Institut des Neurosciences GRENOBLE

Dynamic Causal Modelling for fMRI

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Grenoble Brain Connectivity Course

Outline

- Introduction
- DCM neuronal model
- DCM hemodynamic model
- Canonical example
- Recent DCM developments

Different levels for the study of brain processes

Where is implemented a given neural process?

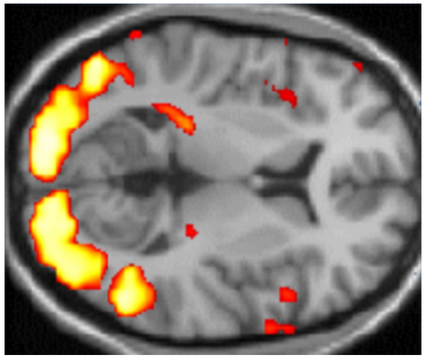
What are the mechanisms that implement this process?

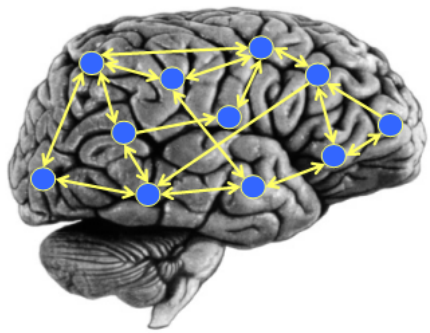
What does mean this process (in computational terms) ?

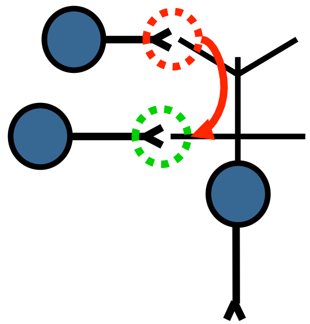
Activation maps

Model of interaction between regions

Models of neural codes







BASICS OF DCM

Effective connectivity
Generative models

Forward problem

Given the generative model, one can **predict** the measured data

NEURONAL VARIABLES

Synaptic time constant

Synaptic efficacy

Inhibition/Excitation

Connectivity

MACROSCOPIC DATA

LFP

EEG/MEG

FMRI

PET

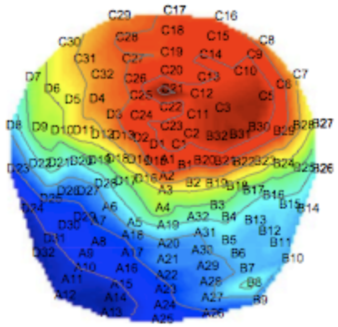
Inverse problem

Given the measured data, one can **estimate** the generative model

Evolution and observation mappings

Hemodynamic observation model: temporal convolution

Electromagnetic observation model: spatial convolution

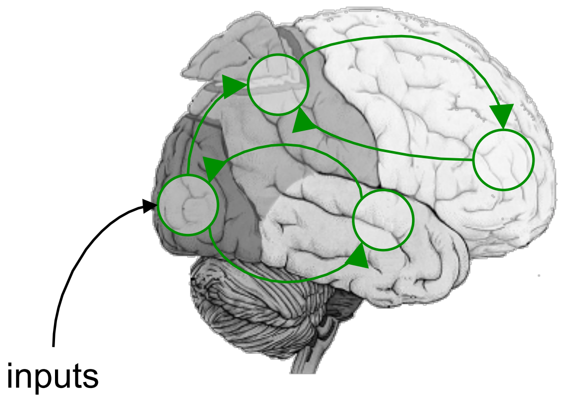


neural states dynamics

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

fMRI

EEG/MEG

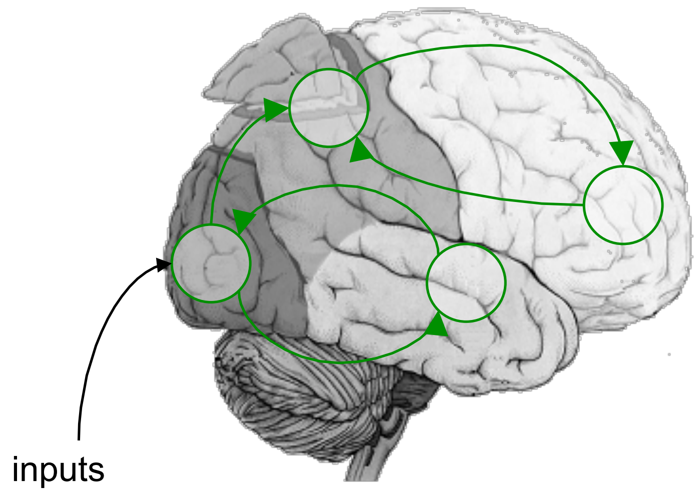


- simple neuronal model
- realistic observation model

- realistic neuronal model
- simple observation model

Basics of DCM

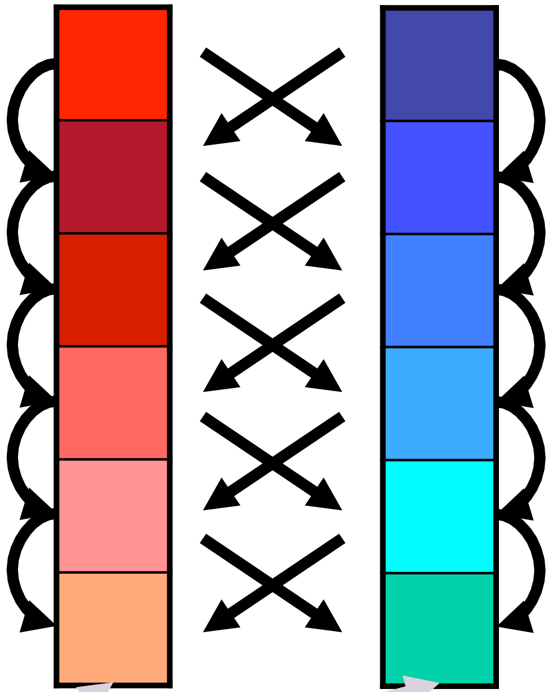
- **DCM allows us**
  - To look at how areas within a network interact
  - To investigate functional integration & modulation of specific cortical pathways
    - **Temporal dependency of activity within and between areas (causality)**



Temporal dependence and causal relations

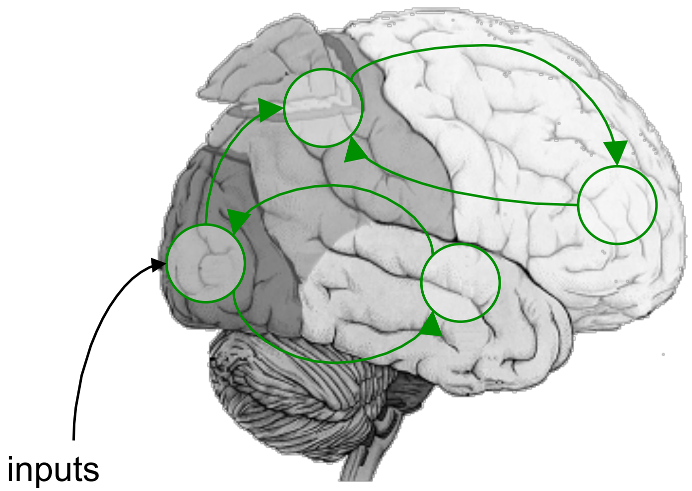
Seed voxel approach, PPI etc.

Dynamic *Causal* Models



Basics of DCM

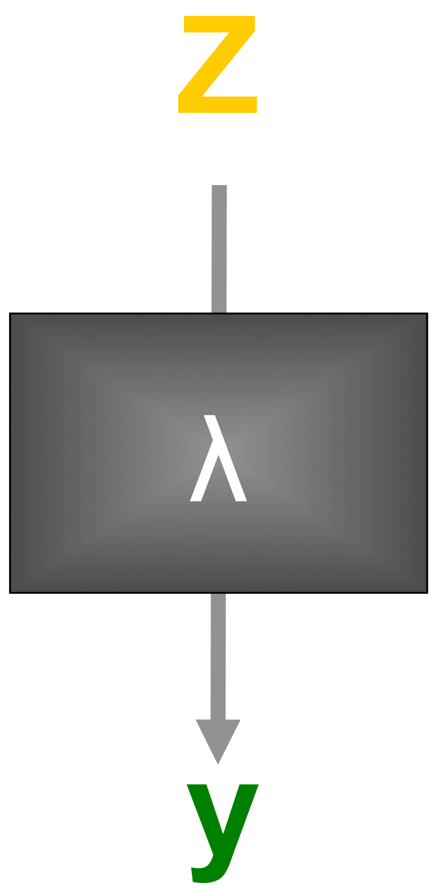
- **DCM allows us**
  - To look at how areas within a network interact
  - To investigate functional integration & modulation of specific cortical pathways
    - Temporal dependency of activity within and between areas (causality)
    - **Separate neuronal activity from observed BOLD responses**



Basics of DCM: Neuronal and BOLD level

- Cognitive system is modelled at its underlying neuronal level (not directly accessible for fMRI)

- The modelled neuronal dynamics (Z) are transformed into area-specific BOLD signals (y) by a hemodynamic model (λ)

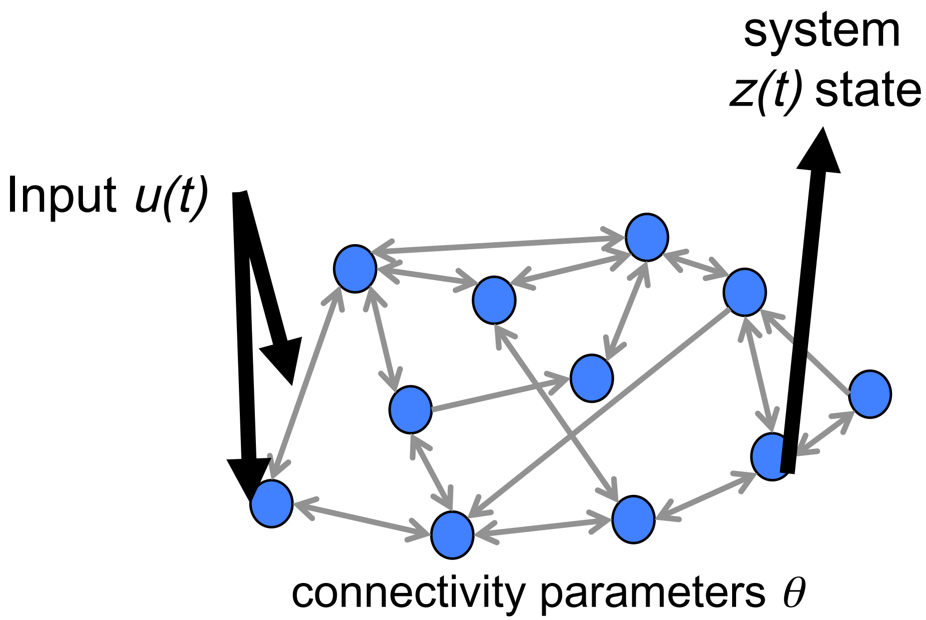


The aim of DCM is to estimate <u>parameters at the neuronal level</u> such that the modelled and measured BOLD signals are optimally similar.

NEURONAL MODEL

Neuronal systems are represented by differential equations

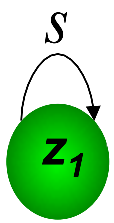
- A system is a set of elements $z_n(t)$ which interact in a spatially and temporally specific fashion
- State changes of the system states are dependent on:
  - the current state z
  - external inputs u
  - its connectivity θ
  - time constants & delays



$$\frac{dz}{dt} = F(z, u, \theta)$$

DCM parameters = rate constants

Generic solution to the ODEs in DCM:

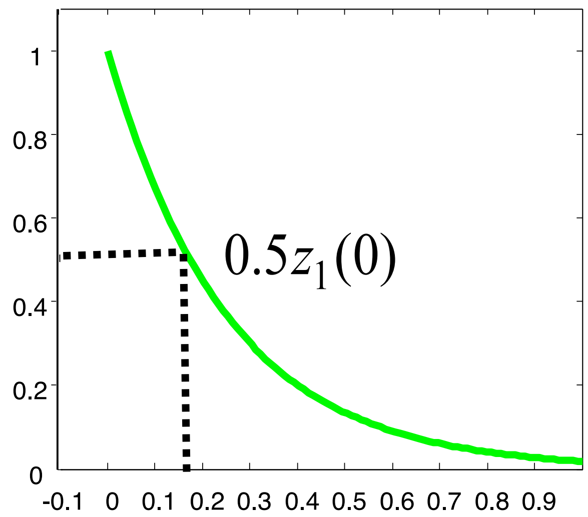


$$\frac{dz_1}{dt} = -sz_1 \quad \Rightarrow \quad z_1(t) = z_1(0)\exp(-st), \qquad z_1(0) = 1$$

Half-life τ

$$z_1(\tau) = 0.5 z_1(0)$$
$$= z_1(0)\exp(-s\tau)$$
$$\Rightarrow \quad s = \ln 2 / \tau$$

Decay function



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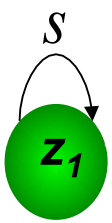
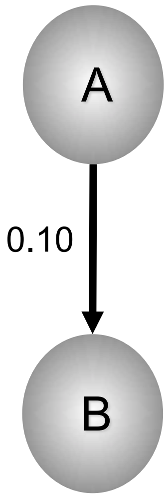
Generic solution to the ODEs in DCM:

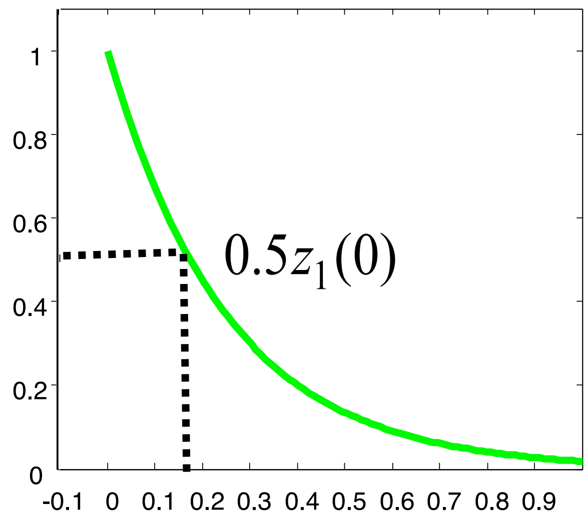


$$\frac{dz_1}{dt} = -sz_1 \Rightarrow z_1(t) = z_1(0)\exp(-st), \qquad z_1(0) = 1$$



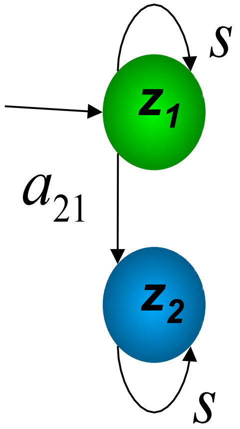
If A→B is 0.10 s^{-1} this means that, per unit time, the increase in activity in B corresponds to 10% of the activity in A

Decay function



$$\tau = \ln 2 / s$$

Linear dynamics
2 nodes

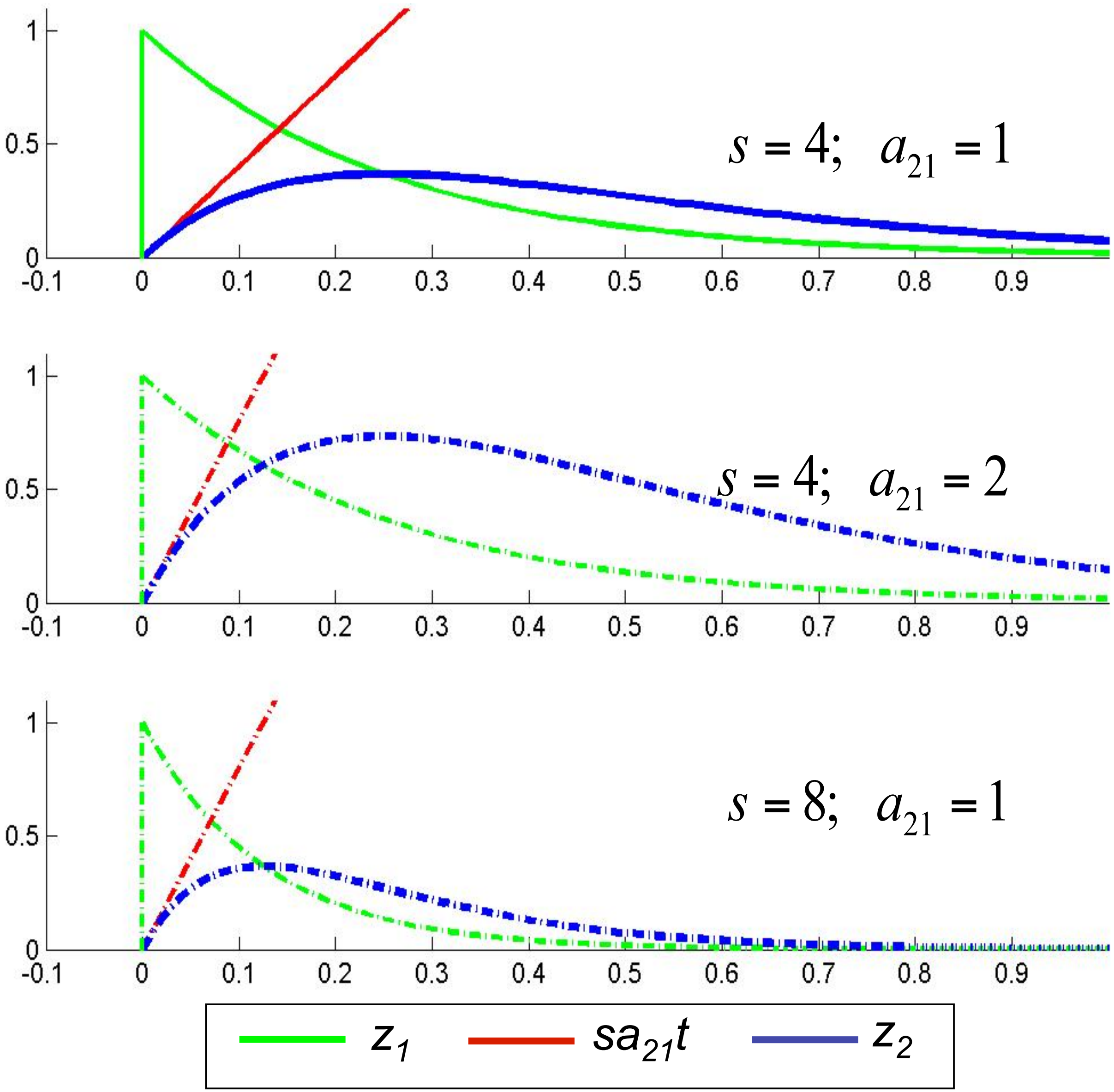


$$\dot{z}_1 = -s z_1$$
$$\dot{z}_2 = s\left(a_{21} z_1 - z_2\right)$$

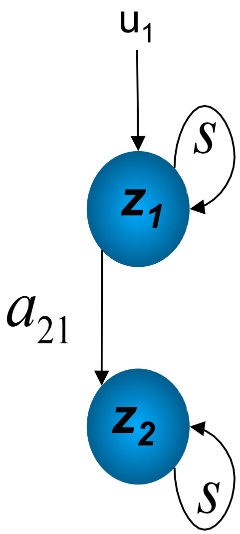
$$z_1(0) = 1$$
$$z_2(0) = 0$$

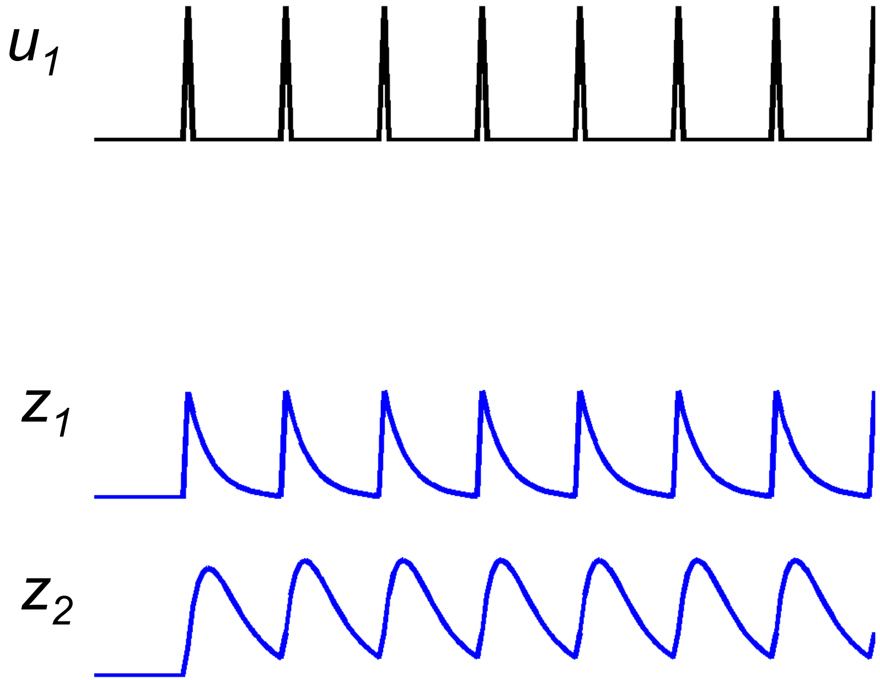
$$z_1(t) = \exp(-st)$$
$$z_2(t) = s a_{21} t \exp(-st)$$

$$a_{21} > 0$$



Neurodynamics
2 nodes with input

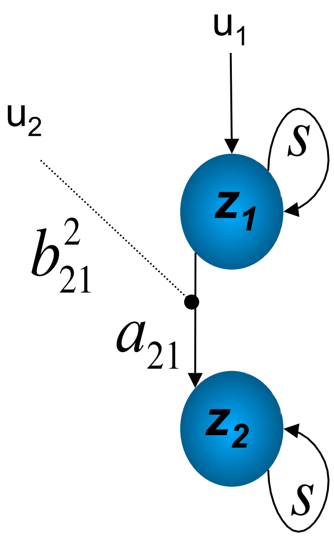


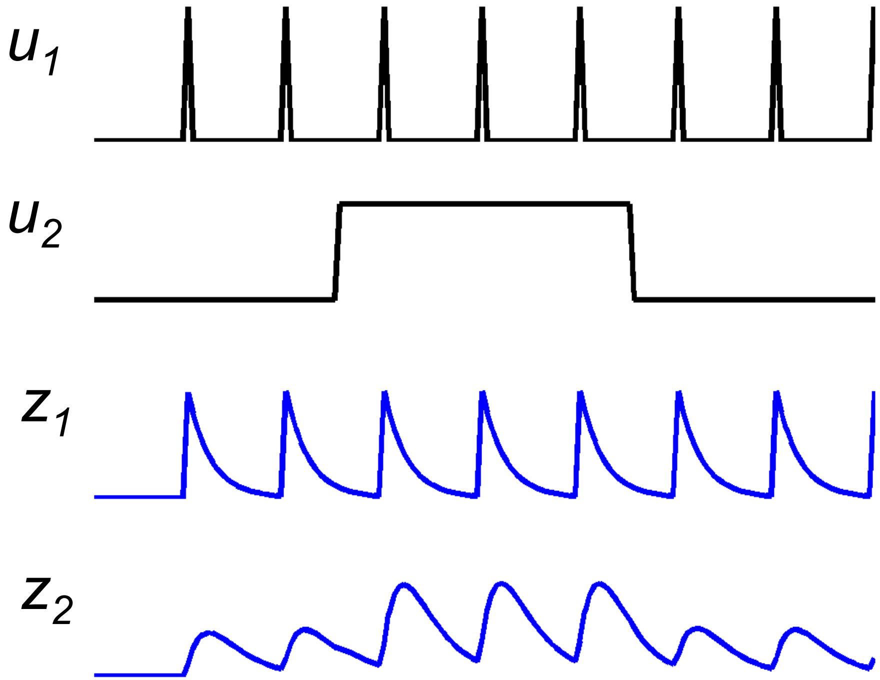


$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = s \begin{bmatrix} -1 & 0 \\ a_{21} & -1 \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} c \\ 0 \end{bmatrix} u_1 \qquad a_{21} > 0$$

activity in z_2 is coupled to z_1 via coefficient a_{21}

Neurodynamics
Positive modulation

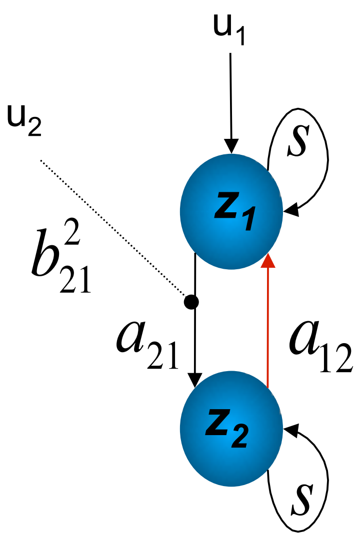


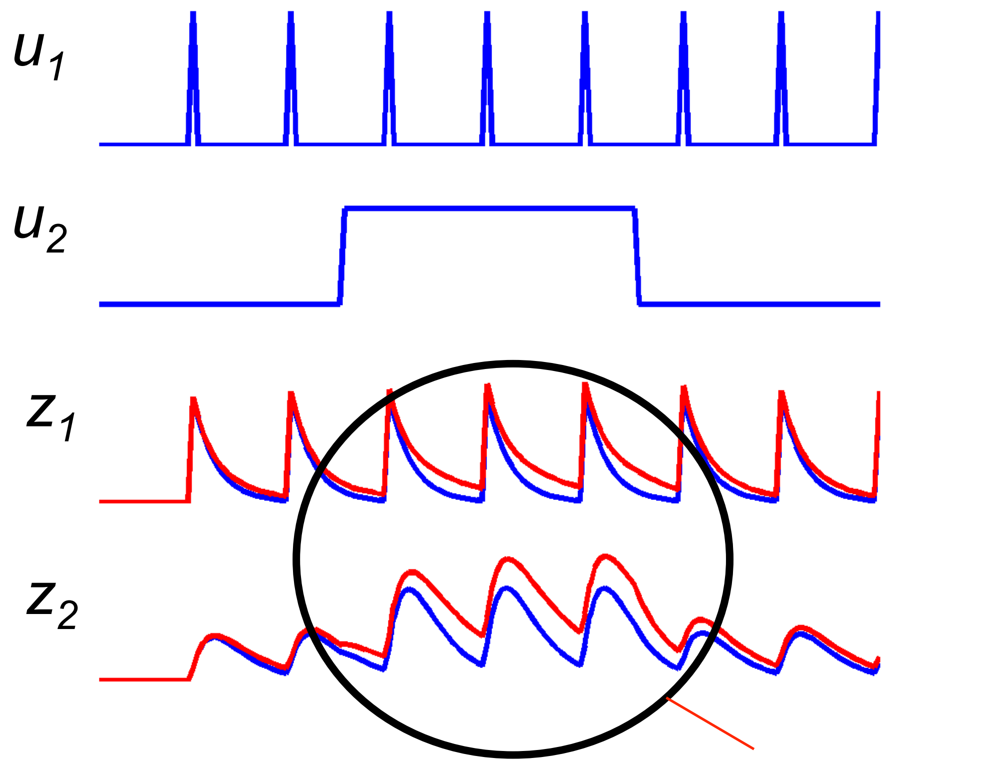


$$\begin{bmatrix}\dot{z}_1\\ \dot{z}_2\end{bmatrix} = s\begin{bmatrix}-1 & 0\\ a_{21} & -1\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + u_2\begin{bmatrix}0 & 0\\ b^2_{21} & 0\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + \begin{bmatrix}c\\ 0\end{bmatrix}u_1 \qquad b^2_{21} > 0$$

activity in z_2 is coupled to z_1 via coefficient a_{21}

Neurodynamics
Reciprocal connections





$$\begin{bmatrix}\dot{z}_1\\ \dot{z}_2\end{bmatrix} = s\begin{bmatrix}-1 & a_{12}\\ a_{21} & -1\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + u_2\begin{bmatrix}0 & 0\\ b_{21}^{2} & 0\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + \begin{bmatrix}c\\ 0\end{bmatrix}u_1 \qquad a_{12}, a_{21}, b_{21}^{2} > 0$$

contextual modulation through coefficient b^2_{21}

Bilinear state equation in DCM for fMRI

state changes → connectivity → modulation of connectivity → state vector → direct inputs → external inputs

$$\begin{bmatrix} \dot{z}_1 \\ \vdots \\ \dot{z}_n \end{bmatrix} = \left\{ \begin{bmatrix} a_{11} & \cdots & a_{1n} \\ \vdots & \ddots & \vdots \\ a_{n1} & \cdots & a_{nn} \end{bmatrix} + \sum_{j=1}^{m} u_j \begin{bmatrix} b_{11}^{j} & \cdots & b_{1n}^{j} \\ \vdots & \ddots & \vdots \\ b_{n1}^{j} & \cdots & b_{nn}^{j} \end{bmatrix} \right\} \begin{bmatrix} z_1 \\ \vdots \\ z_n \end{bmatrix} + \begin{bmatrix} c_{11} & \cdots & c_{1m} \\ \vdots & \ddots & \vdots \\ c_{n1} & \cdots & c_{nm} \end{bmatrix} \begin{bmatrix} u_1 \\ \vdots \\ u_m \end{bmatrix}$$

n regions

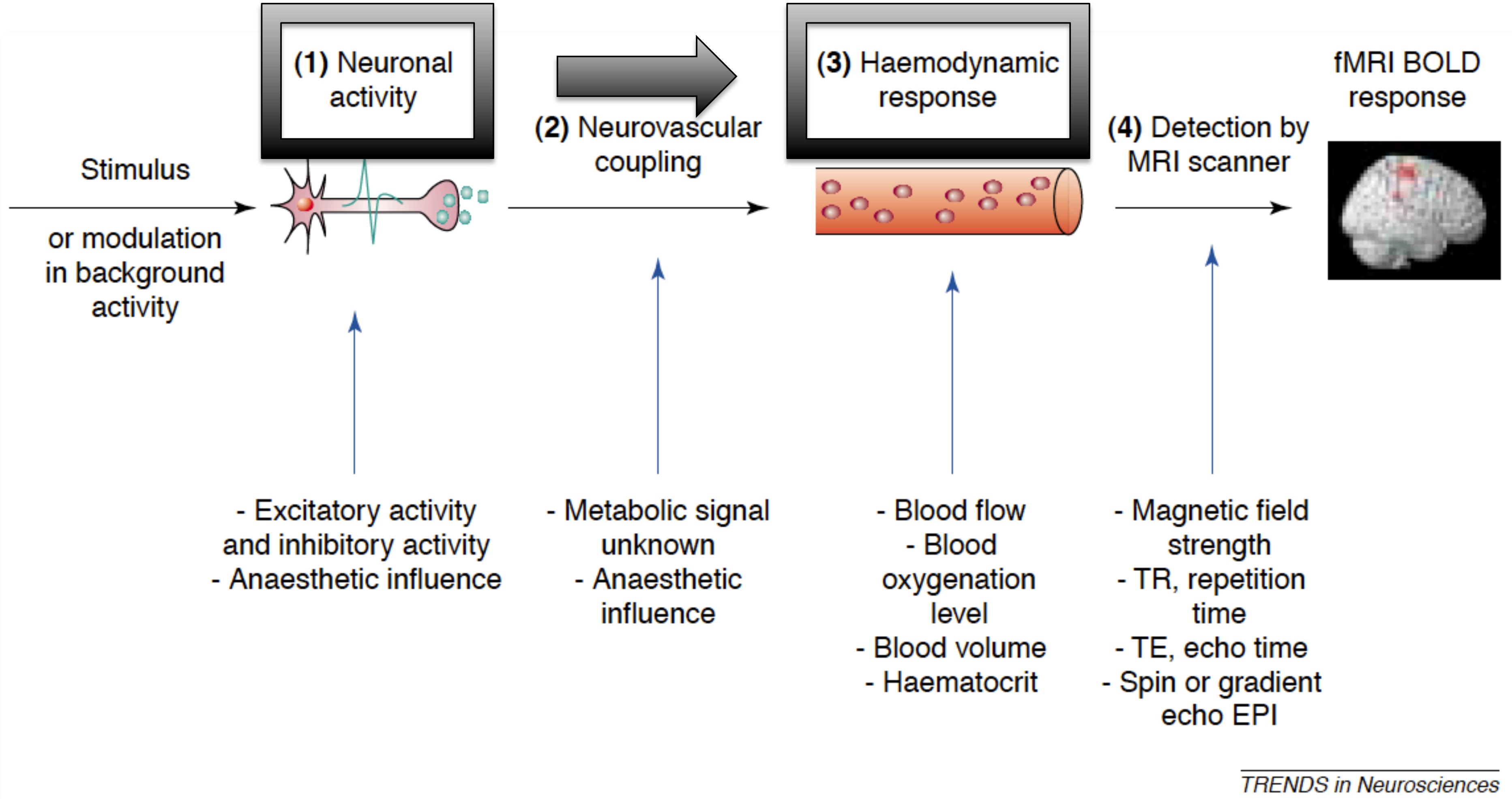
m mod inputs

m drv inputs

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

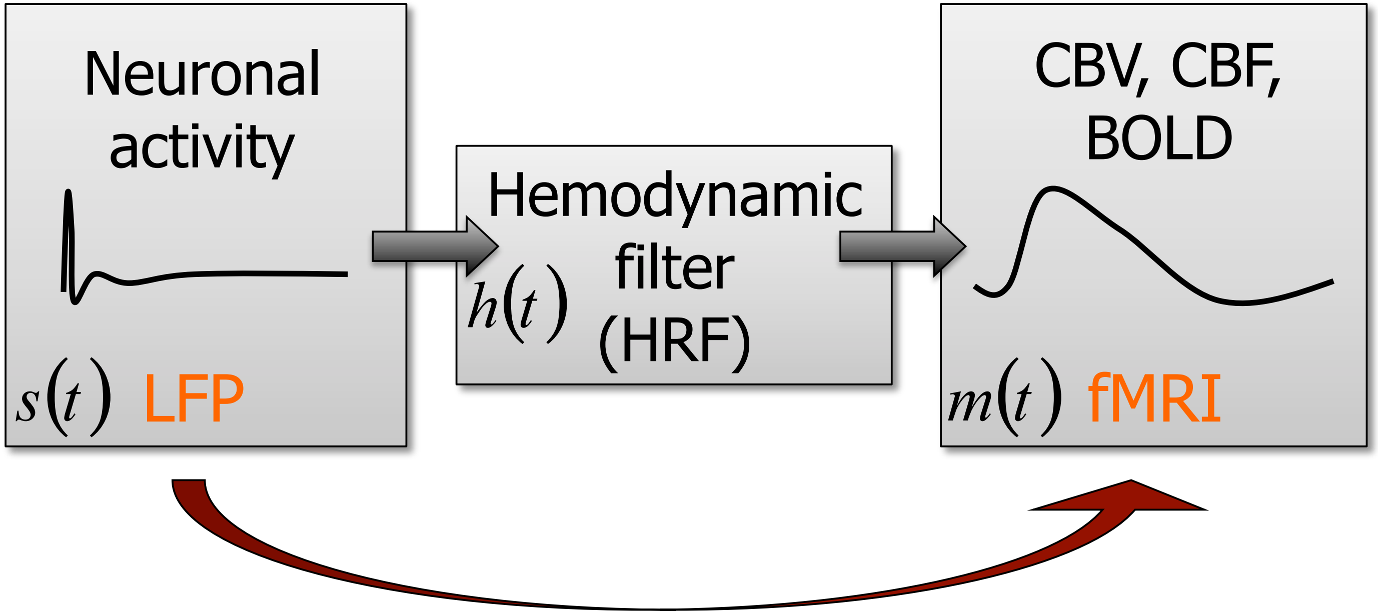
HEMODYNAMIC MODEL

LFP/BOLD
Standard biophysical model



Arthurs & Boniface, TINS, 2000

LFP/BOLD
Standard biophysical model

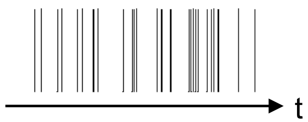


Prediction

$$m(t) = s(t) \otimes h(t) + \varepsilon(t)$$

General Linear Model

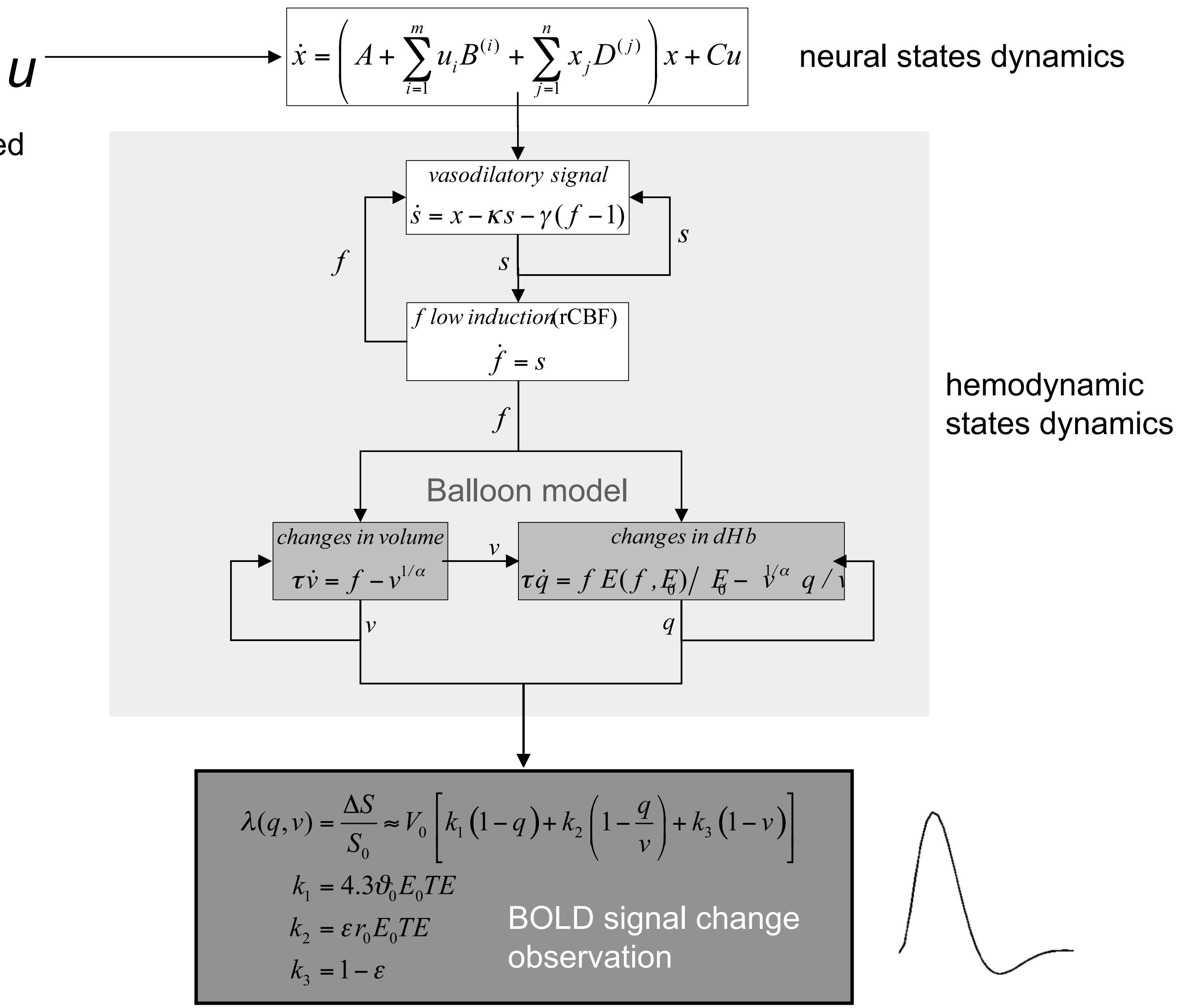
DCM hemodynamic model



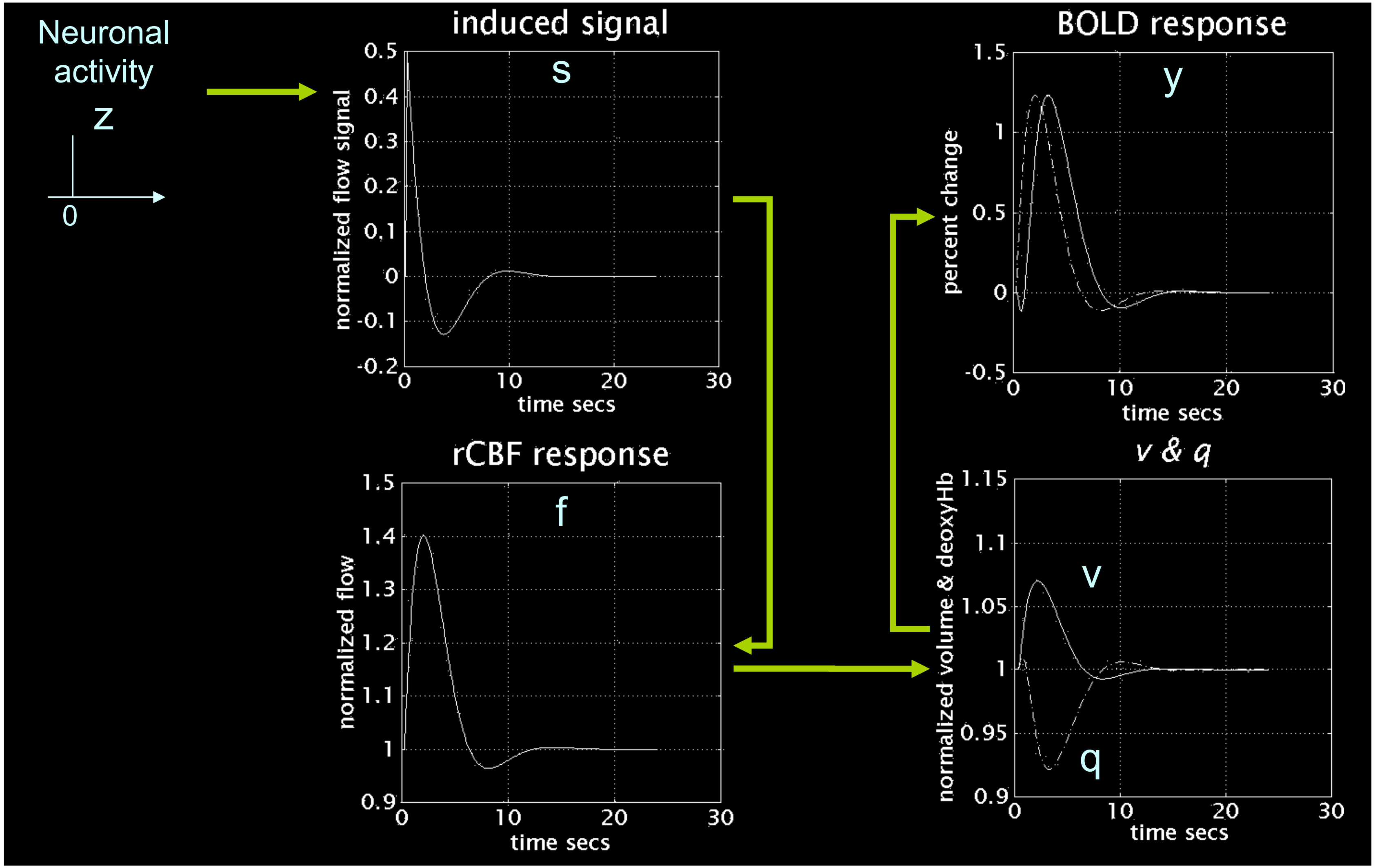
experimentally controlled stimulus

$$\theta^h = \{\kappa, \gamma, \tau, \alpha, E_0, \varepsilon\}$$

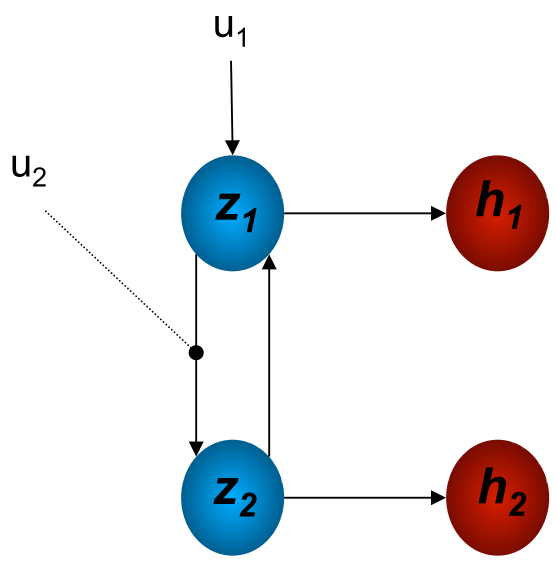
$$\theta^n = \{A, B^{(i)}, C, D^{(j)}\}$$

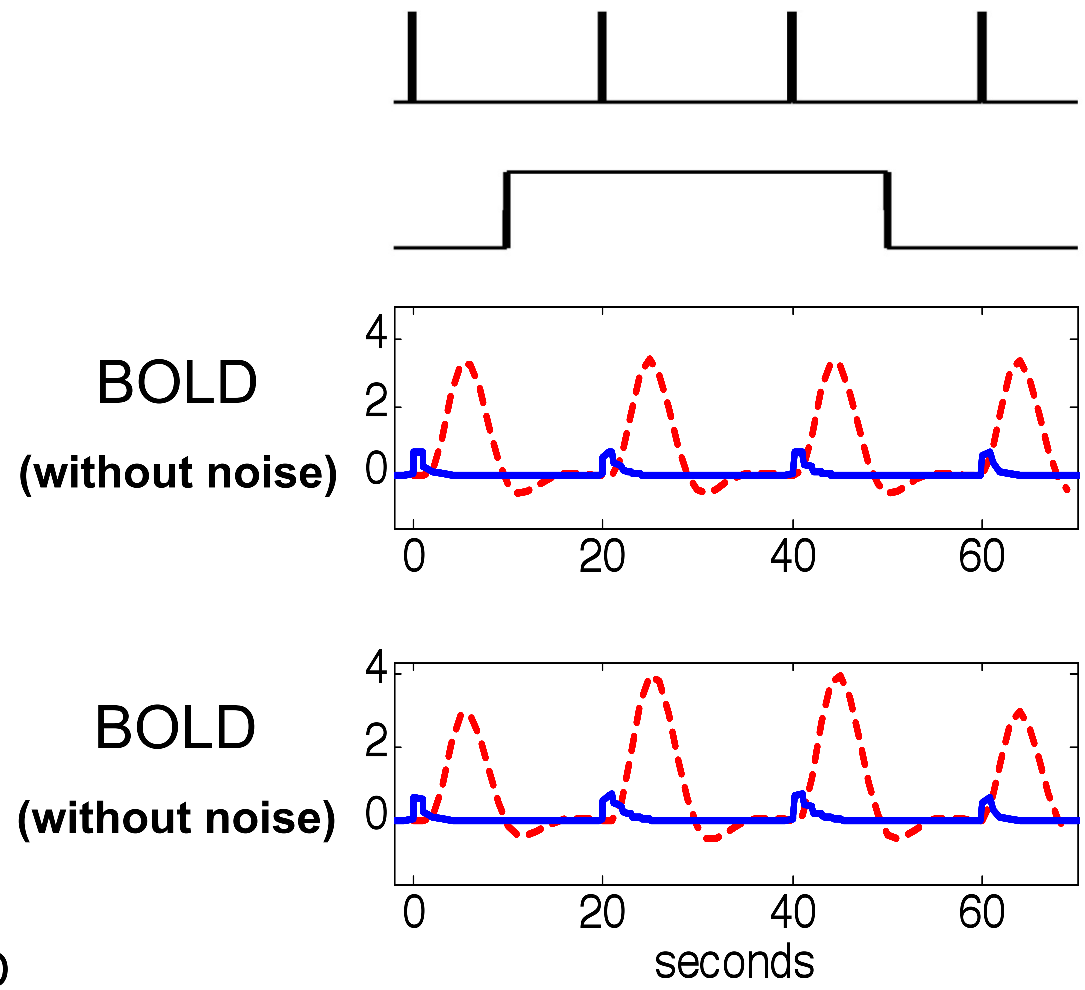


DCM hemodynamic model



Haemodynamics
Reciprocal connections

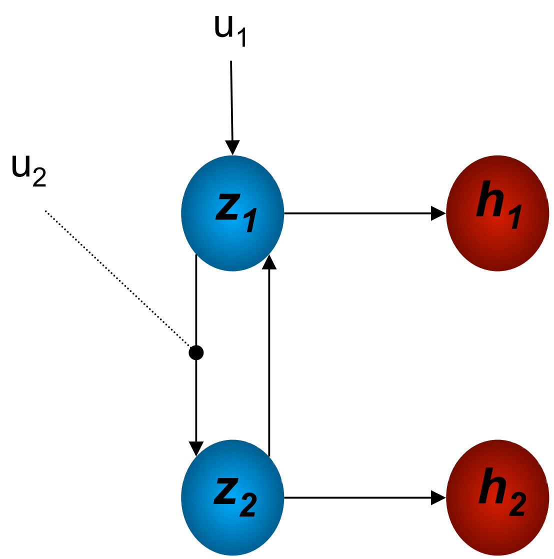




h(u,θ) represents the BOLD response (balloon model) to input

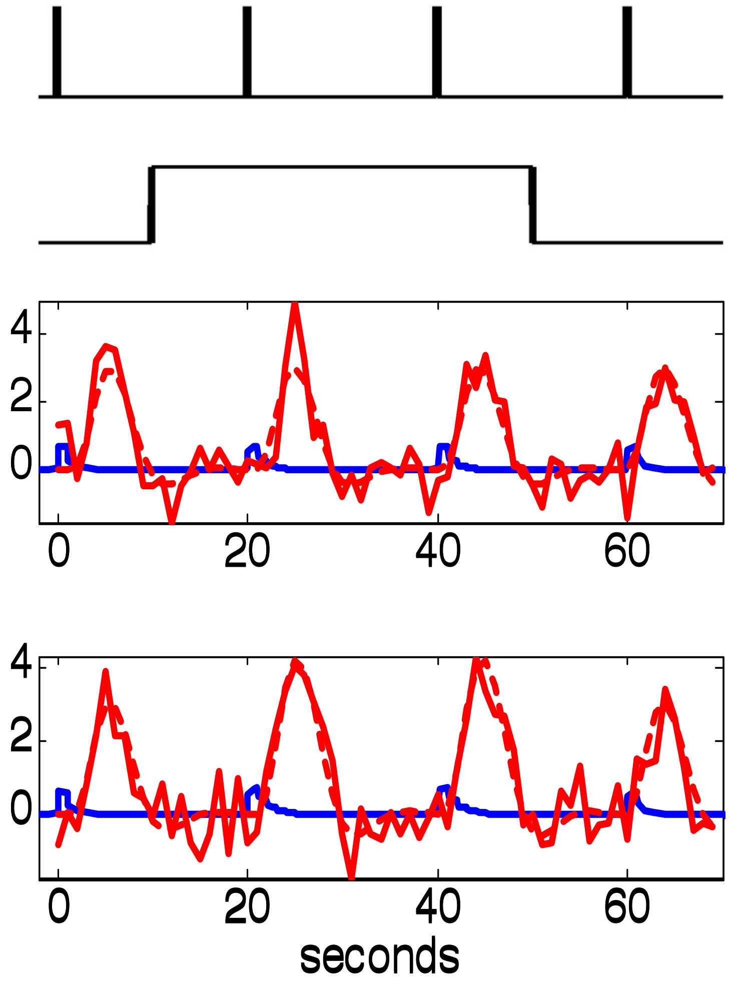
blue: neuronal activity
red: bold response

Haemodynamics
Reciprocal connections



BOLD
(noise added)

BOLD
(noise added)



y represents simulated observation of BOLD response, i.e. includes noise

$$y = h(u, \theta) + e$$

blue: neuronal activity
red: bold response

Conceptual overview

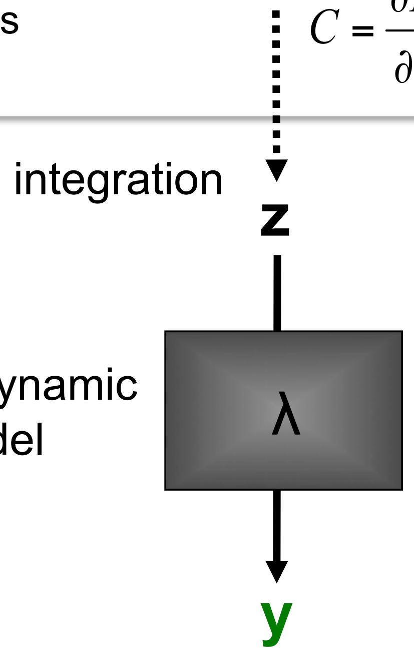
Neuronal state equation $\dot{z} = F(z,u,\theta^n)$

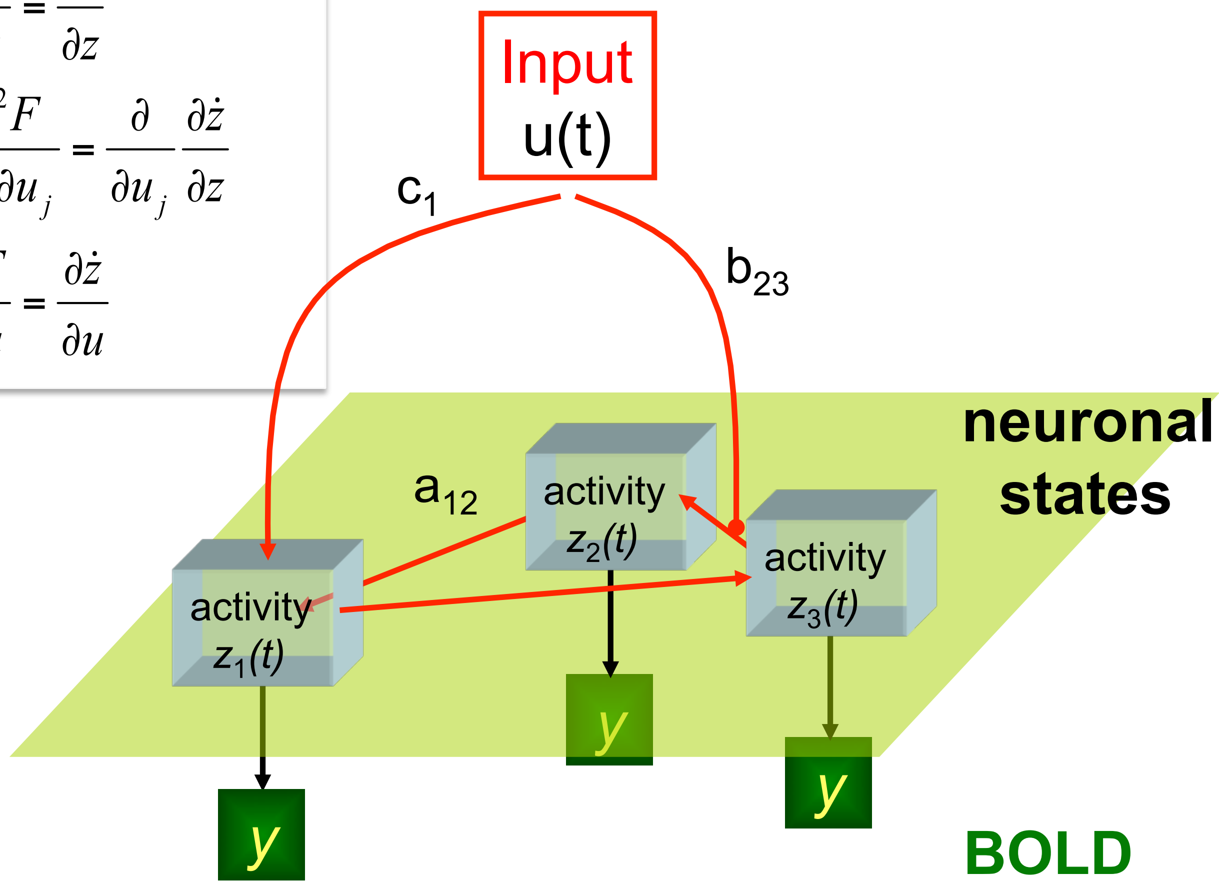
The bilinear model $\dot{z} = (A + \sum u_j B^j)z + Cu$

effective connectivity $A = \frac{\partial F}{\partial z} = \frac{\partial \dot{z}}{\partial z}$

modulation of connectivity $B^j = \frac{\partial^2 F}{\partial z \partial u_j} = \frac{\partial}{\partial u_j}\frac{\partial \dot{z}}{\partial z}$

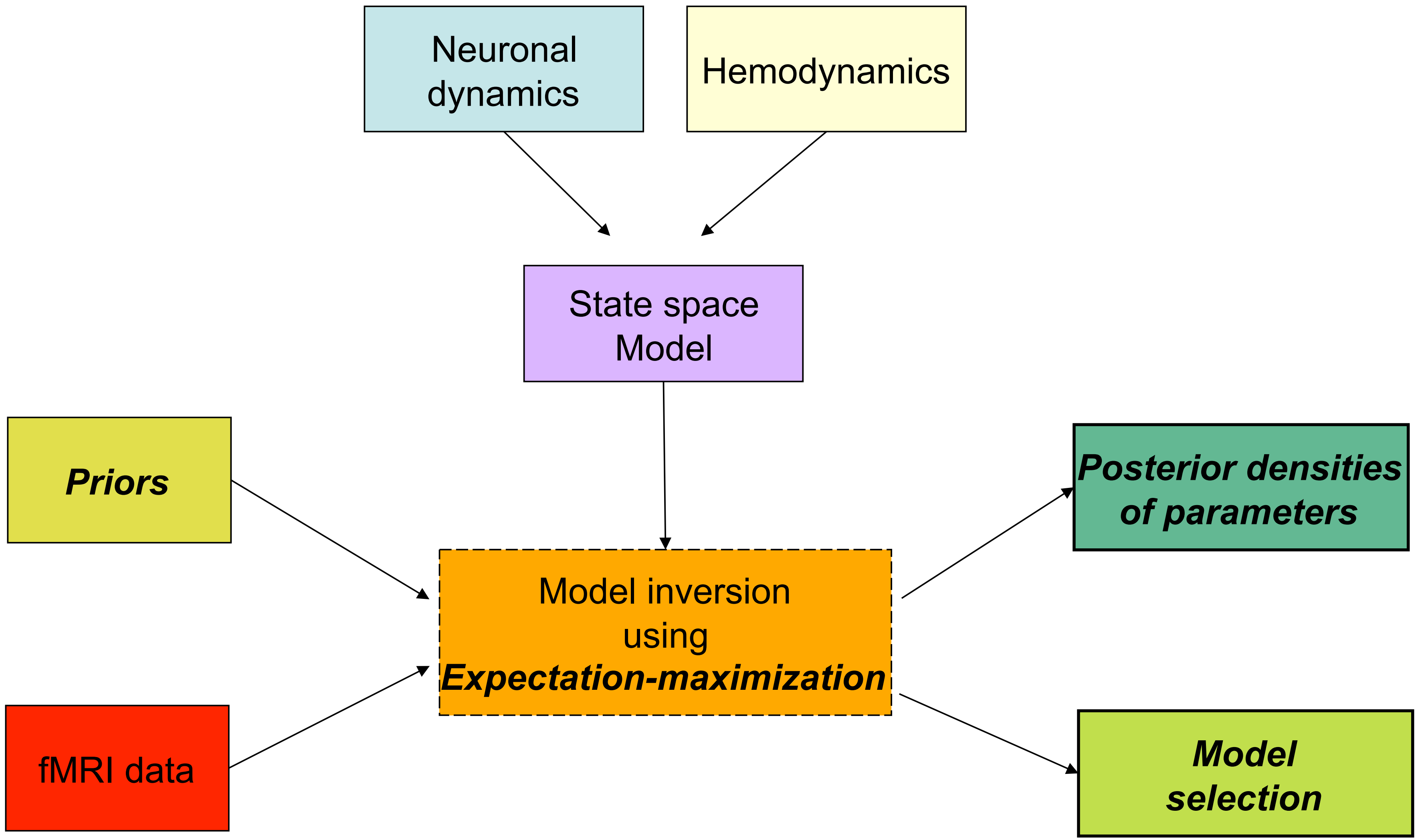
direct inputs $C = \frac{\partial F}{\partial u} = \frac{\partial \dot{z}}{\partial u}$





Friston et al., NeuroImage, 2003

DCM roadmap


Neuronal dynamics
Hemodynamics
State space Model
Priors
fMRI data
Model inversion using *Expectation-maximization*
Posterior densities of parameters
Model selection

Estimation: Bayesian framework

Models of
- Haemodynamics in a single region
- Neuronal interactions

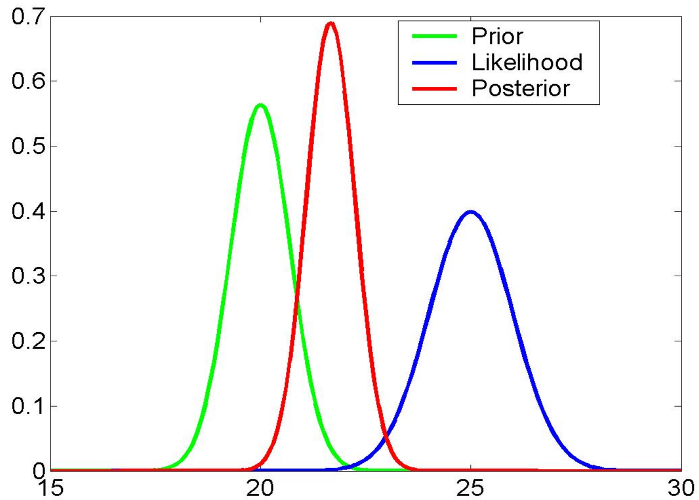
Constraints on
- Haemodynamic parameters
- Connections

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

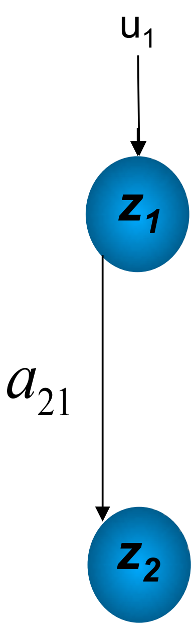
prior $p(\theta)$

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

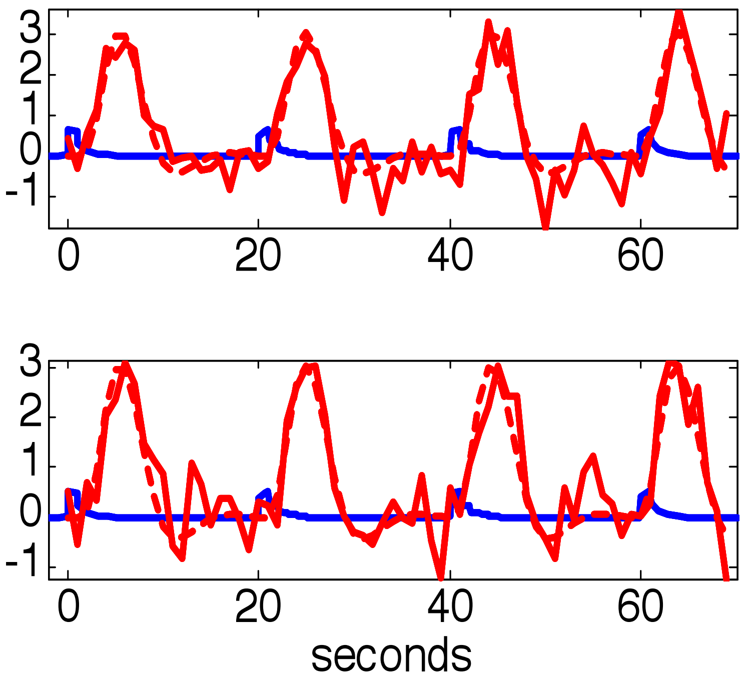
Bayesian estimation



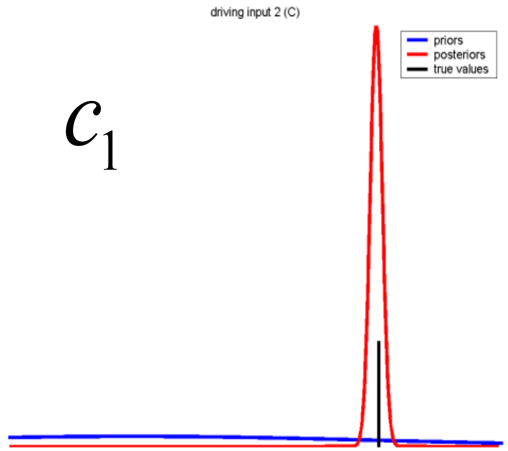
Parameter estimation: an example



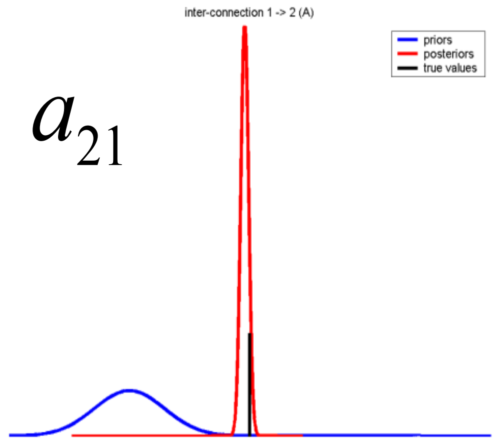
Simulated response



Input coupling, c_1



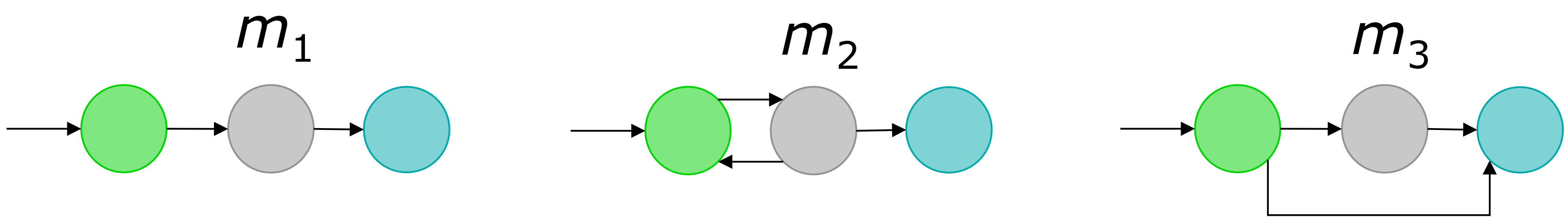
Forward coupling, a_{21}

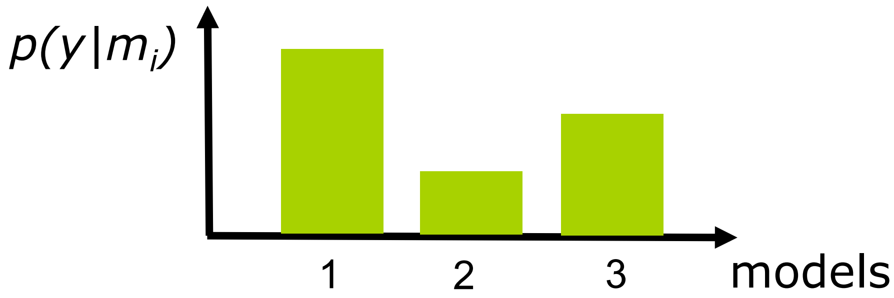


Prior density — Posterior density — true values —

Model comparison

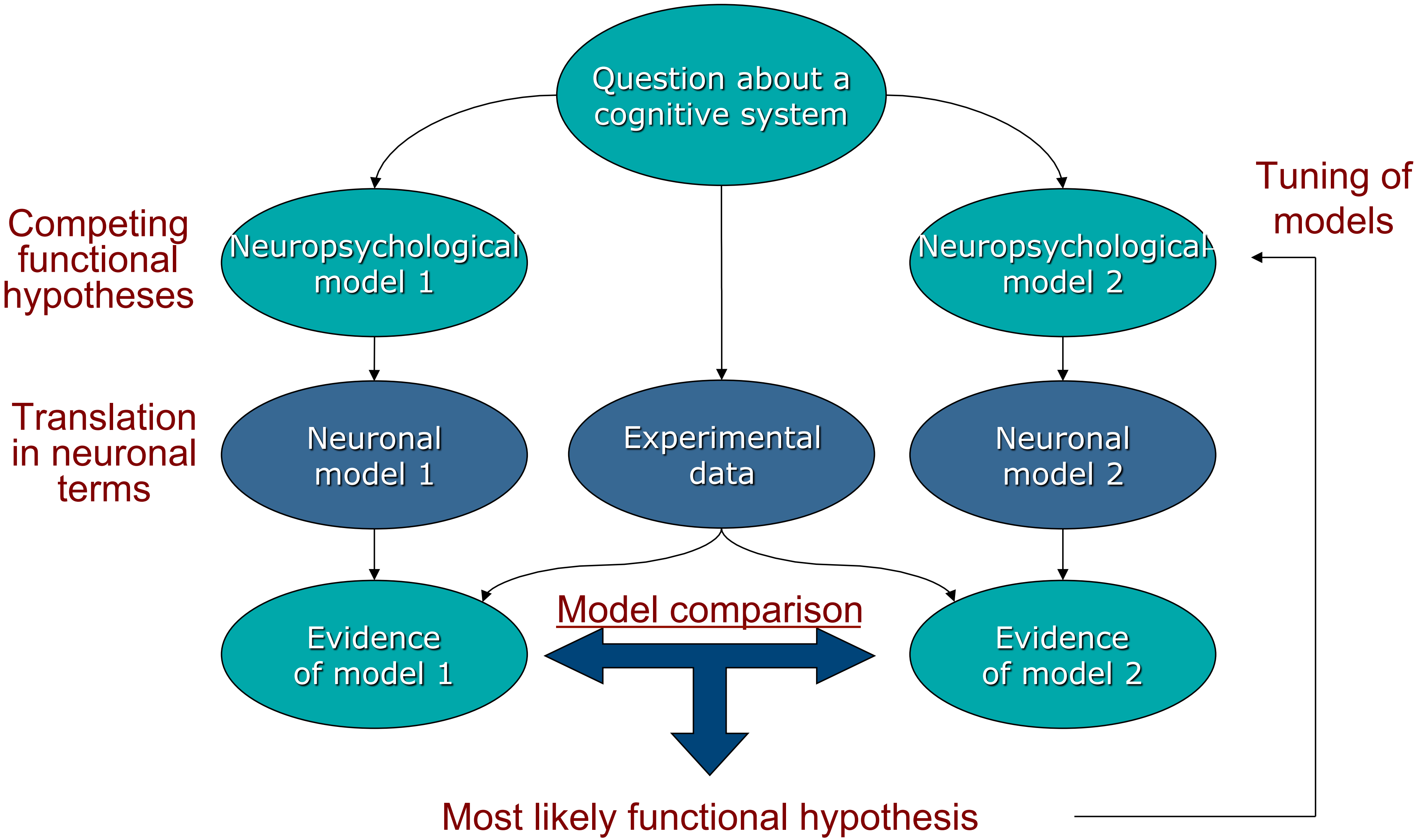
- **Which model is the best among a set of competing models?**
  - Model evidence: $$\log p(y \mid m) = accuracy(m) - complexity(m)$$





Penny et al., NeuroImage, 2004; PLoS Comp Biol, 2010

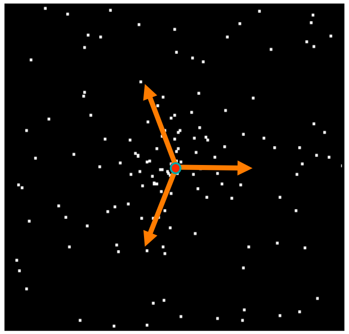
Testing neuropsychological models using DCM

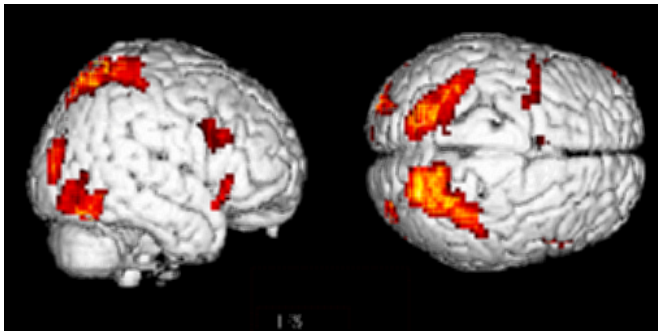


CANONICAL EXAMPLE

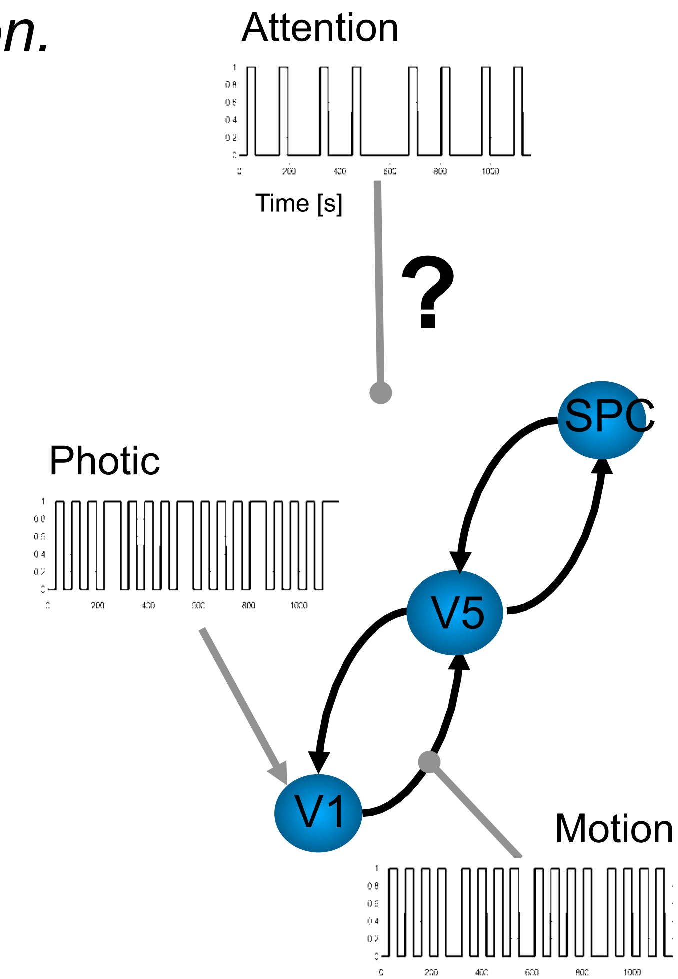
Example
Attention to motion in the visual system

This models is used to assess the site of ***attention modulation*** during *visual motion processing* in an fMRI paradigm reported by *Büchel & Friston.*





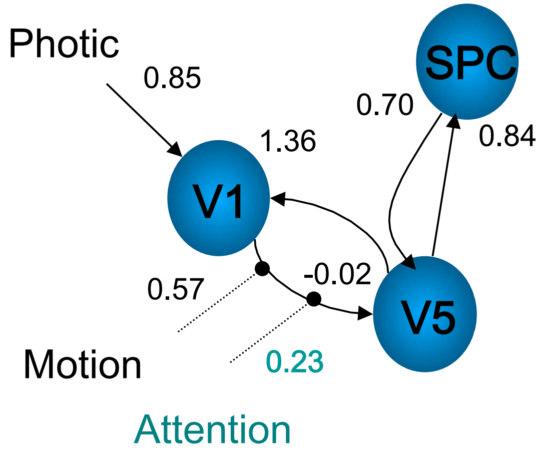
- fixation only
- observe static dots + photic → V1
- observe moving dots + motion → V5
- task on moving dots + attention → V5 + parietal cortex



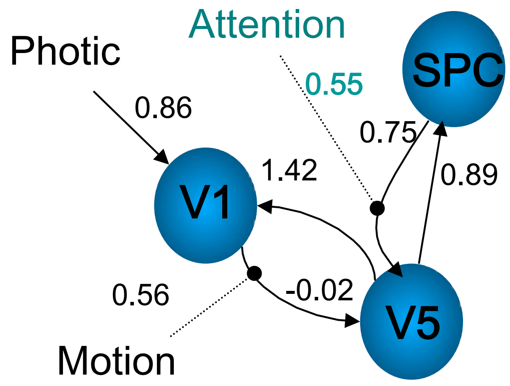
Friston et al., NeuroImage, 2003

Comparison of two simple models

<u>Model 1:</u>
attentional modulation
of V1→V5



<u>Model 2:</u>
attentional modulation
of SPC→V5



Bayesian model selection: Model 1 better than model 2

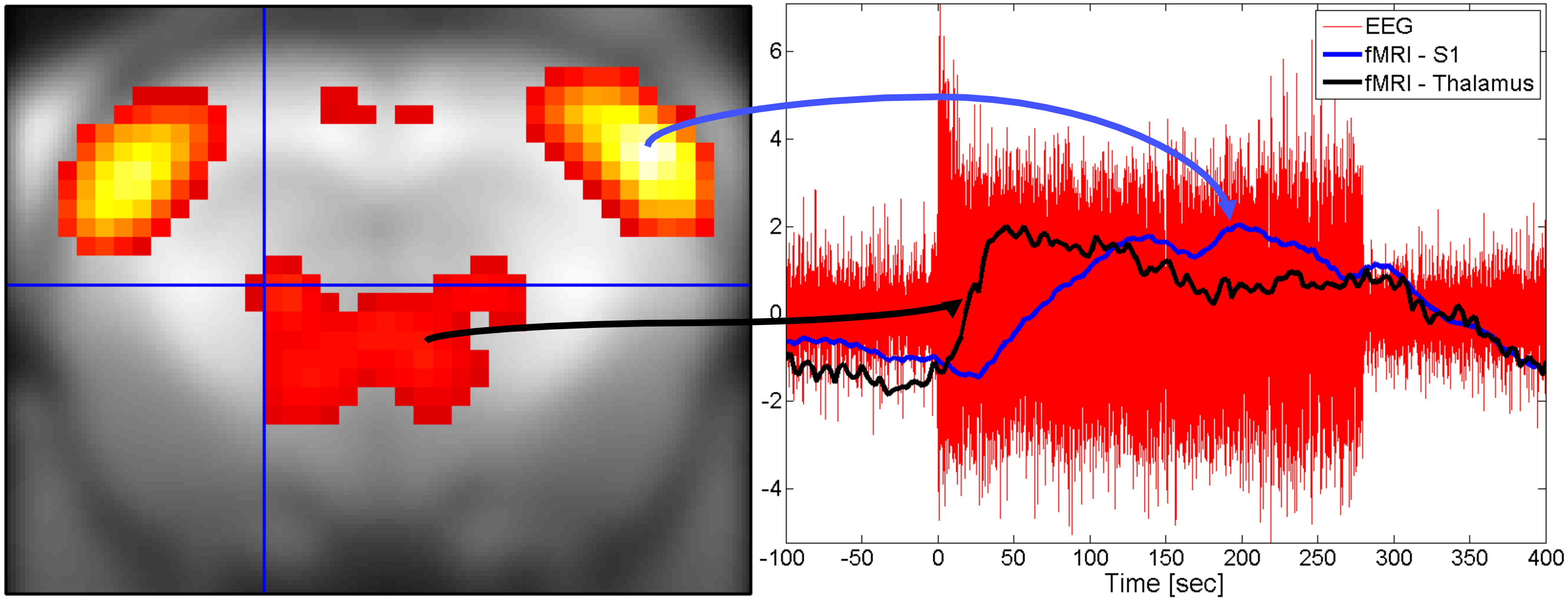
$$\log p(y \mid m_1) >> \log p(y \mid m_2)$$

→ Decision for model 1: in this experiment, attention primarily modulates V1→V5

WHAT ABOUT HEMODYNAMIC PARAMETERS?

Studying neurovascular coupling with DCM

- **Hemodynamics of the epileptic focus in the GAERS model of absence epilepsy**

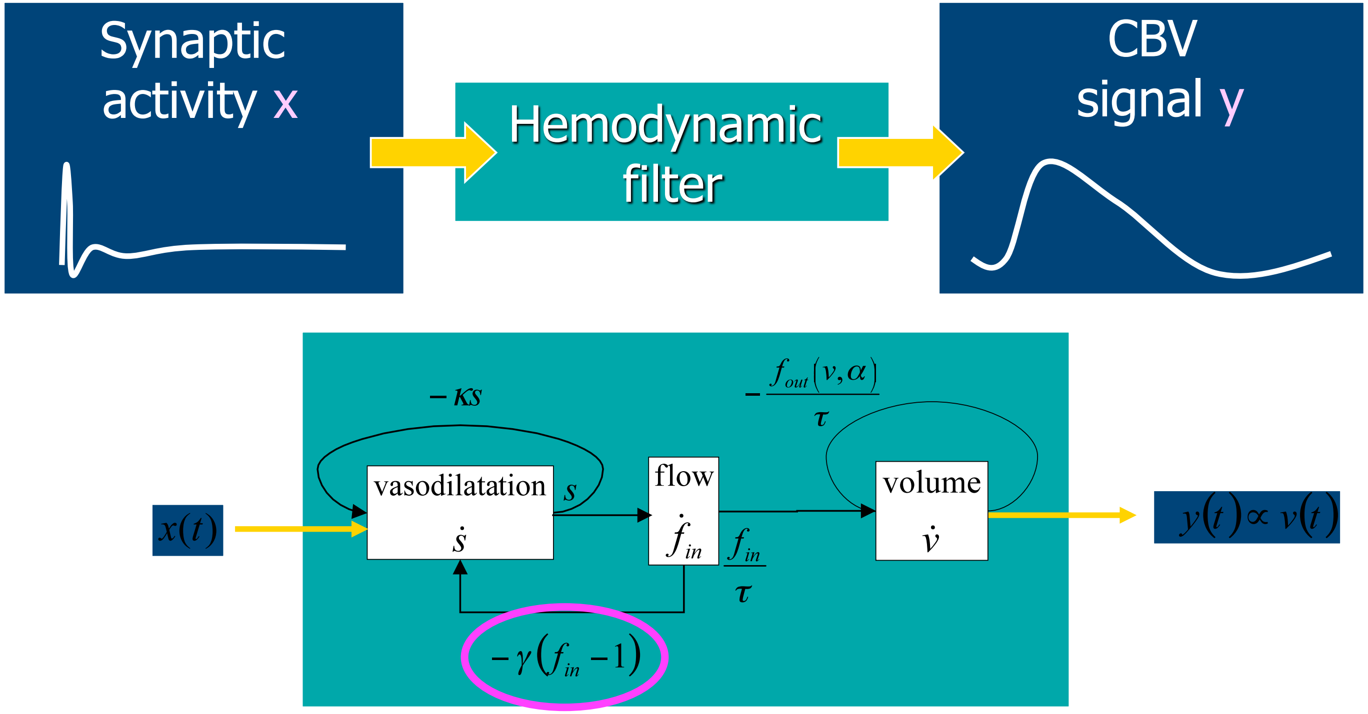


Why such difference of hemodynamics?

David et al., PLoS Biol, 2008

Studying neurovascular coupling with DCM

- DCM performs a biologically informed HRF deconvolution and **estimates hemodynamical parameters for each ROI**



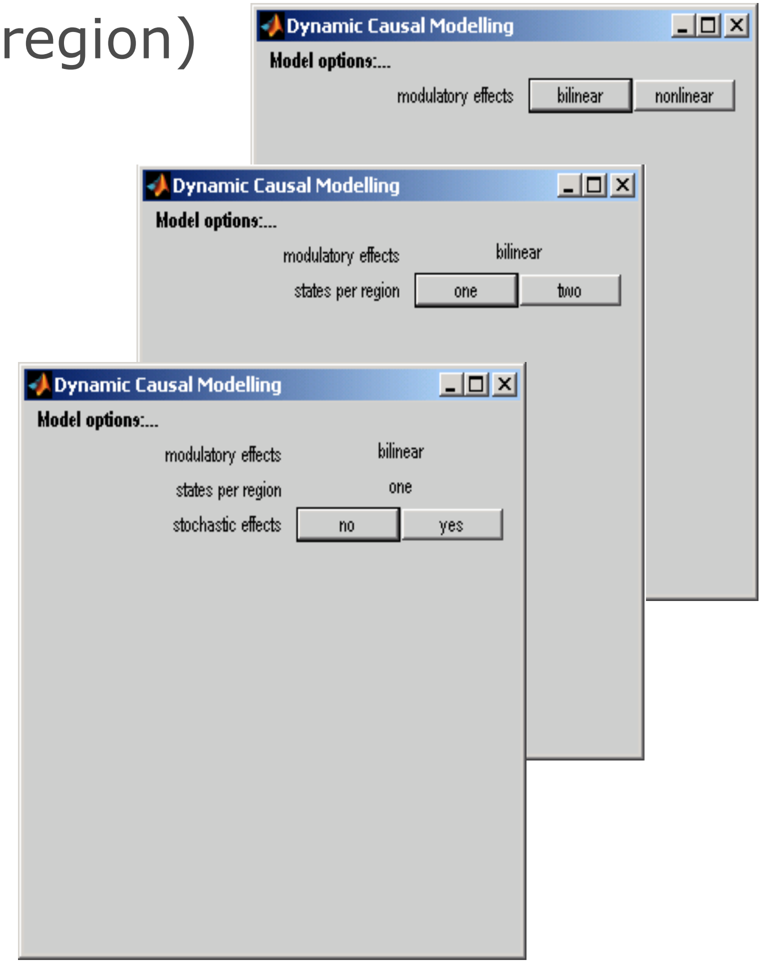
- **Canonical: γ=0.41 Thalamus: γ=0.31 S1: γ=0.03**
- **Deregulation of CBF feedback on vasodilation**
  - Underexpression of NO by astrocytes in the epileptic focus?

David et al., PLoS Biol, 2008

RECENT DCM EXTENSIONS

Factorial structure of model specification in DCM10 (SPM8)

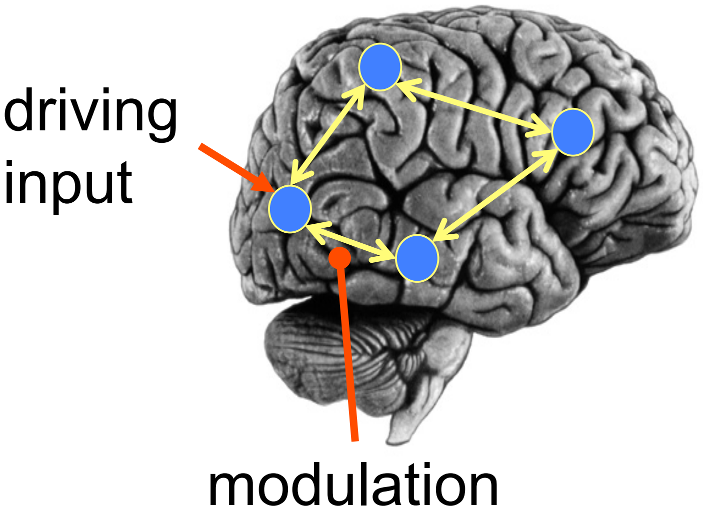
- **Three dimensions of model specification:**
  - bilinear vs. nonlinear
  - single-state vs. two-state (per region)
  - deterministic vs. stochastic



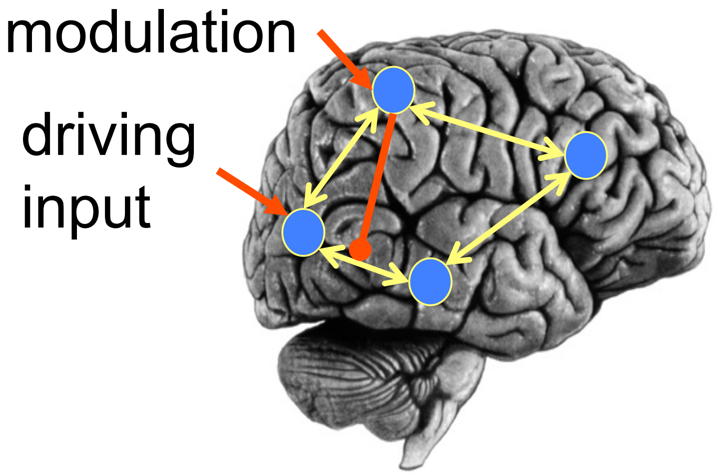
- **Specification via GUI.**

Bilinear vs. nonlinear

bilinear DCM



non-linear DCM



Bilinear state equation:

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

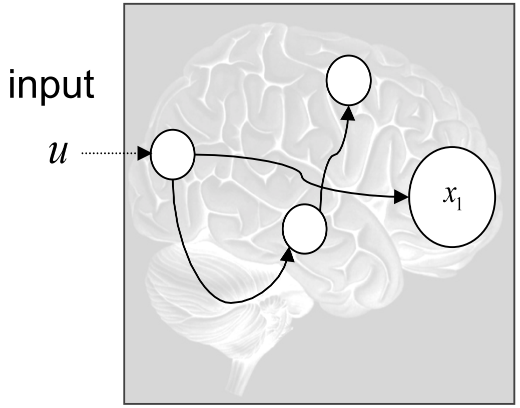
Nonlinear state equation:

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

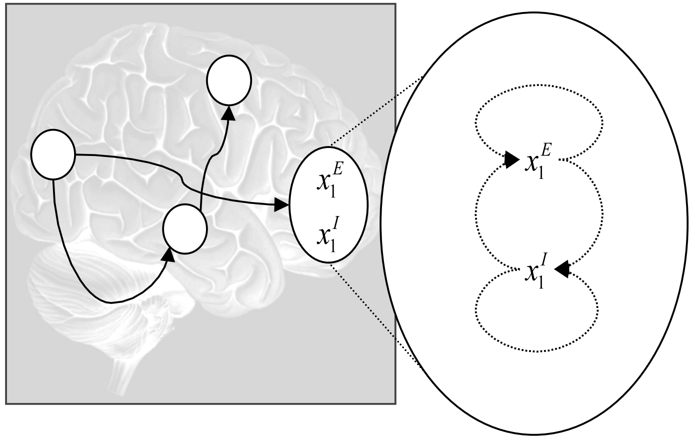
Stephan et al., NeuroImage, 2008

Single-state vs. two-state DCMs

Single-state DCM



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., NeuroImage, 2008

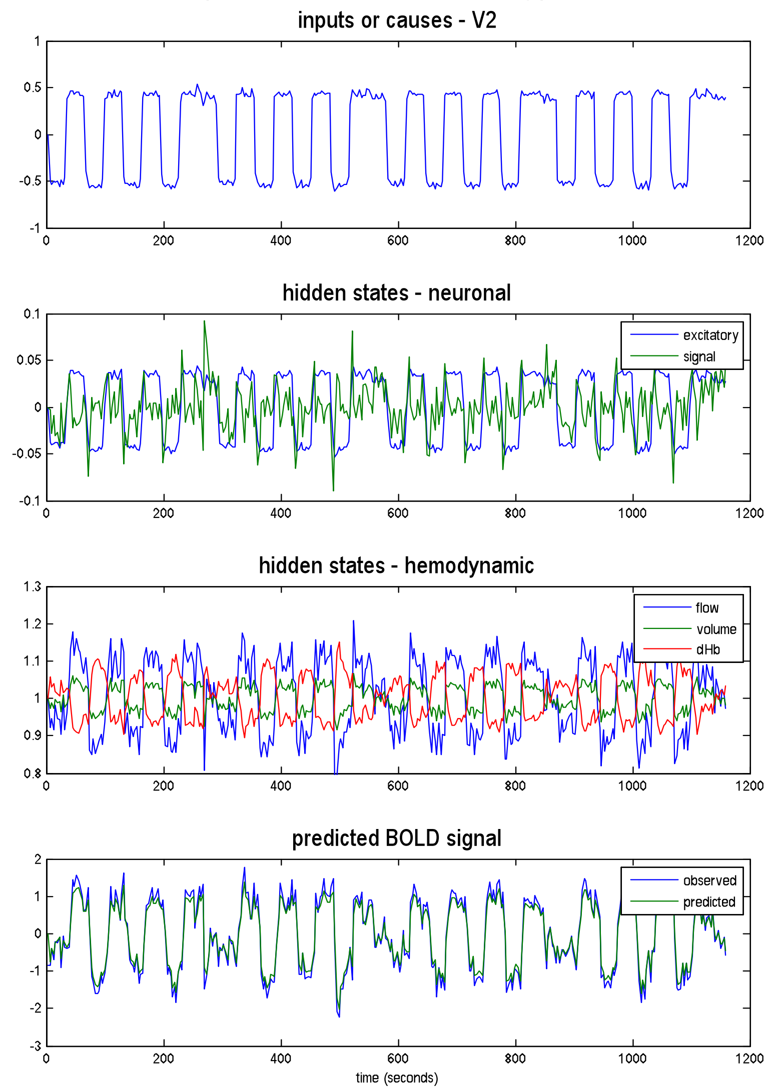
Stochastic DCM

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

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

- 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

Estimates of hidden causes and states (Generalised filtering)



Li et al., NeuroImage, 20011

CONCLUSION

Conclusion
Planning a compatible DCM study

- Hypothesis and model:
  - define specific *a priori* hypothesis
  - which models are relevant to test this hypothesis?
  - check existence of effect on data features of interest

- Suitable experimental design:
  - any design that is suitable for a GLM
  - preferably multi-factorial (e.g. 2 x 2)
    - e.g. one factor that varies the driving (sensory) input
    - and one factor that varies the modulatory input