Dynamic Causal Modelling for fMRI

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SPM fMRI course

Wellcome Trust Centre
for Neuroimaging

London

Overview

Brain connectivity: types & definitions

Anatomical connectivity
Functional connectivity
Effective connectivity

Dynamic causal models (DCMs)

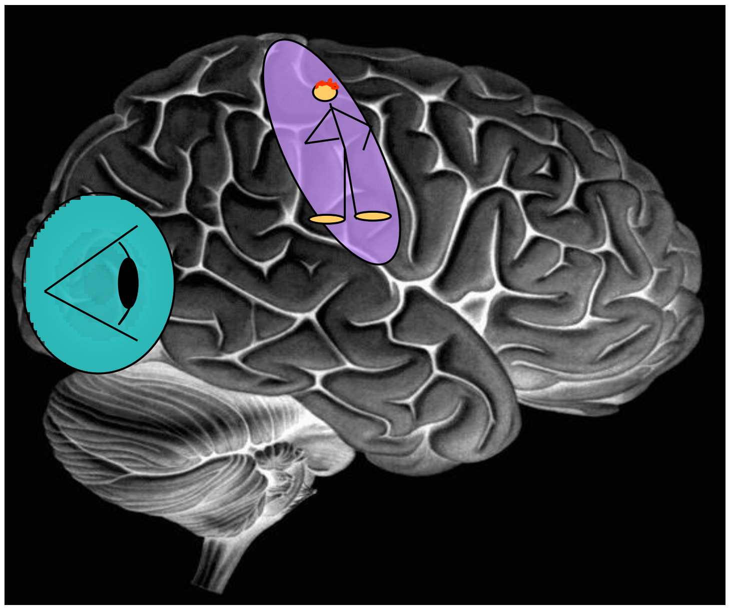
Neuronal model
Hemodynamic model
Estimation: Bayesian framework

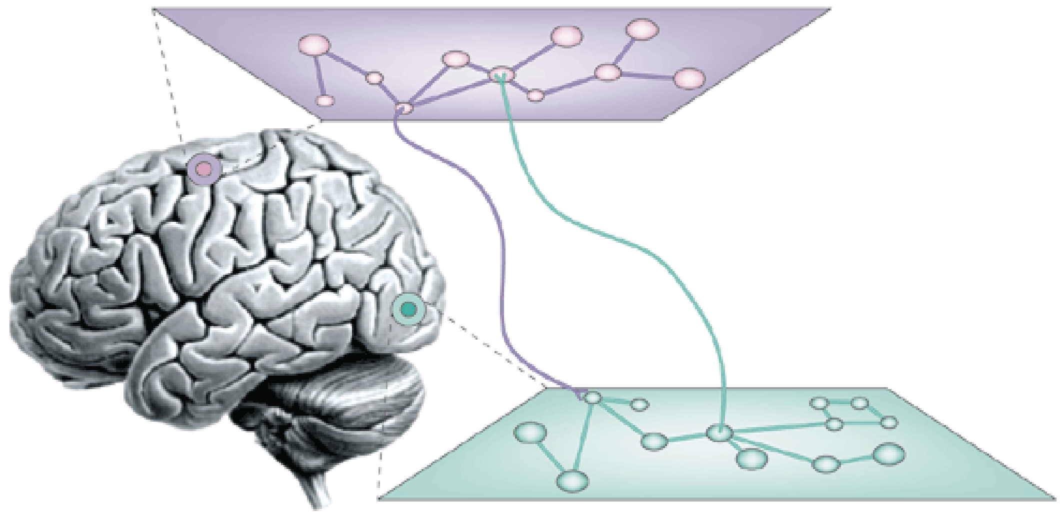
Applications & extensions of DCM to fMRI data

Principles of Organisation

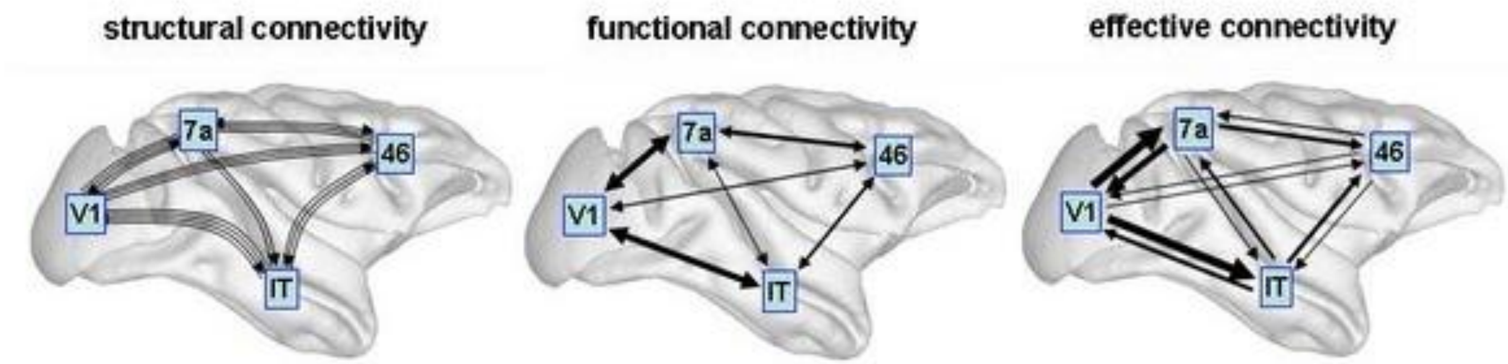
Functional specialization

Functional integration





Structural, functional & effective connectivity



Sporns 2007, *Scholarpedia*

- **anatomical/structural connectivity**
  = presence of axonal connections

- **functional connectivity**
  = statistical dependencies between regional time series

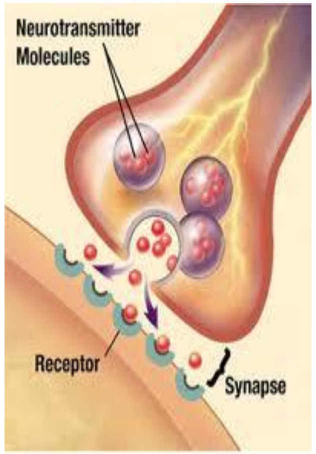
- **effective connectivity**
  = causal (directed) influences between neurons or neuronal populations

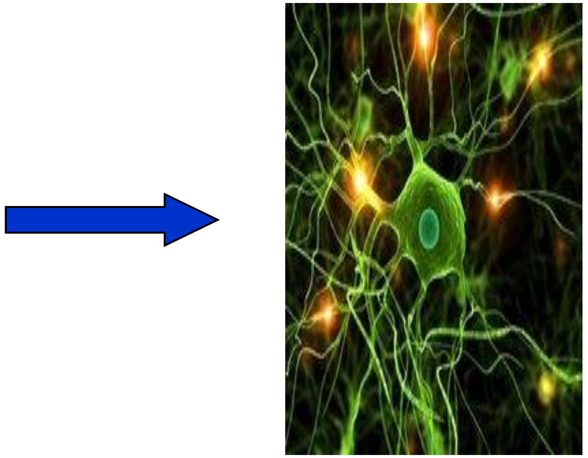
Anatomical connectivity

Definition:

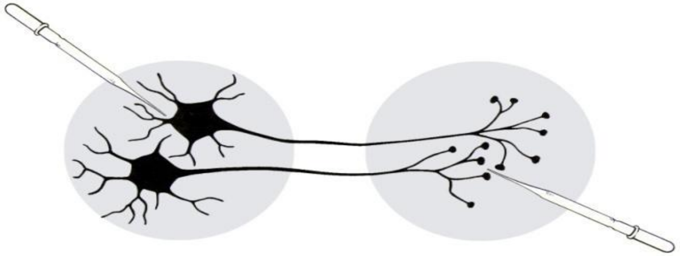
presence of axonal connections

- neuronal communication via synaptic contacts

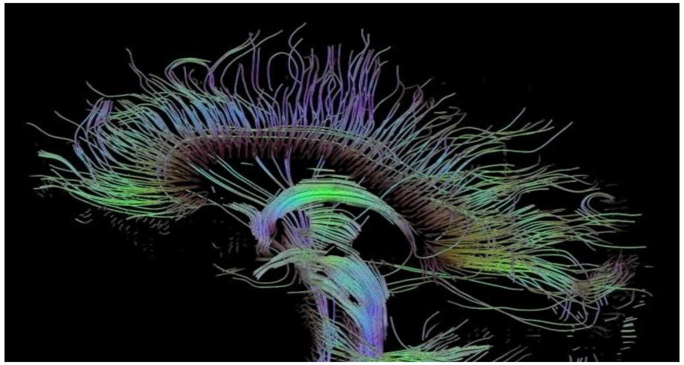




- Measured with
  - tracing techniques



  - diffusion tensor imaging (DTI)

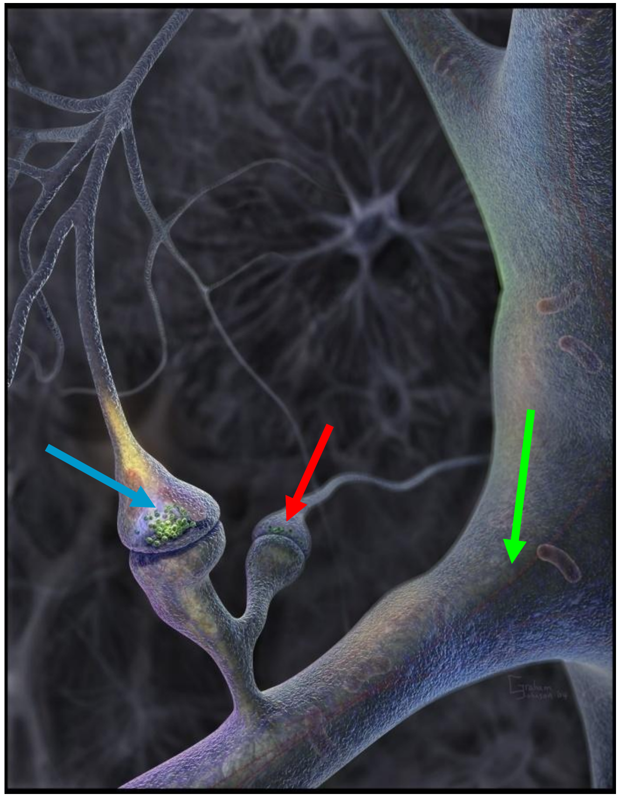


Knowing anatomical connectivity is not enough...

- Context-dependent recruiting of connections :
  - Local functions depend on network activity

- Connections show synaptic plasticity
  - change in the structure and transmission properties of a synapse
  - even at short timescales

→ Look at functional and effective connectivity



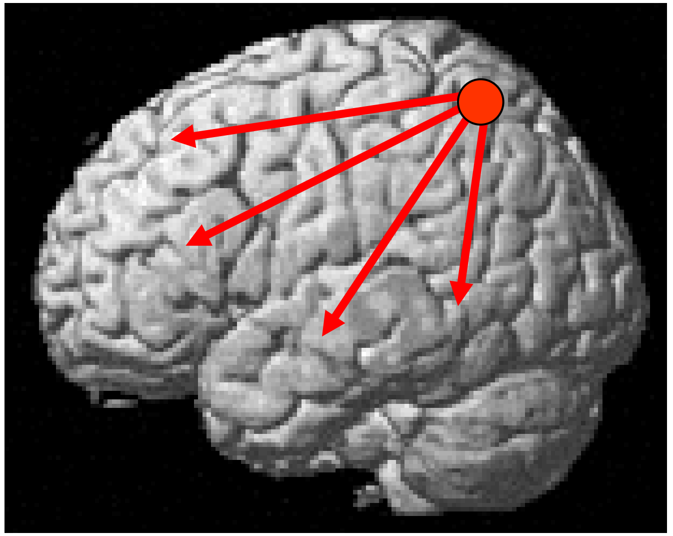
Functional connectivity

Definition: statistical dependencies between regional time series

- Seed voxel correlation analysis
- Coherence analysis
- Eigen-decomposition (PCA, SVD)
- Independent component analysis (ICA)
- any technique describing statistical dependencies amongst regional time series

Seed-voxel correlation analyses

- hypothesis-driven choice of a seed voxel
- extract reference time series
- voxel-wise correlation with time series from all other voxels in the brain

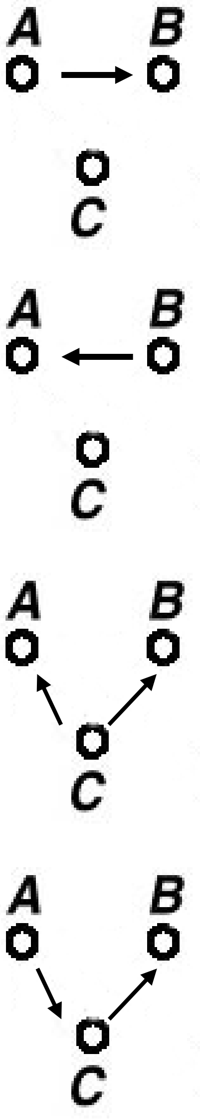


Pros & Cons of functional connectivity analysis

- Pros:
  - useful when we have no experimental control over the system of interest and no model of what caused the data (e.g. sleep, hallucinations, etc.)

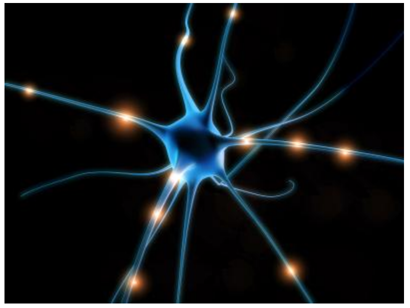
- Cons:
  - interpretation of resulting patterns is difficult / arbitrary
  - no mechanistic insight
  - usually suboptimal for situations where we have a priori knowledge / experimental control

→ Effective connectivity



Effective connectivity

Definition: ***causal*** *(directed) influences between neurons or neuronal populations*

- *In vivo* and *in vitro* stimulation and recording
- 
- Models of causal interactions among neuronal populations
  - explain *regional* effects in terms of *interregional* connectivity

Some models for computing effective connectivity from fMRI data

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

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

- Volterra kernels
  Friston & Büchel 2000

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

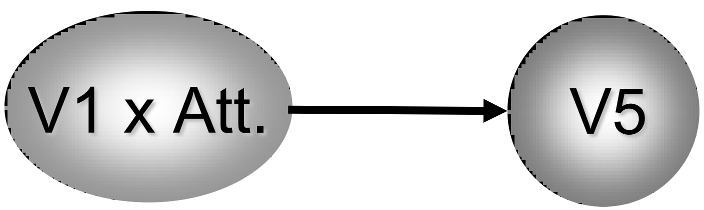
- Dynamic Causal Modelling (DCM)
  bilinear: Friston et al. 2003; *nonlinear:* Stephan et al. 2008

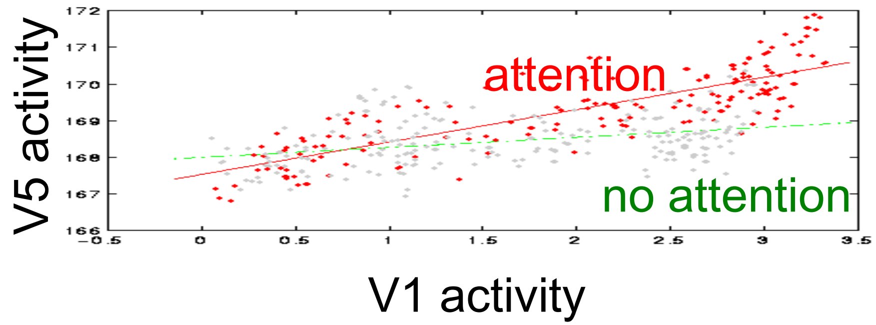
Psycho-physiological interaction (PPI)

- bilinear model of how the psychological context A changes the influence of area B on area C :

$$B \times A \rightarrow C$$

- A PPI corresponds to differences in regression slopes for different contexts.





Friston et al. 1997, *NeuroImage*
Büchel & Friston 1997, *Cereb. Cortex*

Pros & Cons of PPIs

- Pros:
  - given a single source region, we can test for its context-dependent connectivity across the entire brain
  - easy to implement
- Cons:
  - only allows to model contributions from a single area
  - operates at the level of BOLD time series (SPM 99/2).

    SPM 5/8 deconvolves the BOLD signal to form the proper interaction term, and then reconvolves it.
  - ignores time-series properties of the data

→ *Dynamic Causal Models*

needed for more robust statements of effective connectivity.

Overview

Brain connectivity: types & definitions

Anatomical connectivity
Functional connectivity
Effective connectivity

Dynamic causal models (DCMs)

Basic idea
Neuronal model
Hemodynamic model
Parameter estimation, priors & inference

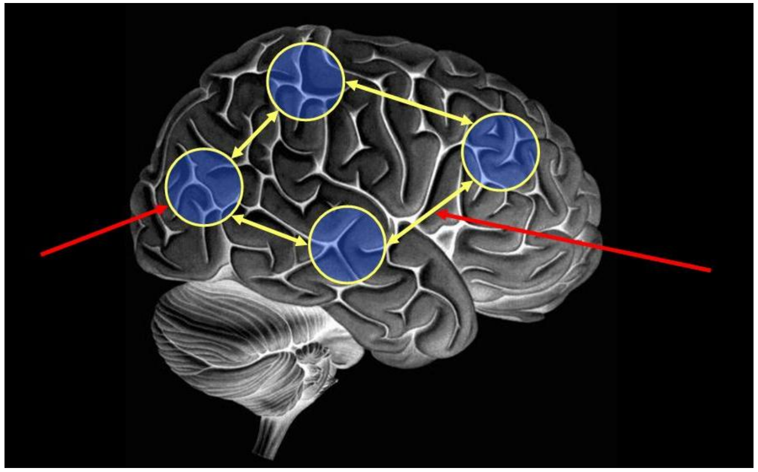
Applications & extensions of DCM to fMRI data

Basics of Dynamic Causal Modelling

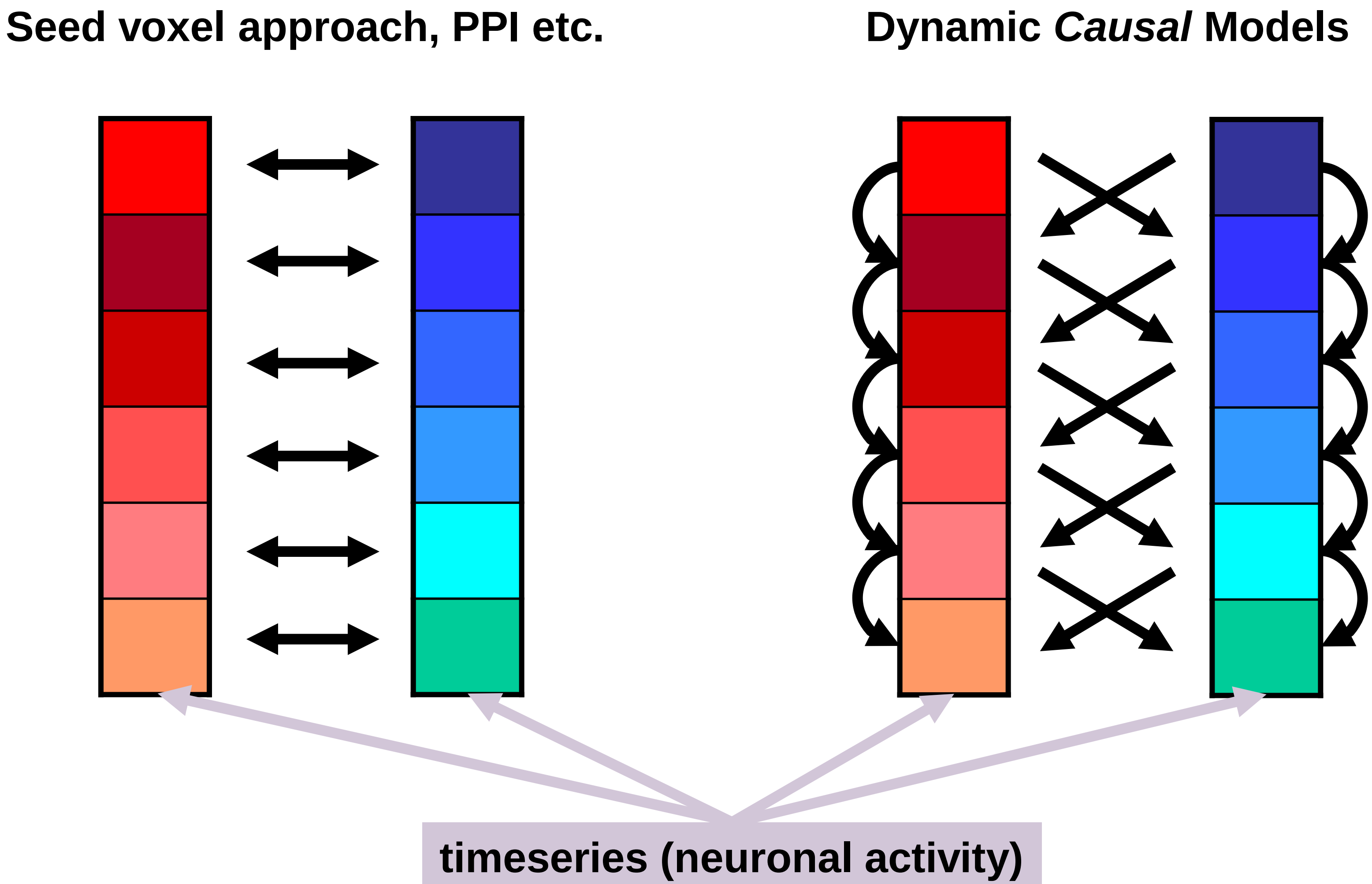
DCM allows us to look at how areas within a network interact:

Investigate functional integration & modulation of specific cortical pathways

- Temporal dependency of activity within and between areas (causality)



Temporal dependence and causal relations

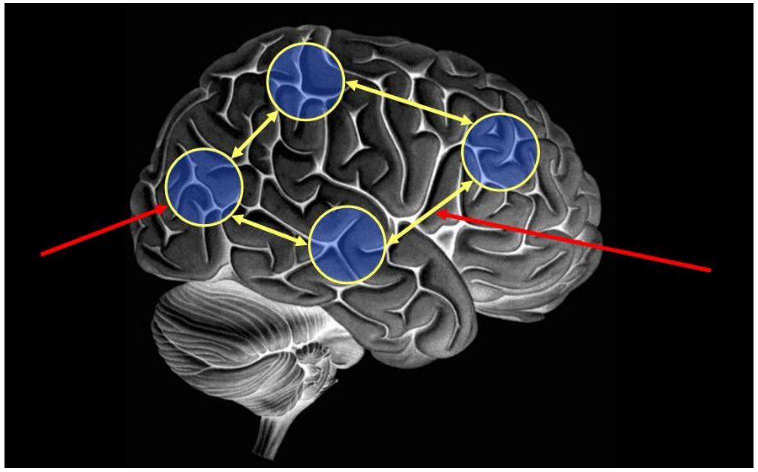


Basics of Dynamic Causal Modelling

DCM allows us to look at how areas within a network interact:

Investigate functional integration & modulation of specific cortical pathways

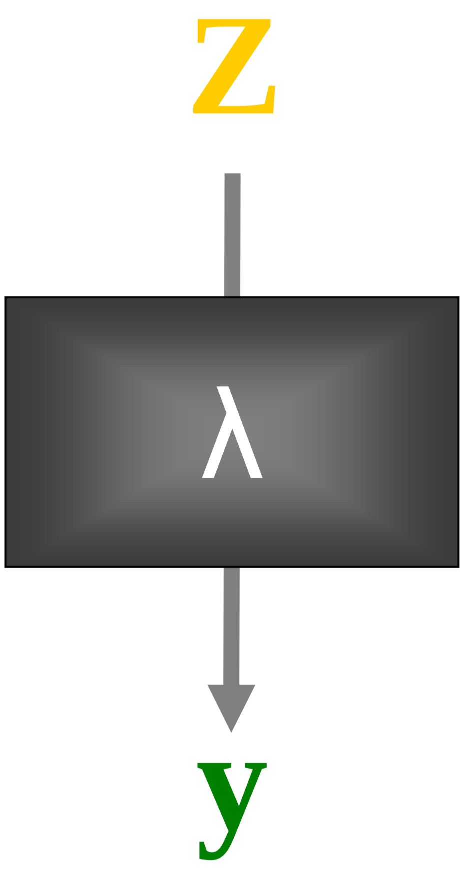
- Temporal dependency of activity within and between areas (causality)
- Separate neuronal activity from observed BOLD responses



Basics of DCM:
Neuronal and BOLD level

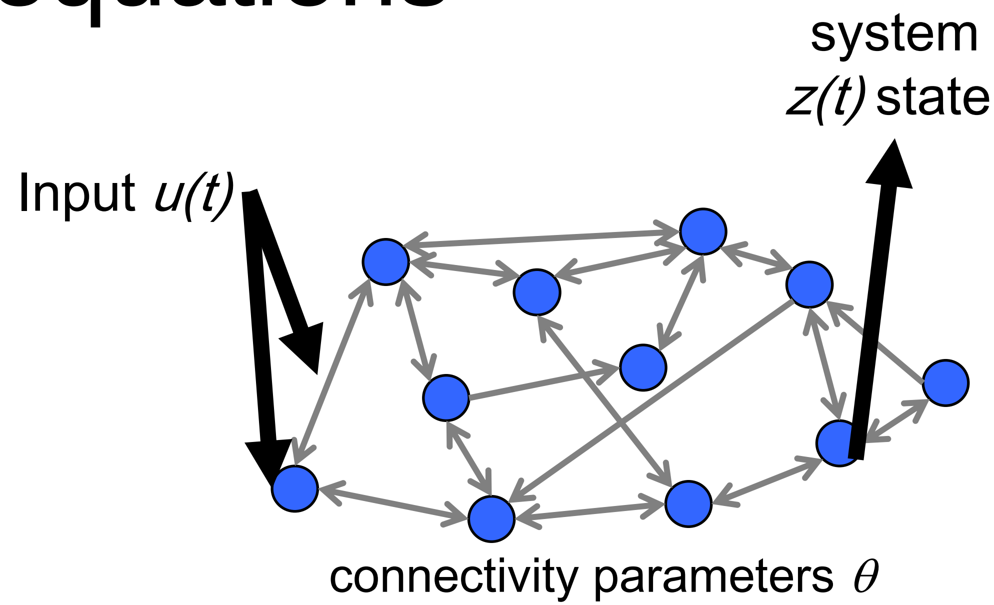
- Cognitive system is modelled at its underlying neuronal level (not directly accessible for fMRI).
- The modelled neuronal dynamics (Z) are transformed into area-specific BOLD signals (y) by a hemodynamic model (λ).

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



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



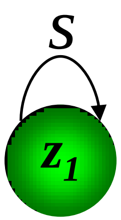
State changes of the system states are dependent on:

– 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:



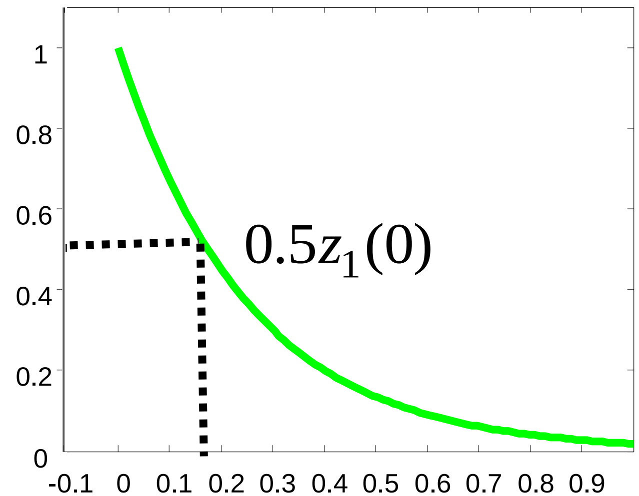
$$\frac{dz_1}{dt} = -sz_1 \;\Rightarrow\; z_1(t) = z_1(0)\exp(-st), \qquad z_1(0) = 1$$

Half-life τ

$$z_1(\tau) = 0.5z_1(0)$$
$$= z_1(0)\exp(-s\tau)$$

$$\Rightarrow \boxed{s = \ln 2 / \tau}$$

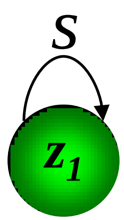
Decay function



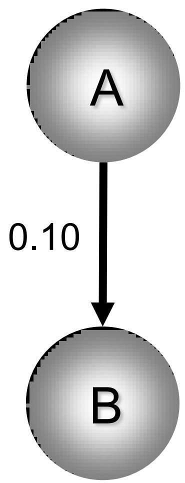
$$\tau = \ln 2 / s$$

DCM parameters = rate constants

Generic solution to the ODEs in DCM:

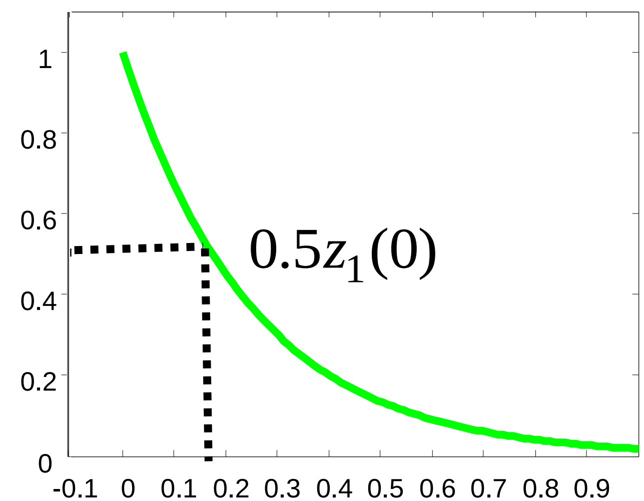


$$\frac{dz_1}{dt} = -sz_1 \quad \Rightarrow \quad z_1(t) = z_1(0)\exp(-st), \qquad z_1(0) = 1$$



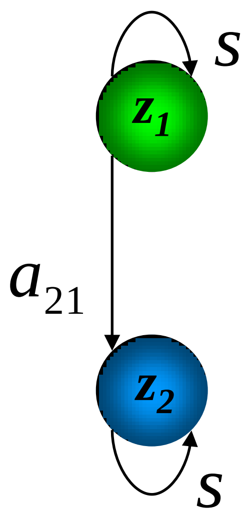
If A→B is 0.10 s^{-1} this means that, per unit time, the increase in activity in B corresponds to 10% of the activity in A

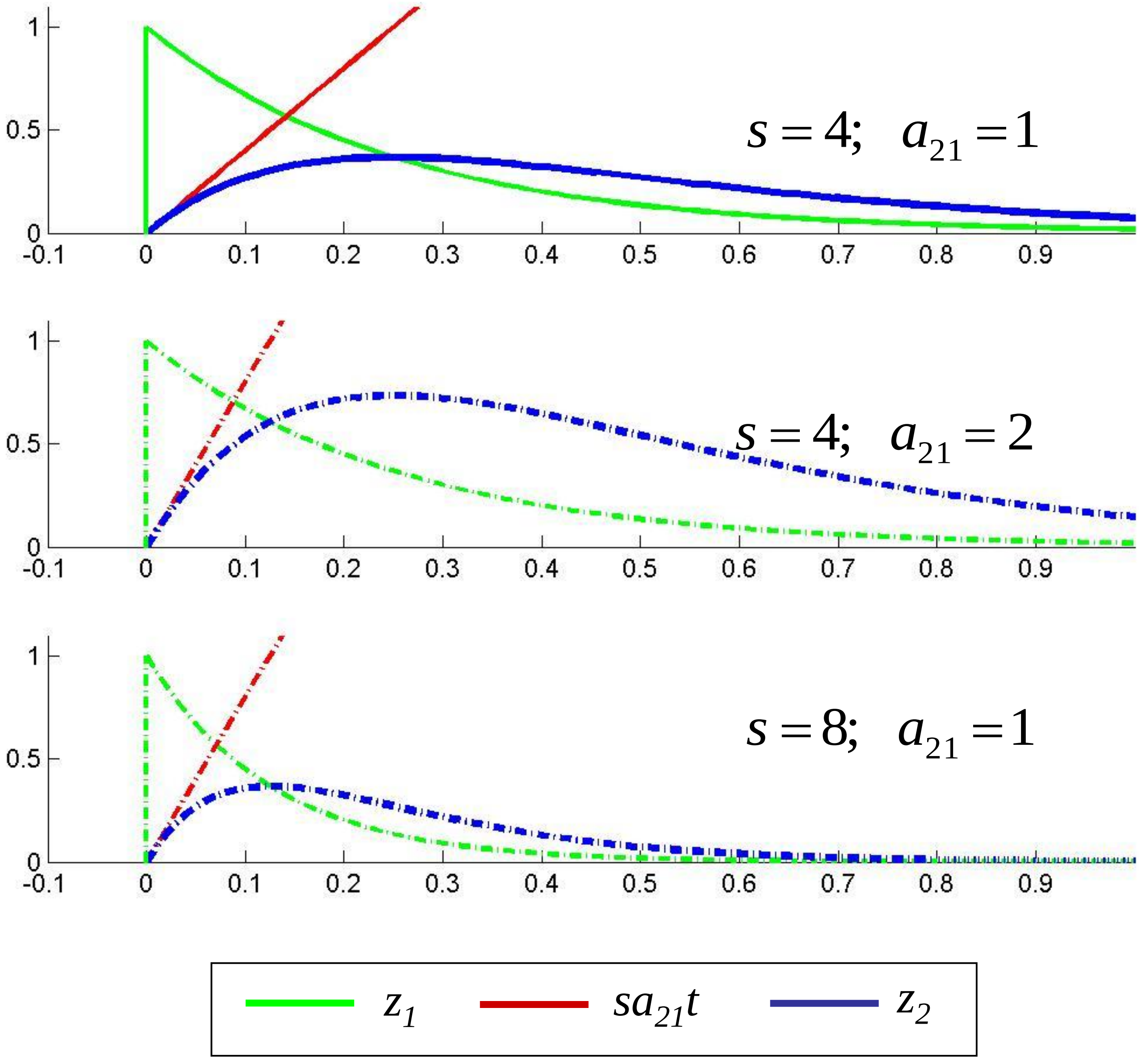
Decay function



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

Linear dynamics: 2 nodes





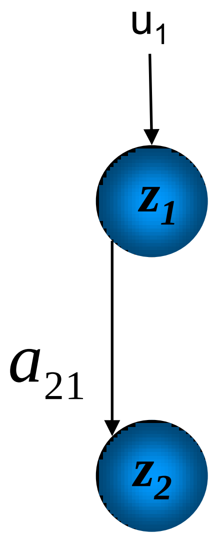
$$\dot{z}_1 = -sz_1$$
$$\dot{z}_2 = s\left(a_{21}z_1 - z_2\right)$$

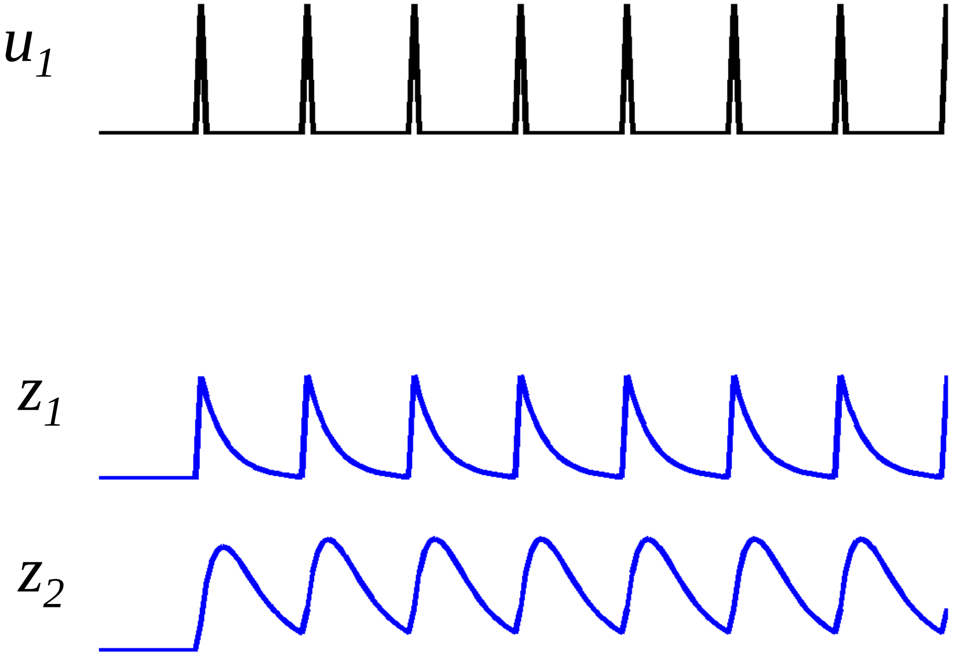
$$z_1(0) = 1$$
$$z_2(0) = 0$$

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

$$a_{21} > 0$$

Neurodynamics: 2 nodes with input

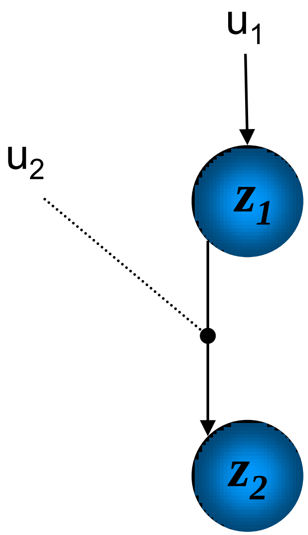


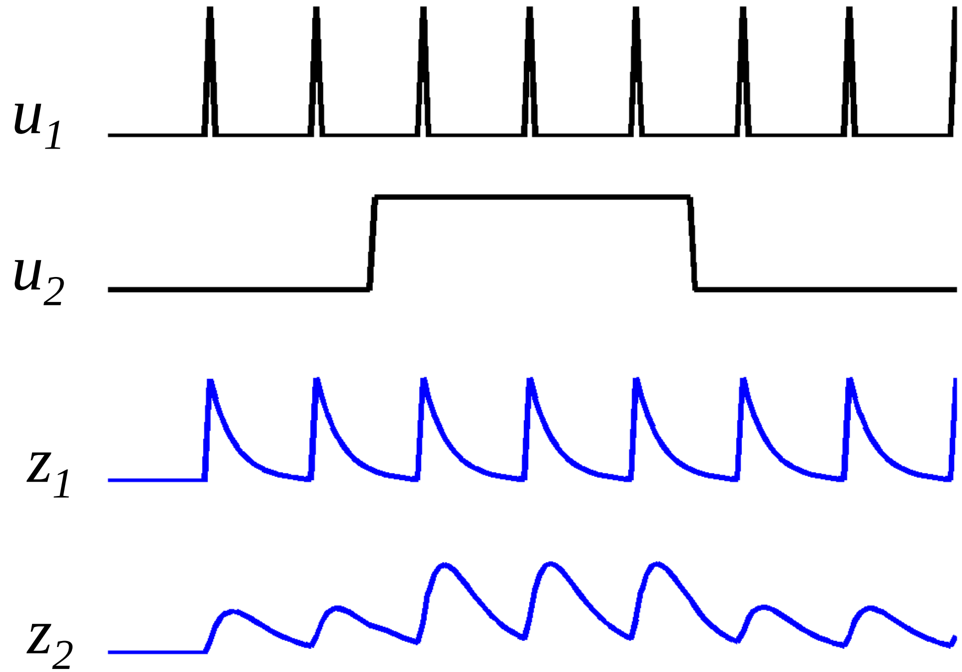


$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = s \begin{bmatrix} -1 & 0 \\ a_{21} & -1 \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} c \\ 0 \end{bmatrix} u_1 \qquad a_{21} > 0$$

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

Neurodynamics: positive modulation



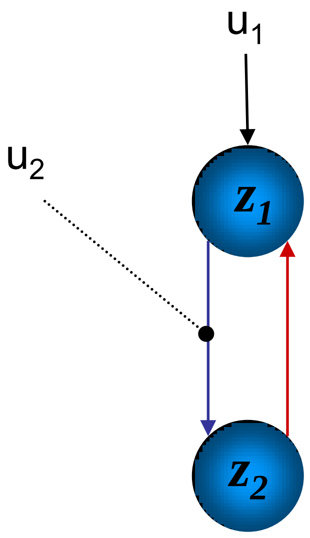


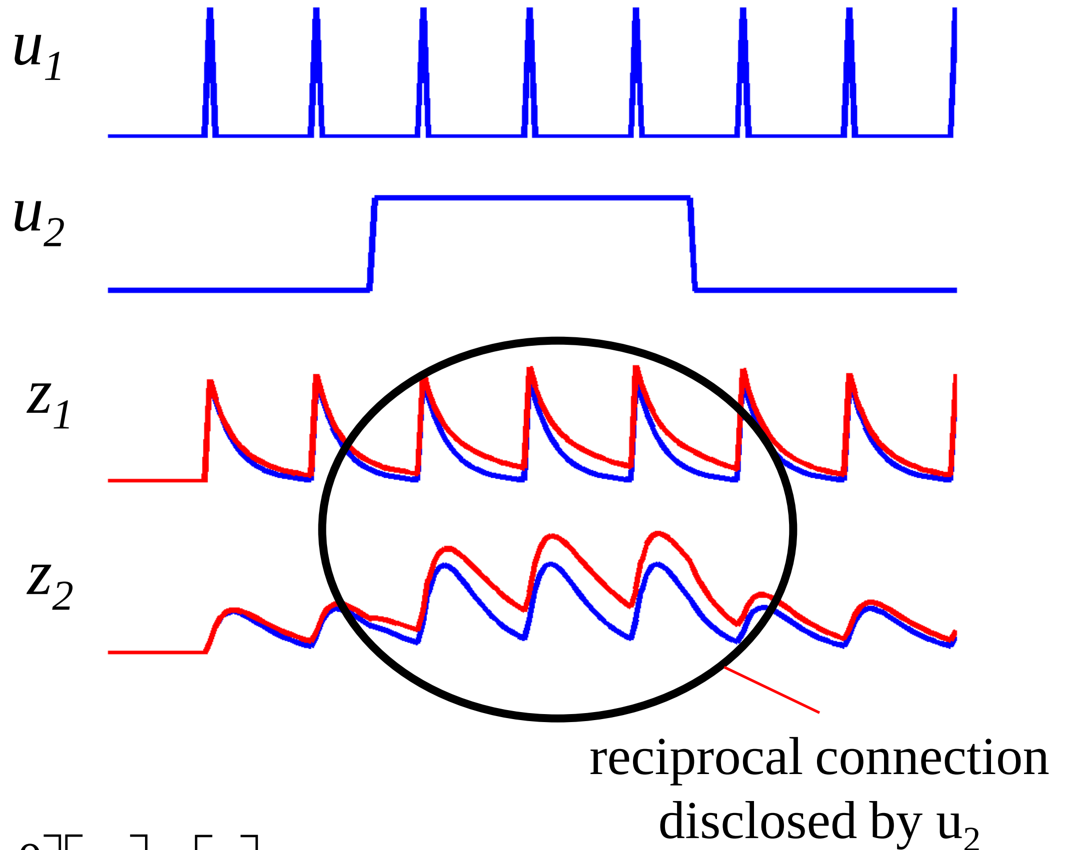
index, not squared

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

modulatory input u_2 activity through the coupling a_{21}

Neurodynamics: reciprocal connections

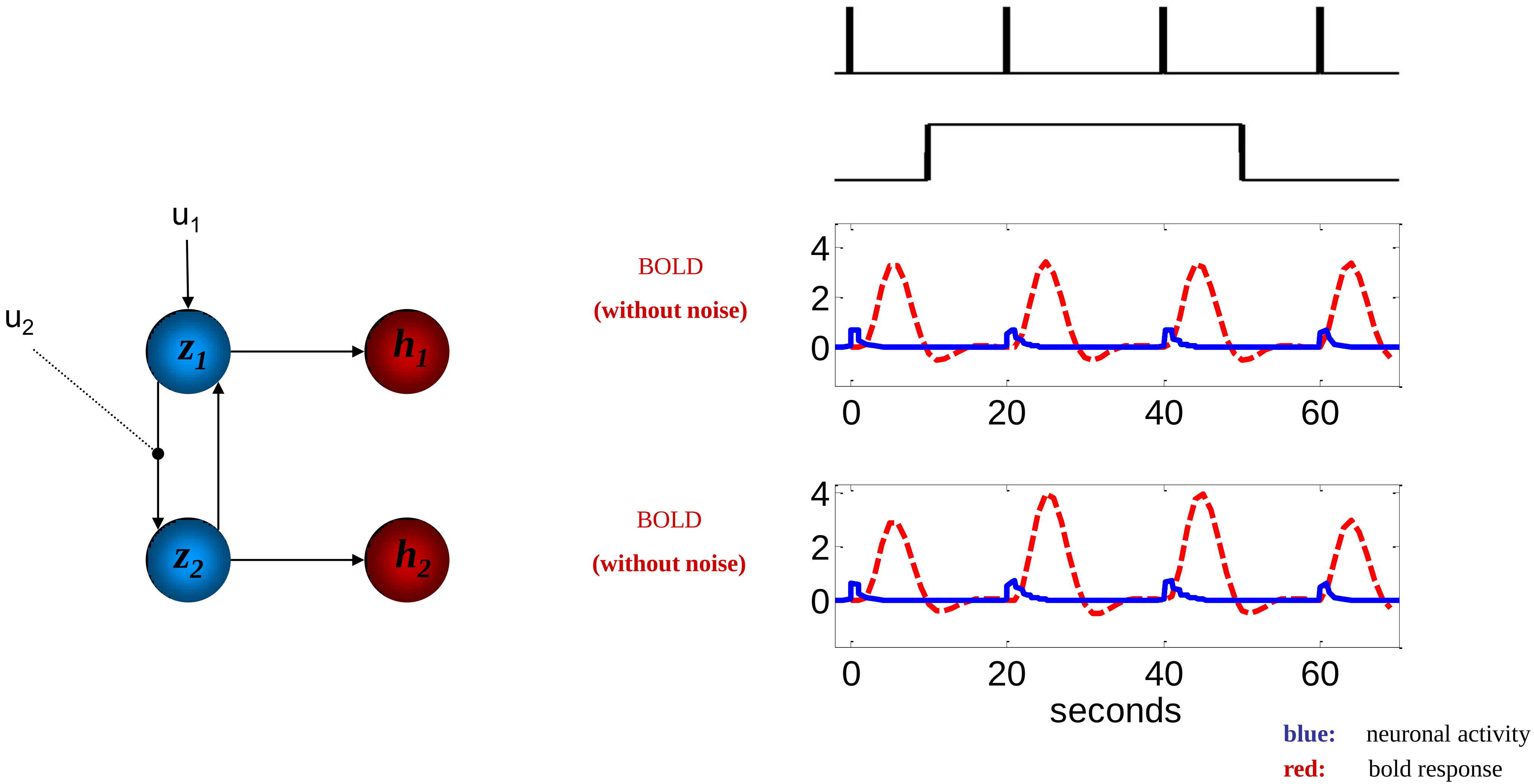




$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = s \begin{bmatrix} -1 & a_{12} \\ a_{21} & -1 \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ b_{21}^2 & 0 \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} c \\ 0 \end{bmatrix} u_1$$

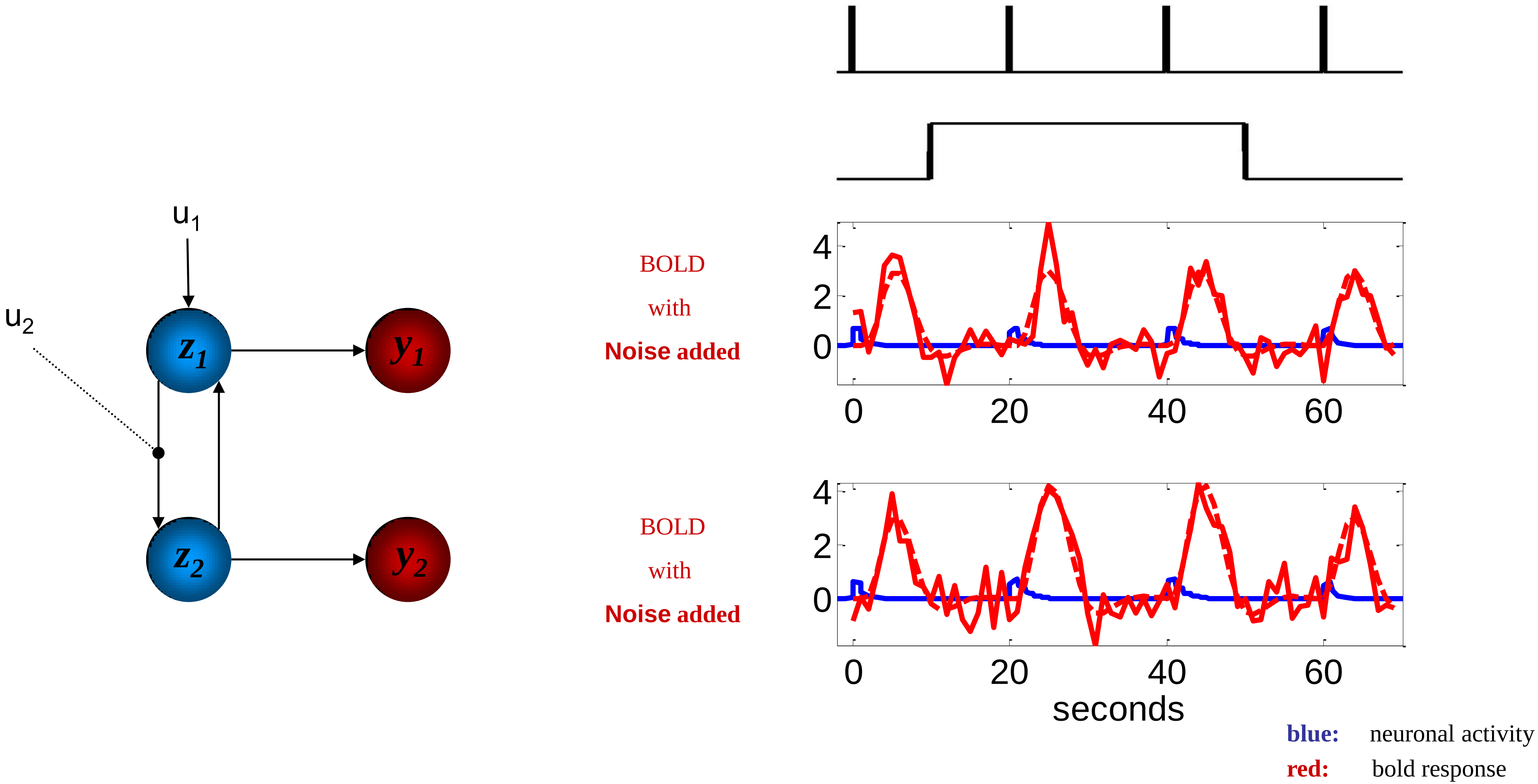
$$a_{12}, a_{21}, b_{21}^2 > 0$$

Haemodynamics: reciprocal connections



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

Haemodynamics: reciprocal connections



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

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

Bilinear state equation in DCM for fMRI

state changes → $\begin{bmatrix}\dot{z}_1\\ \vdots\\ \dot{z}_n\end{bmatrix}$; **connectivity** → A; **modulation of connectivity** → B^j; **state vector** → z; **direct inputs** → C; **external inputs** → u

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

n regions | *m mod* inputs | *m drv* inputs

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

Conceptual overview

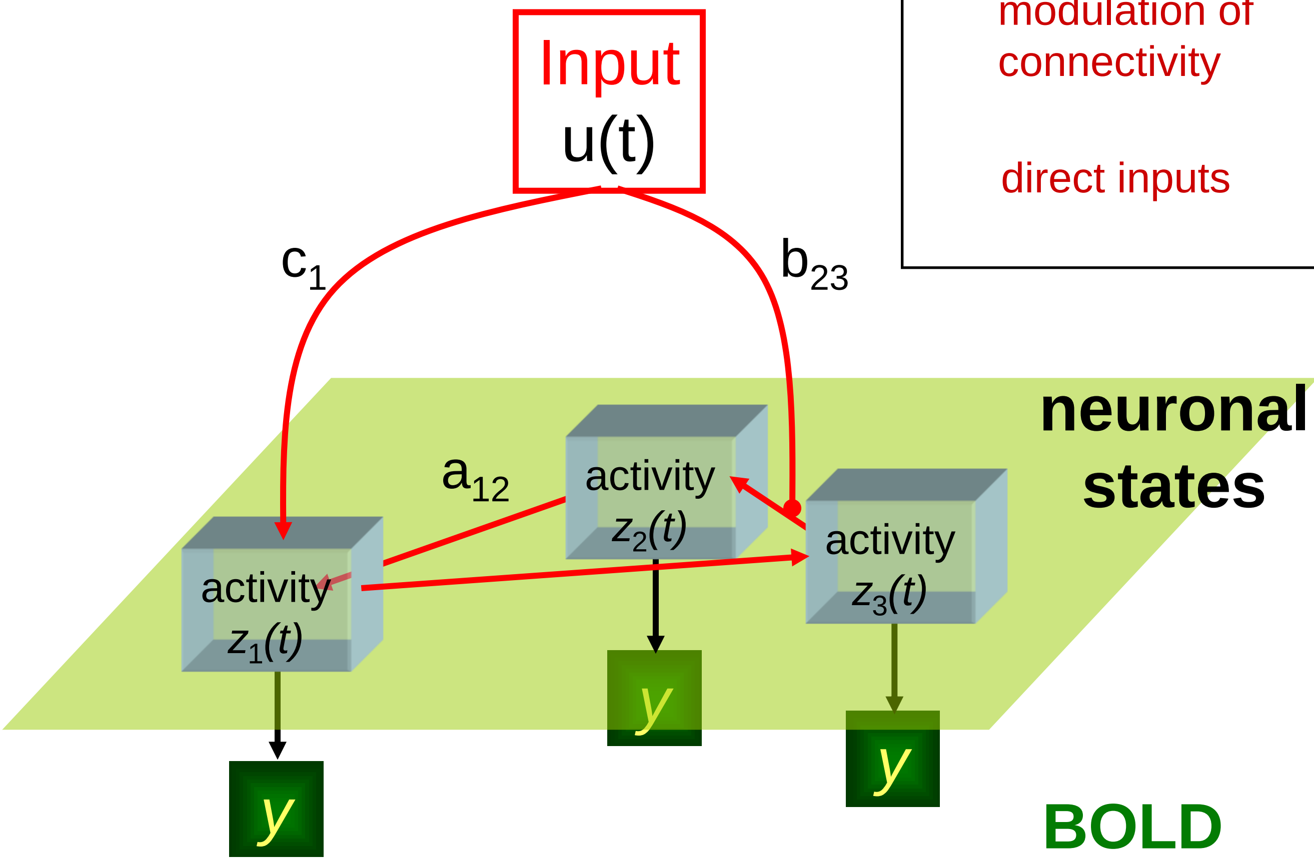
Neuronal state equation $\dot{z} = F(z, u, \theta^n)$

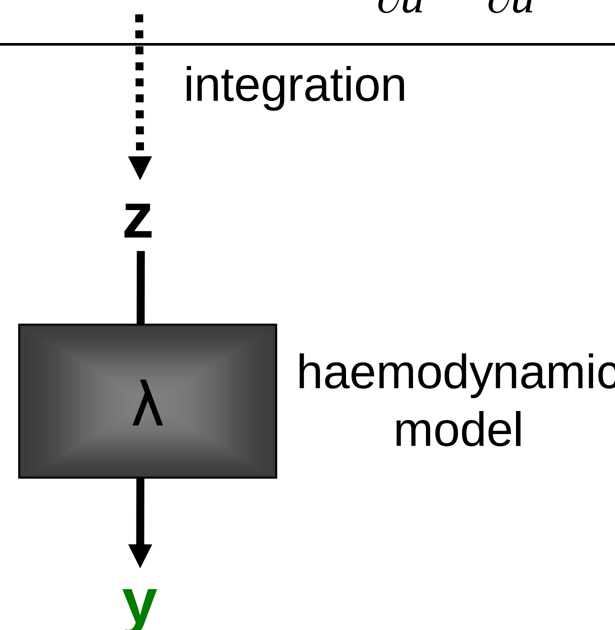
The bilinear model $\dot{z} = (A + \sum u_j B^j) z + Cu$

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

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

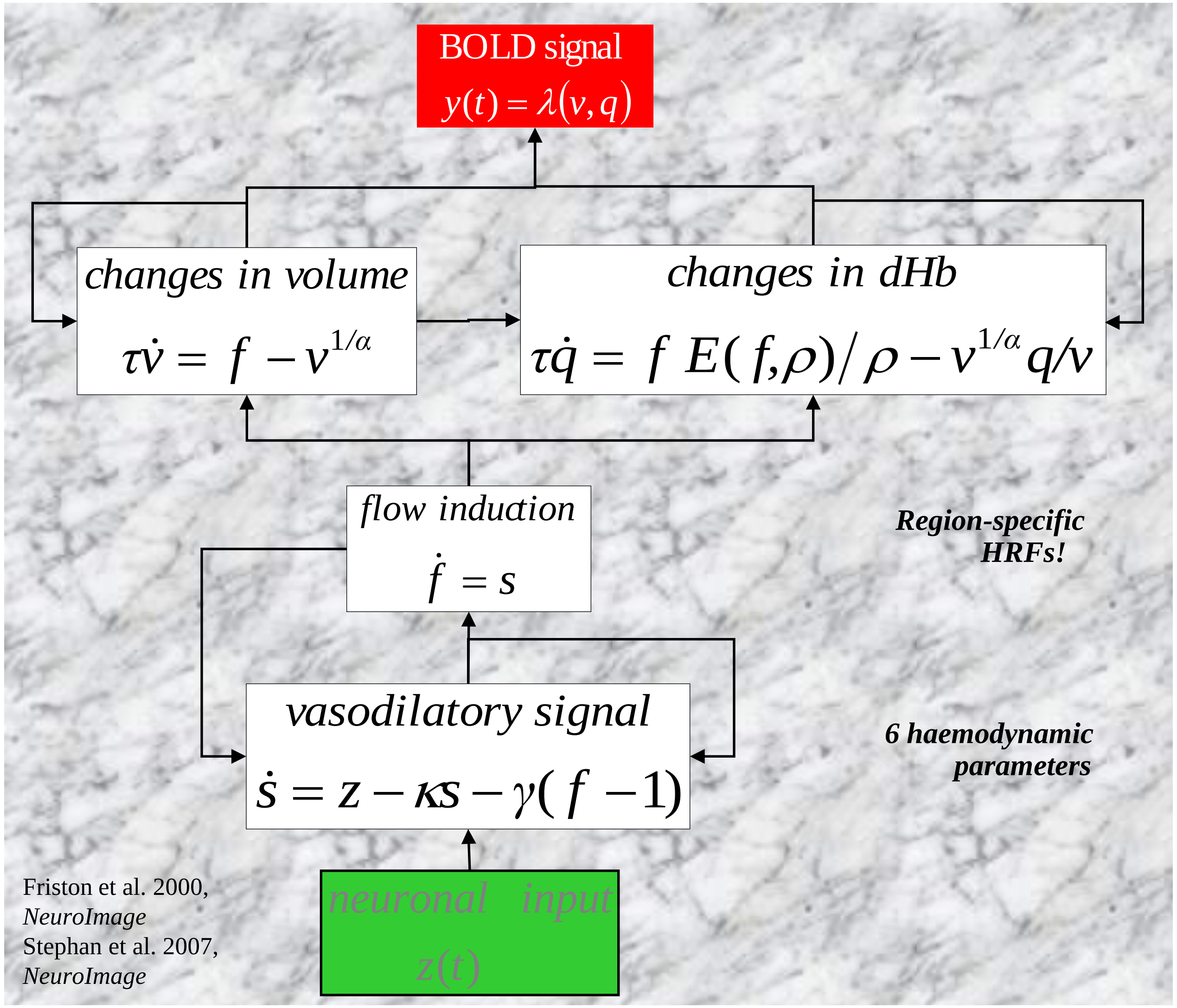
direct inputs $C = \frac{\partial F}{\partial u} = \frac{\partial \dot{z}}{\partial u}$

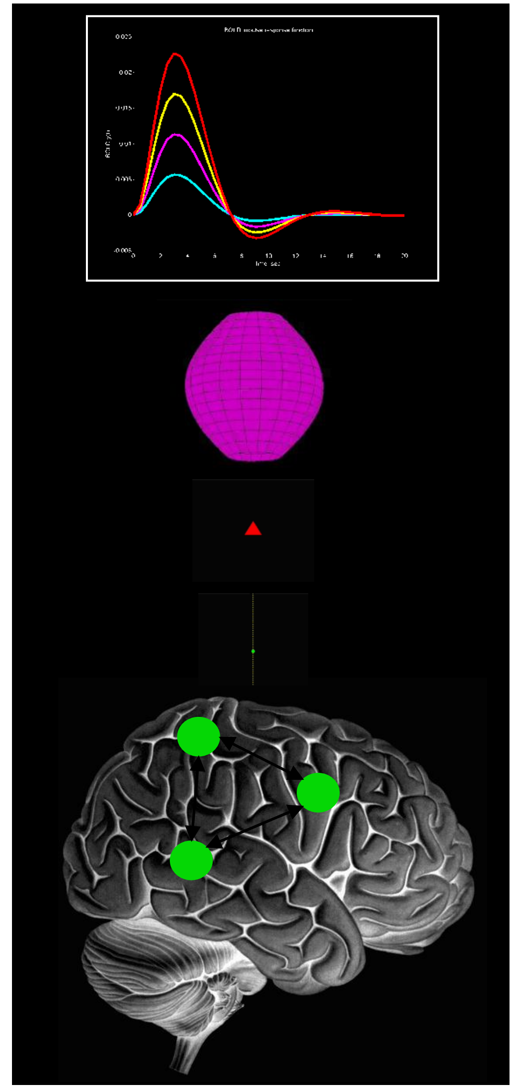




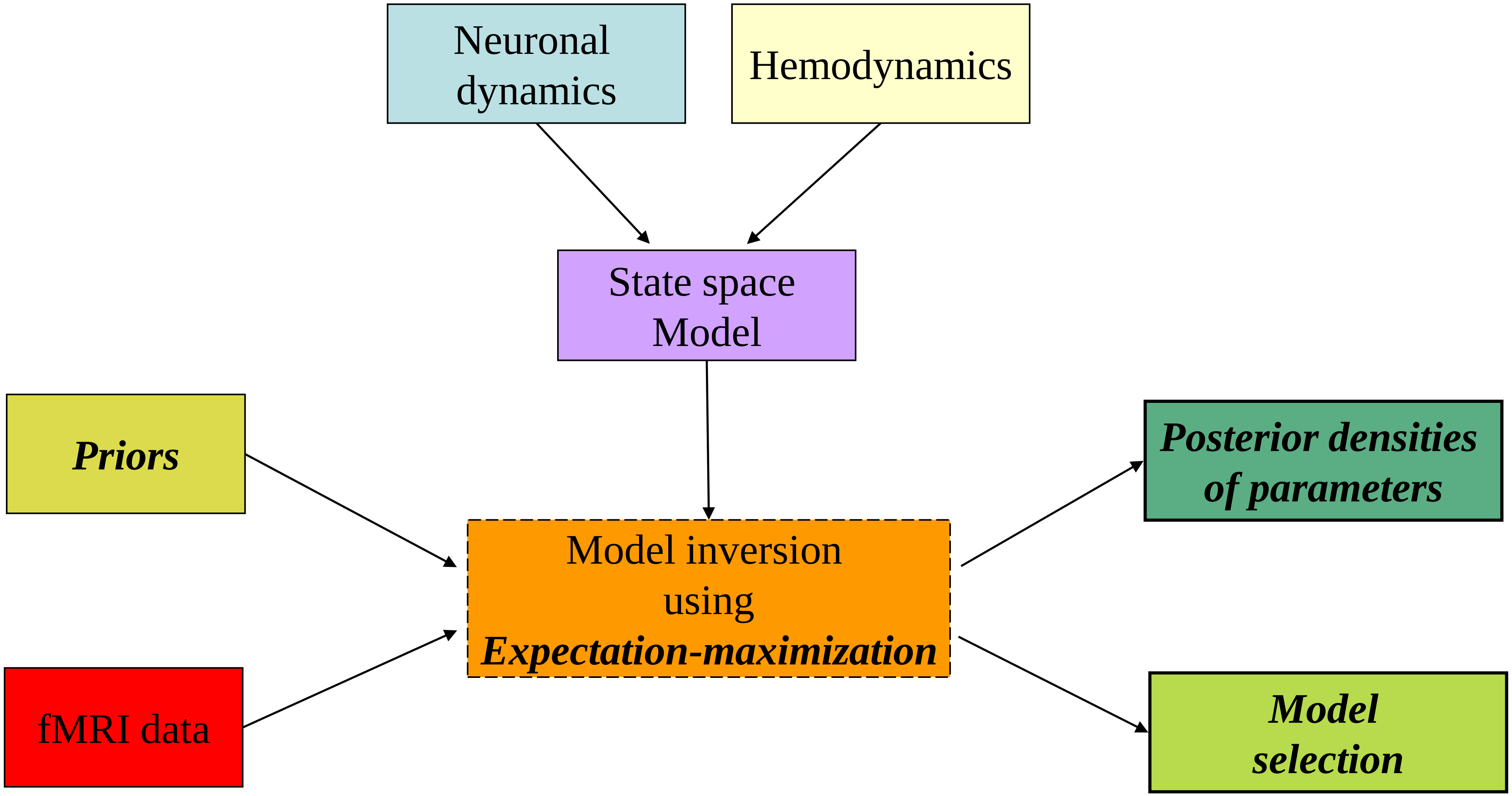
Friston et al. 2003, *NeuroImage*

The hemodynamic "Balloon" model





DCM roadmap



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

Estimation: Bayesian framework

Models of
•Haemodynamics in a single region
•Neuronal interactions

$p(y \mid \theta)$

likelihood term

Constraints on
•Haemodynamic parameters
•Connections

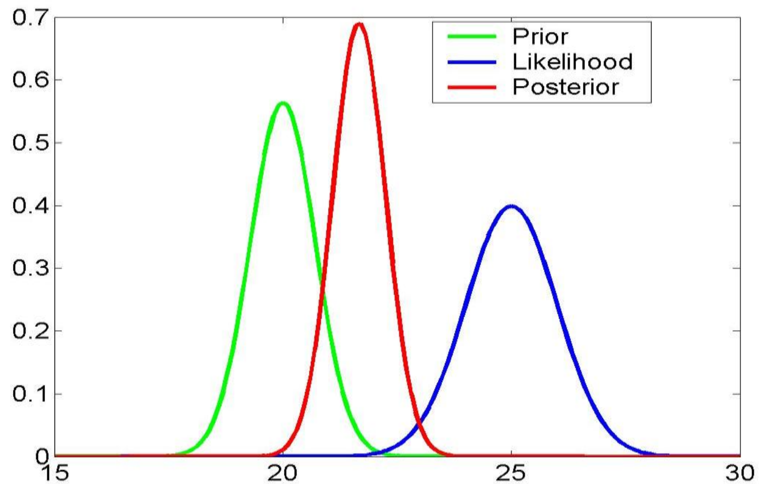
$p(\theta)$

prior

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

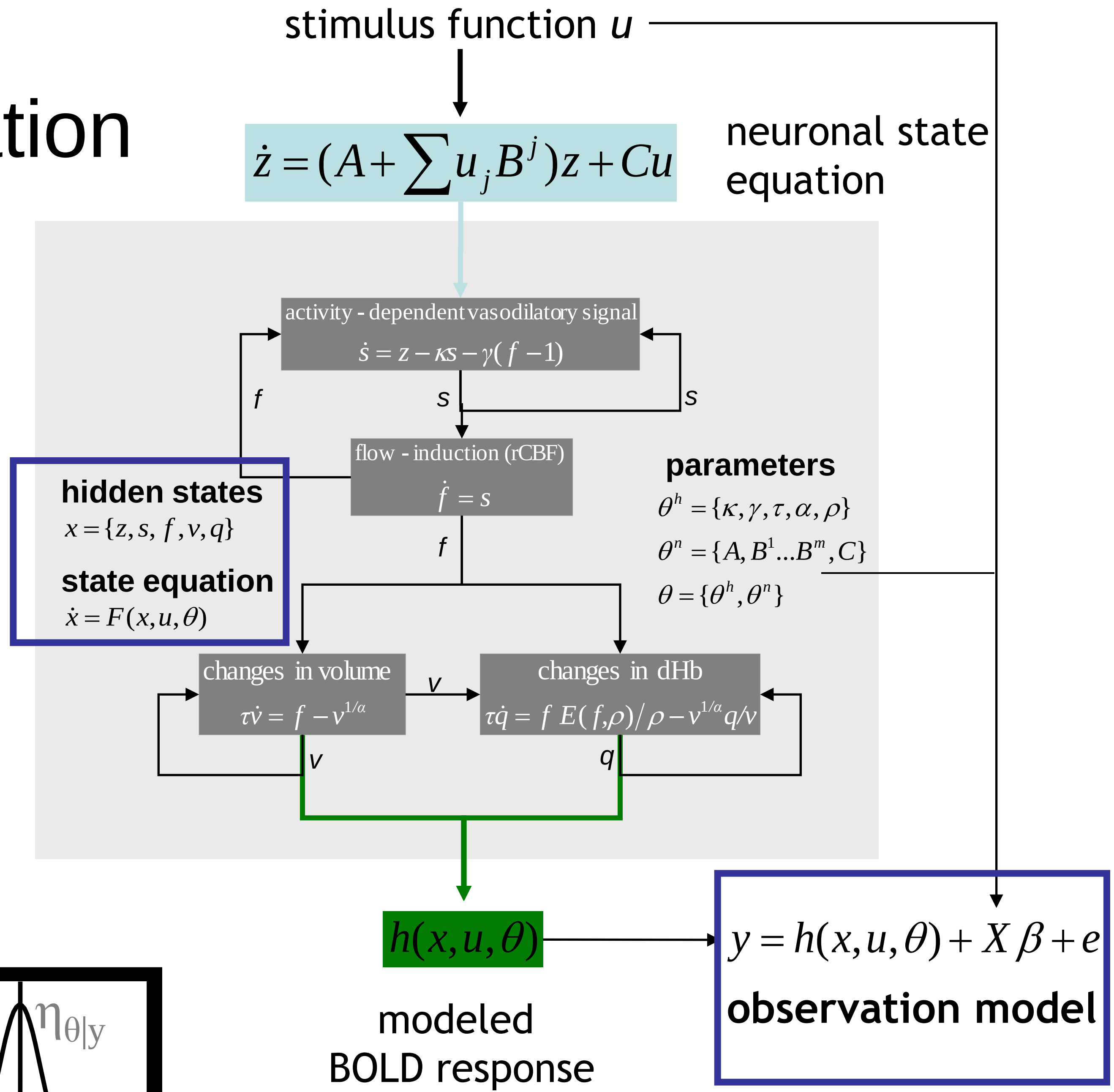
posterior

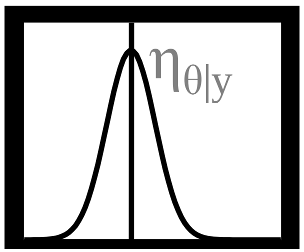
Bayesian estimation



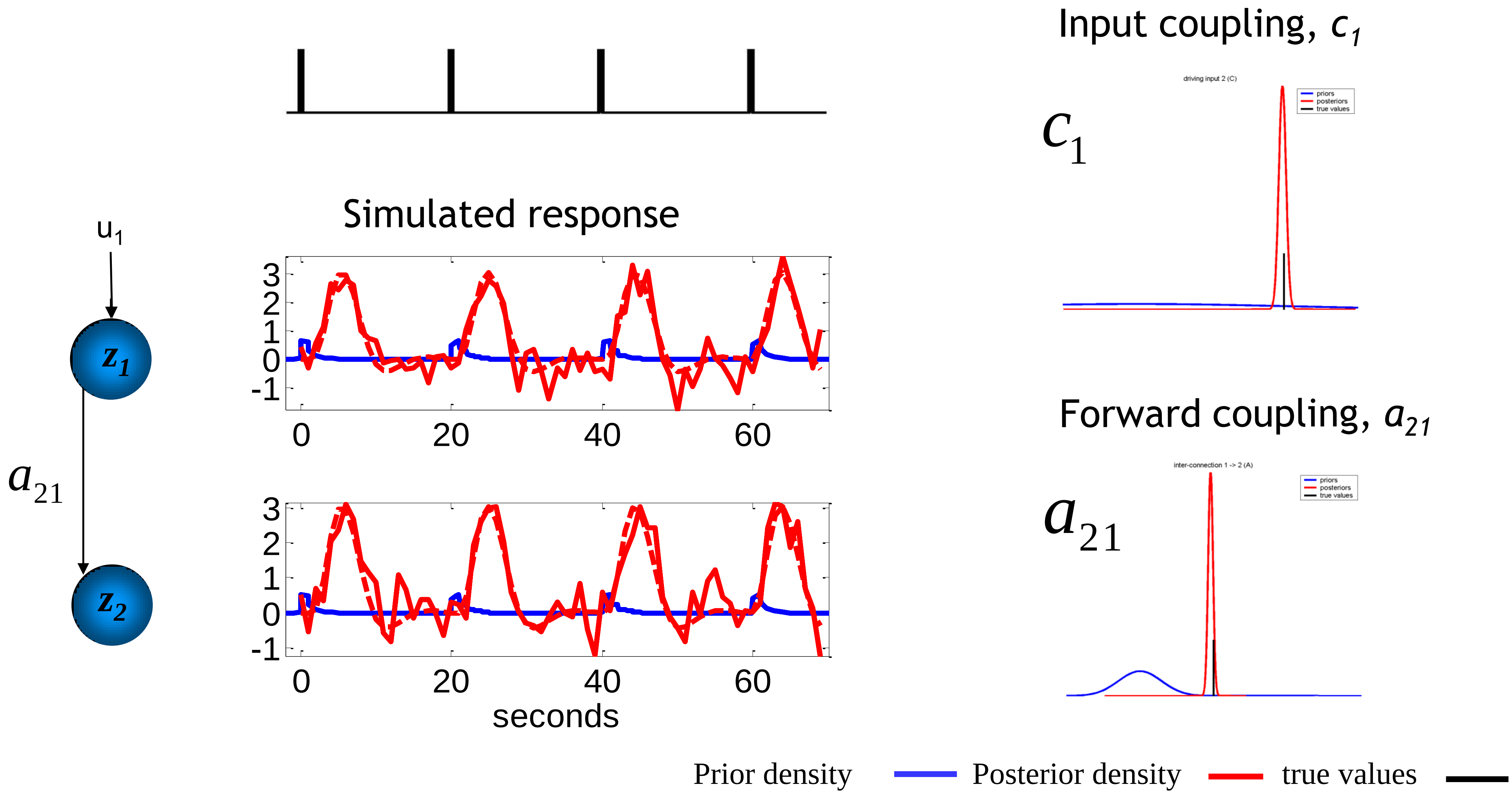
Overview: parameter estimation

- Specify model (neuronal and haemodynamic level)
- Make it an observation model by adding measurement error *e* and confounds *X* (e.g. drift).
- Bayesian parameter estimation using expectation-maximization.
- Result:
  (Normal) posterior parameter distributions, given by mean $\eta_{\theta|y}$ and Covariance $C_{\theta|y}$.





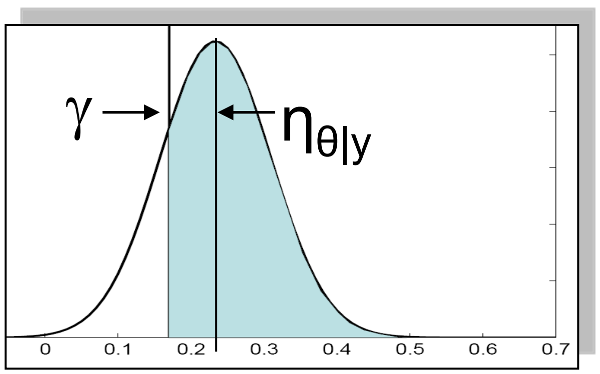
Parameter estimation: an example



Inference about DCM parameters

Bayesian single subject analysis

- The model parameters are distributions that have a mean $\eta_{\theta|y}$ and covariance $C_{\theta|y}$.
  - Use of the cumulative normal distribution to test the probability that a certain parameter is above a chosen threshold γ:



Classical frequentist test across groups

- Test summary statistic: mean $\eta_{\theta|y}$
  - One-sample t-test: Parameter > 0?
  - Paired t-test: parameter 1 > parameter 2?
  - rmANOVA: e.g. in case of multiple sessions per subject

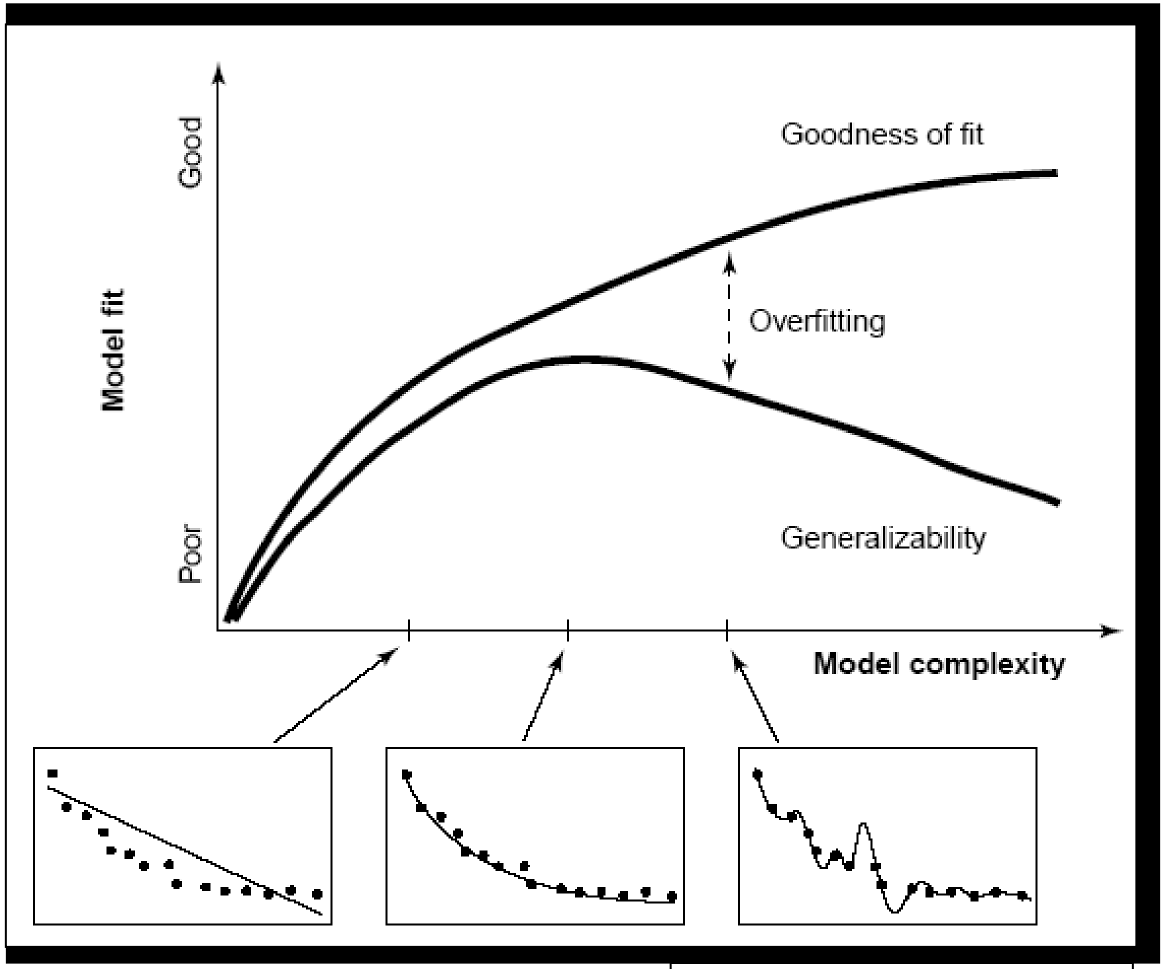
Bayesian parameter averaging

Model comparison and selection

Given competing hypotheses, which model is the best?

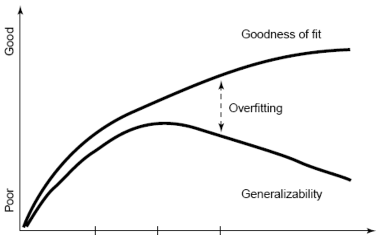
$$\log p(y \mid m) = accuracy(m) - complexity(m)$$

$$B_{ij} = \frac{p(y \mid m = i)}{p(y \mid m = j)}$$



Pitt & Miyung (2002), *TICS*

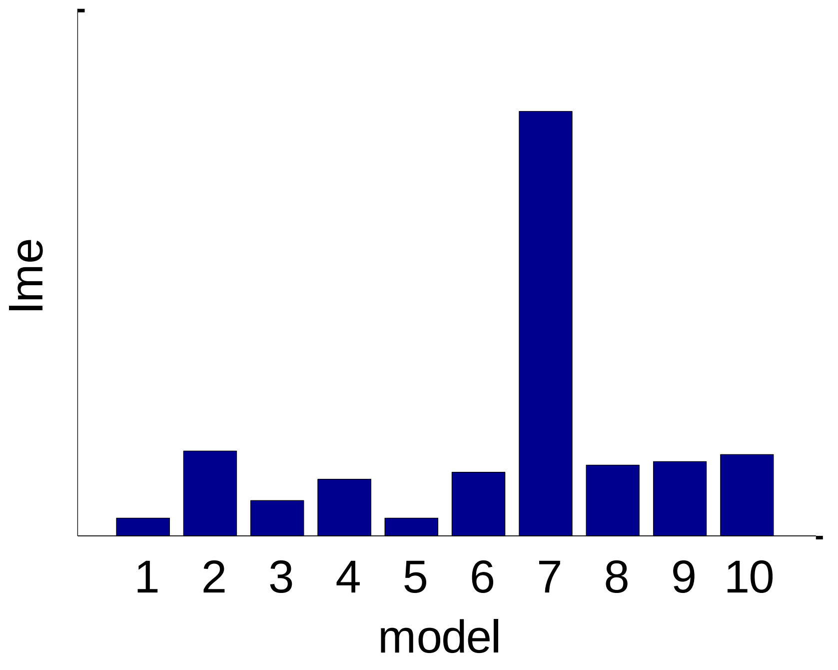
Inference on model space



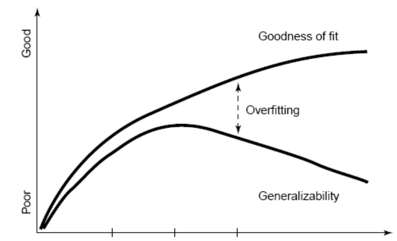
Model evidence: The optimal balance of fit and complexity

Comparing models

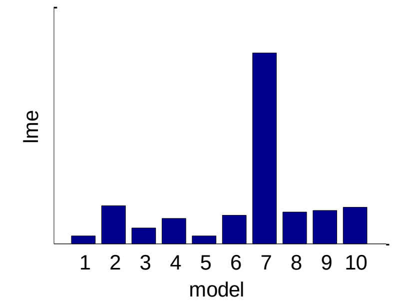
- Which is the best model?



Inference on model space



Model evidence: The optimal balance of fit and complexity

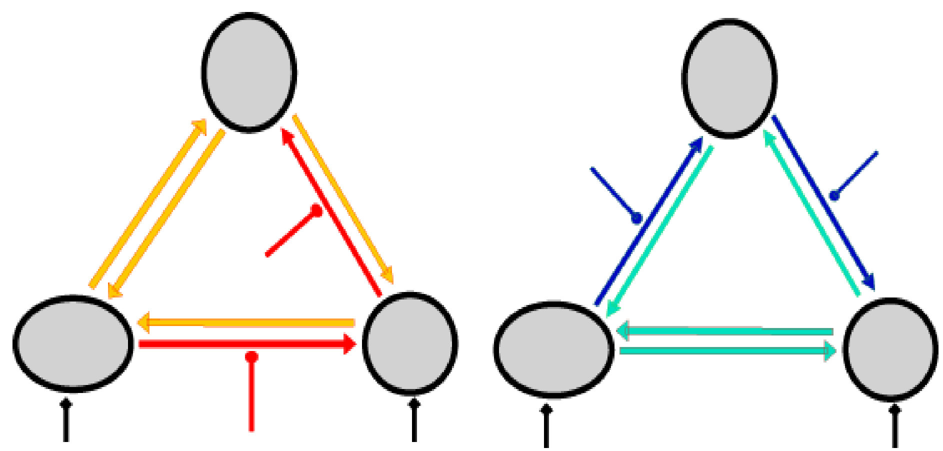


Comparing models

- Which is the best model?

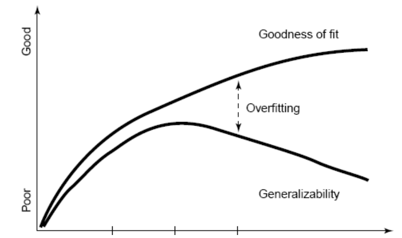
Comparing families of models

- What type of model is best?
    - Feedforward vs feedback
    - Parallel vs sequential processing
    - With or without modulation



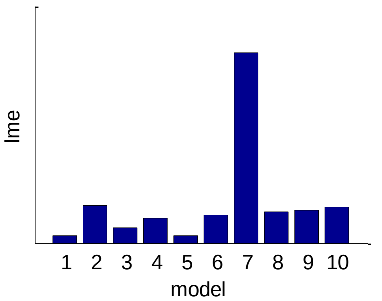
Inference on model space

Model evidence: The optimal balance of fit and complexity



Comparing models

- Which is the best model?



Comparing families of models

- What type of model is best?
  - Feedforward vs feedback
  - Parallel vs sequential processing
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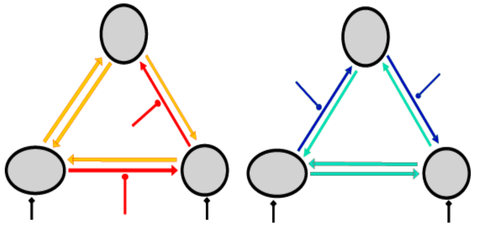
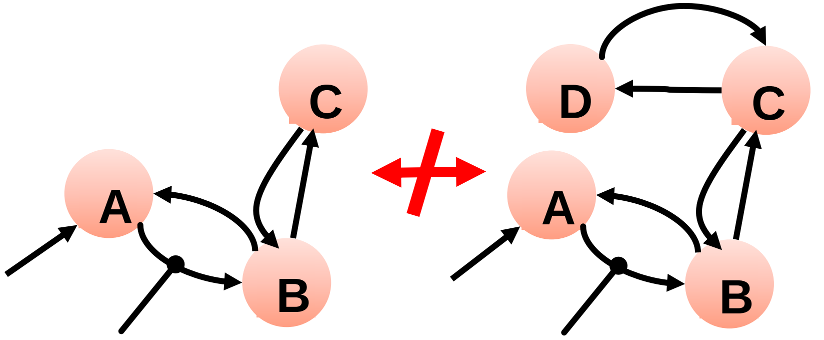


Only compare models with the same data



Overview

Brain connectivity: types & definitions

Anatomical connectivity
Functional connectivity
Effective connectivity

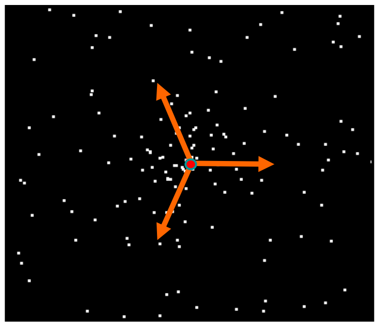
Dynamic causal models (DCMs)

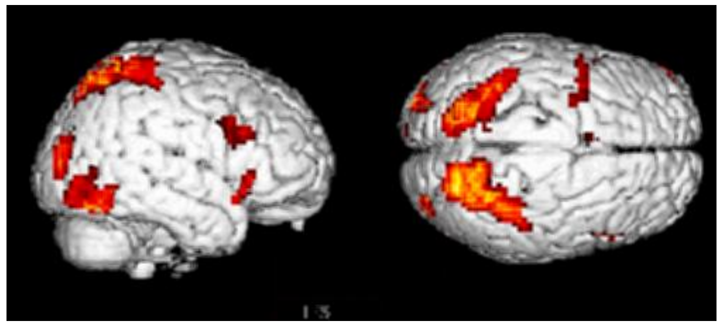
Neuronal model
Hemodynamic model
Estimation: Bayesian framework

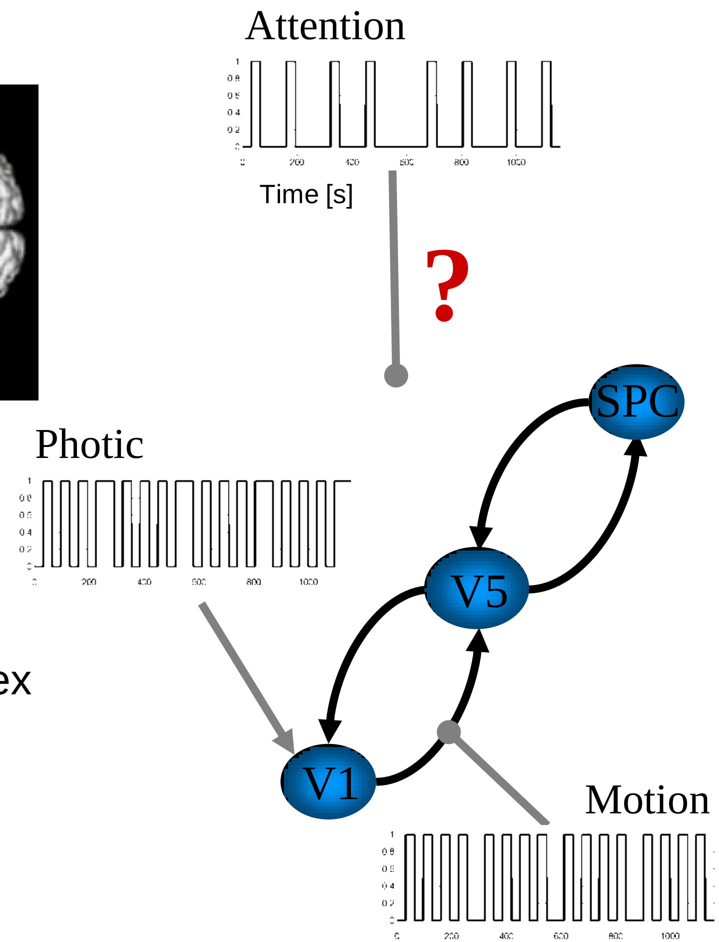
Applications & extensions of DCM to fMRI data

Attention to motion in the visual system

We used this model to assess the site of ***attention modulation*** during *visual motion processing* in an fMRI paradigm reported by *Büchel & Friston.*





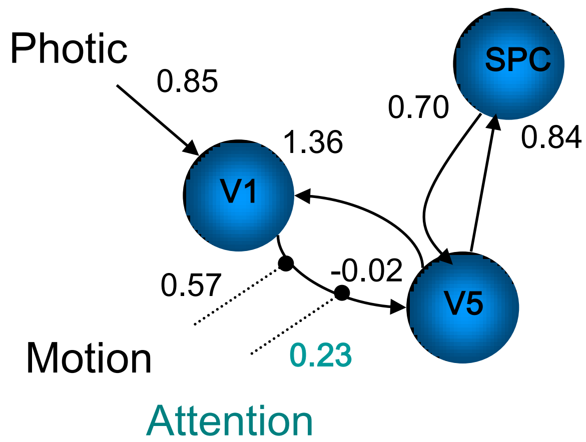


- fixation only
- observe static dots + photic → V1
- observe moving dots + motion → V5
- task on moving dots + attention → V5 + parietal cortex

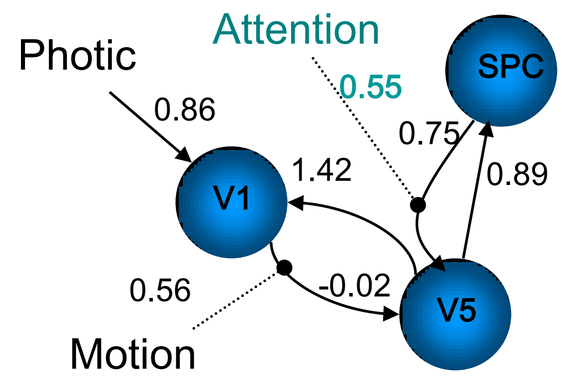
Friston et al. 2003, *NeuroImage*

Comparison of two simple models

Model 1:
attentional modulation
of V1→V5



Model 2:
attentional modulation
of SPC→V5



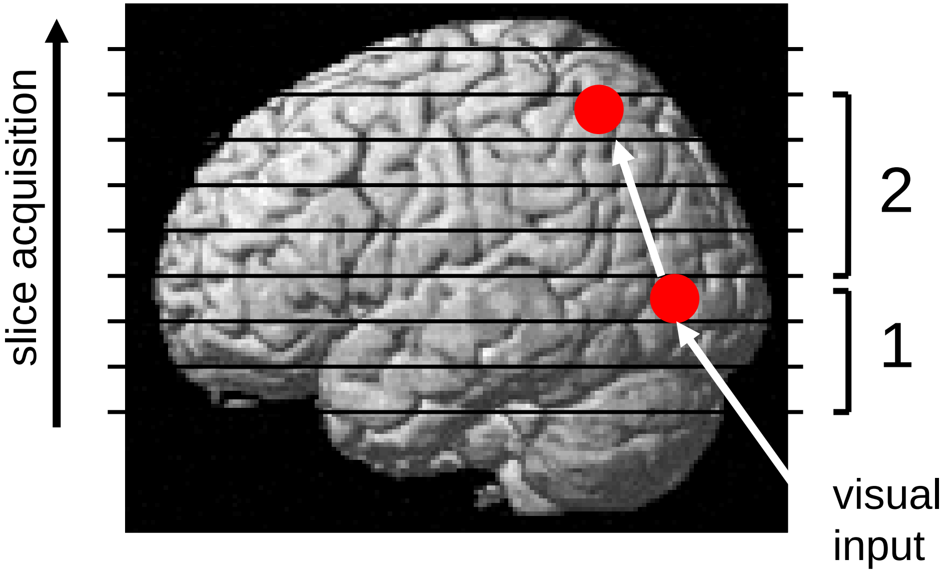
Bayesian model selection: Model 1 better than model 2

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

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

Extension I: Slice timing model

- potential timing problem in DCM:
  temporal shift between regional time series because of multi-slice acquisition



- Solution:
  - Modelling of (known) slice timing of each area.

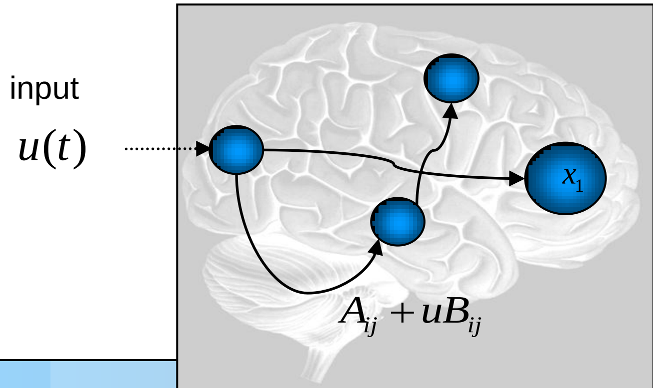
Slice timing extension now allows for any slice timing differences!

Long TRs (> 2 sec) no longer a limitation.

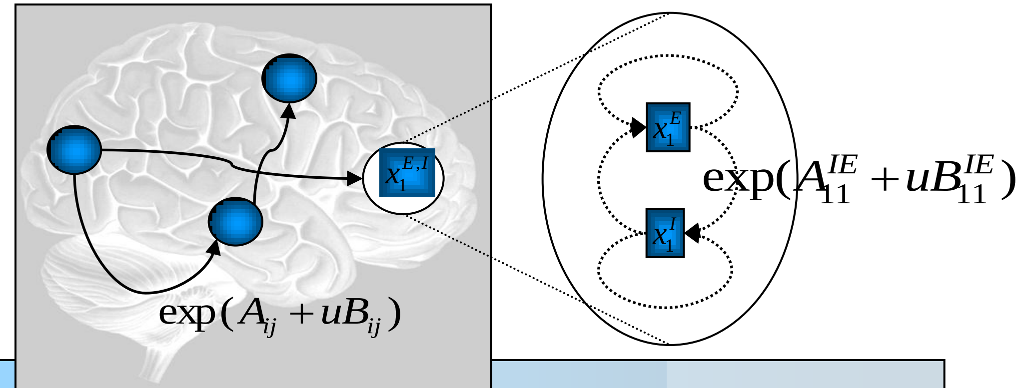
(Kiebel et al., 2007)

Extension II: Two-state model

Single-state DCM



Two-state DCM



$$\frac{\partial x}{\partial t} = (A + uB)x + Cu$$

$$A = \begin{bmatrix} A_{11} & \cdots & A_{1N} \\ \vdots & \ddots & \vdots \\ A_{N1} & \dots & A_{NN} \end{bmatrix} \quad x(t) = \begin{bmatrix} x_1 \\ \vdots \\ x_N \end{bmatrix}$$

$$\dot{z} = Az + \sum u_j B_j z + Cu$$

$$\frac{\partial x}{\partial t} = (AB^u)x + Cu$$

$$A = \begin{bmatrix} -e^{A_{11}^{EE}} & -e^{A_{11}^{EI}} & \cdots & e^{A_{1N}} & 0 \\ e^{A_{11}^{IE}} & -e^{A_{11}^{II}} & & 0 & 0 \\ \vdots & & \ddots & & \vdots \\ e^{A_{N1}} & 0 & & -e^{A_{NN}^{EE}} & -e^{A_{NN}^{EI}} \\ 0 & 0 & \cdots & e^{A_{NN}^{IE}} & -e^{A_{NN}^{II}} \end{bmatrix} \quad x(t) = \begin{bmatrix} x_1^E \\ x_1^I \\ \vdots \\ x_N^E \\ x_N^I \end{bmatrix}$$

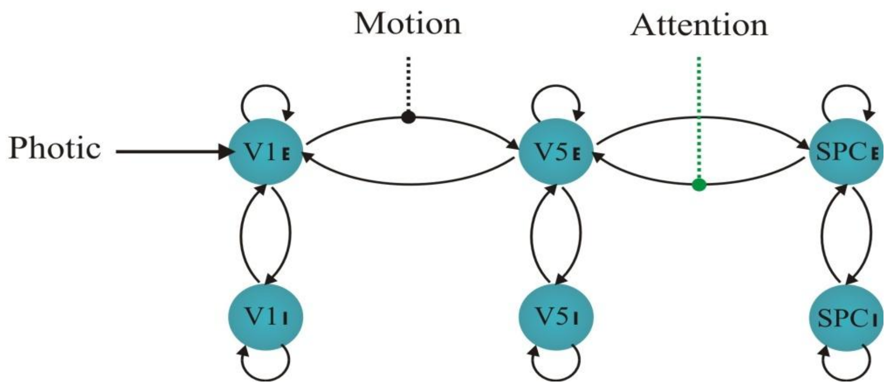
Extrinsic (between-region) coupling

Intrinsic (within-region) coupling

DCM for *Büchel & Friston*

Example: Two-state Model Comparison

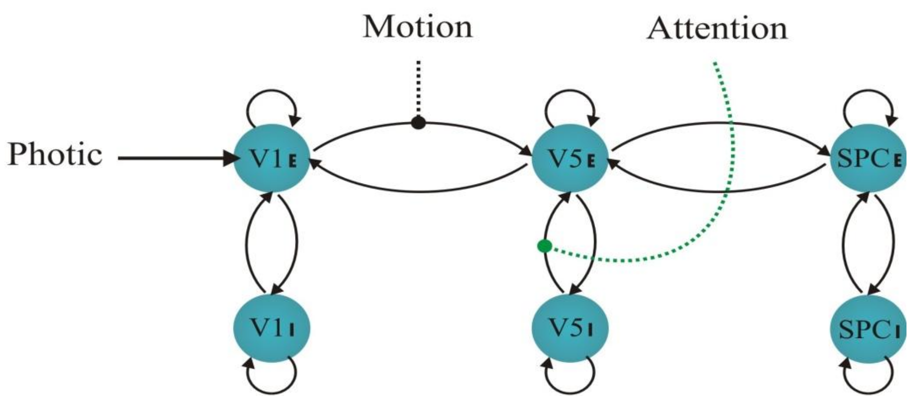
Model 1 - BCW



Attention

$$A=\begin{bmatrix} -EE_{V1} & -EI_{V1} & E_{V1}E_{V5} & 0 & 0 & 0 \\ IE_{V1} & -II_{V1} & 0 & 0 & 0 & 0 \\ E_{V5}E_{V1} & 0 & -EE_{V5} & -EI_{V5} & \boxed{E_{V5}E_{SPC}} & 0 \\ 0 & 0 & IE_{V5} & -II_{V5} & 0 & 0 \\ 0 & 0 & E_{SPC}E_{V5} & 0 & -EE_{SPC} & -EI_{SPC} \\ 0 & 0 & 0 & 0 & IE_{SPC} & -II_{SPC} \end{bmatrix}$$

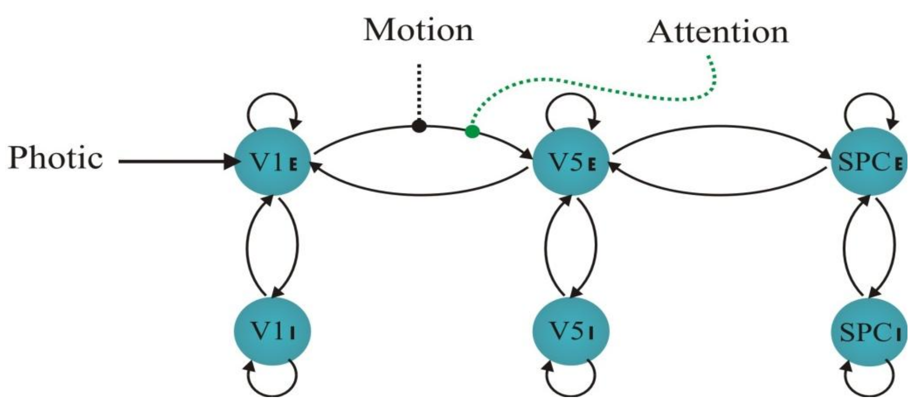
Model 2 - Intr



Attention

$$A=\begin{bmatrix} -EE_{V1} & -EI_{V1} & E_{V1}E_{V5} & 0 & 0 & 0 \\ IE_{V1} & -II_{V1} & 0 & 0 & 0 & 0 \\ E_{V5}E_{V1} & 0 & -EE_{V5} & \boxed{-EI_{V5}} & E_{V5}E_{SPC} & 0 \\ 0 & 0 & IE_{V5} & -II_{V5} & 0 & 0 \\ 0 & 0 & E_{SPC}E_{V5} & 0 & -EE_{SPC} & -EI_{SPC} \\ 0 & 0 & 0 & 0 & IE_{SPC} & -II_{SPC} \end{bmatrix}$$

Model 3 - FWD

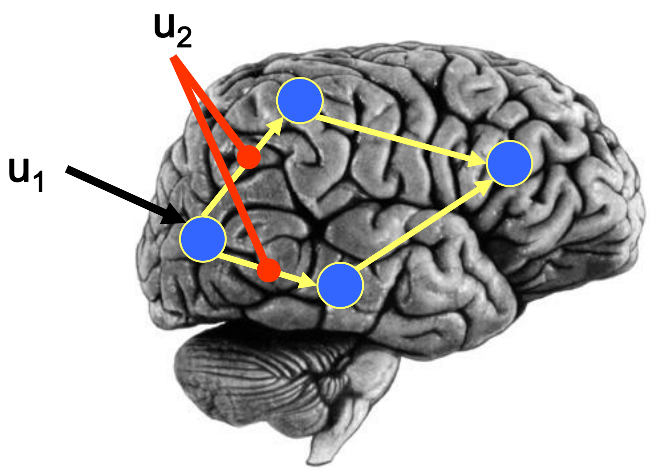


Attention

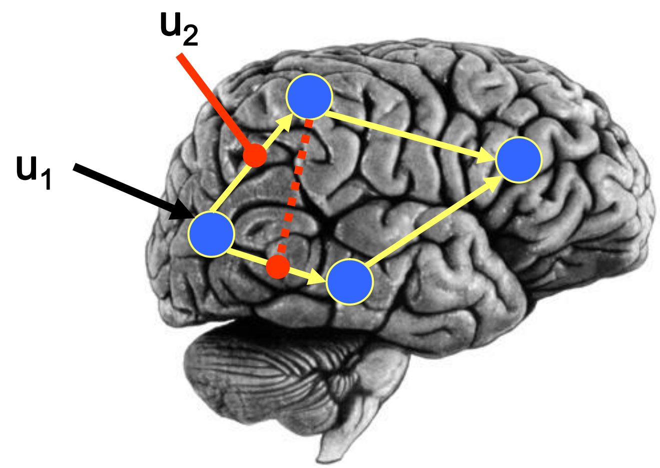
$$A=\begin{bmatrix} -EE_{V1} & -EI_{V1} & E_{V1}E_{V5} & 0 & 0 & 0 \\ IE_{V1} & -II_{V1} & 0 & 0 & 0 & 0 \\ \boxed{E_{V5}E_{V1}} & 0 & -EE_{V5} & -EI_{V5} & E_{V5}E_{SPC} & 0 \\ 0 & 0 & IE_{V5} & -II_{V5} & 0 & 0 \\ 0 & 0 & E_{SPC}E_{V5} & 0 & -EE_{SPC} & -EI_{SPC} \\ 0 & 0 & 0 & 0 & IE_{SPC} & -II_{SPC} \end{bmatrix}$$

Extension III: Nonlinear DCM for fMRI

bilinear DCM



nonlinear DCM



Bilinear state equation

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

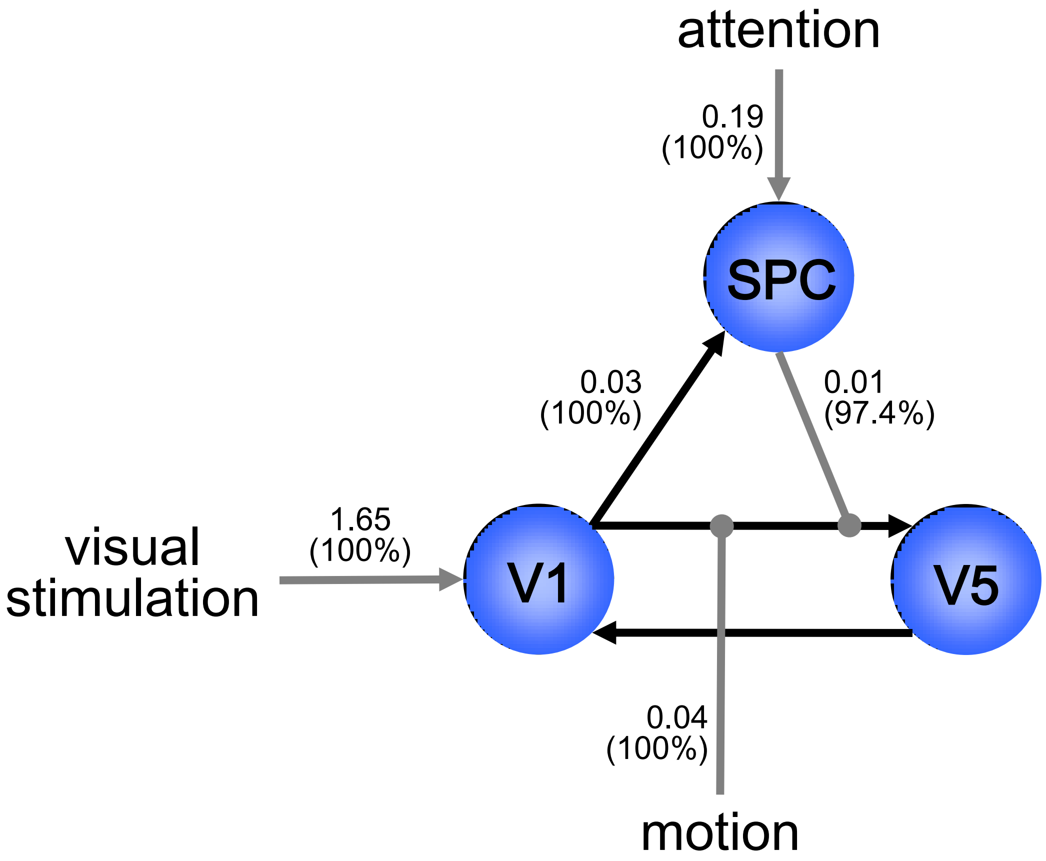
Nonlinear state equation

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

Here DCM can model activity-dependent changes in connectivity; how connections are enabled or gated by activity in one or more areas.

Extension III: Nonlinear DCM for fMRI

Can V5 activity during attention to motion be explained by allowing activity in SPC to modulate the V1-to-V5 connection?



The posterior density of $D^{(SPC)}_{V5,V1}$ indicates that this gating existed with 97% confidence.

(The D matrix encodes which of the n neural units gate which connections in the system)

So, DCM….

- enables one to **infer hidden neuronal processes** from fMRI data
- allows one to **test mechanistic hypotheses** about observed effects
  - uses a deterministic differential equation to model neuro-dynamics (represented by matrices A,B and C).
- is informed by anatomical and physiological principles.
- uses a **Bayesian framework** to estimate model parameters
- is a generic approach to modelling experimentally perturbed dynamic systems.
  - provides an observation model for neuroimaging data, e.g. fMRI, M/EEG
  - DCM is **not model or modality specific** (Models will change and the method extended to other modalities e.g. ERPs, LFPs)

Some useful references

- **The first DCM paper:** Dynamic Causal Modelling (2003). Friston et al. *NeuroImage* 19:1273-1302.
- **Physiological validation of DCM for fMRI:** Identifying neural drivers with functional MRI: an electrophysiological validation (2008). David et al. *PLoS Biol.* 6 2683–2697
- **Hemodynamic model:** Comparing hemodynamic models with DCM (2007). Stephan et al. *NeuroImage* 38:387-401
- **Nonlinear DCMs:**Nonlinear Dynamic Causal Models for FMRI (2008). Stephan et al. *NeuroImage* 42:649-662
- **Two-state model:** Dynamic causal modelling for fMRI: A two-state model (2008). Marreiros et al. *NeuroImage* 39:269-278
- **Group Bayesian model comparison:** Bayesian model selection for group studies (2009). Stephan et al. *NeuroImage* 46:1004-10174
- **10 Simple Rules for DCM** (2010). Stephan et al. *NeuroImage 52*.

Thank you for your attention!!!