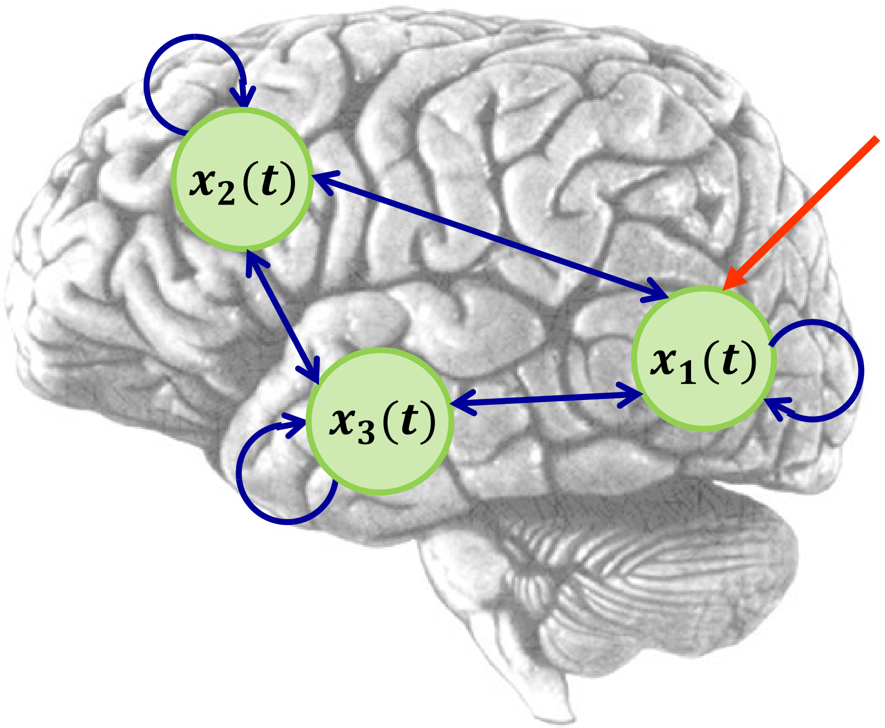
University of Zurich[UZH] | ETH zürich

Translational Neuromodeling Unit

Modeling connectivity: Dynamic Causal Modeling for fMRI



Jakob Heinzle

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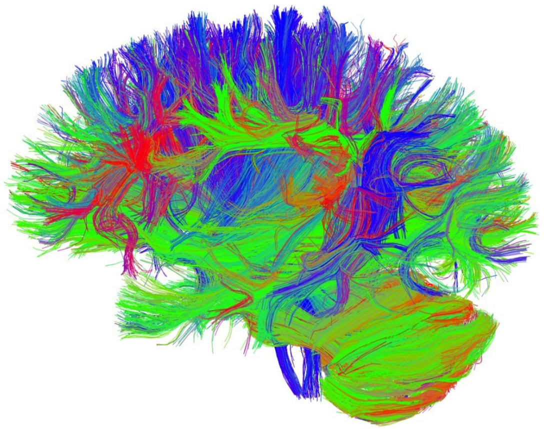
University and ETH Zürich

CP Course 2024, Zürich, Switzerland

Structural, functional & effective connectivity

anatomical/structural

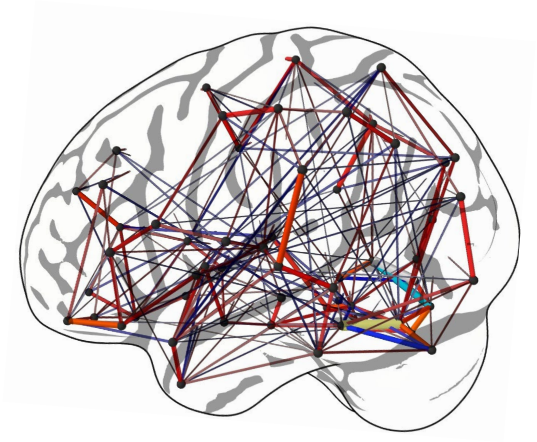


https://optimalsurgerytle.weebly.com/imaging-and-dataset.html

- presence of physical connections
→ *DWI, tractography, tracer studies (animals)*

Context - independent

functional

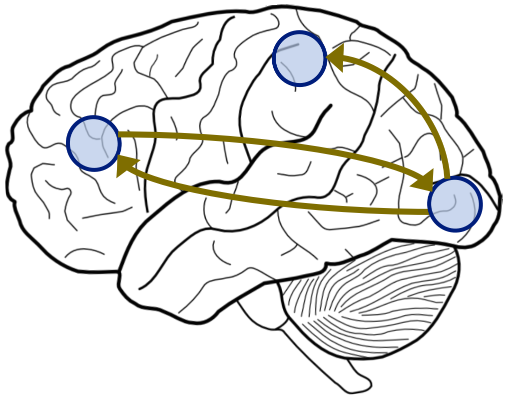


https://team.inria.fr/parietal/files/2013/02/pc_dag.jpg

- statistical dependency between regional time series
→ *correlations, ICA*

Mechanism - free

effective



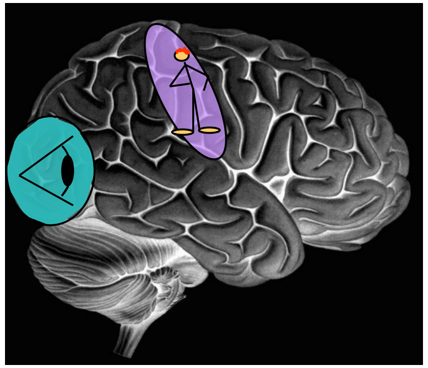
http://www.clker.com/cliparts/e/5/Q/i/e/o/brain-line-drawing-md.png

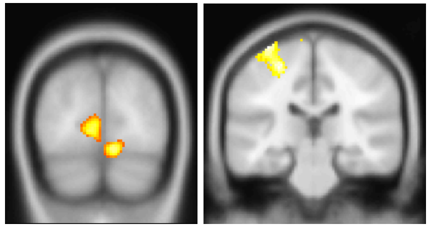
- direct influences between neuronal populations
→ *DCM*

Mechanistic

Specialisation vs. Integration

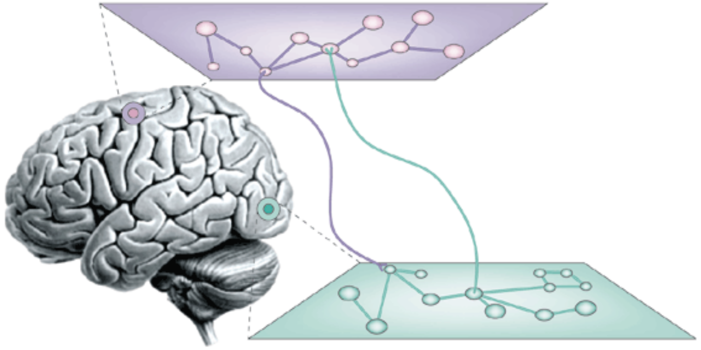
Functional Specialisation

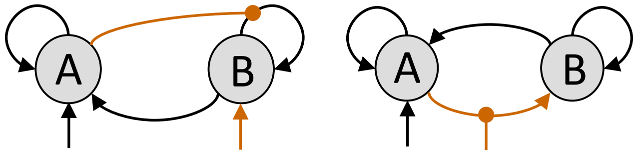




*«**Where**, in the brain, did my experimental manipulation have **an effect**?»*

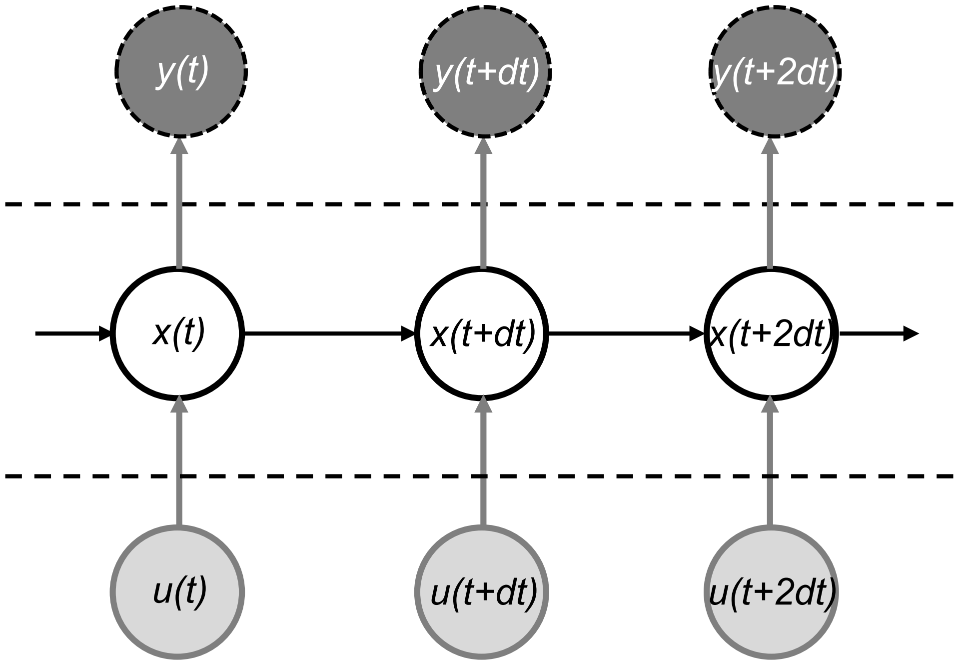
Functional Integration





*«**How** did my experimental manipulation **propagate through the network**?»*

A reminder – generative models



Observed data (fMRI)

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

Hidden states (Brain activity)

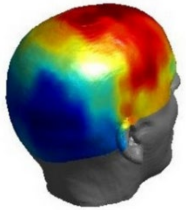
$$\frac{dx}{dt} = f(x, u, \theta_f) + \omega$$

Inputs (Exp. manipulations)

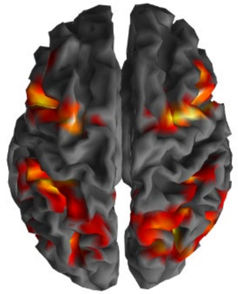
$$u(t)$$

Dynamic causal modelling

EEG,
MEG



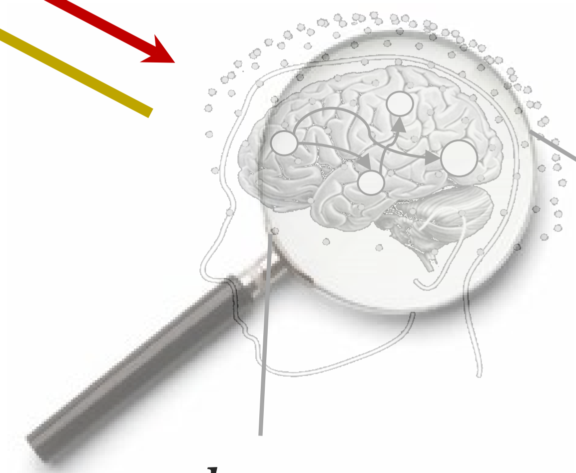
Model inversion:
Estimating
neuronal
mechanisms



fMRI

Forward model:
Predicting
measured activity

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



$$\frac{dx}{dt} = f(x, u, \theta) + \omega$$

State equation:
Describing neuronal
dynamics (and
hemodynamics)

DCM for EEG
→ later today

Friston et al., 2003, NeuroImage; David et al., 2006, NeuroImage

Dynamic causal modelling

ACADEMIC PRESS

Available online at www.sciencedirect.com

SCIENCE DIRECT

NeuroImage 19 (2003) 1273–1302

NeuroImage

www.elsevier.com/locate/ynimg

Dynamic causal modelling

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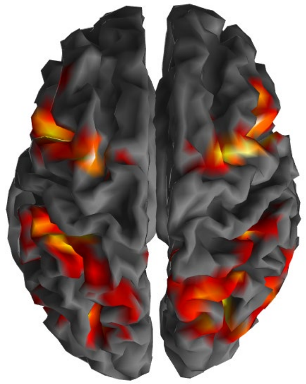
The Wellcome Department of Imaging Neuroscience, Institute of Neurology, Queen Square, London WC1N 3BG, UK

Received 18 October 2002; revised 7 March 2003; accepted 2 April 2003

DCM for fMRI - overview



fMRI

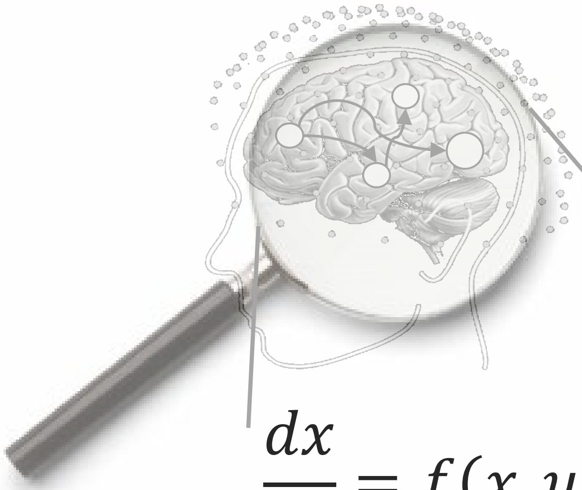
Model inversion:

Estimating neuronal mechanisms

Forward model:

Predicting measured activity

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

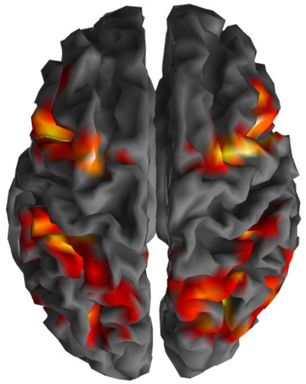


$$\frac{dx}{dt} = f(x, u, \theta)$$

Neural state equation:

Describing neuronal dynamics

DCM for fMRI - overview



fMRI

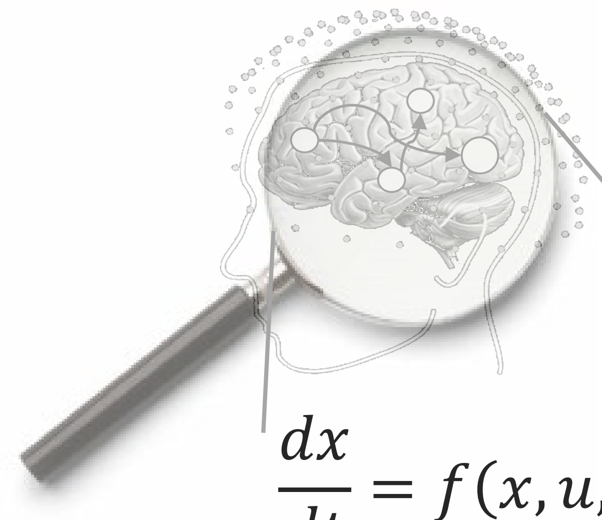
Model inversion:

Estimating neuronal mechanisms

Forward model:

Predicting measured activity

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



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

Neural state equation:

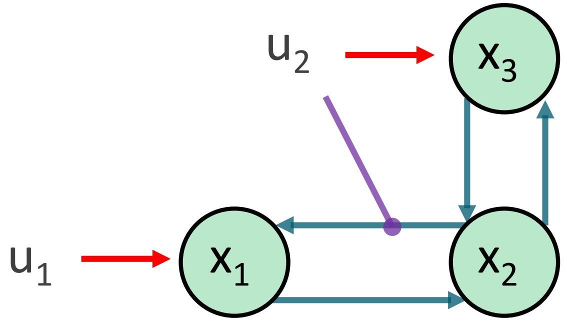
Describing neuronal dynamics

Neuronal state equations

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

Neuronal state equations

$$\frac{dx}{dt} = f(x,u) \approx f(x_0,0) + \underbrace{\frac{\partial f}{\partial x}}_{A} x + \underbrace{\frac{\partial f}{\partial u}}_{C} u + \underbrace{\frac{\partial^2 f}{\partial x \partial u}}_{B} ux + \frac{\partial^2 f}{\partial x^2}\frac{x^2}{2} + \cdots$$

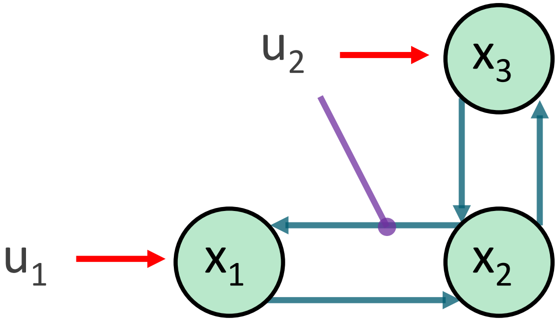


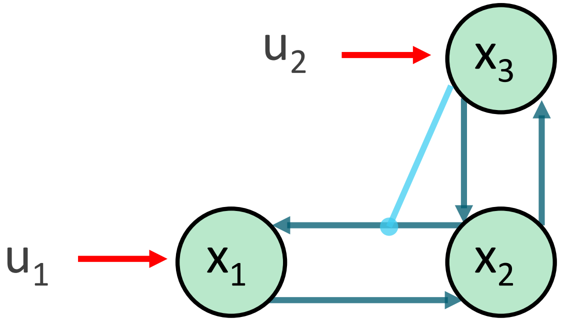
Neuronal state equations

$$\frac{dx}{dt} = f(x,u) \approx f(x_0,0) + \overset{A}{\frac{\partial f}{\partial x}}x + \overset{C}{\frac{\partial f}{\partial u}}u + \overset{B}{\frac{\partial^2 f}{\partial x \partial u}}ux + \overset{D}{\frac{\partial^2 f}{\partial x^2}}\frac{x^2}{2} + \cdots$$

bilinear model

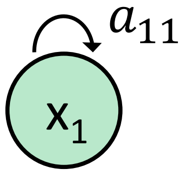
nonlinear model



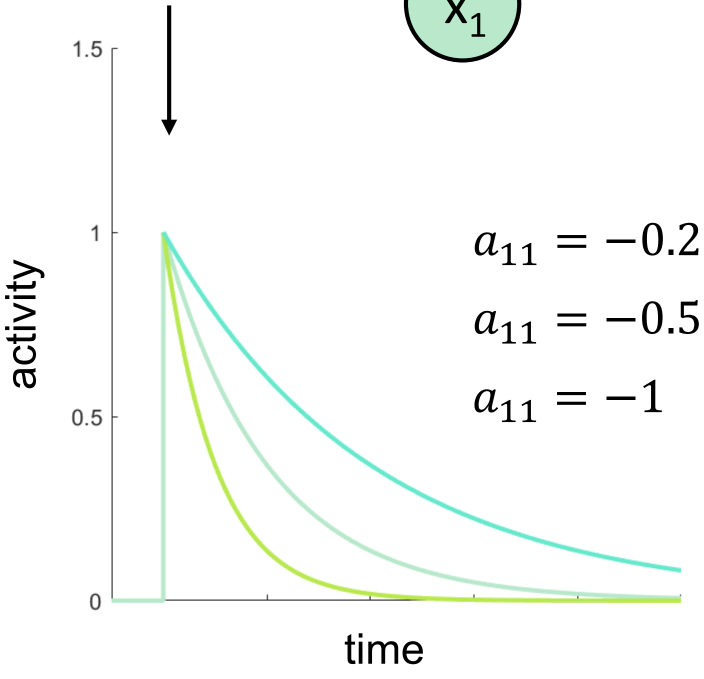


Neuronal state equations

DCM effective connectivity parameters are rate constants



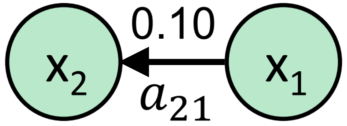
$$\frac{dx_1}{dt} = a_{11}x_1 \longrightarrow x_1(t) = x_1(0) \cdot exp(a_{11}t)$$



$a_{11} = -0.25$

$a_{11} = -0.5$

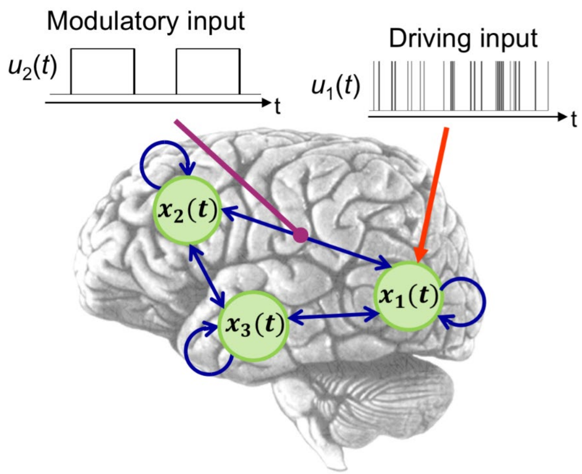
$a_{11} = -1$



If a_{21} is 0.10s^{-1}, this means that, per unit time, the increase in activity in x_2 corresponds to 10% of the current activity in x_1

Neuronal state equations

Interim summary: bilinear neuronal state equation



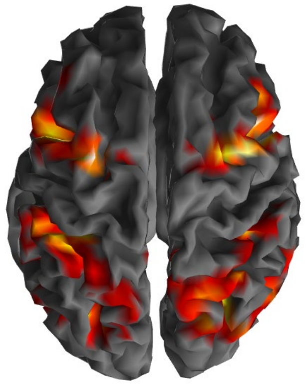
State change | External inputs | Current state

$$\frac{dx}{dt} = \underbrace{\left(A + \sum_{j=1}^{m} u_j B^{(j)}\right)}_{\text{connectivity}} x + Cu$$

$$\theta = \{A, B^{(1)}, \dots, B^{(m)}, C\}$$

Endogenous connectivity | Modulatory connectivity | Driving input weights

DCM for fMRI - overview



fMRI

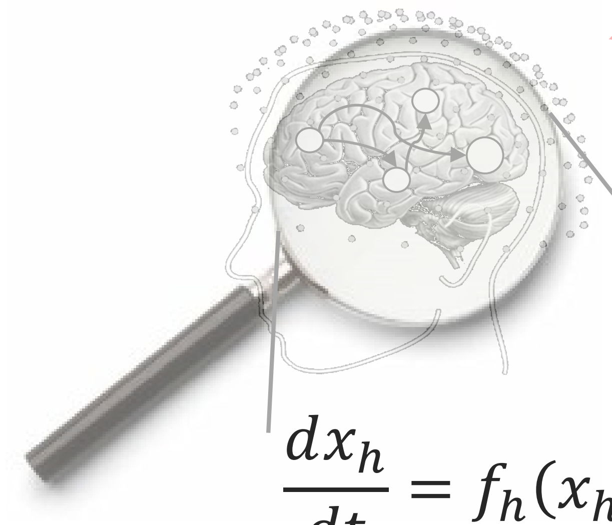
Model inversion:

Estimating neuronal mechanisms

Forward model:

Predicting measured activity

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



$$\frac{dx_h}{dt} = f_h(x_h, x, \theta)$$

Hemodynamic state equation:

Describing hemodynamics

The hemodynamic response

Neuronal dynamics only indirectly observable via hemodynamic response

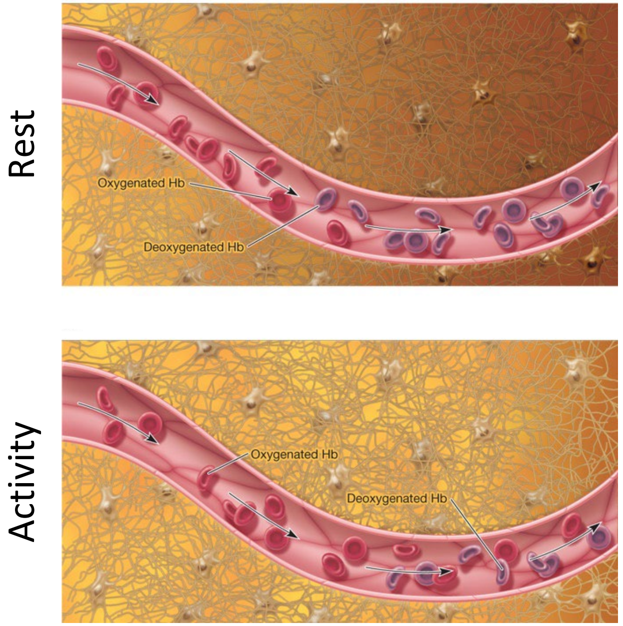
↑ neuronal activity

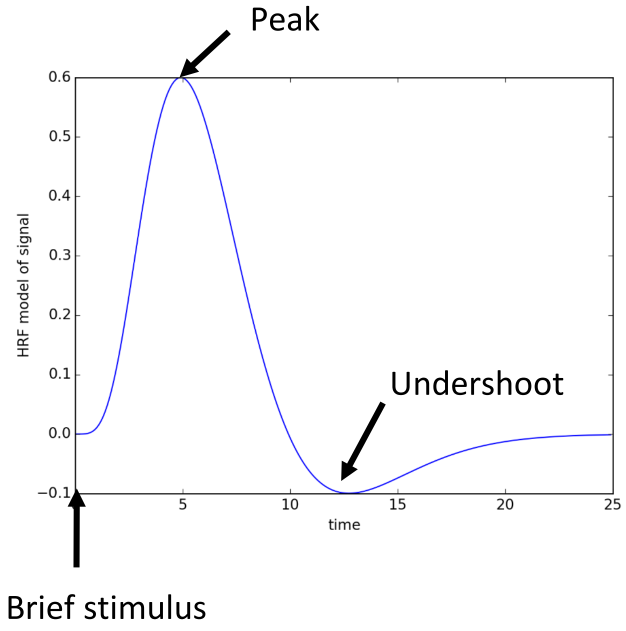
↑ blood flow

↑ oxygenated Hb

↑ T2*

↑ fMRI signal





Huettel et al, 2004, fMRI (Book)

The hemodynamic model

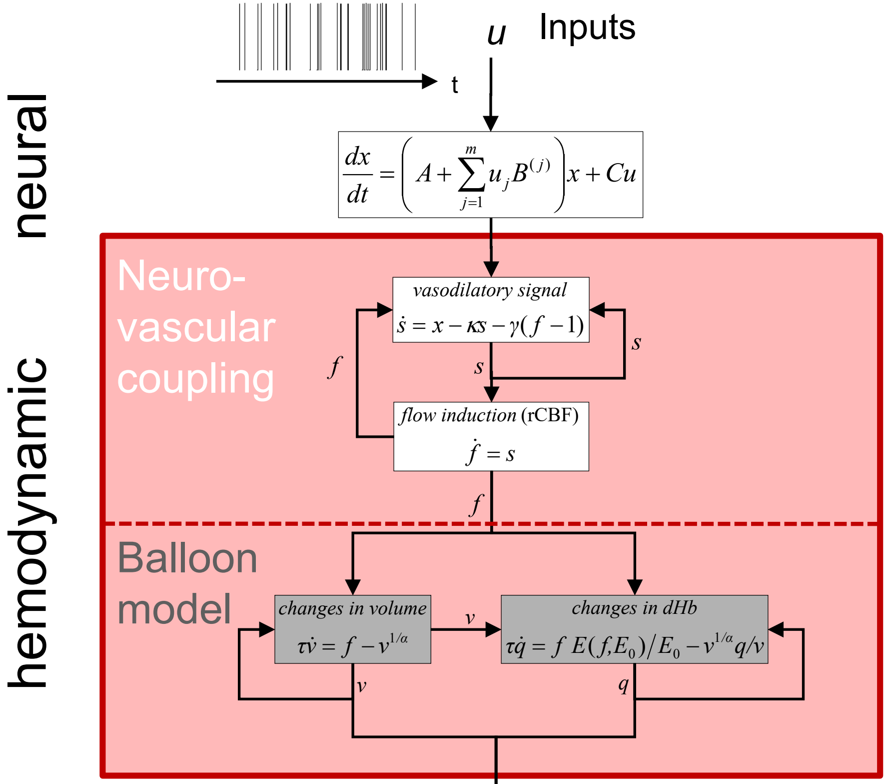
6 parameters:

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

Important for model fitting, but typically of no interest for statistical inference.

Region specific HRF

→ Parameters computed separately for each region



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

$k_1 = 4.3\vartheta_0 E_0 TE$

$k_2 = \varepsilon r_0 E_0 TE$

$k_3 = 1 - \varepsilon$

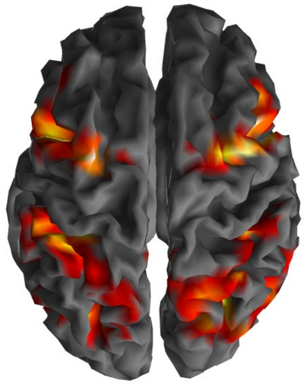
BOLD signal change equation

Vasodilation (s) and blood flow changes (f)

Relative blood volume (v) and deoxyHB (q)

Stephan et al., 2007, NeuroImage

DCM for fMRI - overview

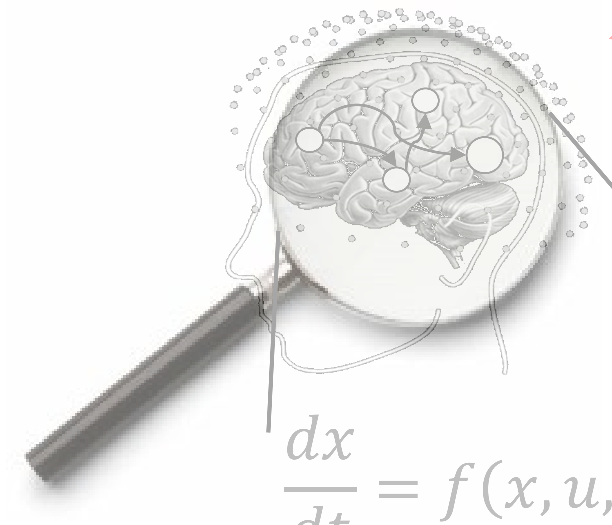


fMRI

Model inversion:
Estimating
neuronal
mechanisms

Forward model:
Predicting
measured activity

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



$$\frac{dx}{dt} = f(x, u, \theta) + \omega$$

Neural state equation:
Describing neuronal
dynamics

Friston et al., 2003, NeuroImage; David et al., 2006, NeuroImage

The BOLD signal equation

Resting blood volume

Deoxyhemoglobin content

Blood volume

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

BOLD-Signal Parameters:

$k_1 = 4.3\vartheta_0 E_0 TE$

$k_2 = \varepsilon r_0 E_0 TE$

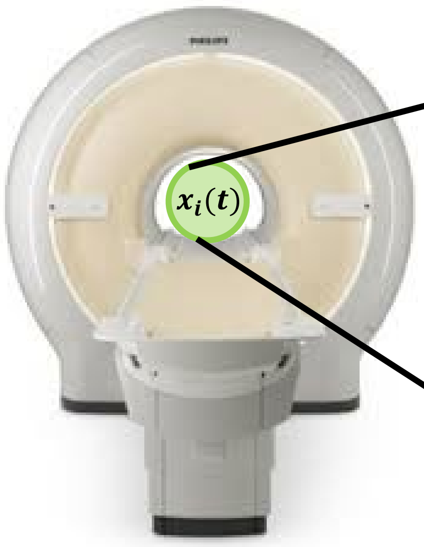
$k_3 = 1 - \varepsilon$

$V_0 = 0.04 \qquad E_0 = 0.32 - 0.4$

At 1.5 Tesla	At 3 Tesla	At 7 Tesla
$\vartheta_0 \approx 40.3\ \mathrm{s}^{-1}$	$\vartheta_0 \approx 80.6\ \mathrm{s}^{-1}$	$\vartheta_0 \approx 188\ \mathrm{s}^{-1}$
$r_0 \approx 25\ \mathrm{s}^{-1}$	$r_0 \approx 110\ \mathrm{s}^{-1}$	$r_0 \approx 340\ \mathrm{s}^{-1}$
$TE \approx 0.04\ s$	$TE \approx 0.035\ s$	$TE \approx 0.025\ s$
$\varepsilon \approx 1.28$	$\varepsilon \approx 0.47$	$\varepsilon \approx 0.026$

Heinzle et al., 2016, NeuroImage

From neural activity to the BOLD signal: summary



Neurovascular coupling

x

Vasodilation (s) and blood flow changes (f)

f

Balloon model

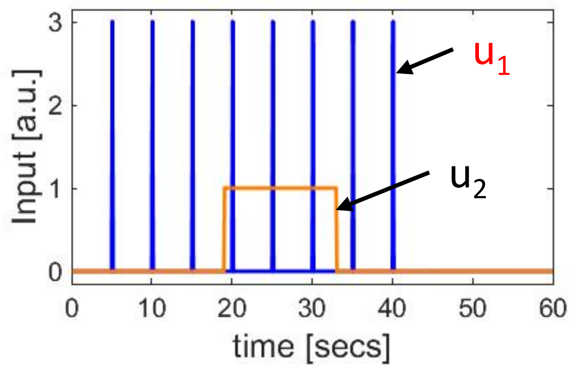
Relative blood volume (v) and deoxyHB (q)

v, q

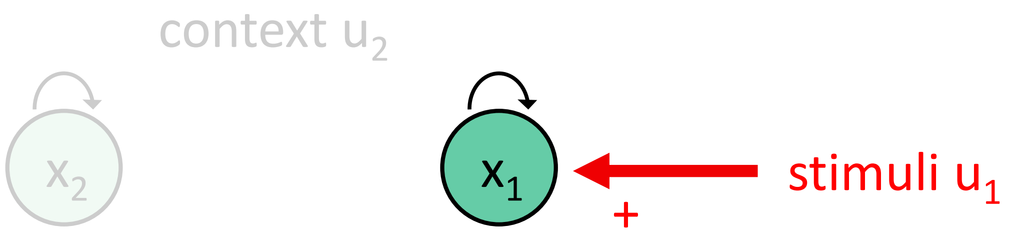
BOLD signal is a **direct function** of v and q

$$y = \frac{\Delta S}{S_0} = g(v, q) + \varepsilon$$

Simulation example: What can DCM explain?



Example: single node

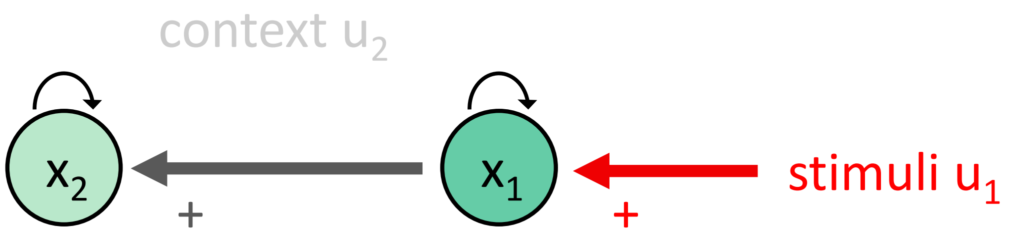


$$\frac{dx}{dt} = \left(A + u_2 B^{(2)}\right)x + C u_1$$

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \end{bmatrix} = \left(\begin{bmatrix} a_{11} & 0 \\ 0 & a_{22} \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \right) \cdot \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} + \begin{bmatrix} c_{11} & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

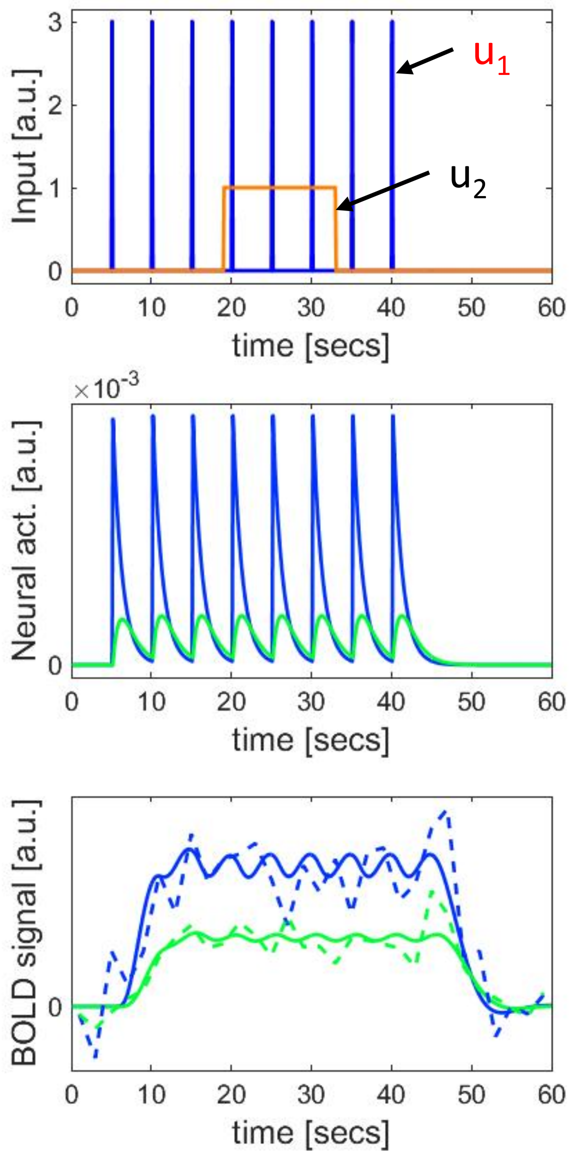
Simulation example: What can DCM explain?

Example: two connected node



$$\frac{dx}{dt} = \left(A + u_2 B^{(2)}\right)x + C u_1$$

$$\begin{bmatrix}\dot{x}_1\\ \dot{x}_2\end{bmatrix} = \left(\begin{bmatrix}a_{11} & 0\\ \boldsymbol{a_{21}} & a_{22}\end{bmatrix} + u_2\begin{bmatrix}0 & 0\\ 0 & 0\end{bmatrix}\right)\cdot\begin{bmatrix}x_1\\ x_2\end{bmatrix} + \begin{bmatrix}c_{11} & 0\\ 0 & 0\end{bmatrix}\cdot\begin{bmatrix}u_1\\ u_2\end{bmatrix}$$



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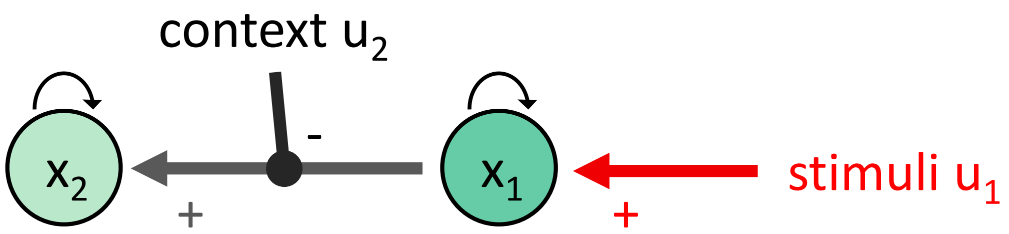
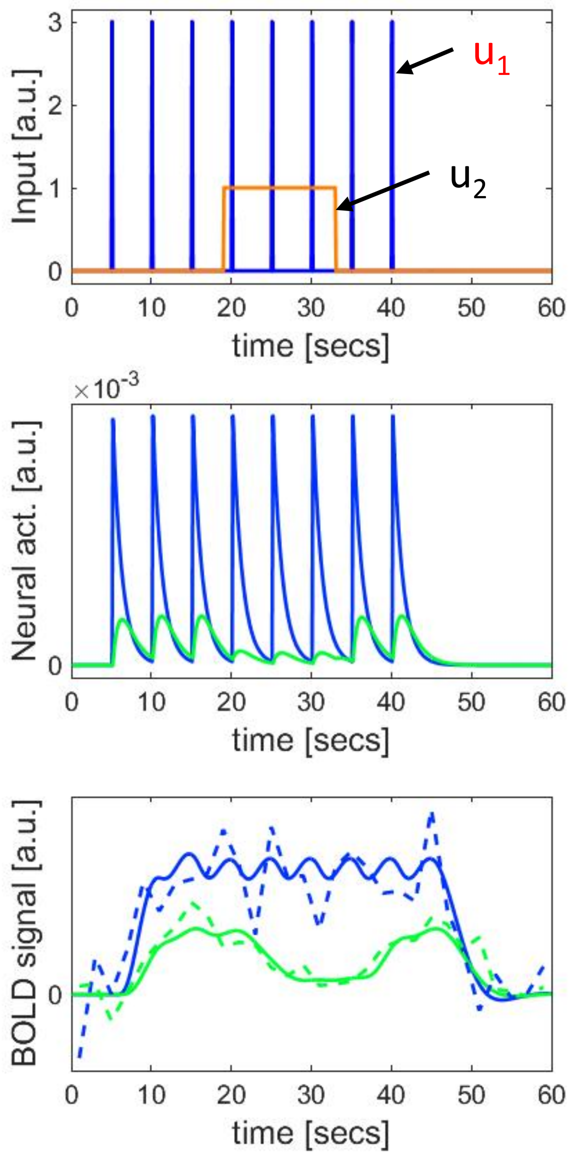
Simulation example: What can DCM explain?

Example: modulation of connection



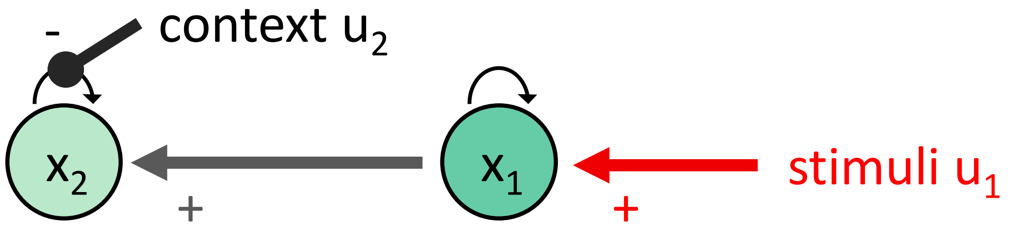
$$\frac{dx}{dt} = (A + u_2 B^{(2)})x + Cu_1$$

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



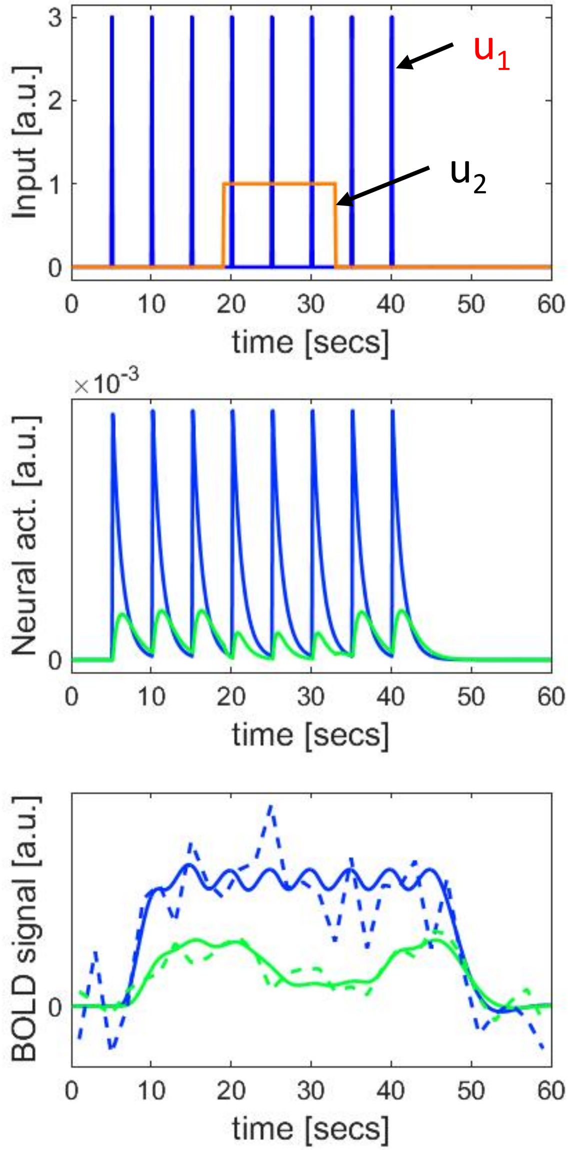
Simulation example: What can DCM explain?

Example: modulation of inhibitory self-connection



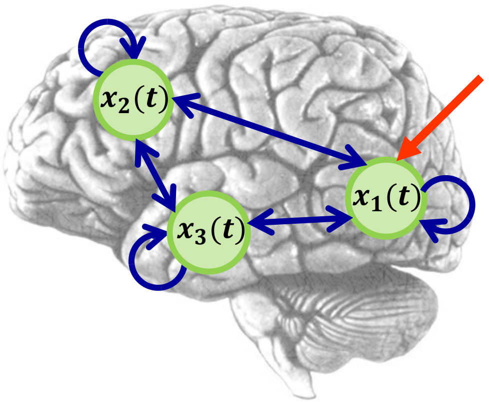
$$\frac{dx}{dt} = \left(A + u_2 B^{(2)}\right)x + Cu_1$$

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



DCM for fMRI

A simple model of a neural network …



$x_i(t)$ Neural node

Input

Connections

… described as a dynamical system …

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

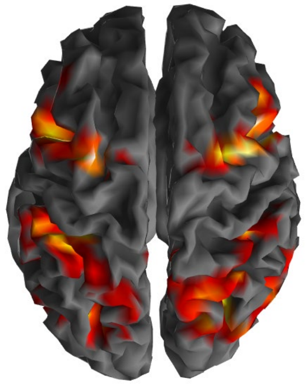
… causes the data (BOLD signal).

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

Simulate the system with input u and parameters θ

→ BOLD signal time course y that can be compared to measured data.

DCM for fMRI - overview

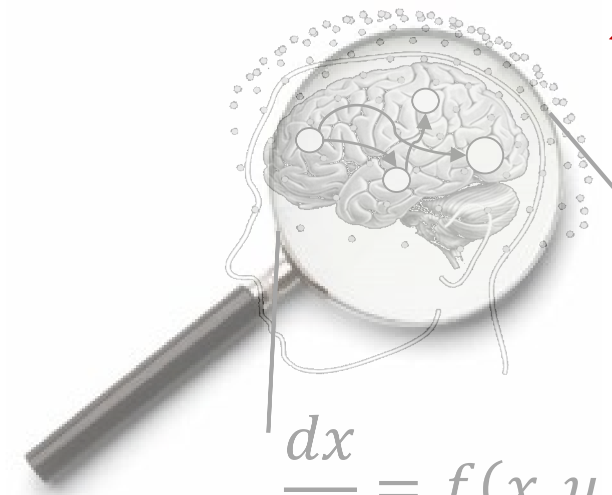


fMRI

Model inversion:
Estimating neuronal mechanisms

Forward model:
Predicting measured activity

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



$$\frac{dx}{dt} = f(x, u, \theta) + \omega$$

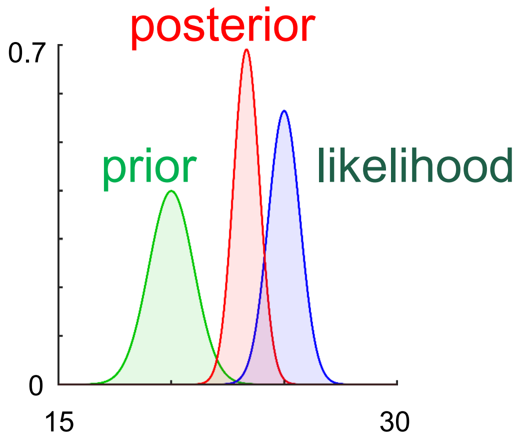
Neural state equation:
Describing neuronal dynamics

Friston et al., 2003, NeuroImage; David et al., 2006, NeuroImage

Bayes' theorem

Reverend Thomas Bayes
(1702-1761)

$$\underbrace{p(\theta|y,m)}_{\text{posterior}} = \frac{\overbrace{p(y|\theta,m)}^{\text{likelihood}}\overbrace{p(\theta|m)}^{\text{prior}}}{\underbrace{p(y|m)}_{\text{model evidence}}}$$



The likelihood function for DCM

$$\underbrace{p(y(t)|\theta,m)}_{\text{likelihood}} = \mathcal{N}\left(y(t); g\left(\theta^n, \theta^h, u(t)\right), \theta^\sigma\right)$$

Assume data is normally distributed around the prediction from the dynamical model (Gaussian noise)

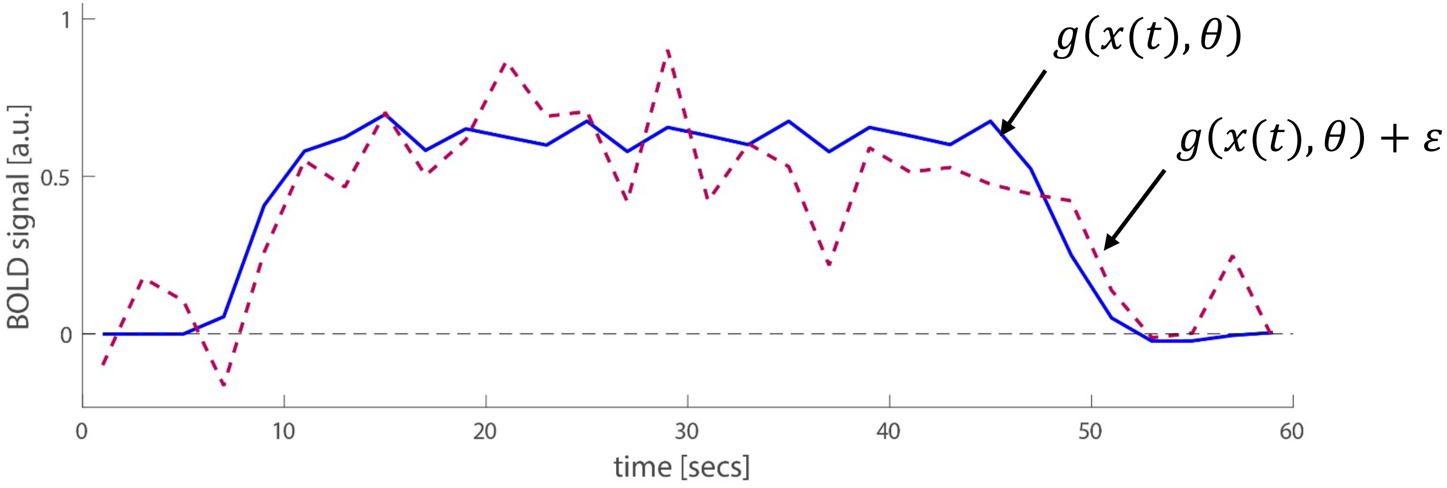
$$y(t) = g(x(t), \theta) + \varepsilon$$

$$\varepsilon \sim \mathcal{N}(0, \sigma^2 I)$$

Data is prediction plus Gaussian noise

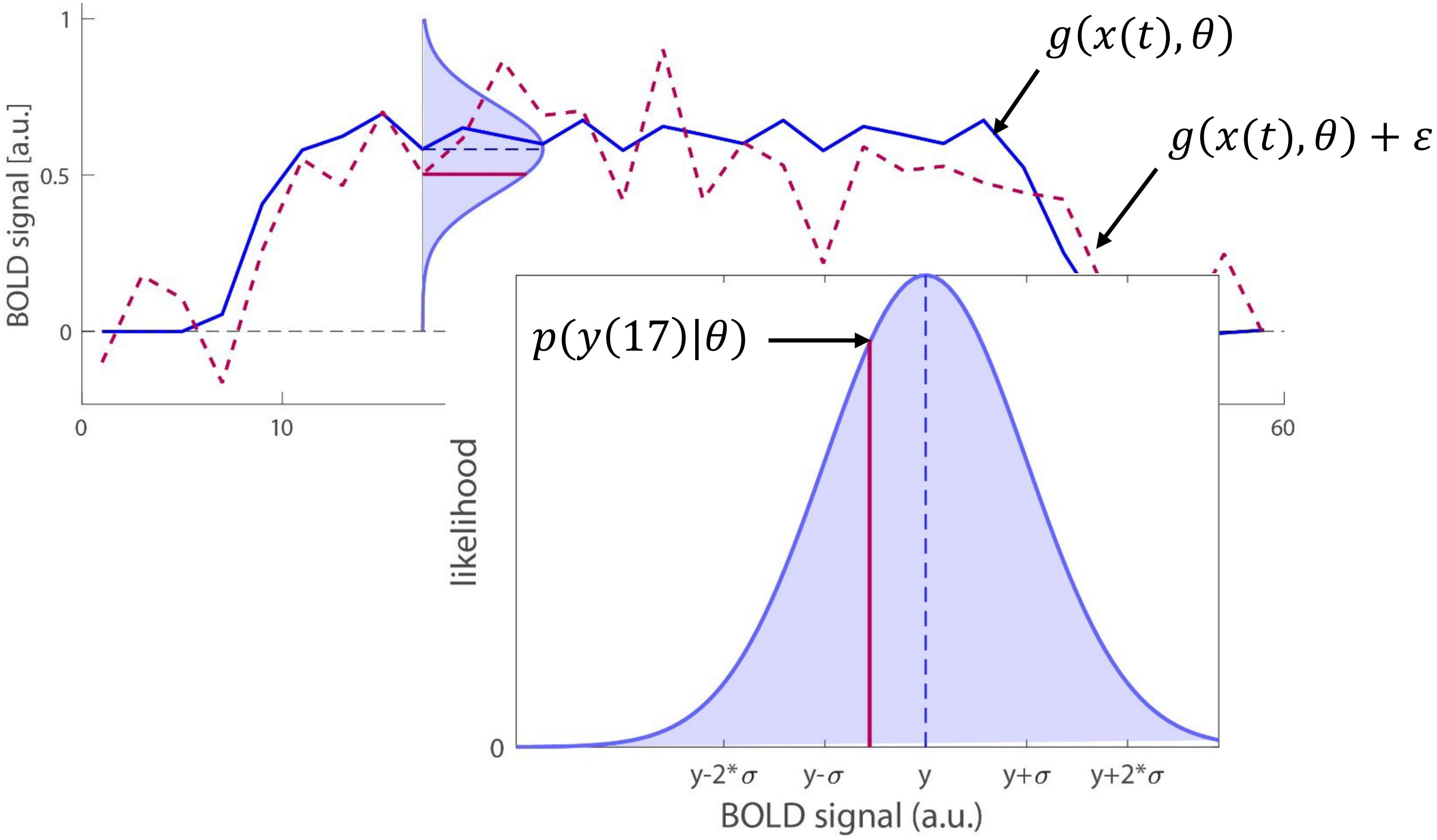
The likelihood function for DCM

$$\underbrace{p(y(t)|\theta,m)}_{\text{likelihood}} = \mathcal{N}\left(y(t); g\left(\theta^n, \theta^h, u\right), \theta^\sigma\right)$$



The likelihood function for DCM

$$\underbrace{p(y(t)|\theta, m)}_{\text{likelihood}} = \mathcal{N}\left(y(t); g\left(\theta^n, \theta^h, u\right), \theta^\sigma\right)$$



The likelihood function for DCM

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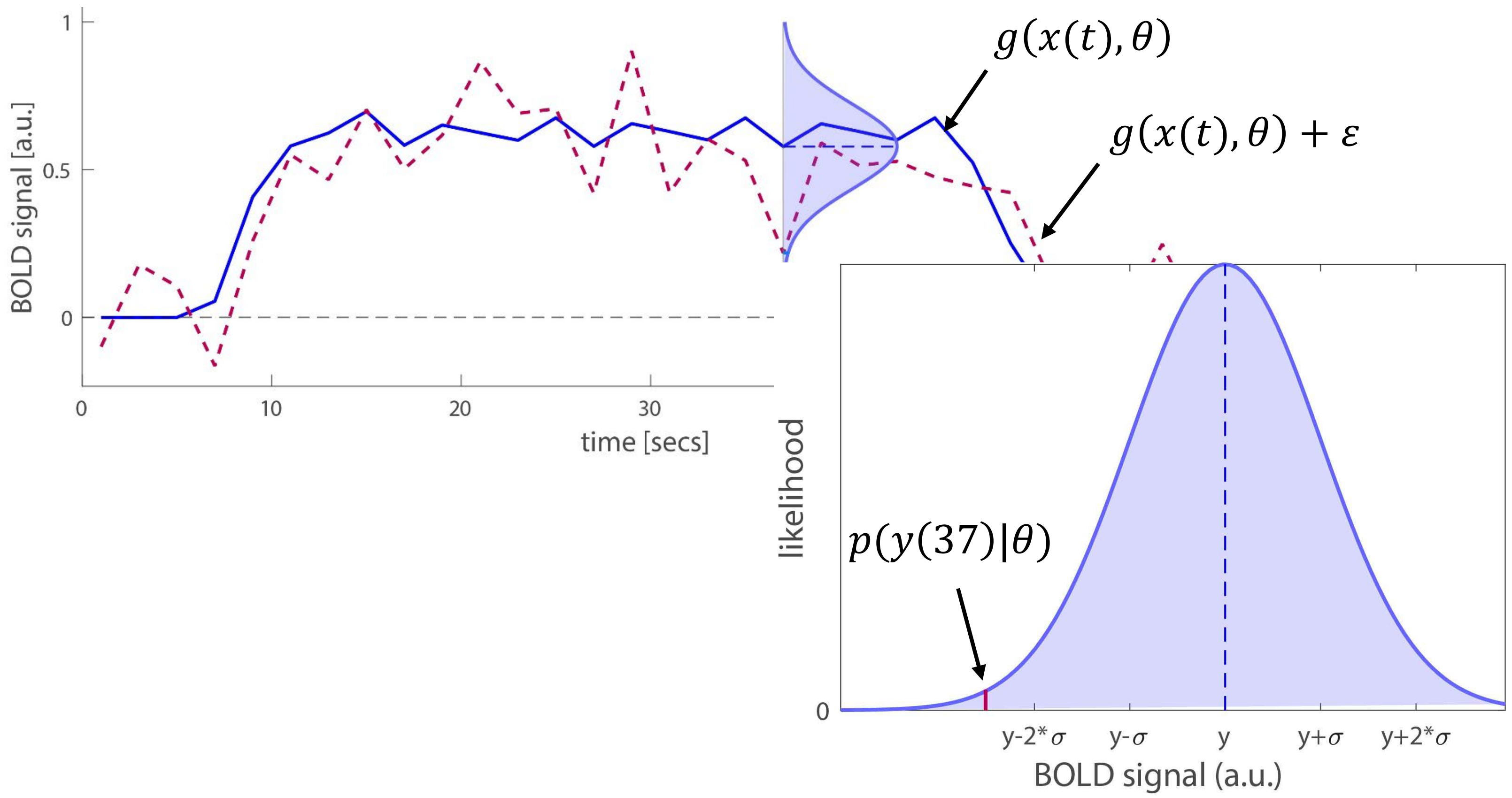


Priors

$$p(\theta|y,m) = \frac{p(y|\theta,m)\overbrace{p(\theta|m)}^{\text{prior}}}{p(y|m)}$$

Neuronal parameters:

- self-connections: principled (to “ensure” that the system is stable)
- other parameters (between—region connections, modulation, inputs): shrinkage priors

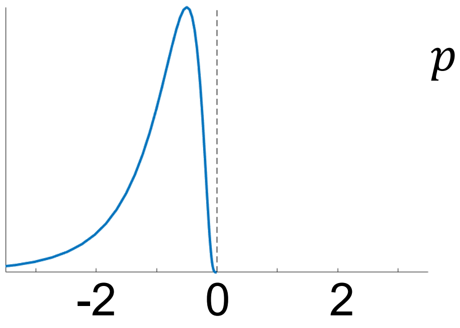
Hemodynamic parameters:

- empirical

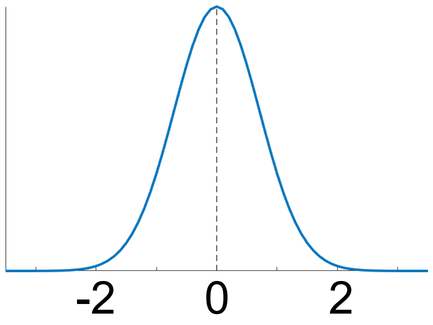
Noise prior (hyperparameter):

- assume relatively noisy data

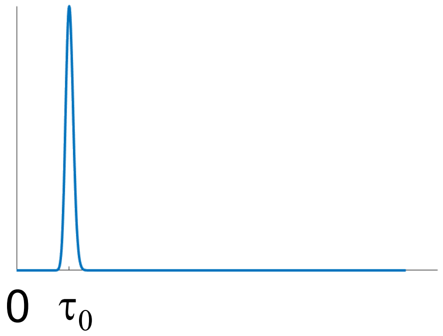
(not default in SPM12 → set DCM.options.hE = 0; DCM.options.hC = 1)



$p(a_{ii}|m)$



$p(a_{ij}|m)$
$p(b_{ij}|m)$
$p(c_{ik}|m)$

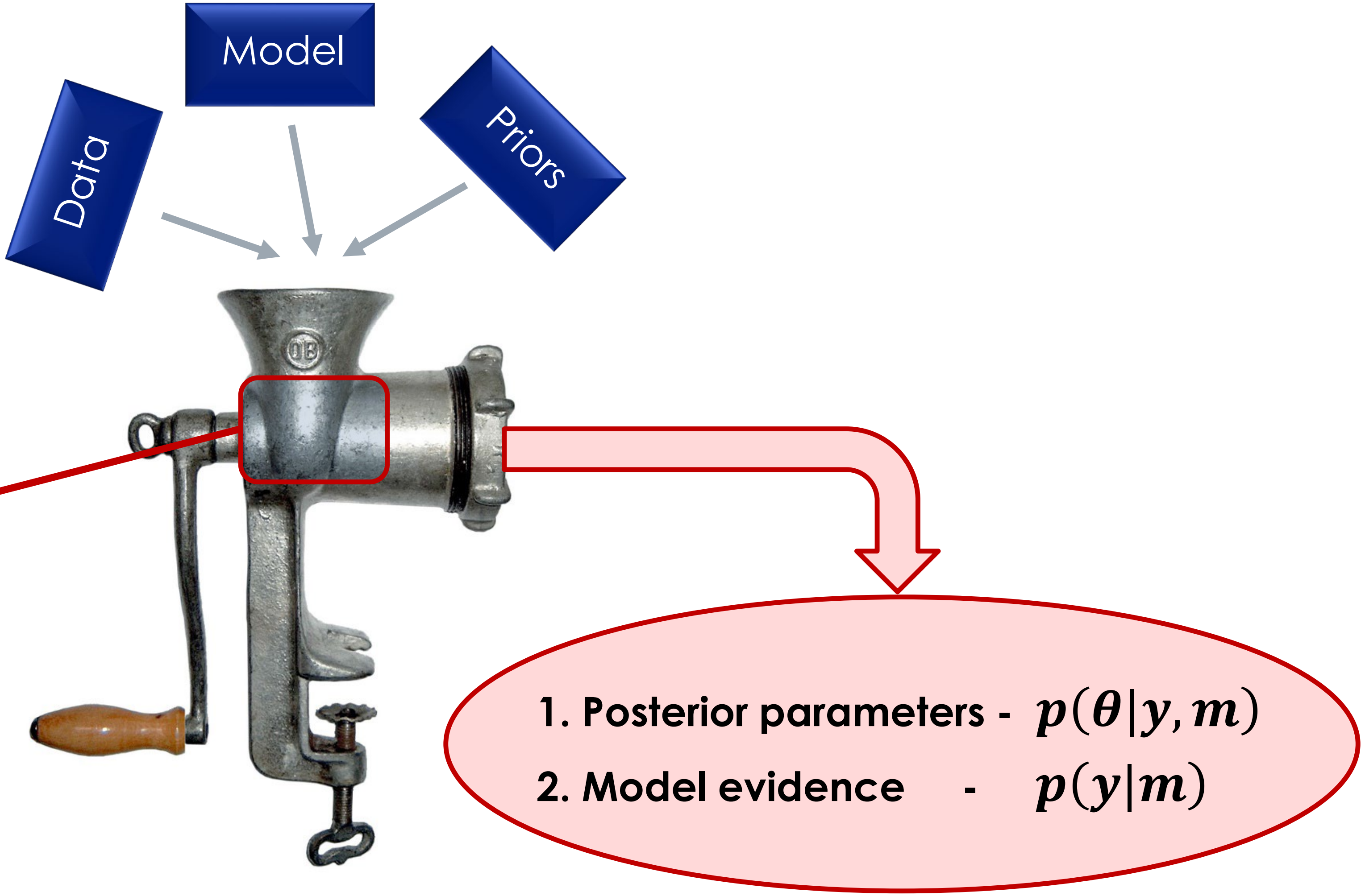


$p(\tau|m)$
$p(\varepsilon|m)$
$p(\alpha|m)$

Model estimation: running the machinery

Free energy approximation
Variational Bayes

Thermodynamic integration
MCMC

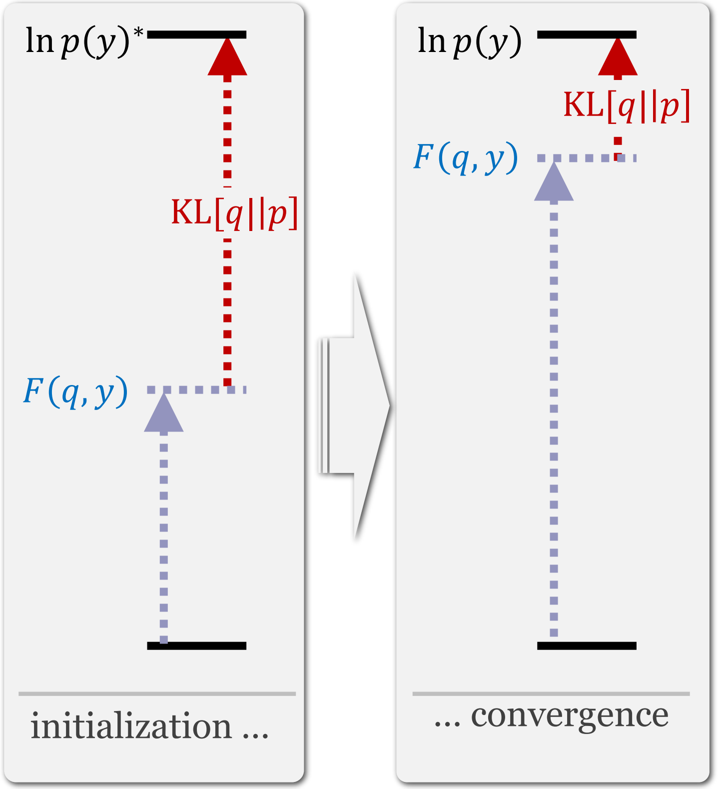


Inversion – variational Free Energy approximation to model evidence

model evidence

$$\ln p(y) = \underbrace{\mathrm{KL}[q||p]}_{\substack{\textbf{divergence} \\ \geq 0 \\ \text{(unknown)}}} + \underbrace{F(q,y)}_{\substack{\textbf{neg. free energy} \\ \text{(easy to evaluate} \\ \text{for a given } q\text{)}}}$$

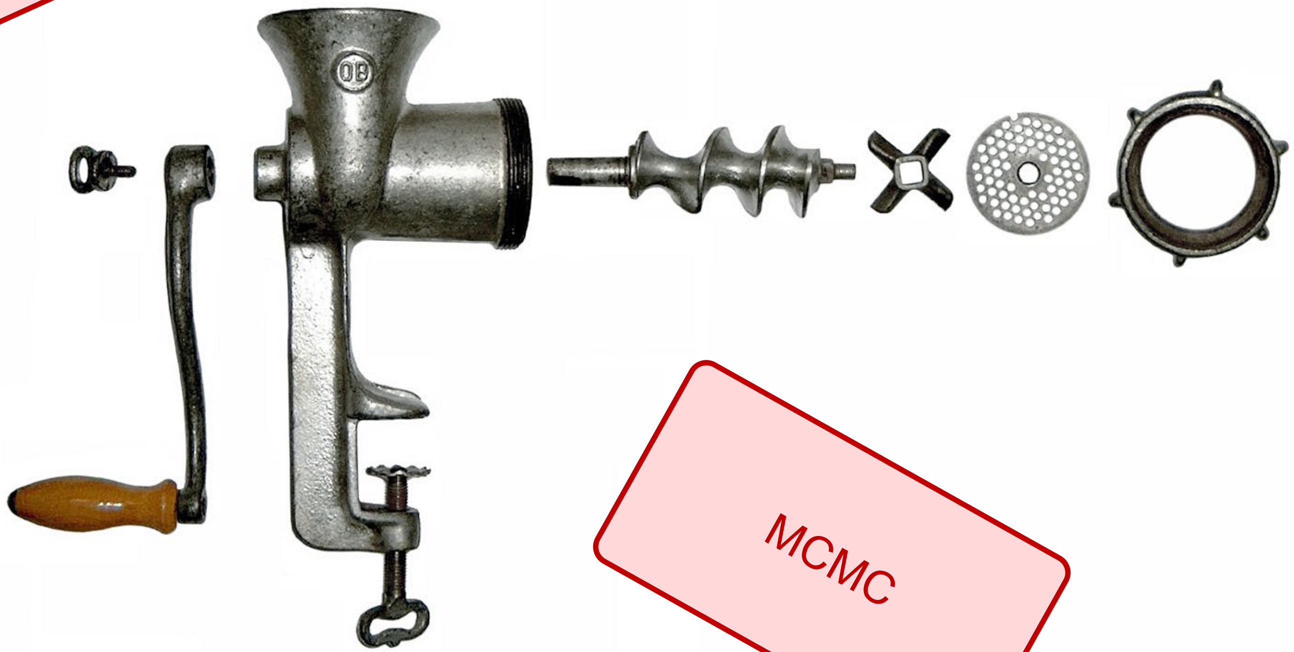
When $F(q,y)$ is maximized, $q(\theta)$ is our best estimate of the true posterior.



Bishop, 2006; Friston et al., 2007, Neuroimage

Model estimation: running the machinery

Variational Bayes

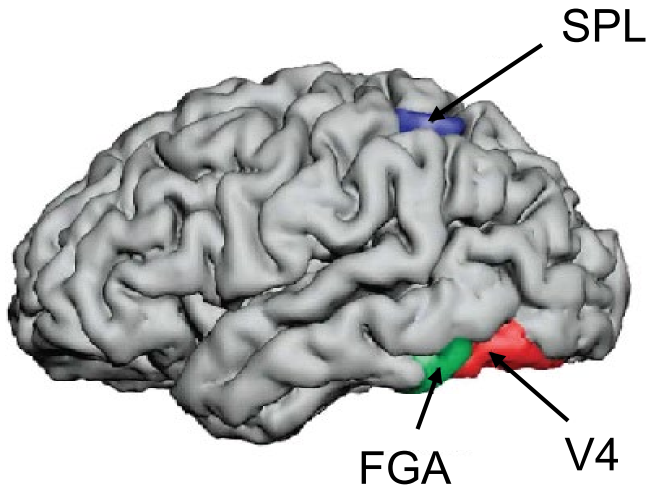


MCMC

BMS and BMA

Model selection example: Synesthesia

- Specific sensory stimuli lead to unusual, additional experiences
- Grapheme-color synesthesia: color
- Involuntary, automatic; stable over time, prevalence ~4%
- Potential cause: aberrant **cross-activation/coupling** between brain areas
  - grapheme encoding area (FGA)
  - color area (V4)
  - superior parietal lobule (SPL)

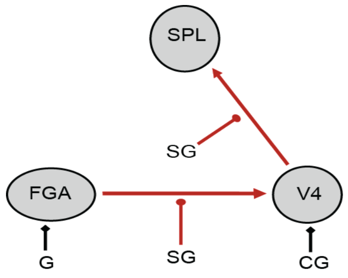


Hubbard, 2007

Bottom-up or Top-down “cross-activation”?

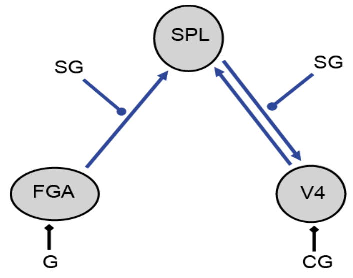
Bottom-up

(*Ramachandran & Hubbard, 2001*)

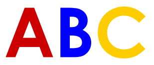


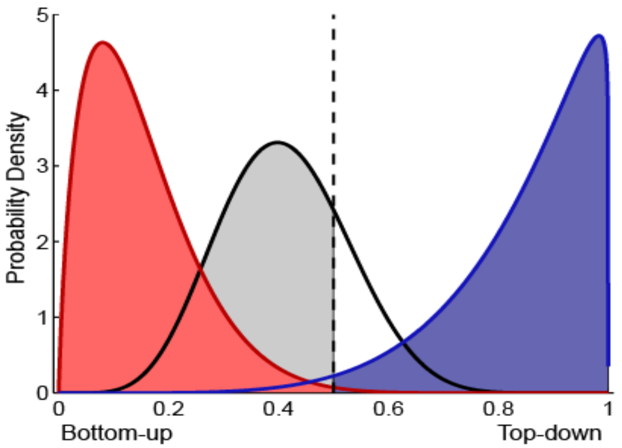
Top-down

(*Grossenbacher & Lovelace, 2001*)

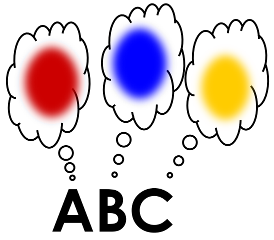


Projectors



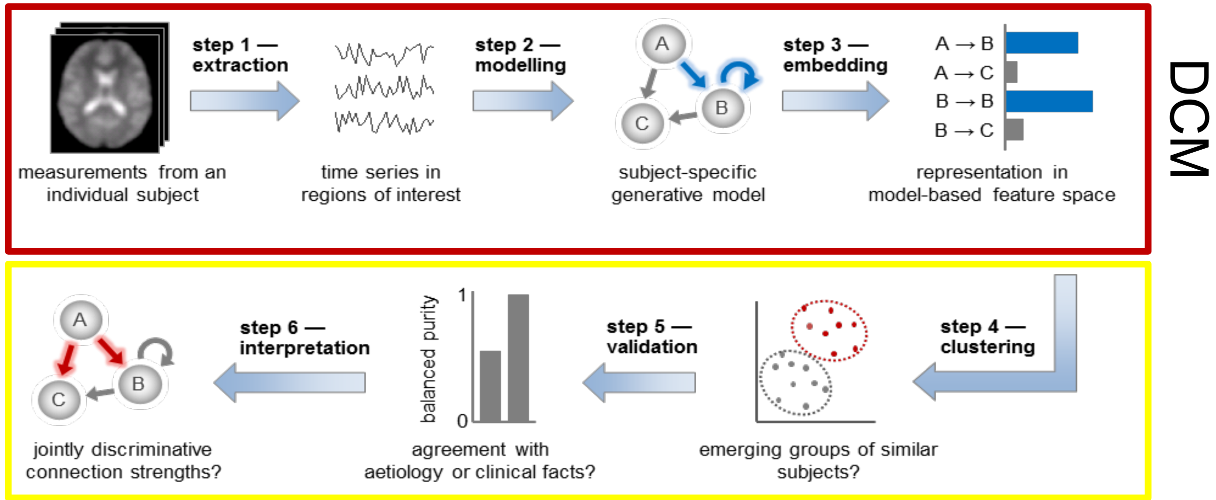


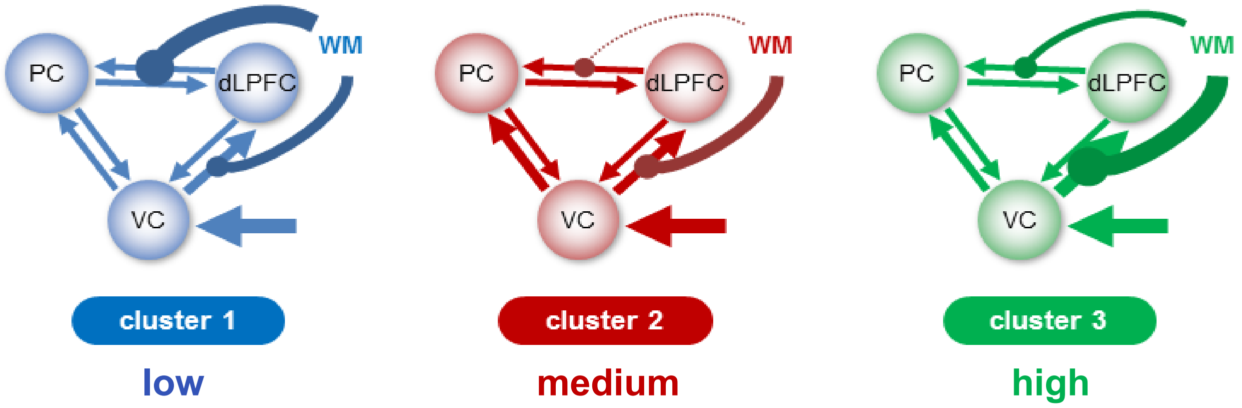
Associators



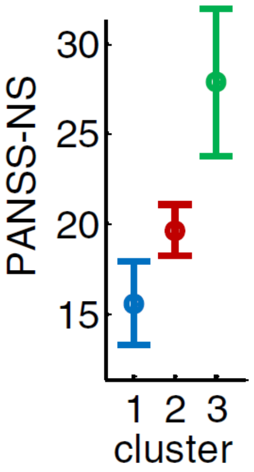
Van Leeuwen et al., JNeurosci, 2011

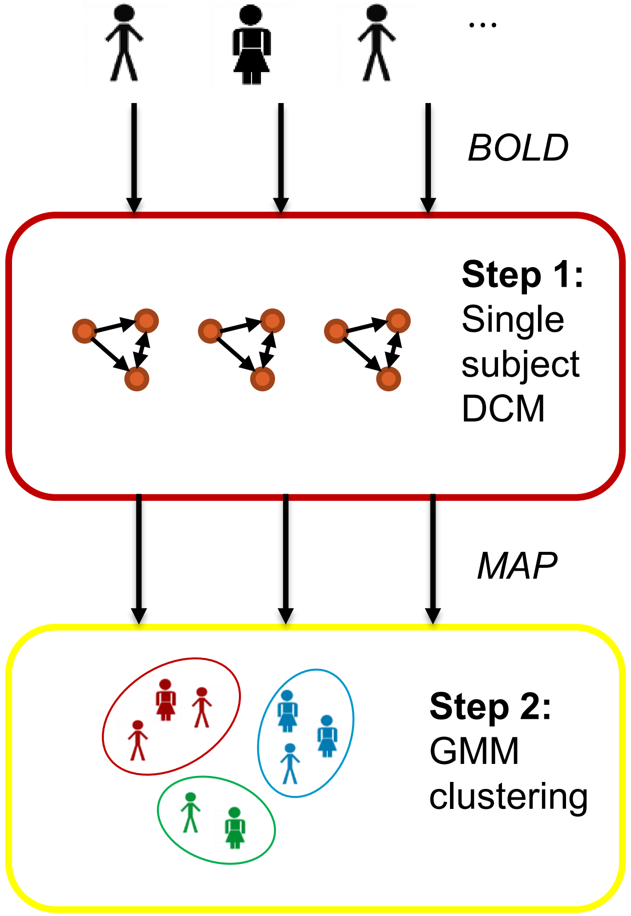
Example: DCM for physiologically plausible feature extraction (generative embedding)





negative symptoms (NS) subscale of the PANSS score





Brodersen et al., NeuroImage: Clinical, 2014

What questions can we answer using DCM?

Model comparison

What is the functional architecture of a network of brain regions?

→ Synesthesia

Are optimal models different between groups?

→ Synesthesia

Which connections are modulated by experimental manipulations?

Parameter inference

Are parameters different between individuals/groups?

Use parameters as physiologically informed summary statistics

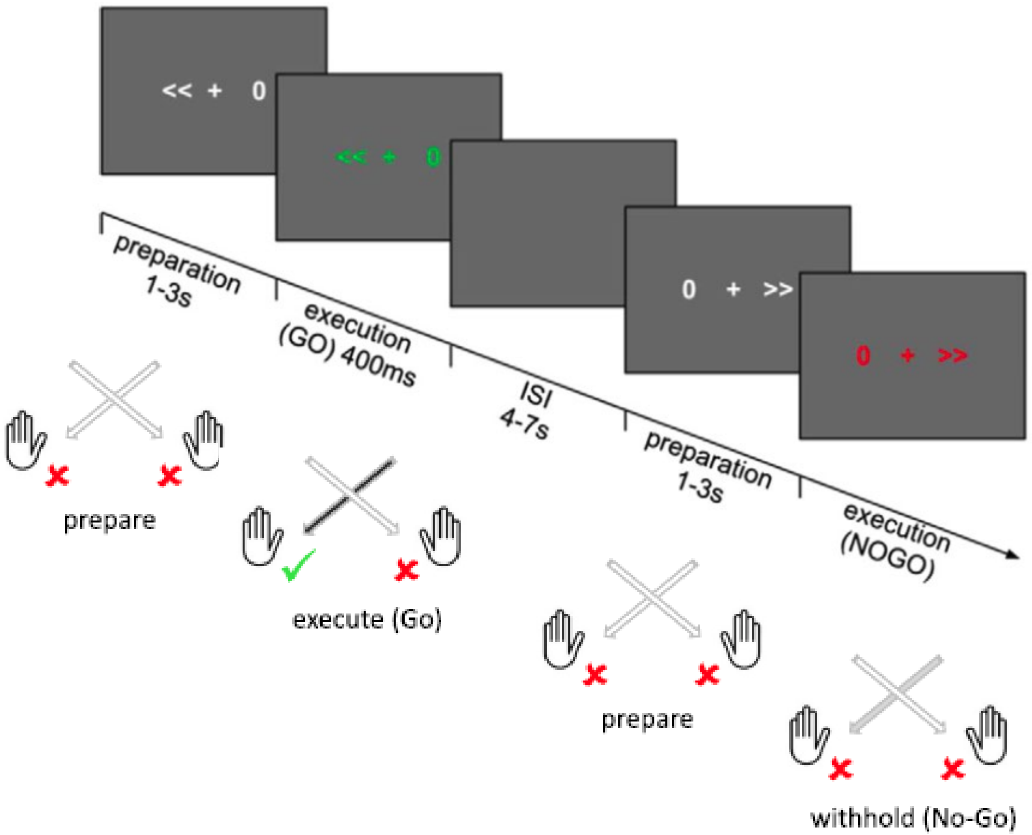
→ Generative embedding

... and of course many more!

Limitations

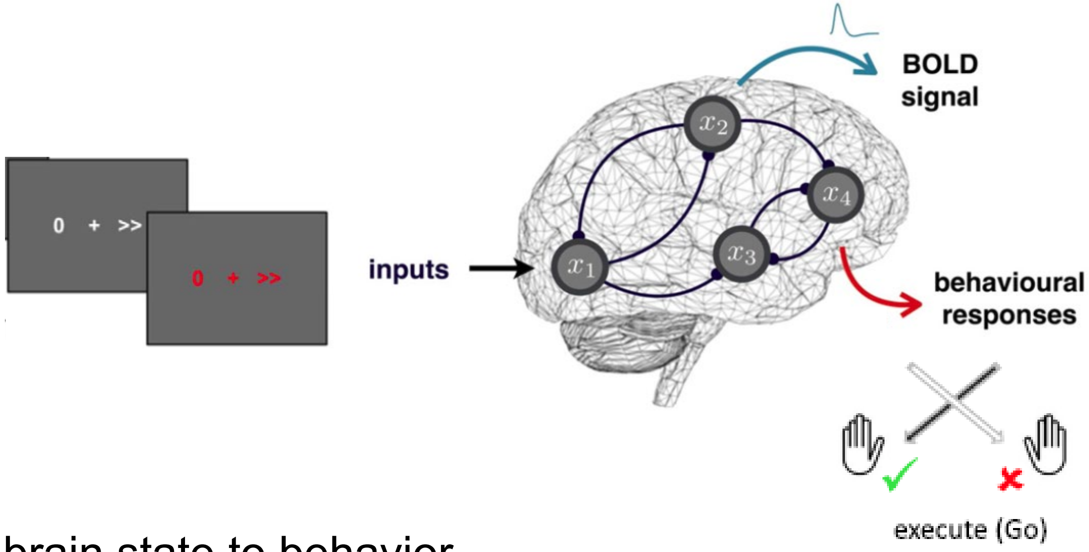
- DCMs only have inputs, no outputs
  - Limits the study of behavioral paradigms
- Local minima
  - Variational approximation can get stuck in local minima of free energy
- Size of networks
  - Standard inversion too slow for large networks (>10 nodes).
- Regularization through fixed priors:
  - Regularization based on other data → empirical Bayes.

Behavioral DCM – a step towards a neurocomputational model

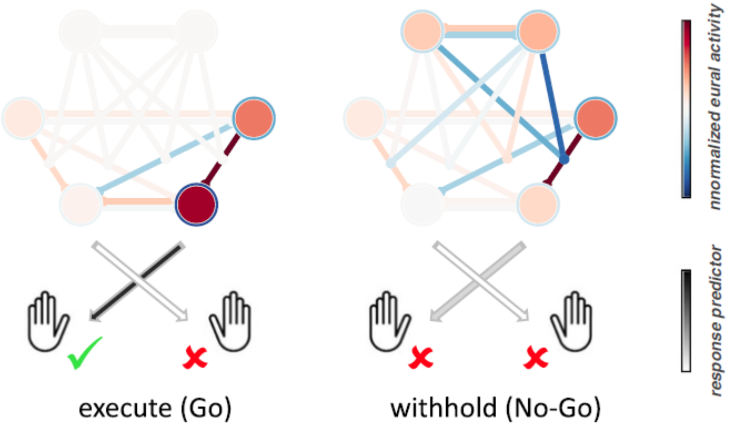


Rigoux and Daunizeau, Neuroimage, 2015

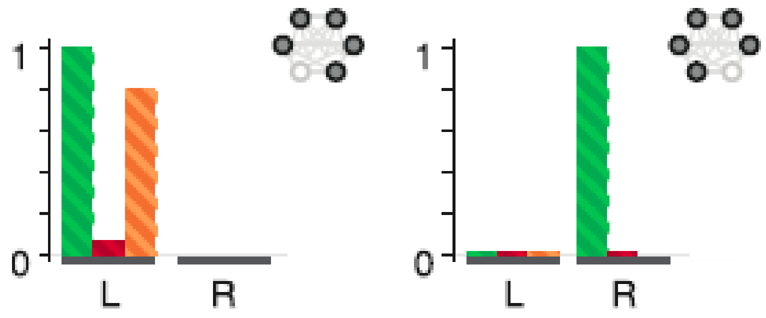
Behavioral DCM – a step towards a neurocomputational model



Mapping brain state to behavior

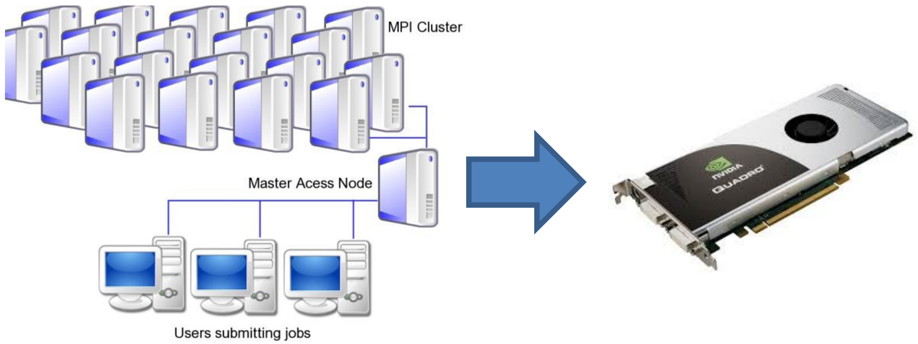


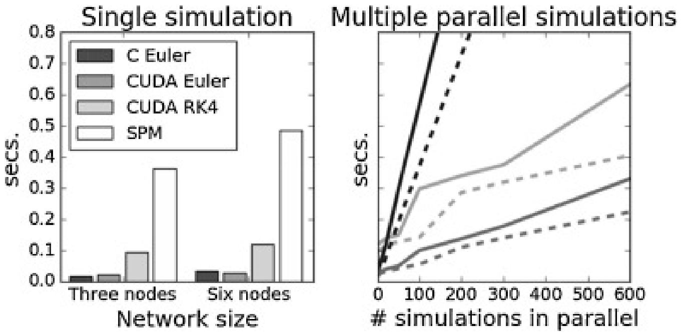
Lesion simulations



Rigoux and Daunizeau, Neuroimage, 2015

MCMC inversion of DCMs: Massively Parallel DCM - mpdcm

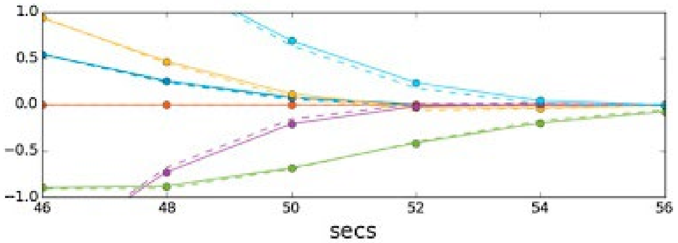




$$\begin{aligned}\dot{x} &= f(x, u_1, \theta_1)\\ \dot{x} &= f(x, u_2, \theta_2)\\ &\vdots\\ \dot{x} &= f(x, u_1, \theta_1)\end{aligned}$$

mpdcm_integrate(dcms)

$$\begin{aligned}&y_1\\ &y_2\\ &\vdots\\ &y_3\end{aligned}$$



- Fast inversion of DCMs
- MCMC based inversion possible

→ **Thermodynamic Integration** (alternative to negative Free Energy)

Aponte, Yao et al., Cogn. Neurodyn., 2021, Aponte et al., J. Neurosci. Meth., 2015

Recent additions to DCM for fMRI

– Massively parallel dynamic causal modelling

➢ mpdcm Aponte et al., J Neuroscience Methods, 2016

– Regression dynamic causal modelling

➢ rDCM Frässle et al., Neuroimage, 2017

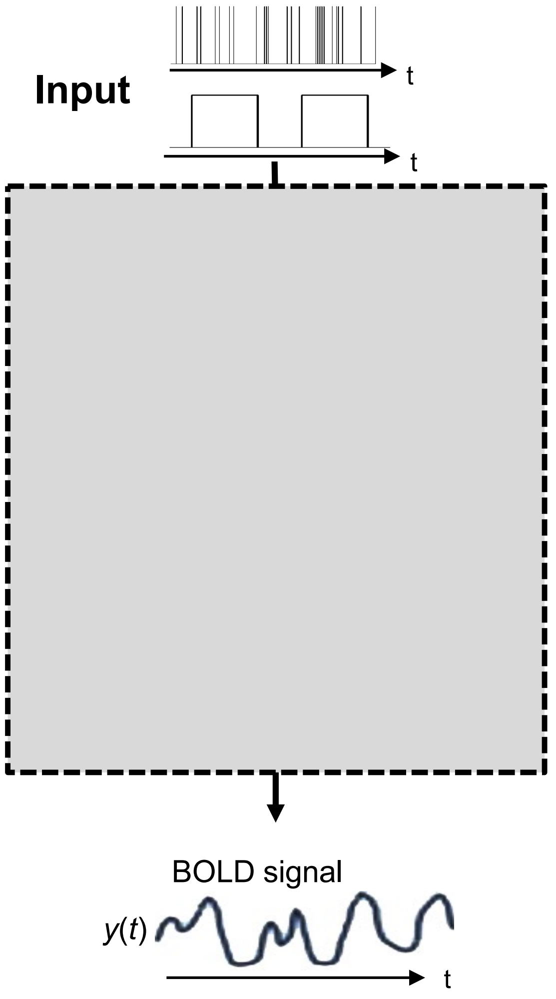
Modeling Connectivity:
Regression DCM for fMRI
→ later today

– Hierarchical unsupervised generative embedding

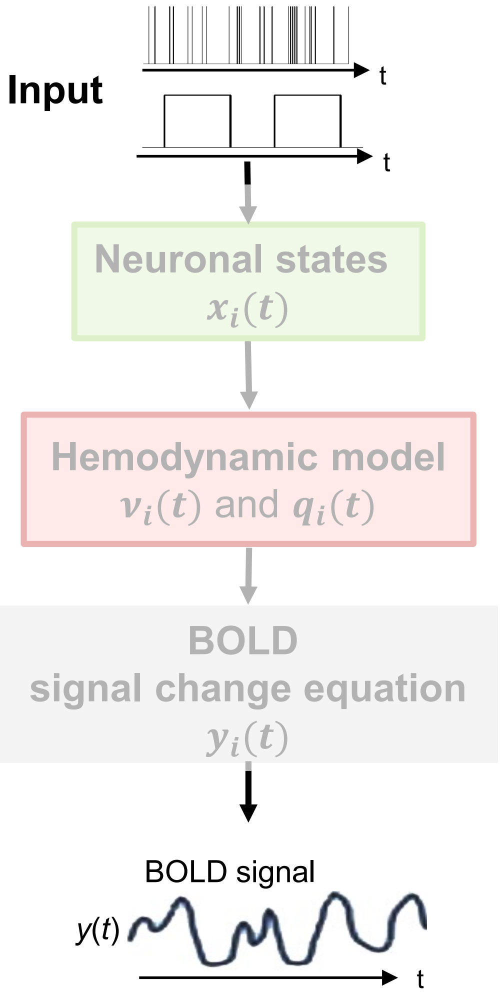
➢ HUGE Yu et al., Neuroimage, 2019

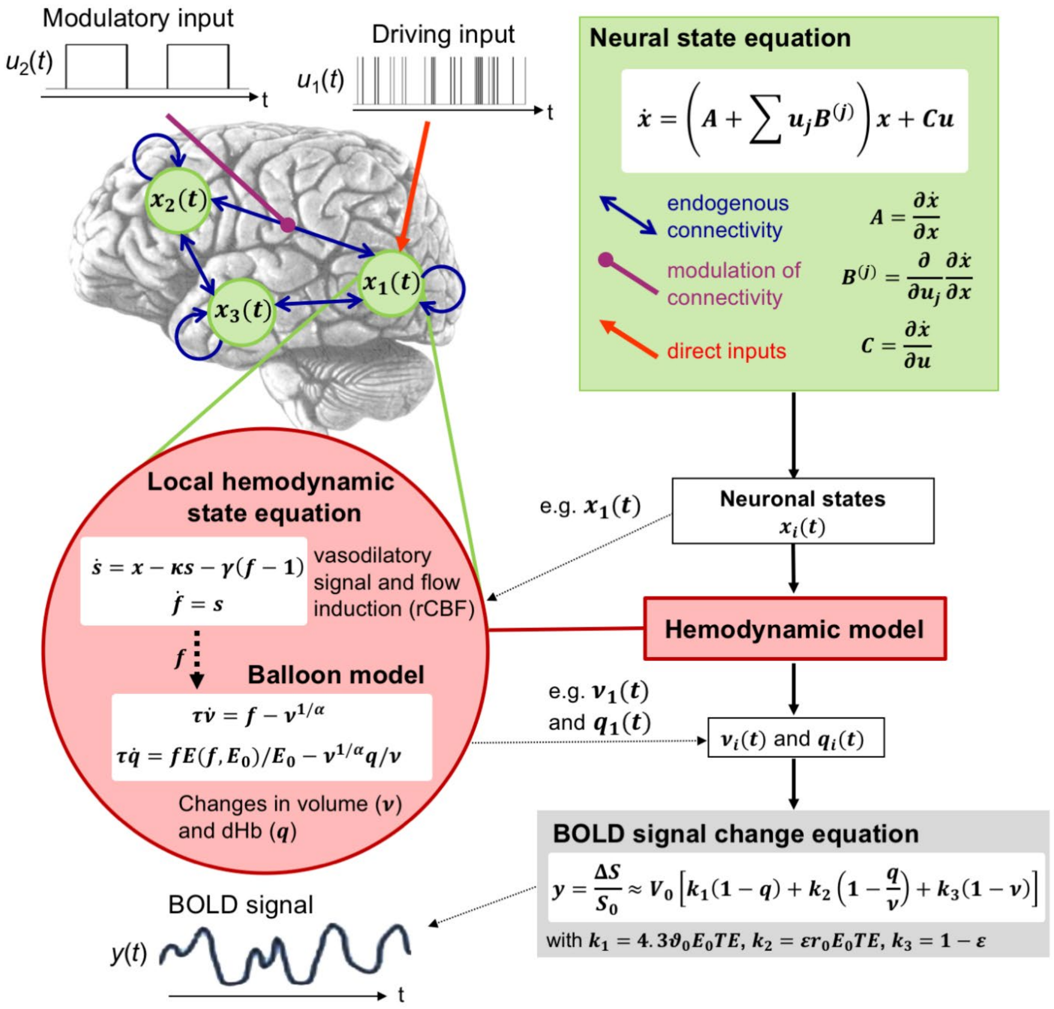
Available in TAPAS:
www.translationalneuromodeling.org/tapas

Summary – generative model



Summary – generative model





Stephan et al., 2015, Neuron

Summary - Bayesian system identification

$$u(t)$$

Neural (and hemo-) dynamics

$$dx/dt = f(x,u,\theta)$$

Observer function

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

$$p(y \mid \theta,m) = N(g(\theta),\Sigma(\theta))$$

$$p(\theta,m) = N(\mu_\theta,\Sigma_\theta)$$

Inference on model structure

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

Inference on parameters

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

Design experimental inputs

↓

Define likelihood model

↓

Specify priors

↓

Invert model

↓

Make inferences

DCM software note

Basic functionality for DCM for fMRI is provided within

SPM
https://www.fil.ion.ucl.ac.uk/spm/

Thank you!

Many thanks to Stefan Frässle,
Klaas Enno Stephan, Hanneke den Ouden
and Jean Daunizeau for many of the slides!

List with suggested DCM literature in Appendix of this presentation!

DCM literature (1)

- **Aponte EA, Raman S, Sengupta B, Penny WD, Stephan KE, Heinzle J (2016). mpdcm: A Toolbox for Massively Parallel Dynamic Causal Modeling. Journal of Neuroscience Methods 257: 7-16.**
- **Aponte EA, Yao Y, Raman S, Frässle S, Heinzle J, Penny WD, Stephan KE (2021). An introduction to thermodynamic integration and application. Cognitive Neurodynamics 16: 1-15.**
- Brodersen KH, Schofield TM, Leff AP, Ong CS, Lomakina EI, Buhmann JM, Stephan KE (2011) Generative embedding for model-based classification of fMRI data. PLoS Computational Biology 7: e1002079.
- Brodersen KH, Deserno L, Schlagenhauf F, Lin Z, Penny WD, Buhmann JM, Stephan KE (2014) Dissecting psychiatric spectrum disorders by generative embedding. NeuroImage: Clinical 4: 98-111
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- Daunizeau J, Stephan KE, Friston KJ (2012) Stochastic Dynamic Causal Modelling of fMRI data: Should we care about neural noise? NeuroImage 62: 464-481.
- **Friston KJ, Harrison L, Penny W (2003) Dynamic causal modelling. NeuroImage 19:1273-1302.**
- Friston KJ, Mattout J, Trujill-Barreto, Ashburner J, Penny W (2007) Variational free energy and the Laplace approximation. NeuroImage 34: 220-234.
- Friston K, Stephan KE, Li B, Daunizeau J (2010) Generalised filtering. Mathematical Problems in Engineering 2010: 621670.
- Friston KJ, Li B, Daunizeau J, Stephan KE (2011) Network discovery with DCM. NeuroImage 56: 1202–1221.
- Friston K, Penny W (2011) Post hoc Bayesian model selection. Neuroimage 56: 2089-2099.
- Friston KJ, Kahan J, Biswal B, Razi A (2014) A DCM for resting state fMRI. Neuroimage 94:396-407.
- Friston KJ, Preller KH, Mathys C, Cagnan H, Heinzle J, Razi A, Zeidman P (2017) Dynamic causal modelling revisited. Neuroimage. 199:730-744.

DCM literature (2)

- Frässle S, Yao Y, Schöbi S, Aponte EA, Heinzle J, Stephan KE (in press) Generative models for clinical applications in computational psychiatry. Wiley Interdisciplinary Reviews: Cognitive Science.
- **Frässle S, Lomakina EI, Razi A, Friston KJ, Buhmann JM, Stephan KE (2017) Regression DCM for fMRI. NeuroImage 155:406-421.**
- Kiebel SJ, Kloppel S, Weiskopf N, Friston KJ (2007) Dynamic causal modeling: a generative model of slice timing in fMRI. NeuroImage 34:1487-1496.
- Li B, Daunizeau J, Stephan KE, Penny WD, Friston KJ (2011). Stochastic DCM and generalised filtering. NeuroImage 58: 442-457
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- Penny WD, Stephan KE, Mechelli A, Friston KJ (2004a) Comparing dynamic causal models. NeuroImage 22:1157-1172.
- Penny WD, Stephan KE, Mechelli A, Friston KJ (2004b) Modelling functional integration: a comparison of structural equation and dynamic causal models. NeuroImage 23 Suppl 1:S264-274.
- Penny WD, Stephan KE, Daunizeau J, Joao M, Friston K, Schofield T, Leff AP (2010) Comparing Families of Dynamic Causal Models. PLoS Computational Biology 6: e1000709.
- Penny WD (2012) Comparing dynamic causal models using AIC, BIC and free energy. Neuroimage 59: 319-330
- **Raman S, Deserno L, Schlagenhauf F, Stephan KE (2016). A hierarchical model for integrating unsupervised generative embedding and empirical Bayes. Journal of Neuroscience Methods 269: 6-20.**
- Rigoux L, Stephan KE, Friston KJ, Daunizeau J (2014). Bayesian model selection for group studies – revisited. NeuroImage 84: 971-985.
- **Rigoux L and Daunizeau J (2015). Dynamic causal modelling of brain–behaviour relationships. NeuroImage 117:202-221**

DCM literature (3)

- Stephan KE, Harrison LM, Penny WD, Friston KJ (2004) Biophysical models of fMRI responses. Curr Opin Neurobiol 14:629-635.
- Stephan KE, Weiskopf N, Drysdale PM, Robinson PA, Friston KJ (2007) Comparing hemodynamic models with DCM. NeuroImage 38:387-401.
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- Stephan KE, Penny WD, Daunizeau J, Moran RJ, Friston KJ (2009a) Bayesian model selection for group studies. NeuroImage 46:1004-1017.
- Stephan KE, Tittgemeyer M, Knösche TR, Moran RJ, Friston KJ (2009b) Tractography-based priors for dynamic causal models. NeuroImage 47: 1628-1638.
- **Stephan KE, Penny WD, Moran RJ, den Ouden HEM, Daunizeau J, Friston KJ (2010) Ten simple rules for Dynamic Causal Modelling. NeuroImage 49: 3099-3109.**
- Stephan KE, Mathys C (2014). Computational approaches to psychiatry. Current Opinion in Neurobiology 25: 85-92.
- **Yao Y, Raman SS, Schiek M, Leff A, Frässle S, Stephan KE (2018) Variational Bayesian Inversion for Hierarchical Unsupervised Generative Embedding (HUGE). NeuroImage, 179: 604-619**
- **Zeidman P, Jafarian A, Corbin N, Seghier ML, Razi A, Price CJ, Friston KJ (2019) A guide to group effective connectivity analysis, part 1: First level analysis with DCM for fMRI. NeuroImage, DOI: 10.1016/j.neuroimage.2019.06.031**
- **Zeidman P, Jafarian A, Seghier ML , Litvak V, Cagnan H , Price CJ, Friston KJ (2019) A guide to group effective connectivity analysis, part 2: Second level analysis with PEB. NeuroImage, DOI: 10.1016/j.neuroimage.2019.06.032**