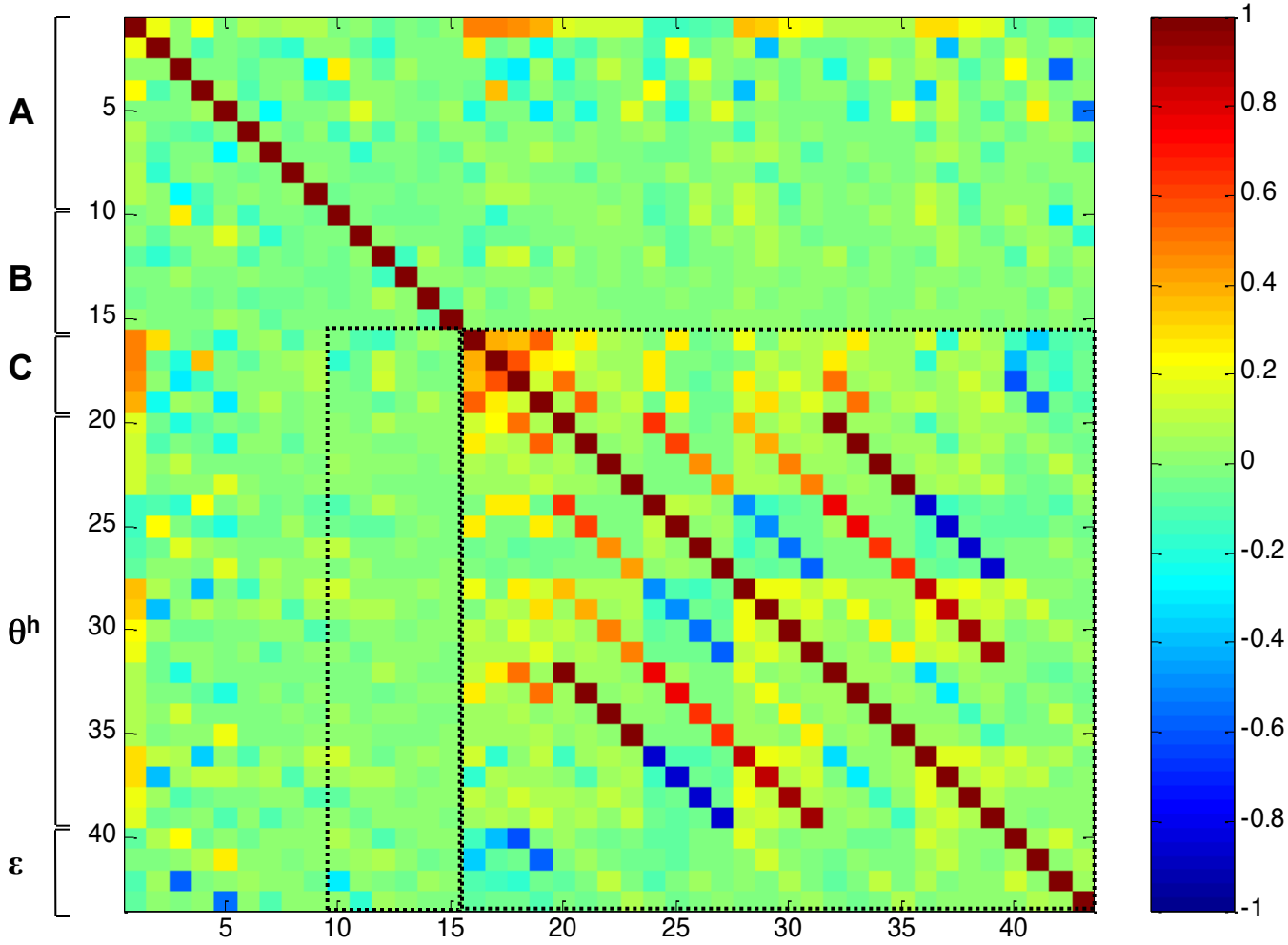
important for model fitting, but usually of no interest for statistical inference

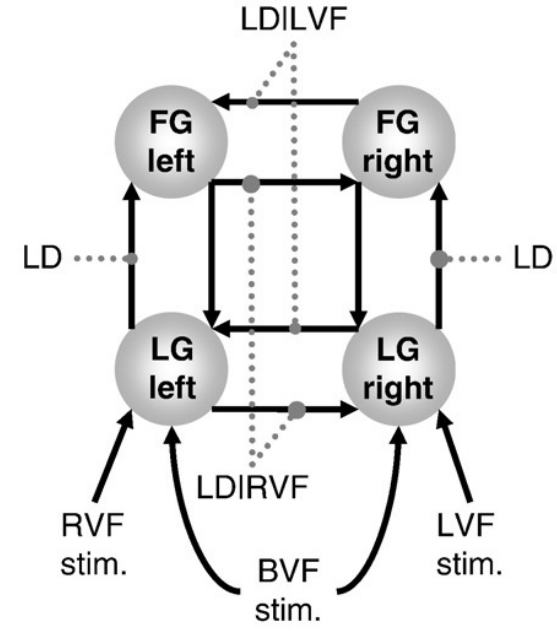
- Computed separately for each area → region-specific HRFs



Friston et al. 2000, *NeuroImage*
Stephan et al. 2007, *NeuroImage*

Hemodynamic and Neural Parameter Correlations





Stephan et al. 2007, *NeuroImage*

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  - Work through example: Attention to Motion
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Inference on Models

Model evidence: $p(y \mid m_i)$

Approximation: Free Energy $F = \ln p(y \mid m_i) - KL[q(\theta), p(\theta \mid G, \lambda)]$

→ accounts for both accuracy and complexity of the model

→ allows for inference about structure (generalisability) of the model

Fixed Effects Model selection via log Group Bayes factor:

$$BF_{1,2} = \sum_k \ln p(y|m_1) - \sum_k \ln p(y|m_2)$$

Random Effects Model selection via Model probability:

$$p(r \mid y, \alpha)$$

$$\langle r_k \rangle_q = \alpha_k / (\alpha_1 + \ldots + \alpha_K)$$

Inference on Models

Model evidence: $p(y \mid m_i)$

Approximation: Free Energy $F = \ln p(y \mid m_i) - KL[q(\theta), p(\theta \mid G, \lambda)]$

balance between fit and complexity = accuracy - *complexity*

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

Deviation of posterior mean from prior mean

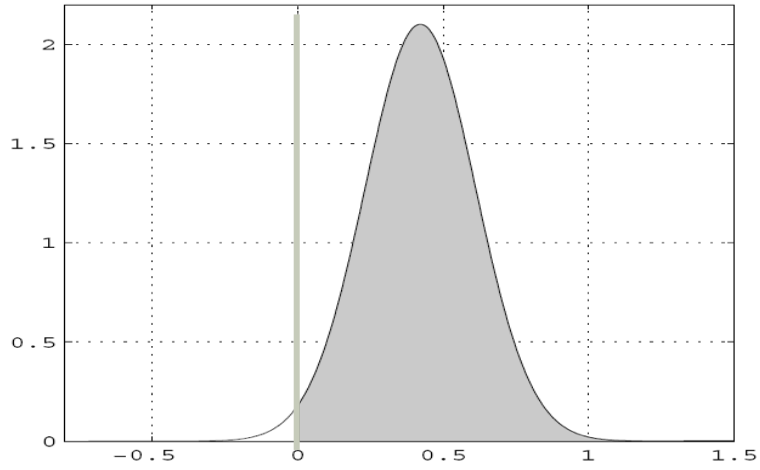
Independent Priors

$$KL_{Laplace} = \frac{1}{2}\ln\left|C_\theta\right| - \frac{1}{2}\ln\left|C_{\theta|y}\right| + \frac{1}{2}\left(\mu_{\theta|y} - \mu_\theta\right)^T C_\theta^{-1}\left(\mu_{\theta|y} - \mu_\theta\right)$$

Dependent Posteriors

Inference on Single Subject Parameters

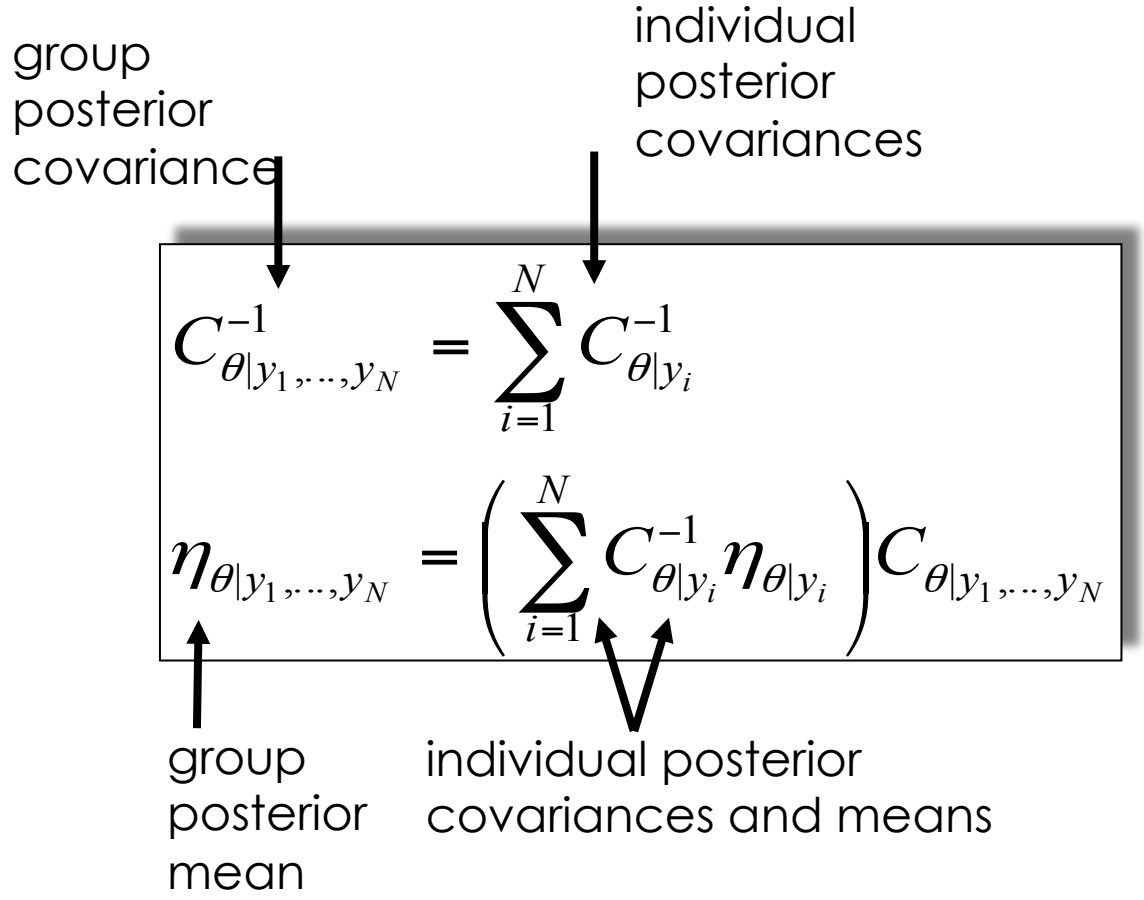
- Gaussian assumptions about the posterior distributions of the parameters
- posterior probability that a certain parameter (or contrast of parameters) is above a chosen threshold γ:
- By default, γ is chosen as zero – the prior ("does the effect exist?").



Inference on Multi Subject Parameters: FFX Bayesian Parameter Averaging

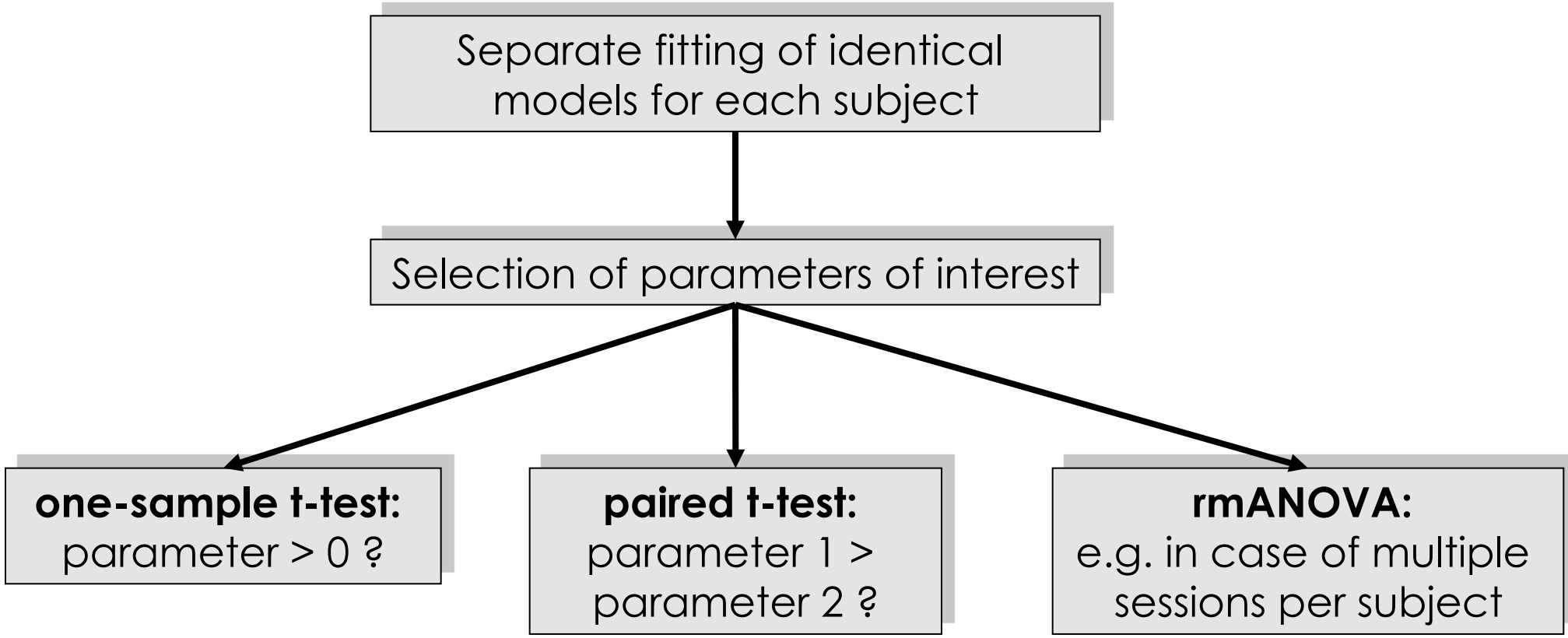
Likelihood distributions from different subjects are independent

Under Gaussian assumptions this is easy to compute:

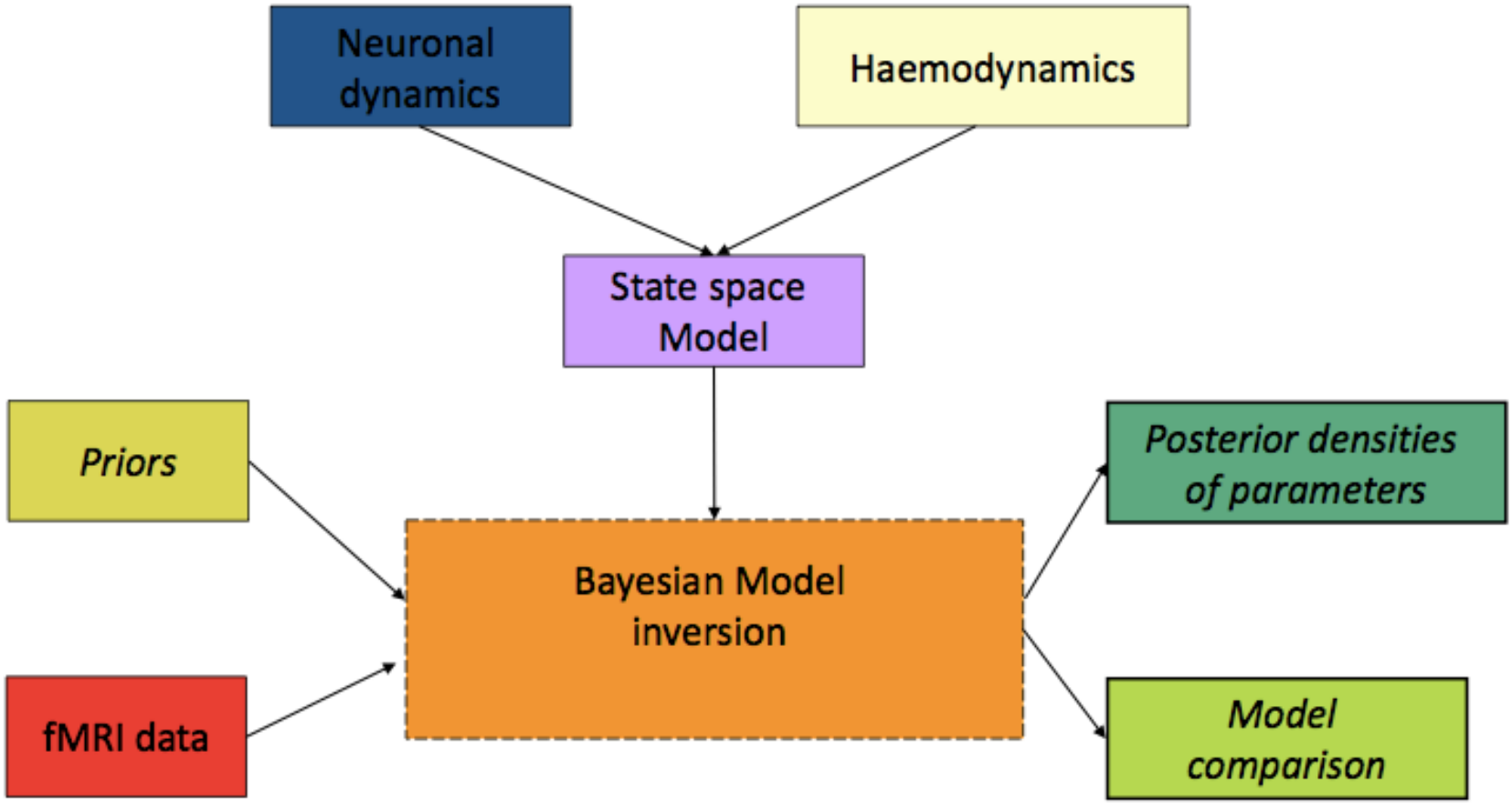


Inference on Multi Subject Parameters: RFX Summary Statistic Approach

- In analogy to "random effects" analyses in SPM, 2nd level analyses can be applied to DCM parameters:



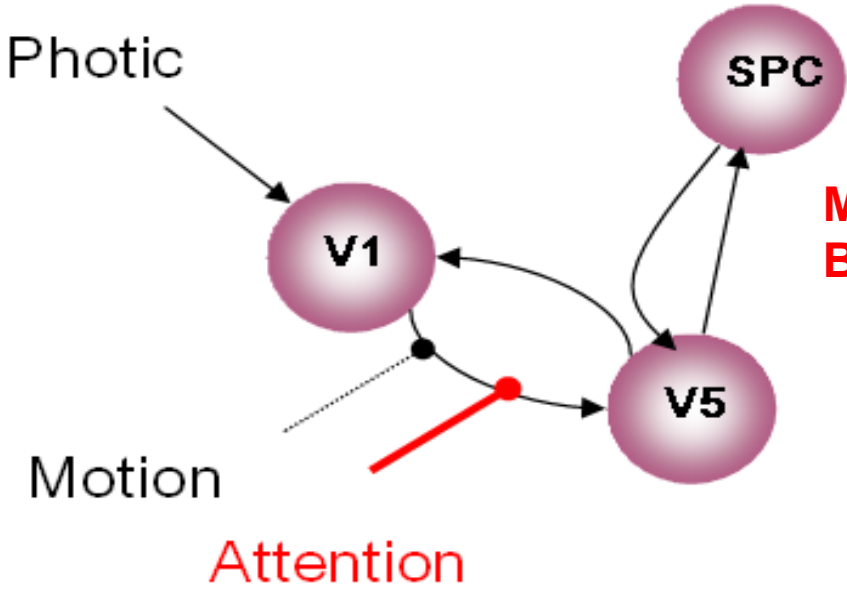
Roadmap


Neuronal dynamics
Haemodynamics
State space Model
Priors
fMRI data
Bayesian Model inversion
Posterior densities of parameters
Model comparison

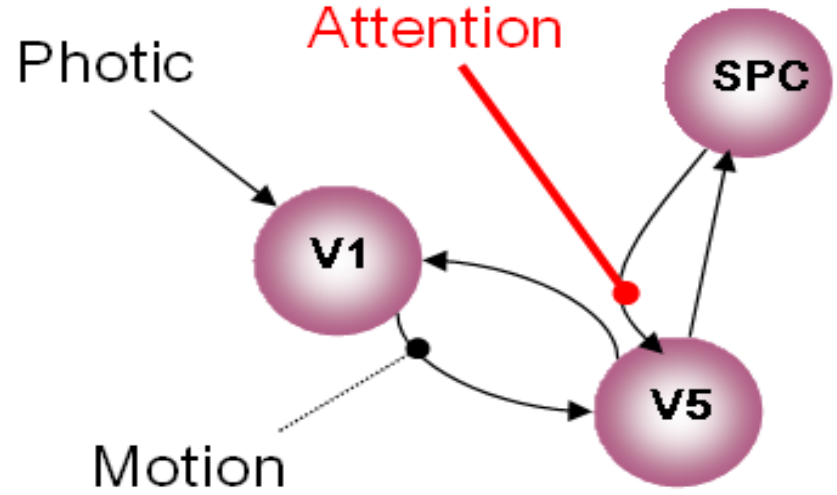
Effects of attention on motion responses in V5

Ingredients for a DCM

Specific hypothesis/question	
Model:	based on hypothesis
Timeseries:	from the SPM
Inputs:	from design matrix



Model 1/Hypothesis 1
Bottom-up Model



Model 2/ Hypothesis 2
Top-down Model

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Dynamic Causal Models and Physiological Inference: A Validation Study Using Isoflurane Anaesthesia in Rodents

Rosalyn J. Moran[1]*, Fabienne Jung[3], Tetsuya Kumagai[3], Heike Endepols[3], Rudolf Graf[3], Raymond J. Dolan[1], Karl J. Friston[1], Klaas E. Stephan[1,2], Marc Tittgemeyer[3]

1 Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, London, United Kingdom, **2** Laboratory for Social and Neural Systems Research, Department of Economics, University of Zurich, Zurich, Switzerland, **3** Max Planck Institute for Neurological Research, Cologne, Germany

Abstract

Generative models of neuroimaging and electrophysiological data present new opportunities for accessing hidden or latent brain states. Dynamic causal modeling (DCM) uses Bayesian model inversion and selection to infer the synaptic mechanisms underlying empirically observed brain responses. DCM for electrophysiological data, in particular, aims to estimate the relative strength of synaptic transmission at different cell types and via specific neurotransmitters. Here, we report a DCM validation study concerning inference on excitatory and inhibitory synaptic transmission, using different doses of a volatile anaesthetic agent (isoflurane) to parametrically modify excitatory and inhibitory synaptic processing while recording local field potentials (LFPs) from primary auditory cortex (A1) and the posterior auditory field (PAF) in the auditory belt region in rodents. We test whether DCM can infer, from the LFP measurements, the expected drug-induced changes in synaptic transmission mediated via fast ionotropic receptors; i.e., excitatory (glutamatergic) AMPA and inhibitory $GABA_A$ receptors. Cross- and auto-spectra from the two regions were used to optimise three DCMs based on biologically plausible neural mass models and specific network architectures. Consistent with known extrinsic connectivity patterns in sensory hierarchies, we found that a model comprising forward connections from A1 to PAF and backward connections from PAF to A1 outperformed a model with forward connections from PAF to A1 and backward connections from A1 to PAF and a model with reciprocal lateral connections. The parameter estimates from the most plausible model indicated that the amplitude of fast glutamatergic excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs) behaved as predicted by previous neurophysiological studies. Specifically, with increasing levels of anaesthesia, glutamatergic EPSPs decreased linearly, whereas fast GABAergic IPSPs displayed a nonlinear (saturating) increase. The consistency of our model-based *in vivo* results with experimental *in vitro* results lends further validity to the capacity of DCM to infer on synaptic processes using macroscopic neurophysiological data.

Citation: Moran RJ, Jung F, Kumagai T, Endepols H, Graf R, et al. (2011) Dynamic Causal Models and Physiological Inference: A Validation Study Using Isoflurane Anaesthesia in Rodents. PLoS ONE 6(8): e22790. doi:10.1371/journal.pone.0022790

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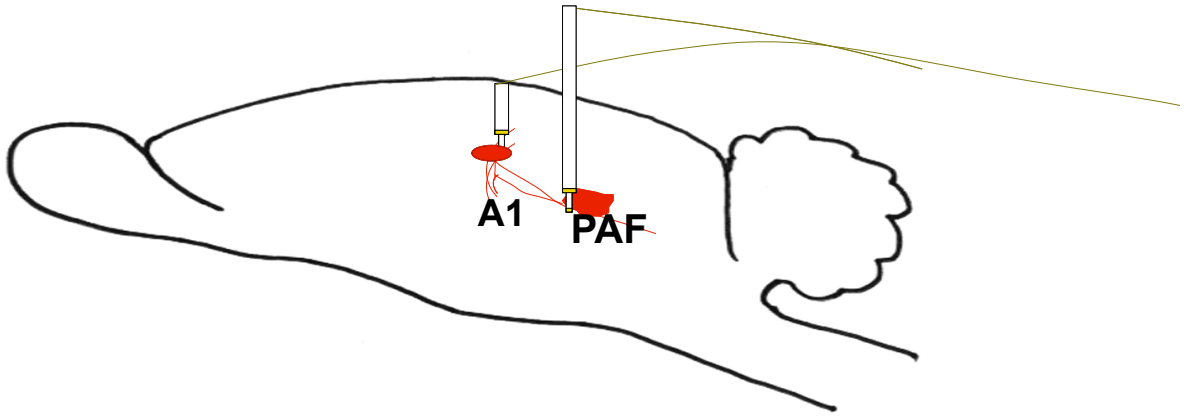
Competing Interests: The authors have declared that no competing interests exist.

* E-mail: r.moran@fil.ion.ucl.ac.uk

Anaesthesia Depth



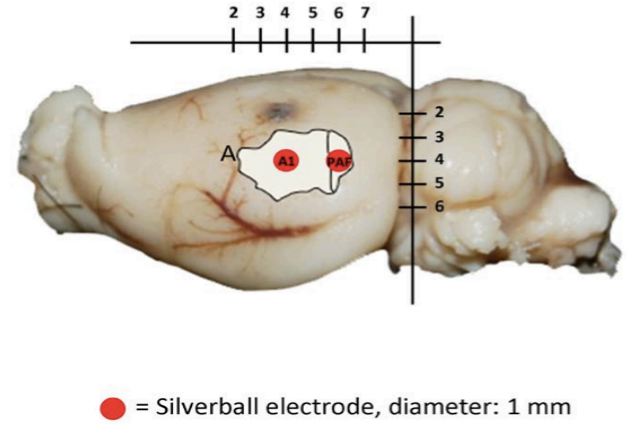
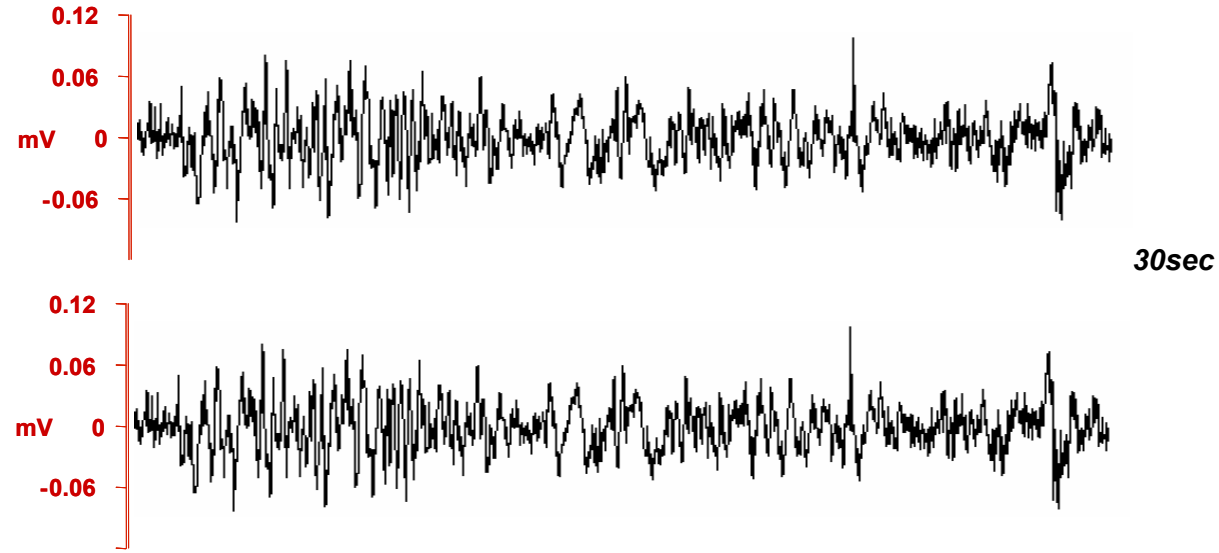


Figure 1. Electrode Placement. Electrode placement (silverball electrodes) in primary auditory cortex (A1) and posterior auditory field (PAF) in auditory cortex (A). The anatomical labelling of auditory fields was taken from [38] and matched to a rat brain from our animals. The indicated scaling is in mm.
doi:10.1371/journal.pone.0022790.g001

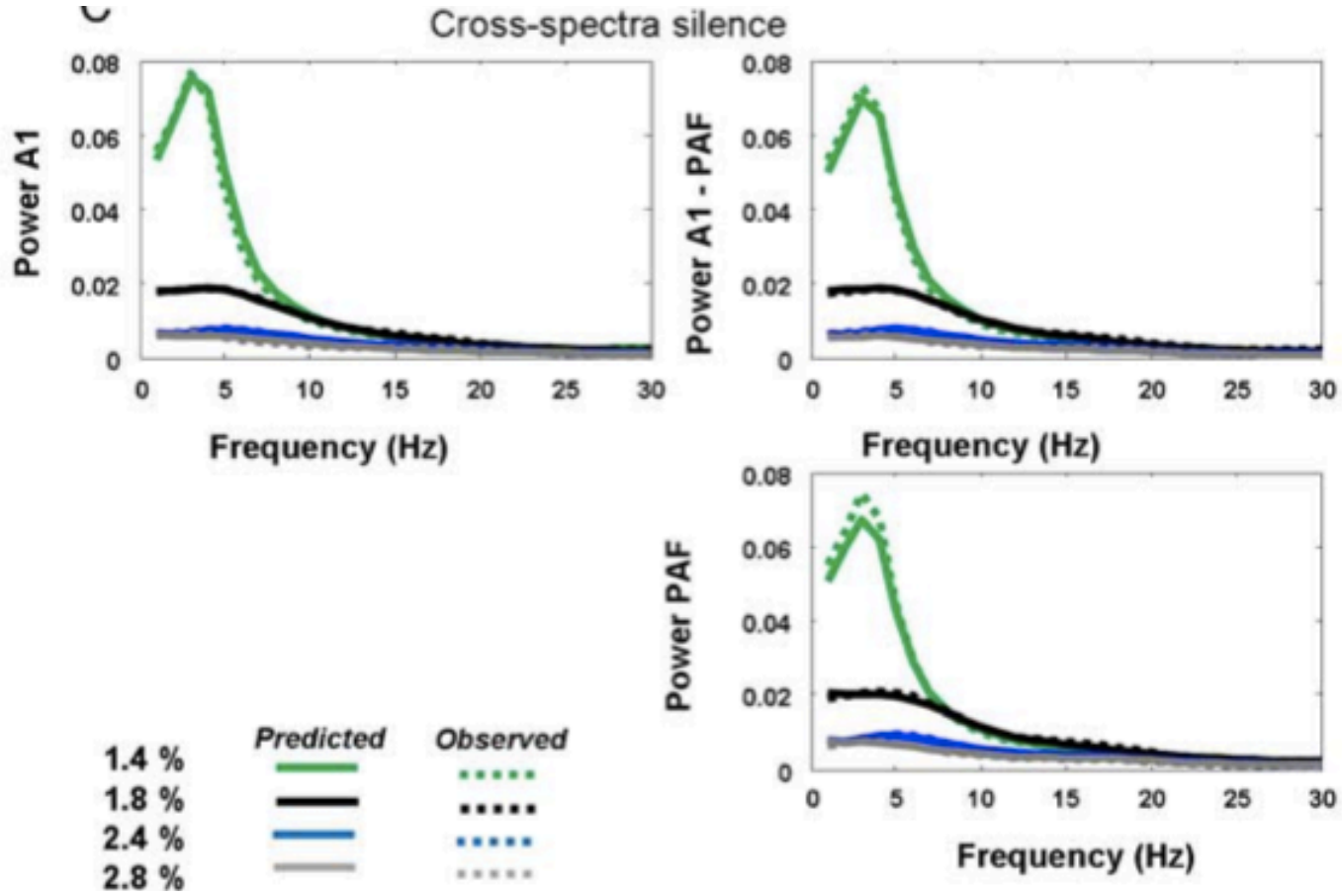
LFP



Trials:
1: 1.4 Mg Isoflourane
2: 1.8 Mg Isoflourane
3: 2.4 Mg Isoflourane
4: 2.8 Mg Isoflourane
5: awake

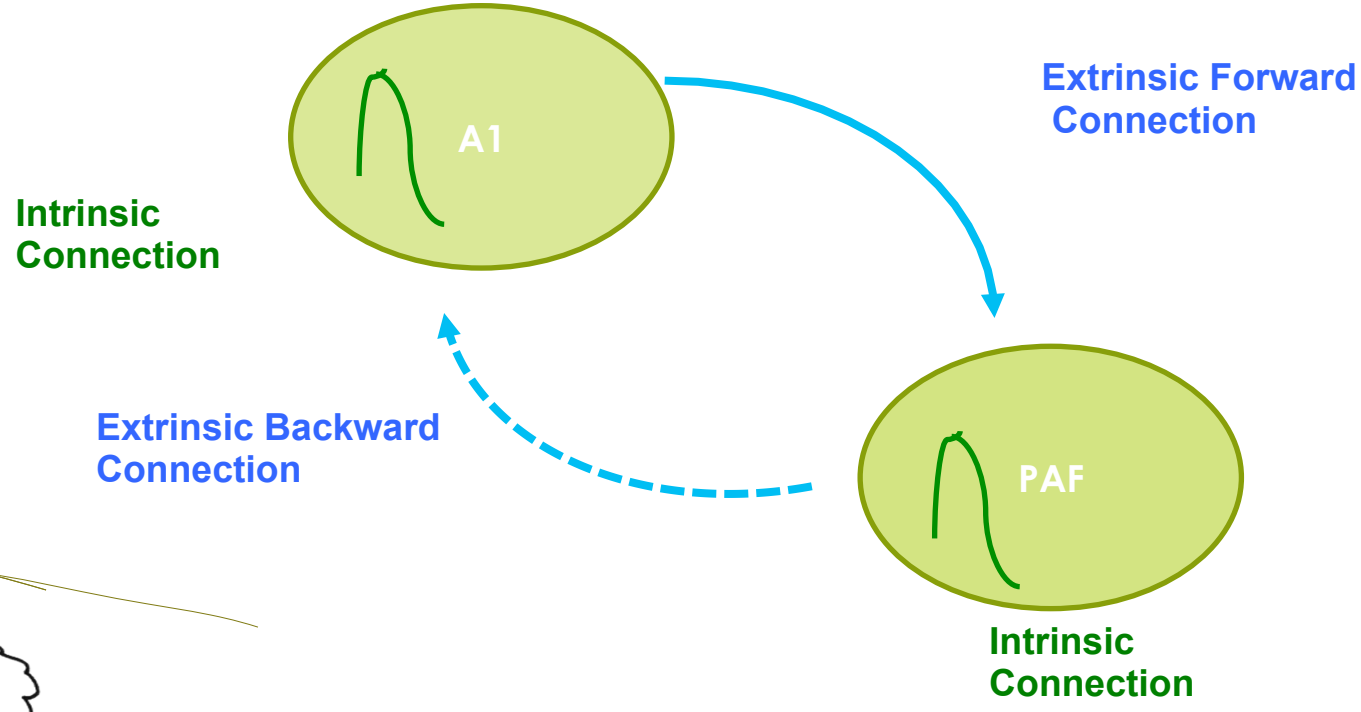
(1 per condition)

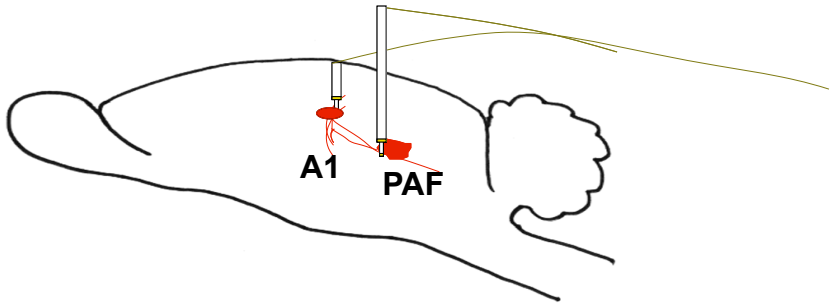
Steady-State Spectral Responses



Hypothesised mechanisms of action

Connectivity effected by Isoflurane:
Extrinsic or Intrinsic? (Bayesian Model Comparison)
How so? (Posterior Parameter Estimates)





Overview

- Dynamic causal models for fMRI

- Work through example: Attention to Motion

- Neural level & Hemodynamic level

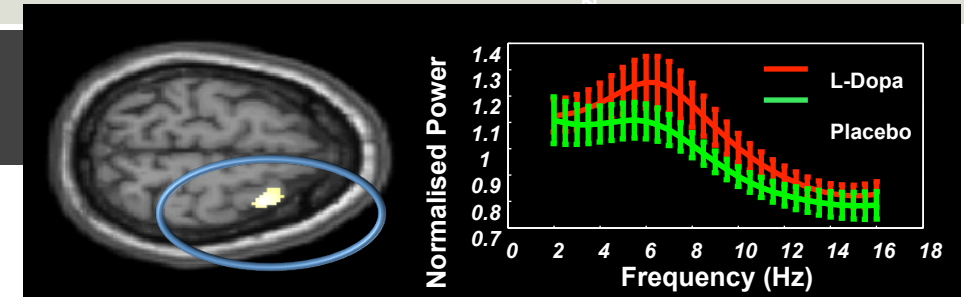
- Parameter estimation, priors & inference

- Dynamic causal models for Steady State Responses (rat LFPs)

- Work through example: Isoflurane effects on connectivity

- Neural mass model

Neural Mass Model



Lateral connections

Intrinsic connections

γ_5

Backward connections

Inhibitory cells in supragranular layers

$$\dot{x}_7 = x_8$$
$$\dot{x}_8 = \kappa_e H_e (B + \gamma_3 I) S(x_9) - 2\kappa_e x_8 - \kappa_e^2 x_7$$
$$\dot{x}_{10} = x_{11}$$
$$\dot{x}_{11} = \kappa_i H_i \gamma_5 S(x_{12}) - 2\kappa_i x_{11} - \kappa_i^2 x_{10}$$
$$\dot{x}_{12} = x_8 - x_{11}$$

γ_4 γ_3

input

u

Excitatory spiny cells in granular layers

$$\dot{x}_1 = x_4$$
$$\dot{x}_4 = \kappa_e H_e ((F + \gamma_1 I) S(x_9) + Cu) - 2\kappa_e x_4 - \kappa_e^2 x_1$$

γ_1 γ_2

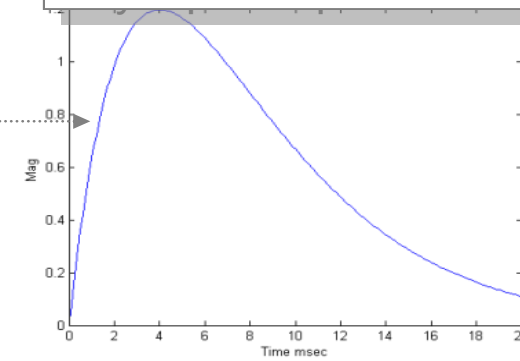
Excitatory pyramidal cells in infragranular layers

$$\dot{x}_2 = x_5$$
$$\dot{x}_5 = \kappa_e H_e (BS(x_9) + \gamma_2 S(x_1)) - 2\kappa_e x_5 - \kappa_e^2 x_2$$
$$\dot{\mu}_3 = x_6$$
$$\dot{x}_6 = \kappa_i H_i \gamma_4 S(x_{12}) - 2\kappa_i x_6 - \kappa_i^2 x_3$$
$$\dot{x}_9 = x_5 - x_6$$

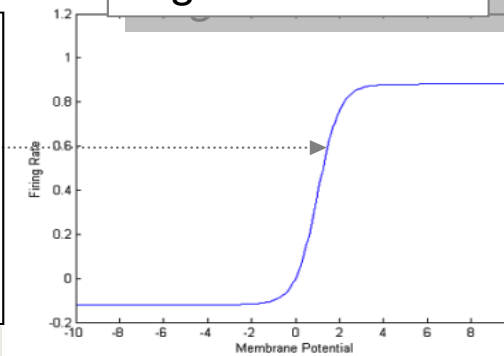
Forward connections

$$\dot{x} = f(x,u)$$

Synaptic 'alpha' kernel



Sigmoid function



Time to Frequency Domain

Linearise around a stable fixed point or LC

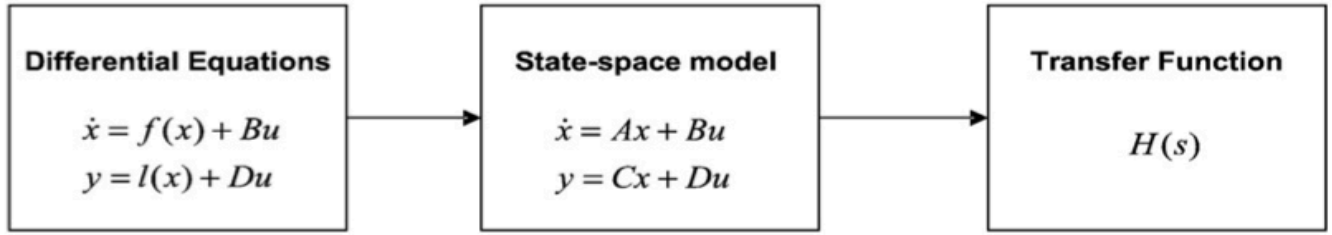


Fig. 1. Conversion scheme to obtain spectral outputs from the systems transfer function.

NeuroImage 44 (2009) 796–811

Contents lists available at ScienceDirect

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

DCM for SSR

Dynamic causal models of

R.J. Moran [a,*], K.E. Stephan [a,b], T. S

[a] Wellcome Trust Centre for Neuroimaging, Institute of N
[b] Laboratory for Social and Neural Systems Research, Insi
[c] Institute of Physiology, University of Münster, Germany

DCM for CSD

NeuroImage 59 (2012) 439–455

Contents lists available at ScienceDirect

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Technical Note

DCM for complex-valued data: Cross-spectra, coherence and phase-delays

K.J. Friston [a], A. Bastos [b,c], V. Litvak [a], K.E. Stephan [a,d], P. Fries [c], R.J. Moran [a,*]

[a] The Wellcome Trust Centre for Neuroimaging, University College London, Queen Square, London WC1N 3BG, UK
[b] Center for Neuroscience and Center for Mind and Brain, University of California-Davis, Davis, CA 95618, USA
[c] Ernst Strüngmann Institute in Cooperation with Max Planck Society, Deutschordenstraße 46, 60528 Frankfurt, Germany
[d] Laboratory for Social and Neural Systems Research, Dept. of Economics, University of Zurich, Switzerland

Hypothesised mechanisms of action

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Extrinsic or Intrinsic? (Bayesian Model Comparison)
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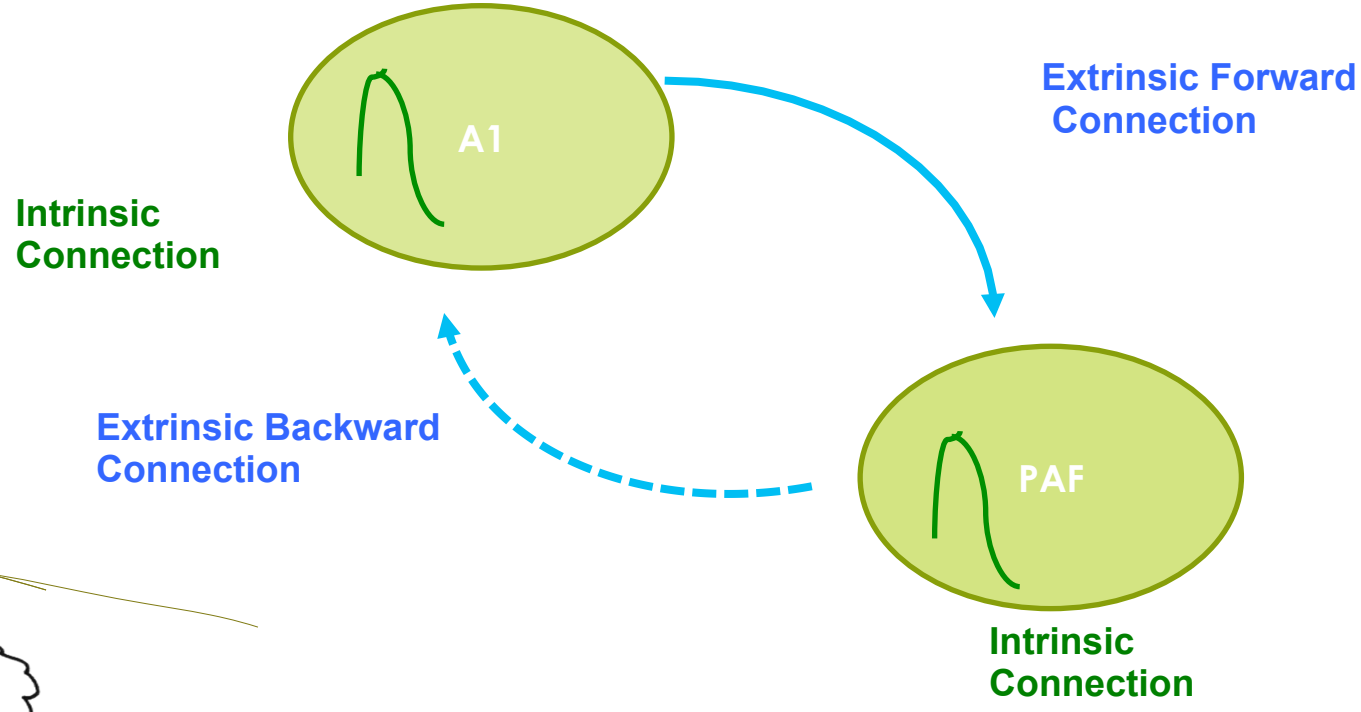

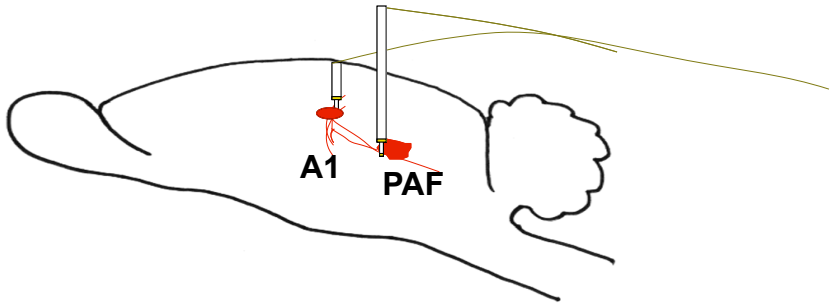

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