University of Zurich[UZH]

Translational Neuromodeling Unit

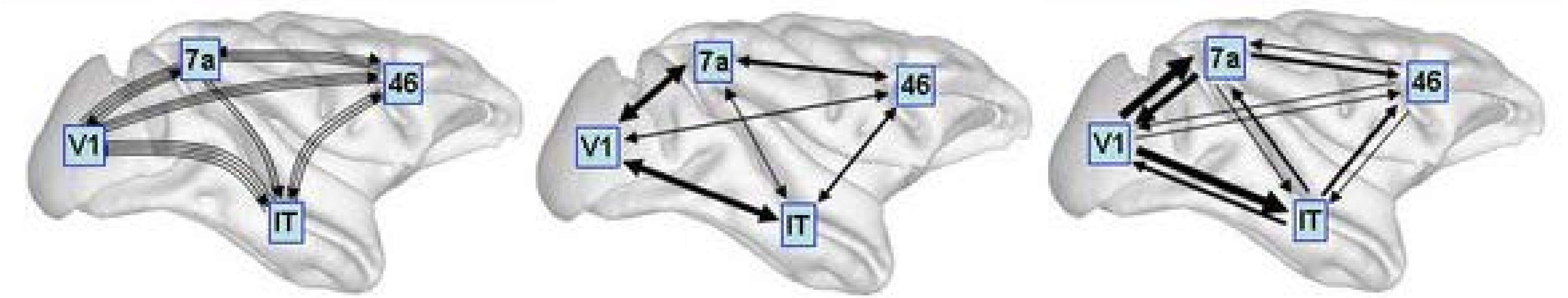
ETH zürich

DCM for fMRI –

Dynamic causal modeling for functional magnetic resonance imaging

Andreea Diaconescu and Jakob Heinzle
Translational Neuromodeling Unit
University and ETH Zürich

Structural, functional & effective connectivity



Sporns 2007, *Scholarpedia*

anatomical/structural connectivity

- presence of physical connections
- DWI, tractography, tracer studies (monkeys)

functional connectivity

- statistical dependency between regional time series
- correlations, ICA

effective connectivity

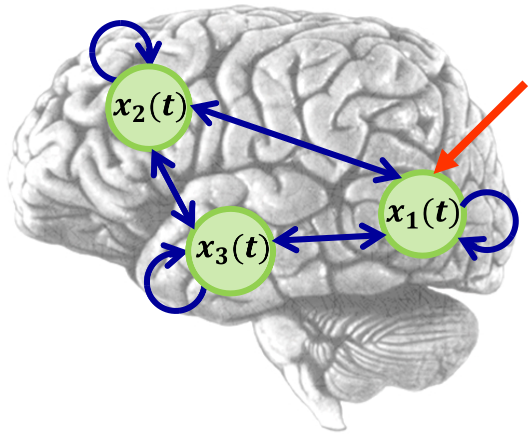
- causal (directed) influences between neuronal populations
- DCM

DCM approach to effective connectivity

A simple model of a neural network …

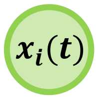
… described as a dynamical system …

… causes the data (BOLD signal).

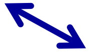


$$\dot{x} = f(x, u, \theta_x)$$

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

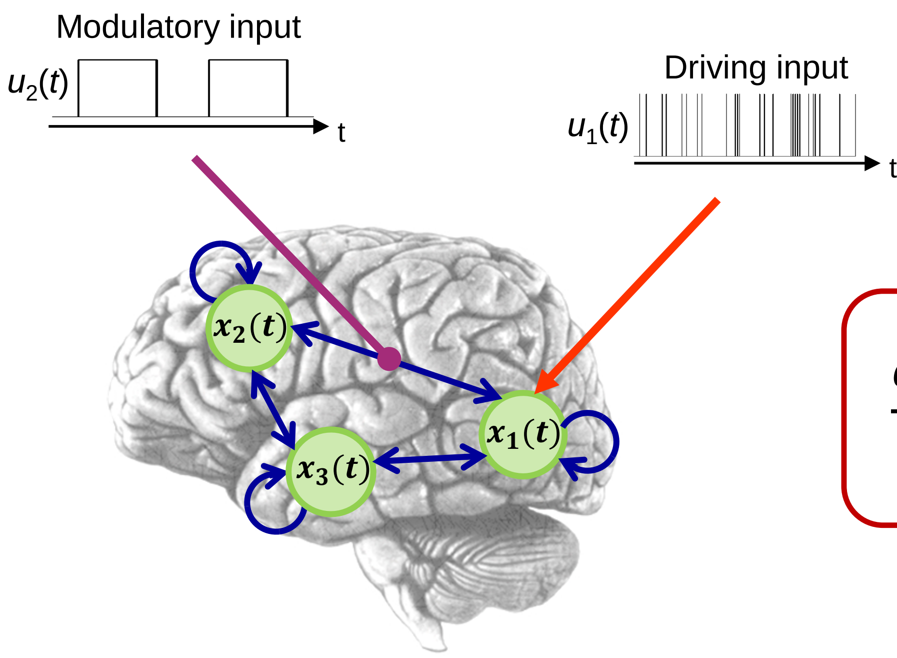
 Neural node

 Input (u)

 Connections (θ)

Let the system run with input (u) and parameters (θ_x, θ_y), and you will get a BOLD signal time course y that you can compare to the measured data.

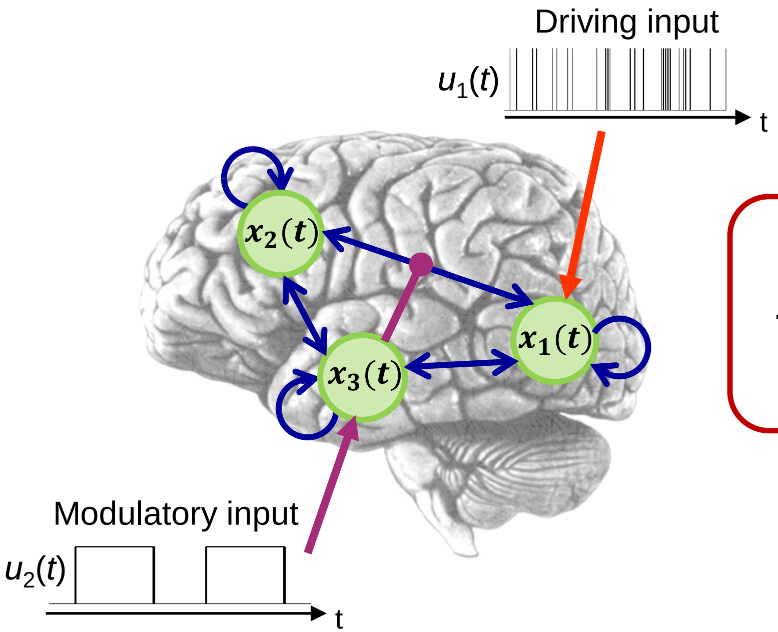
The neural equations – bilinear model



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

Parameters A, B and C define connectivity!

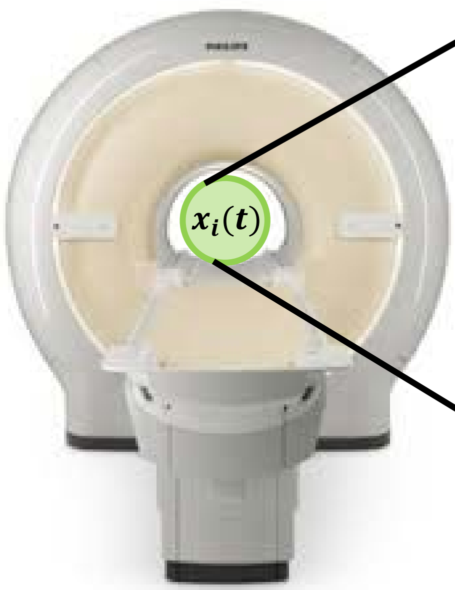
The neural equations – non-linear model



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

Parameters A, B, C and D define connectivity!

From neural activity to the BOLD signal



$x_i(t)$

Local hemodynamic state equation

$$\dot{s} = x - \kappa s - \gamma(f-1)$$
$$\dot{f} = s$$

vasodilatory signal and flow Induction (rCBF)

f

Balloon model

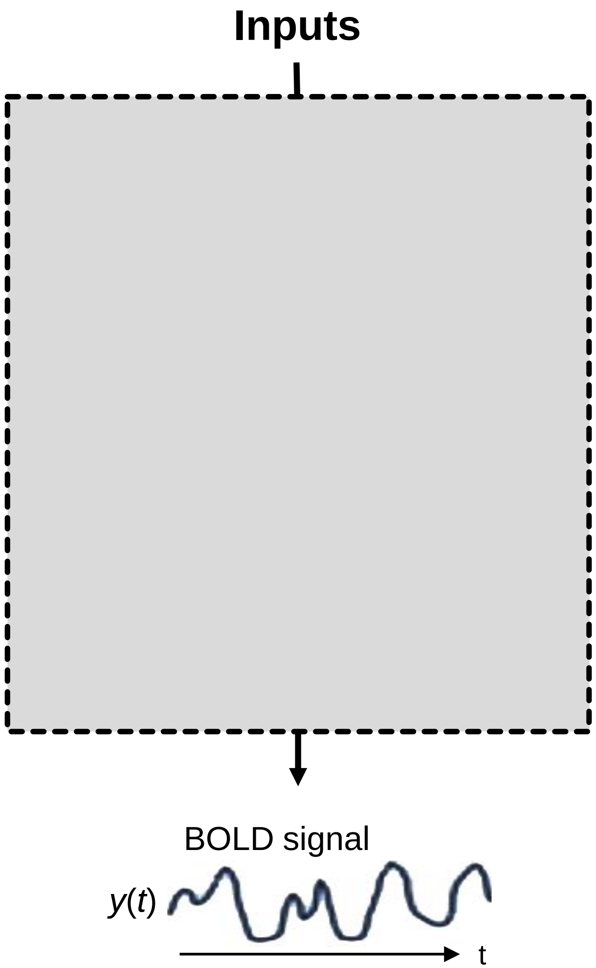
$$\tau\dot{\nu} = f - \nu^{1/\alpha}$$
$$\tau\dot{q} = fE(f, E_0)/E_0 - \nu^{1/\alpha}q/\nu$$

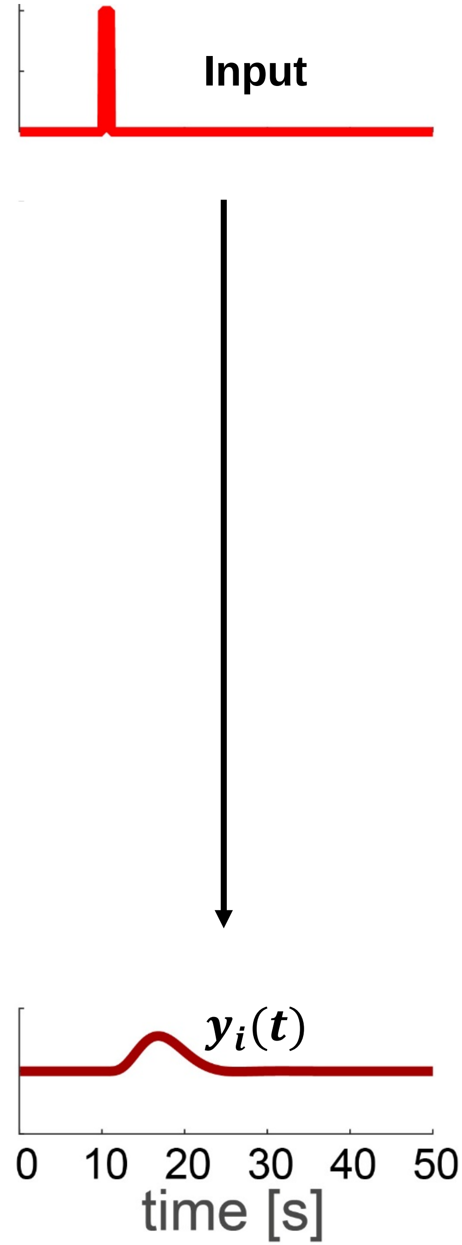
Changes in volume (ν) and dHb (q)

BOLD signal change equation

$$y = \frac{\Delta S}{S_0} \approx V_0\left[k_1(1-q) + k_2\left(1-\frac{q}{\nu}\right) + k_3(1-\nu)\right]$$

Summary – the full model





Summary – the full model

Inputs

↓

Neuronal states
$x_i(t)$

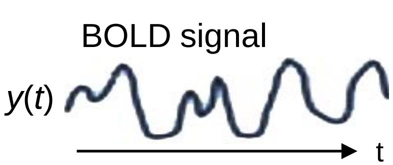
↓

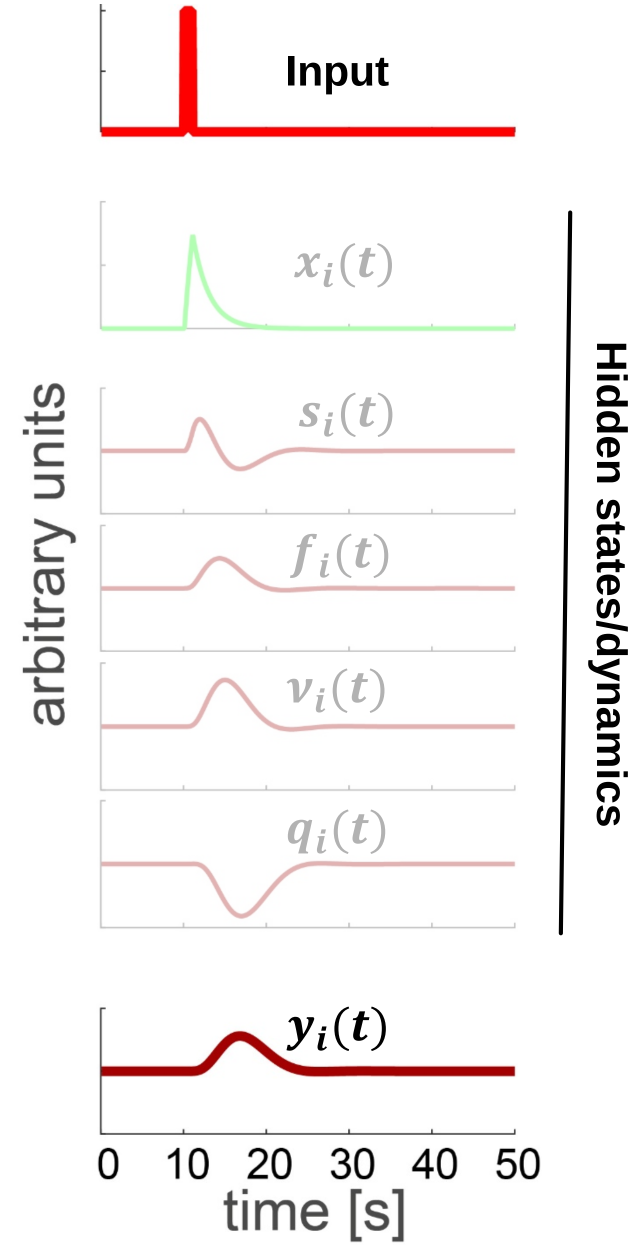
Hemodynamic model
$v_i(t)$ and $q_i(t)$

↓

BOLD
signal change equation
$y_i(t)$

↓





Summary – parameters of interest

Inputs

↓

Neuronal states
$\boldsymbol{x_i(t)}$

← Connection weights: **A, B, C** and **D**

↓

Hemodynamic model
$\boldsymbol{v_i(t)}$ and $\boldsymbol{q_i(t)}$

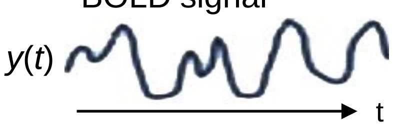
↓

← Hemodynamic parameters: $\boldsymbol{\tau}$, $\boldsymbol{\kappa}$, $\boldsymbol{\varepsilon}$

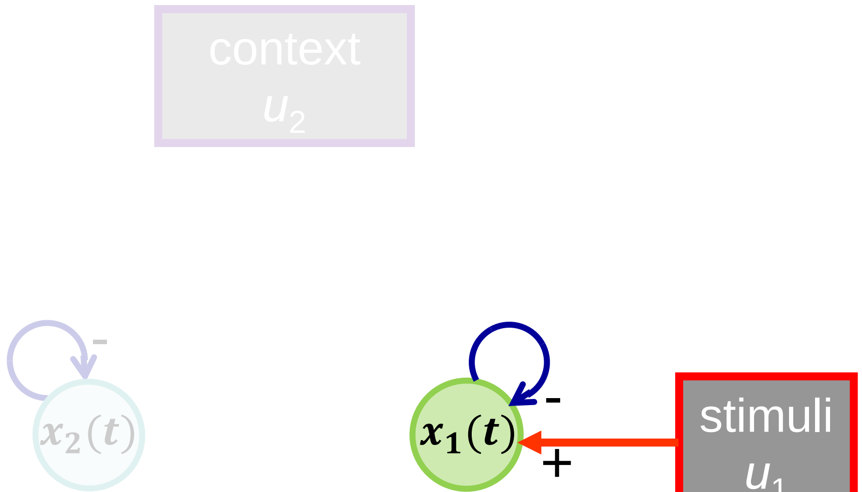
BOLD
signal change equation
$\boldsymbol{y_i(t)}$

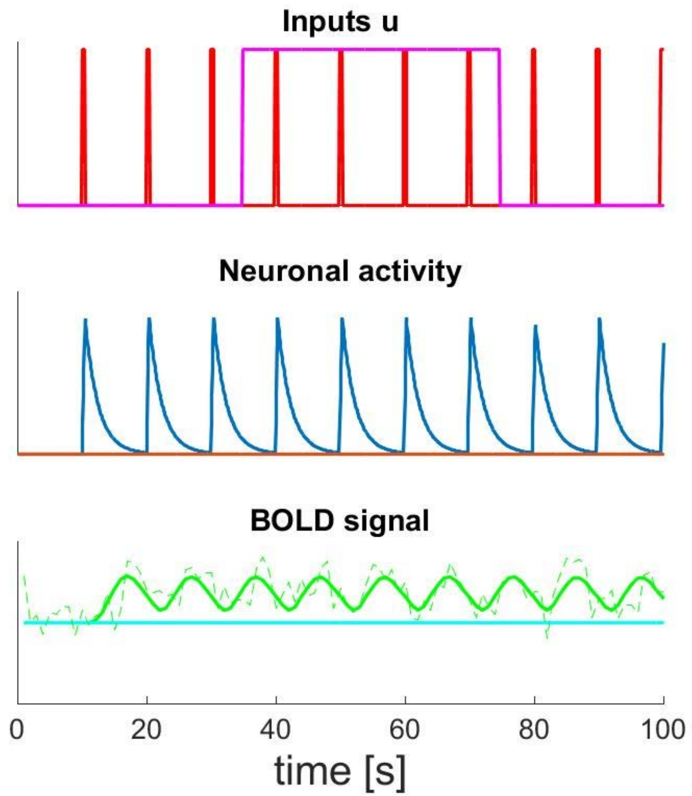
↓

BOLD signal



Example traces 1: Single node

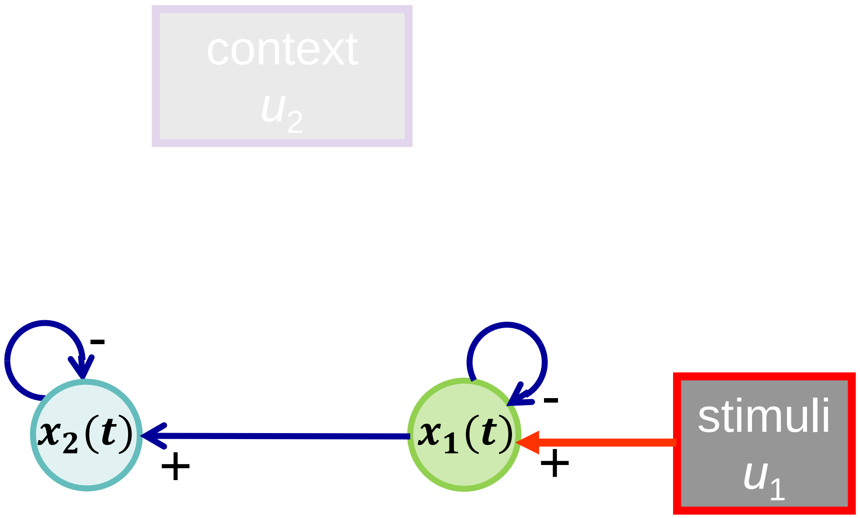


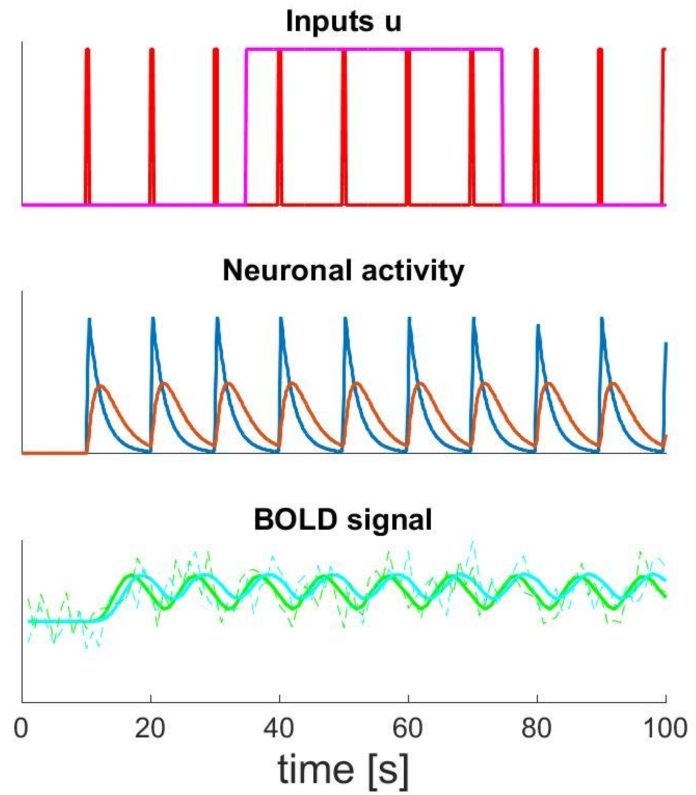


$$\dot{x} = Ax + u_2 B^{(2)} x + C u_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \begin{bmatrix} \sigma & 0 \\ 0 & \sigma \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

Example traces 2: Connected nodes

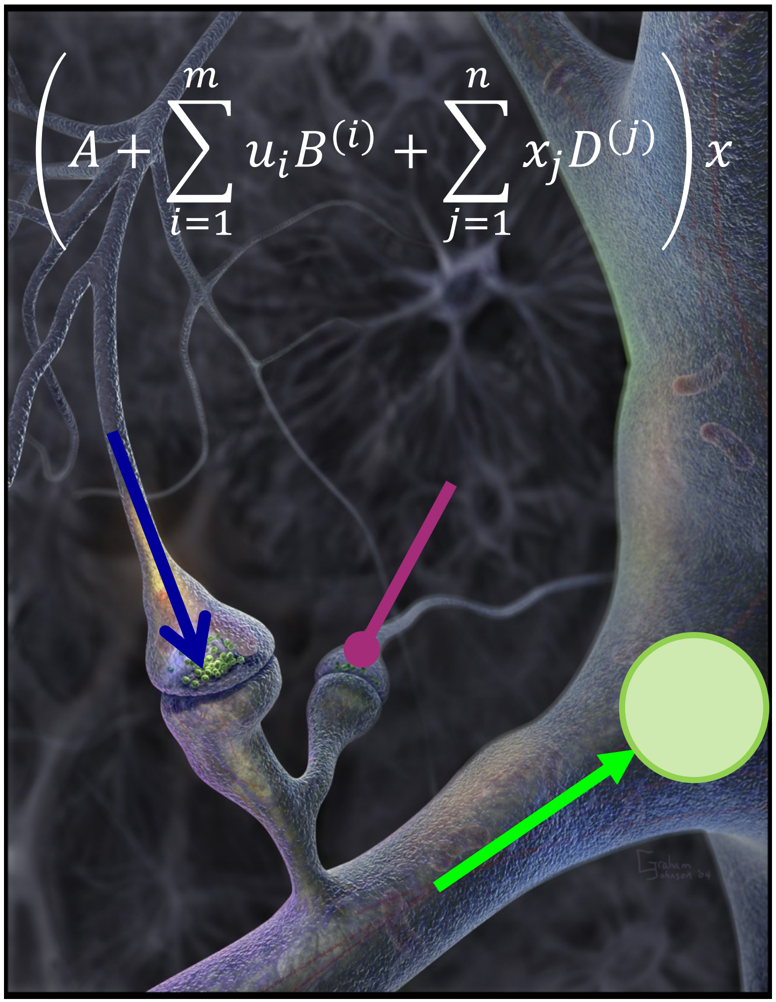


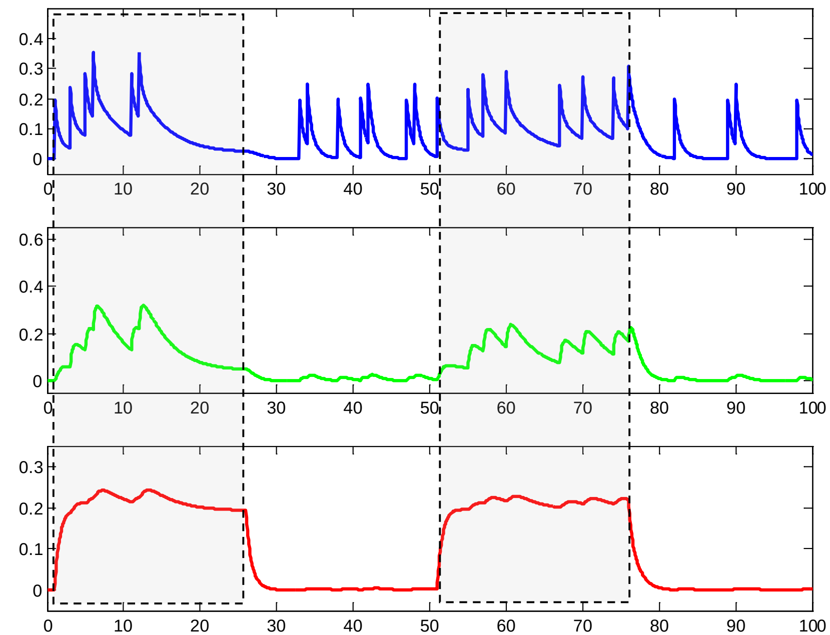


$$\dot{x} = Ax + u_2 B^{(2)} x + C u_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \begin{bmatrix} \sigma & 0 \\ a_{21} & \sigma \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

Context specific «neuro»-modulation

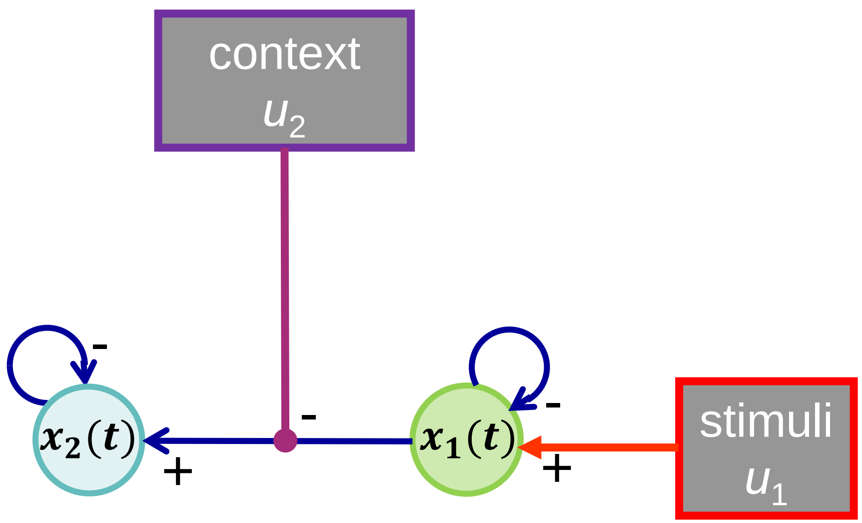


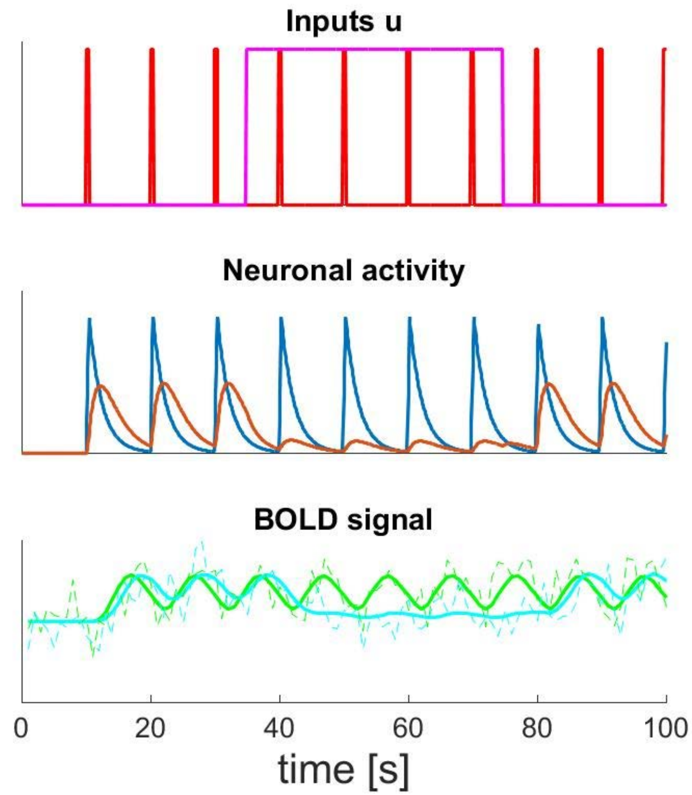


Synaptic strengths are context-sensitive: They depend on spatio-temporal patterns of network activity.

Stephan et al., NeuroImage, 2008

Example traces 3: Modulation of connection

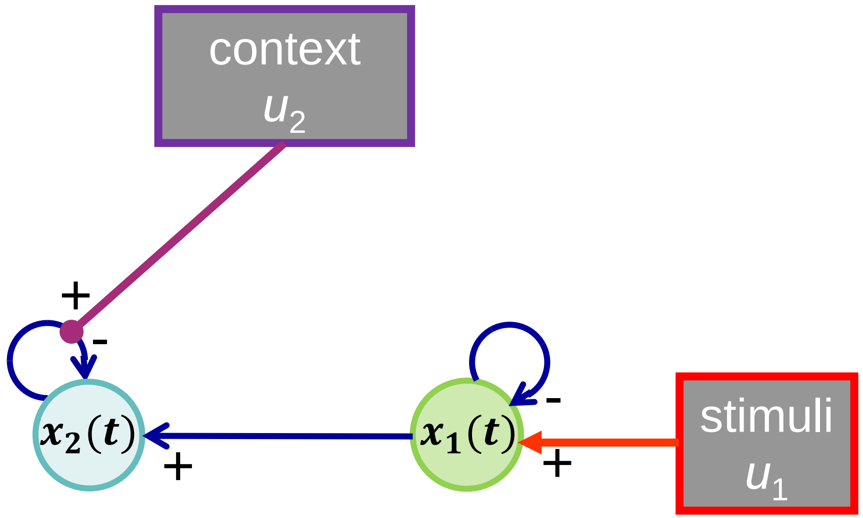


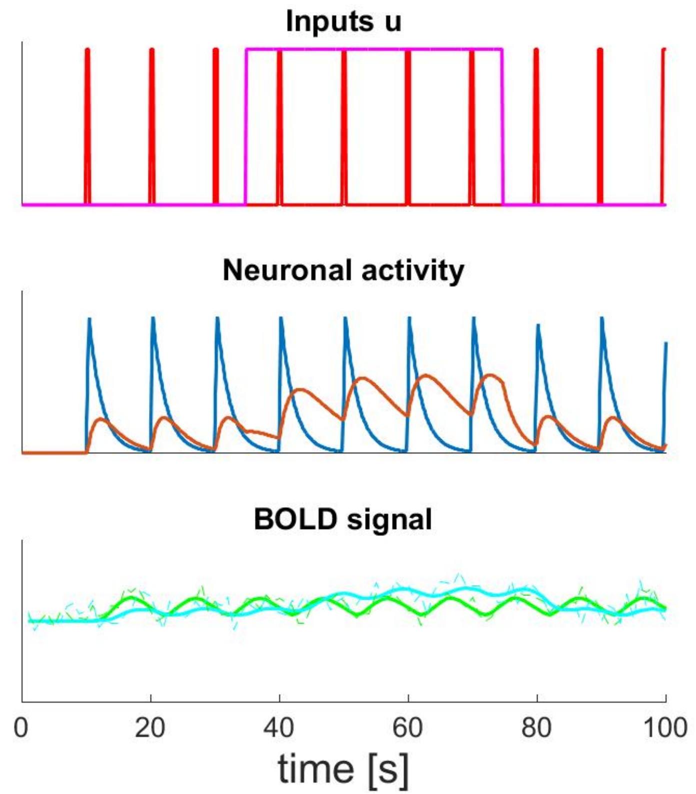


$$\dot{x} = Ax + u_2 B^{(2)} x + C u_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \begin{bmatrix} \sigma & 0 \\ a_{21} & \sigma \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ b_{21}^{(2)} & 0 \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

Example traces 4: Modulation of self-connection





$$\dot{x} = Ax + u_2 B^{(2)} x + C u_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \begin{bmatrix} \sigma & 0 \\ a_{21} & \sigma \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ 0 & b_{22}^{(2)} \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

How to introduce dynamical systems in Bayes' world

$$p(\theta|y,m) = \frac{\boxed{p(y|\theta,m)}\,p(\theta|m)}{p(y|m)}$$ Bayes' formula

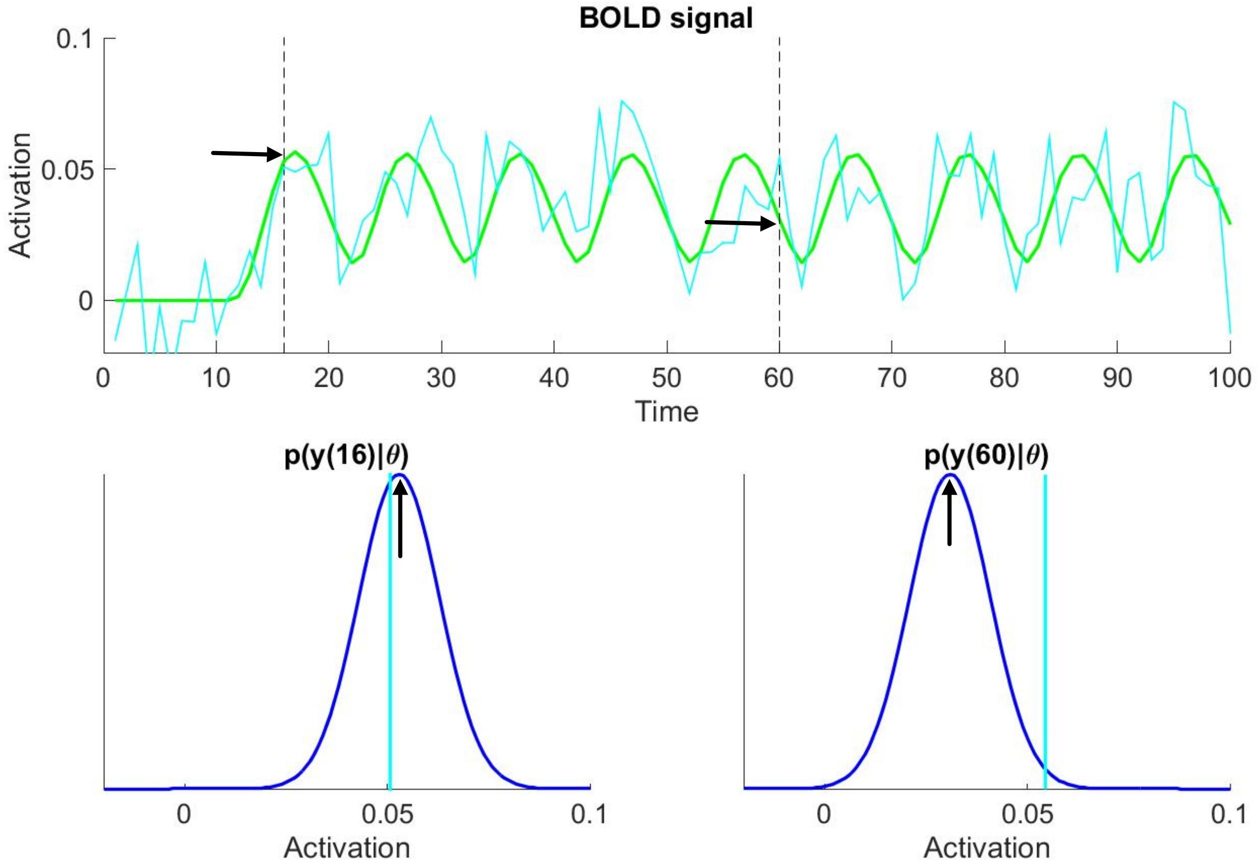
Assume data is normally distributed around the prediction from the dynamical model.

$$y = g(x,\theta_y) + \varepsilon \quad \text{with} \quad \varepsilon \sim \mathcal{N}(0, \Sigma(\theta_\sigma))$$

$$\Longrightarrow \quad p(y(t)|\theta,m) = \mathcal{N}(g(x,\theta_y), \Sigma(\theta_\sigma))$$

Dynamical model defines the likelihood!

Illustration of likelihood



$$p(y|\theta, m) = \prod_t p(y(t)|\theta, m)$$

Define priors

$$p(\theta|y,m) = \frac{p(y|\theta,m)\boxed{p(\theta|m)}}{p(y|m)}$$

- In order to be able to apply Bayesian Inference, we also need to define the priors for the model.
- And now, we can let the machinery run …

DCM inversion – running the machinery
(not the main topic here)

- Goal: Find posterior of parameters $p(\theta|y,m)$ and model evidence $p(y|m)$ given data and priors.
- Analytically often non-tractable
  → Approximations needed (cf. Saturday lectures)
- Variational Bayes (Jean Daunizeau)
- MCMC, Thermodynamic integration (Sudhir Shankar & Eduardo Aponte)
- BMS/BMA (Klaas Enno Stephan)

Bayesian system identification

$$u(t)$$

Neural dynamics

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

Observer function

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

$$p(y|\theta, m) = \mathcal{N}(g(x, \theta_y), \Sigma(\theta_\sigma))$$

$$p(\theta|m) = \mathcal{N}(\mu_\theta, \Sigma_\theta)$$

Inference on model structure

$$p(y|m) = \int p(y|\theta, m)p(\theta|m)d\theta$$

Inference on parameters

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

Design experimental inputs

Define likelihood model

Specify priors

Invert model

Make inferences

What to do with DCM? 3 Example applications

- Inferring on models

  →Which model best explains the data - BMS

- Inferring on parameters

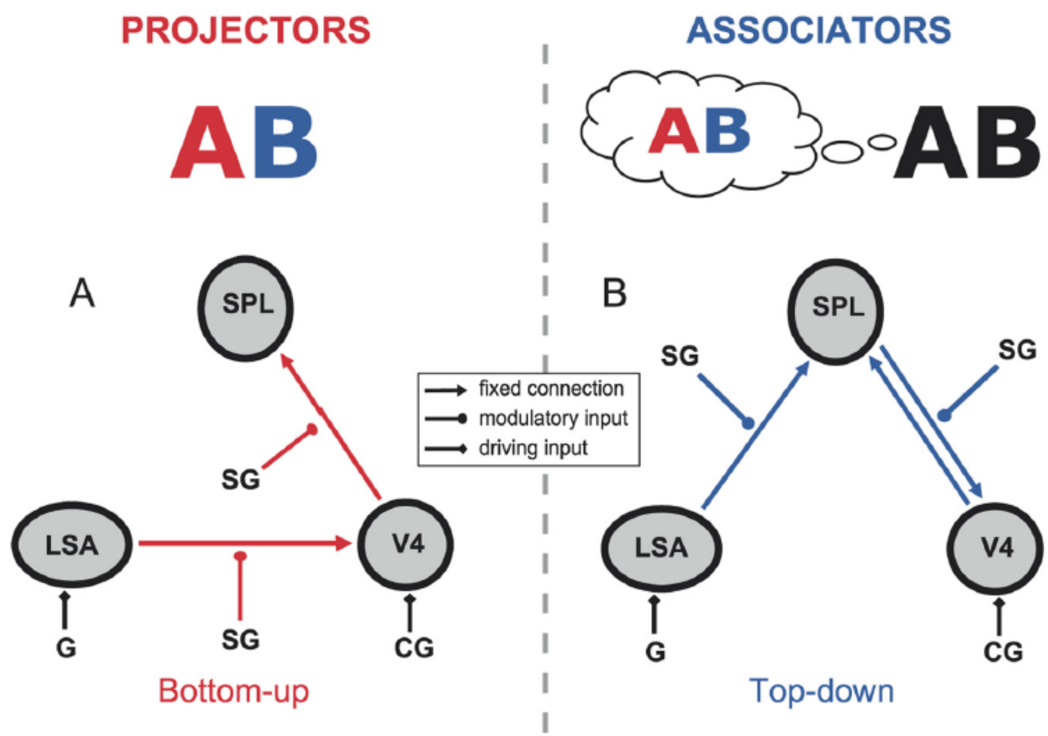
  → Do the parameters show an effect (or group difference) - BMA

- Generative embedding

  →Can we use DCM as a «clever» feature extraction for classification ot clustering.

Model comparison: Synesthesia

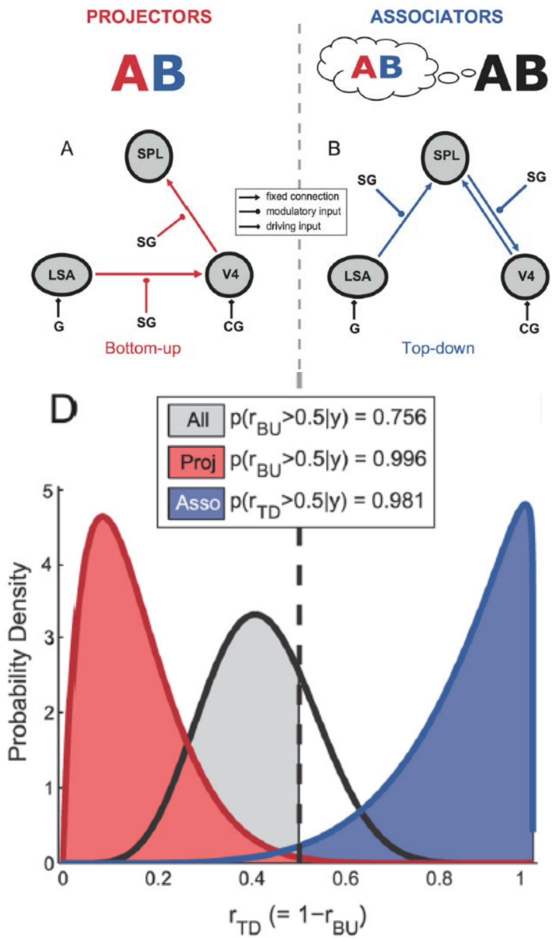
- “projector” synesthetes experience color externally co-localized with a presented grapheme
- “associators” report an internally evoked association



van Leeuwen et al., J Neurosci 2011

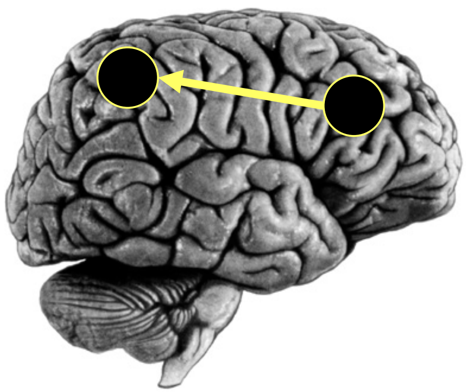
Model comparison: Synesthesia

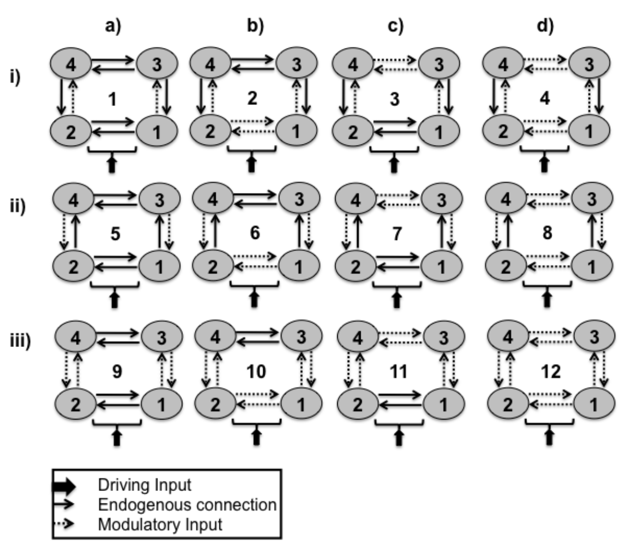
- “projector” synesthetes experience color externally co-localized with a presented grapheme
- “associators” report an internally evoked association
- across all subjects: no evidence for either model
- but splitting into synesthesia types gives very strong evidence for bottom-up (projectors) and top-down (associators) mechanisms, respectively

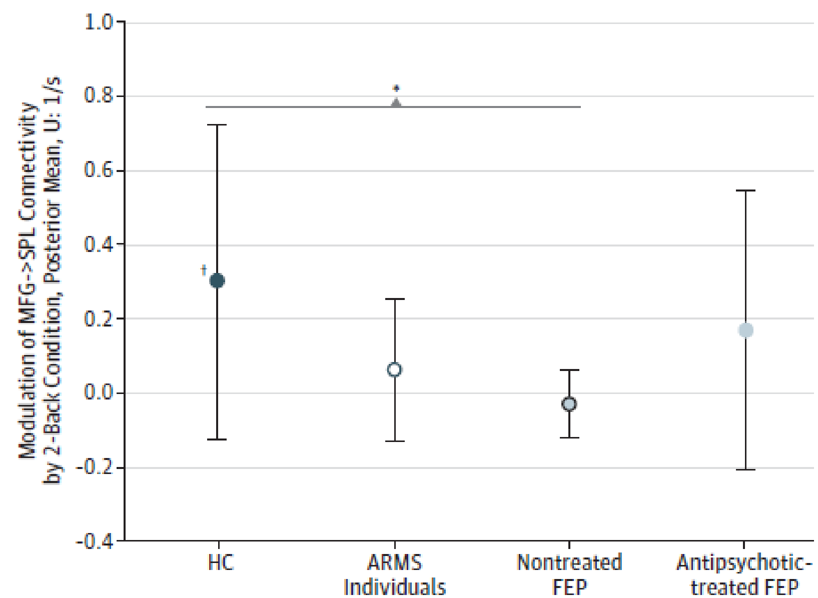


van Leeuwen et al., J Neurosci 2011

Prefrontal-parietal connectivity during working memory in schizophrenia



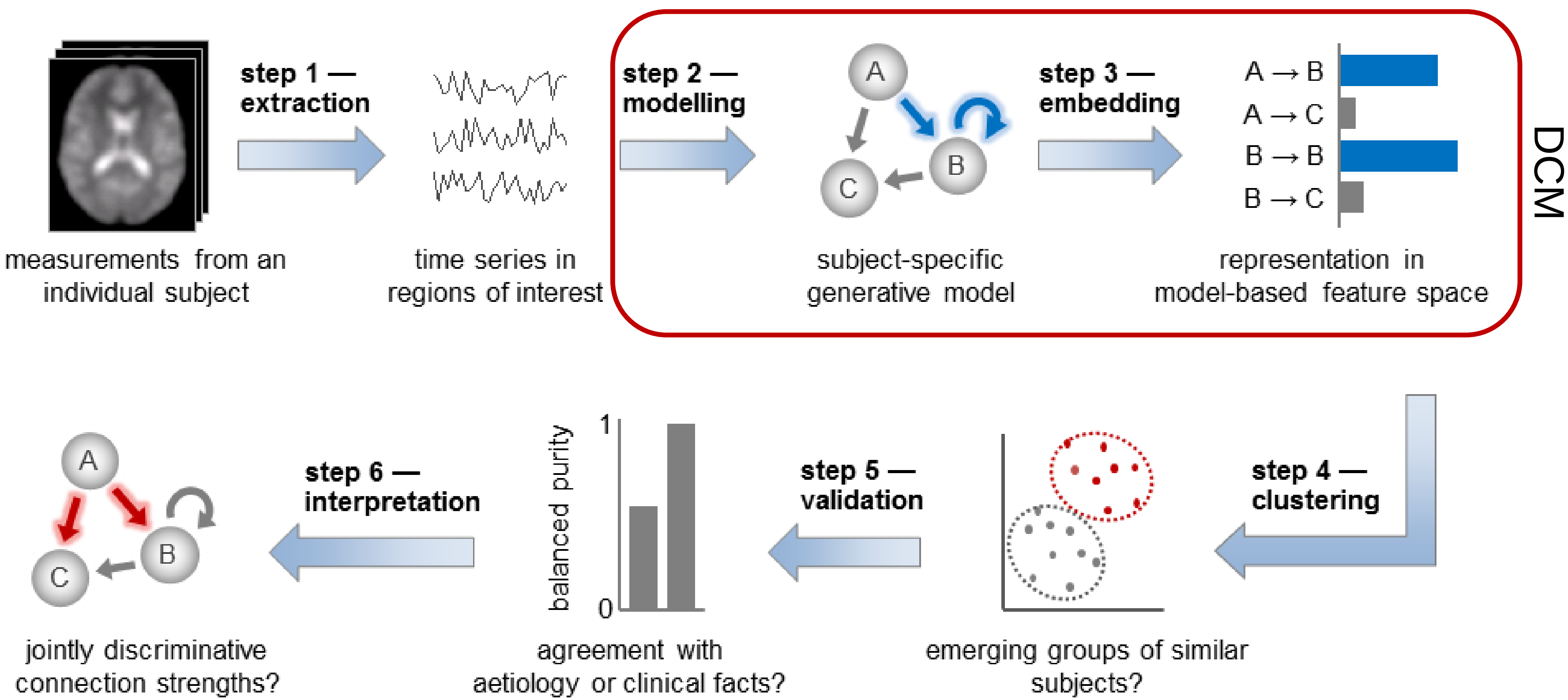




17 ARMS, 21 first-episode (13 non-treated), 20 controls

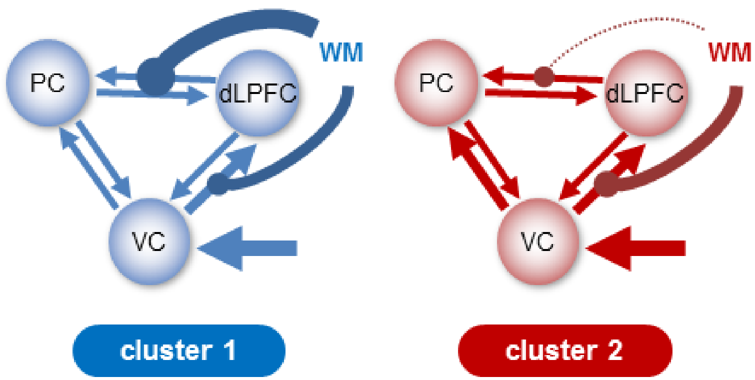
Schmidt et al., JAMA Psychiatry 2013

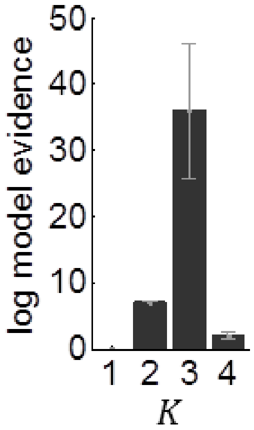
Generative embedding – using DCM as physiologically motivated feature extraction



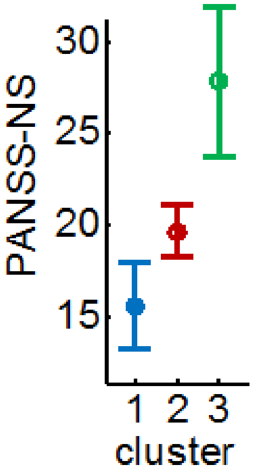
Brodersen et al., NeuroImage: Clinical, 2014

Generative embedding – Detecting subgroups of patients in schizophrenia





Optimal cluster solution



Relation to clinical score

- three distinct subgroups (total N=41)
- subgroups differ ($p < 0.05$) wrt. negative symptoms on the *positive and negative symptom scale* (PANSS)

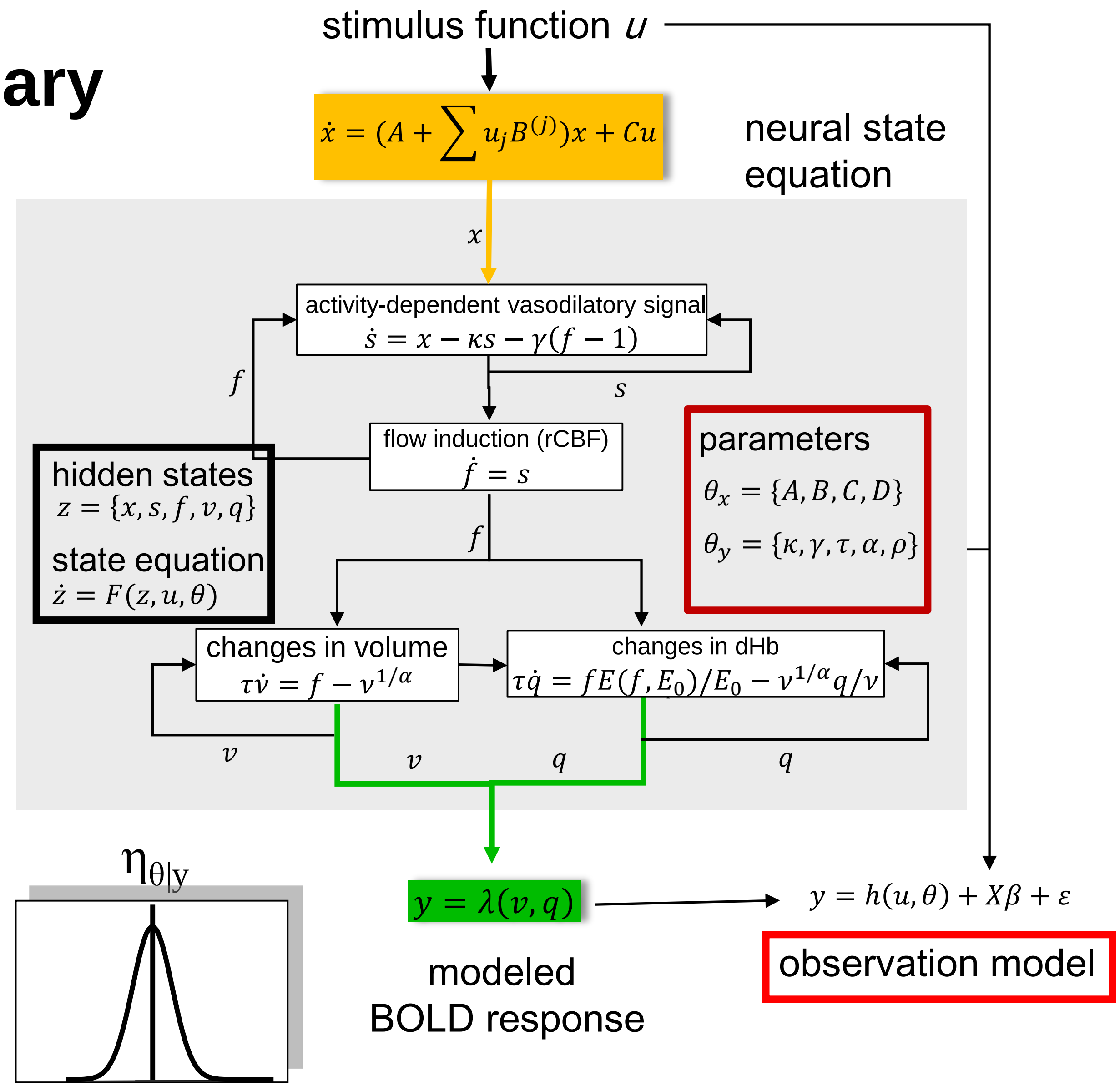
Brodersen et al., NeuroImage: Clinical, 2014

Extensions - software

- MCMC: Would help to avoid local minima (but can be slow)
- Simulation of traces in C: used for hierarchical model (Raman & Stephan, in preparation) → soon TAPAS
- mpdcm-Toolbox: Computations on GPU → massive speed increase (Aponte et al., J Neurosci Methods, 2016) → TAPAS
- Alternative HRF model (Havlicek et al., Neuroimage, 2015) → soon in SPM.
- Layered DCM for fMRI (Heinzle et al., Neuroimage, 2016) → soon in TAPAS.

One slide summary

- Combining the neural and hemodynamic states gives the complete forward model.
- Observation model includes measurement error e and confounds X (e.g. drift).
- Bayesian inversion: parameter estimation variational Bayes or MCMC
- Result 1: A posteriori parameter distributions $p(\theta|y,m)$, characterised by mean $\eta_{\theta|y}$ and covariance $C_{\theta|y}$.
- Result 2: Estimate of model evidence $p(y|m)$.



Discussion questions

- Why is this model useful?
  - Allows for mechanistic explanation of fMRI data and to compare this between groups.
- Where can we use it?
  - For example in the settings discussed.
- Where can‘t we use it?
  - It is not optimal for data mining
- What do you like about it?
  - Forces thinking about mechanisms and, if successful, provides “close” link to physiology
- What are the most common mistakes made?
  - No careful specification of model space. Interpretation of results.

That’s it!

- Thank you!