Testing hypotheses with SPM & DCM

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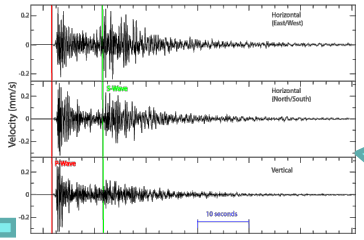
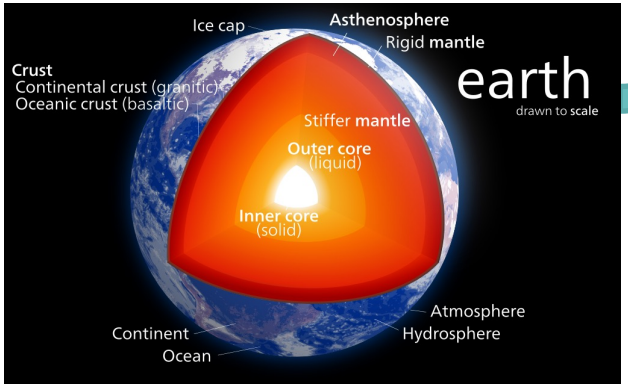
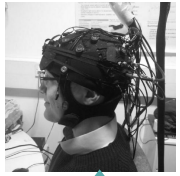
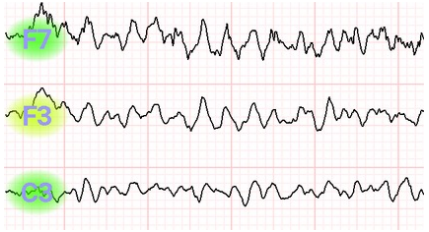
University College London

Inverse problems









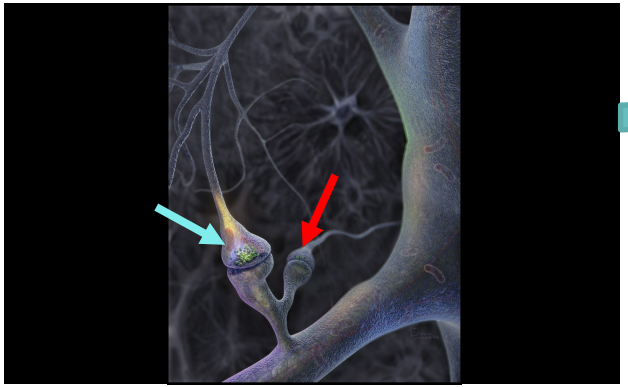


Image credits: Pekachu, Anastasiia Starikova, Kelvinsong from Wikipedia

Empirical science

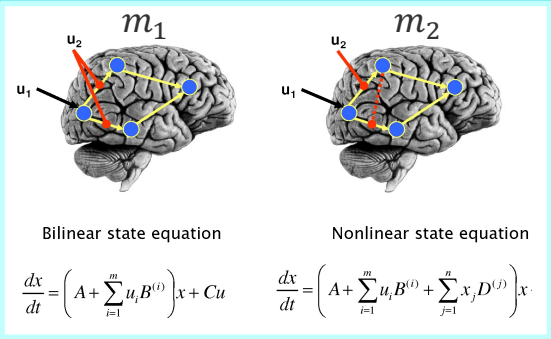
Which hypothesis (model) offers the best explanation for my data?

Model evidence (marginal likelihood)

$$\frac{p(y|m_1)}{p(y|m_2)}$$

Likelihood ratio (Bayes factor)

Bayesian model comparison



Stephan et al., NeuroImage, 2008

Eight steps to DCM for fMRI success

1. Write down some **hypotheses**
2. **Design** an experiment
3. Data collection and **pre-processing**
4. Functional **localisation**
5. First-level **DCM**
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8. Assess **predictive** validity

9. (Write the paper)
10. (Nobel Prize)

1. Write down some hypotheses

DCM is a tool for scoring the evidence for different hypotheses. It is not an exploratory technique.

Commonalities

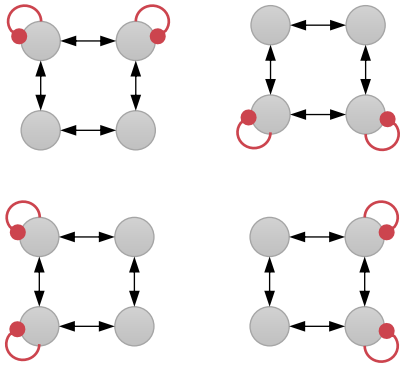
"I hypothesise that top-down connections from parietal cortex are modulated by attention to visual stimuli."

Differences

"I hypothesise that people with a diagnosis of Mild Cognitive Impairment (MCI) have weaker modulation of top-down connections by attention."

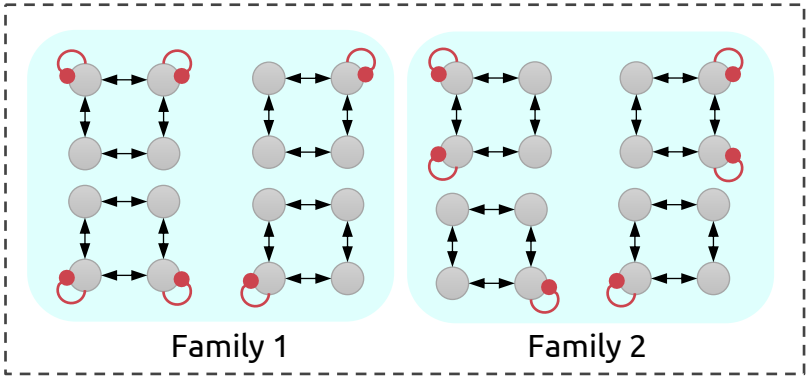
1. Write down some hypotheses

One hypothesis → one model



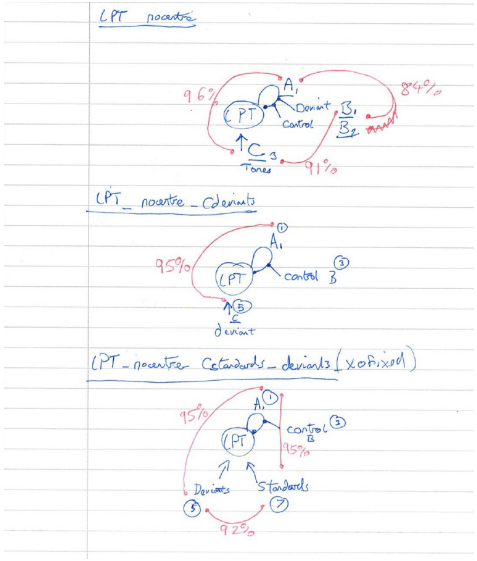
One hypothesis → one family of models

A “model space”



1. Write down some hypotheses

Drawing a diagram for each hypothesis can help!



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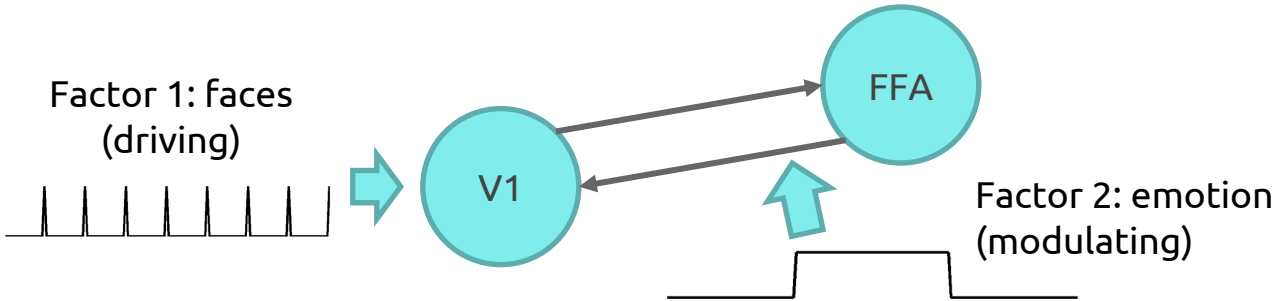
2. Design an experiment

Use a factorial design where possible

e.g. [2 x 2] design:

Factor 1: faces or upside down faces
Factor 2: attend to emotion or attend to hair colour



2. Design an experiment

Favour controlled tasks over resting state where possible

Rest is great when…

- Participants cannot perform tasks
- You are interested in resting state brain dynamics

Any others?

There's a DCM for that

- Use DCM for cross-spectral densities (Spectral DCM)
- Studies often have a factorial design at the between-subjects level (e.g. two groups, pre- and post-intervention)

Friston, K.J., Kahan, J., Biswal, B. and Razi, A., 2014. A DCM for resting state fMRI. Neuroimage, 94, pp.396-407.

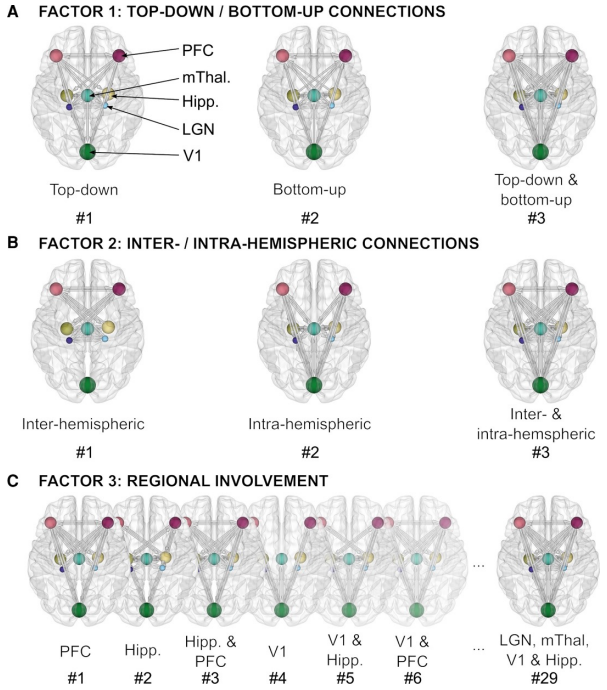
Resting state example

"Are visual hallucinations in Parkinson's disease explained by **impaired bottom-up integration** of sensory information and **overweighting of top-down perceptual priors** within the visual system?"

Participants:

- 15 Parkinson's disease visual hallucinators
- 75 Parkinson's disease non-visual hallucinators.

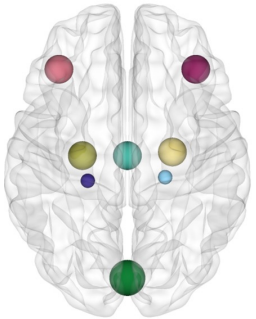
Model space



Thomas, G.E., et al., 2023. *Brain Communications*, *5*(1)

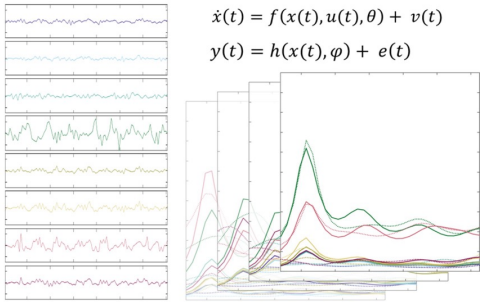
Resting state example

Visual network nodes



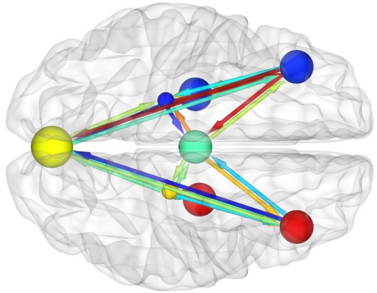
Spectral dynamic causal modelling

$$\dot{x}(t) = f(x(t), u(t), \theta) + v(t)$$
$$y(t) = h(x(t), \varphi) + e(t)$$

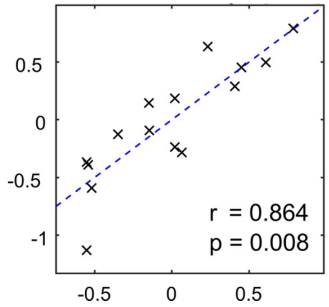


90 participants with Parkinson's disease
15 with visual hallucinations

Connectivity differences in visual hallucinatiors



Connectivity association with hallucination severity



Thomas, G.E., et al., 2023. *Brain Communications*, *5*(1)

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3. Data collection and pre-processing

No special considerations for DCM

Functional MRI acquisition and image reconstruction

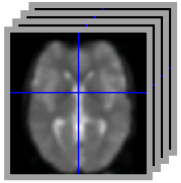
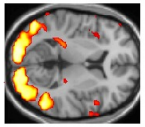
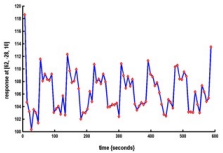


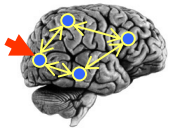
Image pre-processing (realignment, co-registration, normalisation, smoothing)



Statistical Parameter Mapping (SPM) / General Linear Model



Timeseries extraction from Regions of Interest (ROIs)



Dynamic Causal Modelling (DCM)

DCM

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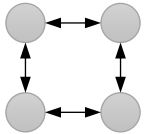
4. Functional localisation



A network consists of nodes (brain regions) and connections. We need to select the nodes.

Task based experiments

The purpose of DCM is to infer the underlying neural connectivity that gave rise to your SPM results.

→ **Select Regions of Interest using your contrasts**

Resting state experiments

The purpose of DCM is to infer the underlying neural connectivity that caused the functional connectivity (correlations or cross-spectral density) among pre-selected brain regions.

→ Select Regions of Interest from previous literature, anatomical hypotheses or an initial PCA or ICA

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5. First level DCM

Two outputs:

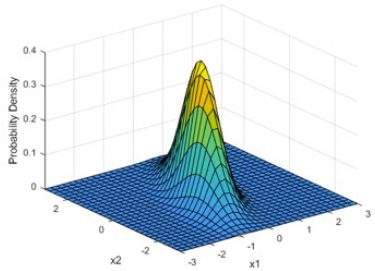
Free energy

Approximation of the log model evidence $P(Y|m)$

$$F \approx \log P(Y|m) = \text{accuracy} - \text{complexity}$$

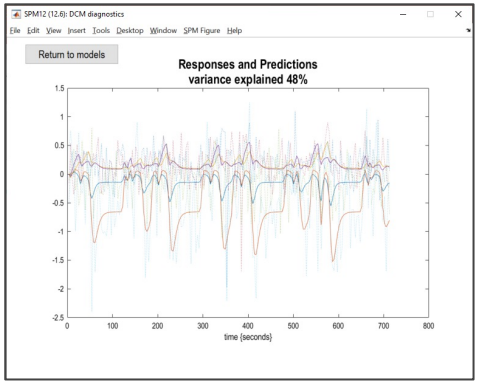
Estimated parameters

Posterior (multivariate Gaussian) probability $P(\theta|Y,m)$



5. First level DCM

Check the variance explained by your models



spm_dcm_fmri_check(DCM);

(10% or more is considered non-trivial)

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6. Group analysis using Parametric Empirical Bayes (PEB)

Group-level questions:

- Are the strength of particular connections changed by an experimental manipulation?
- Does belonging to a diagnostic **group** determine the strength of these connections?
- Does the strength of the connections correlate with **behavioural or clinical variables**?
- Could we **predict** a new participant's disease status or behavioural scores using our estimate of their connections?

6. Group analysis using Parametric Empirical Bayes (PEB)

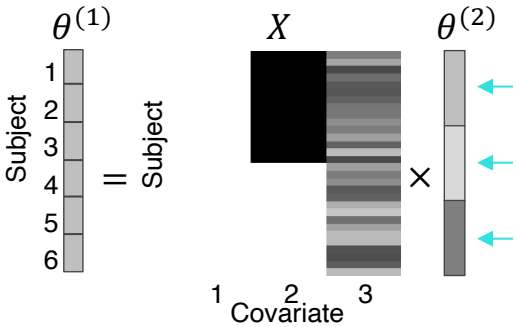
The connectivity parameters are taken to the group level and modelled using a General Linear Model

Design matrix (covariates)

Group level parameters

$$\theta^{(1)} = X\theta^{(2)} + \epsilon^{(2)}$$

Unexplained between-subject variability



Group average connection strength

Effect of group on the connection

Effect of age on the connection

Outputs:

- One free energy for the entire group-level model (DCMs and GLM).
- Group-level parameters (effect of each covariate on each connection)

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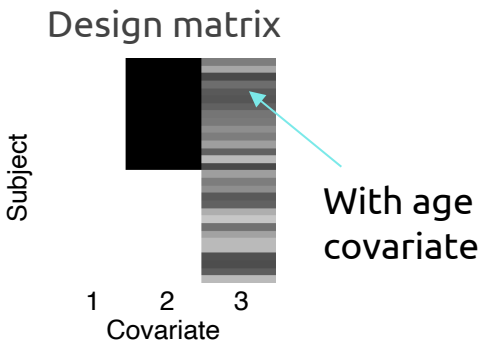
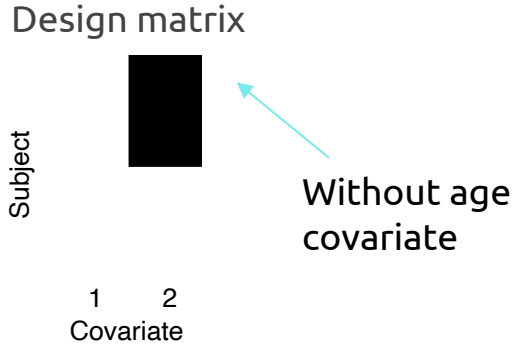
7. Bayesian model comparison

PEB model 1



Free energy F_1

PEB model 2



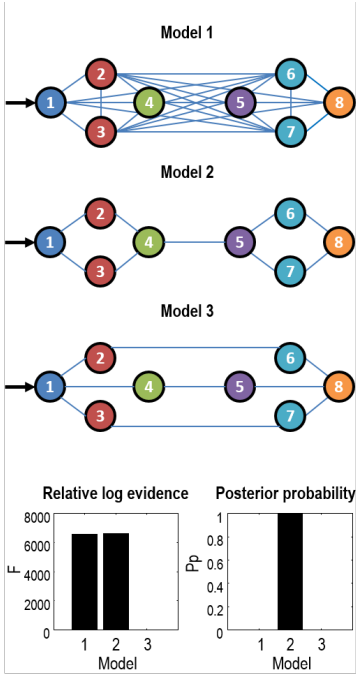
Free energy F_2

$$\log BF = F_1 - F_2$$

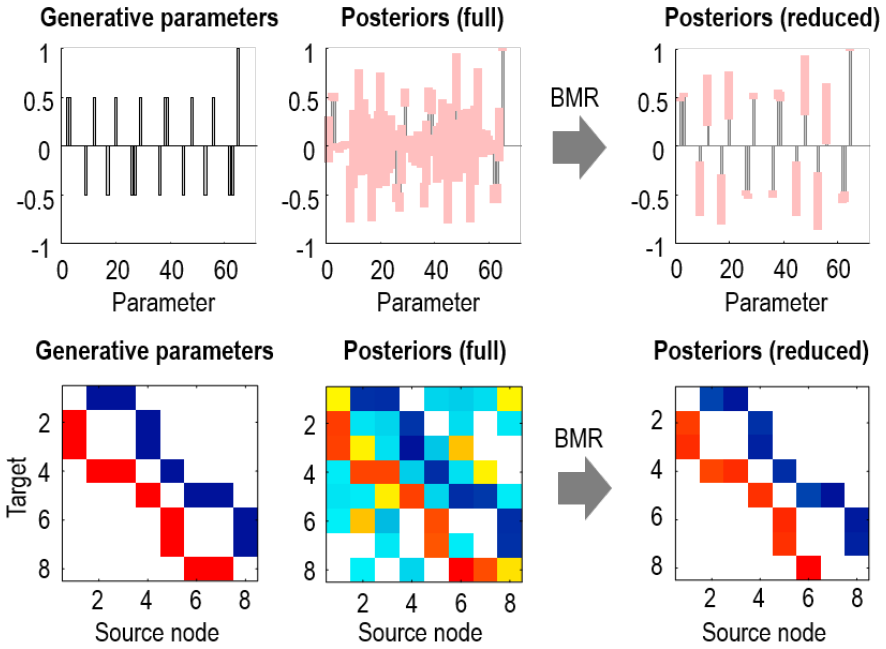
(The free energy for nested models is derived analytically using Bayesian Model Reduction)

Bayesian model reduction

Pre-defined models



Automatic search



Friston, Parr, Zeidman. *Bayesian model reduction*. arXiv preprint arXiv:1805.07092.

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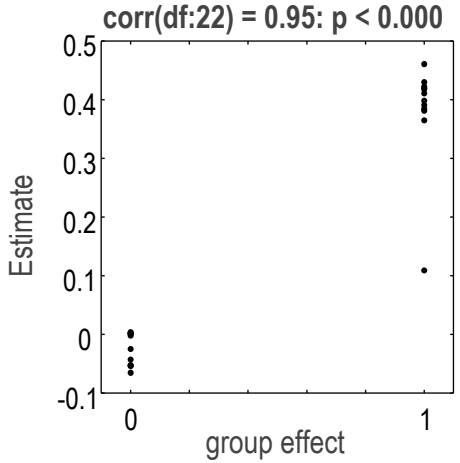
8. Assess predictive validity

The question

Are the effect sizes I detected large enough to predict the group membership or clinical scores of new participants?

→ Leave-one-out (LOO) cross-validation

Predicted vs actual covariates



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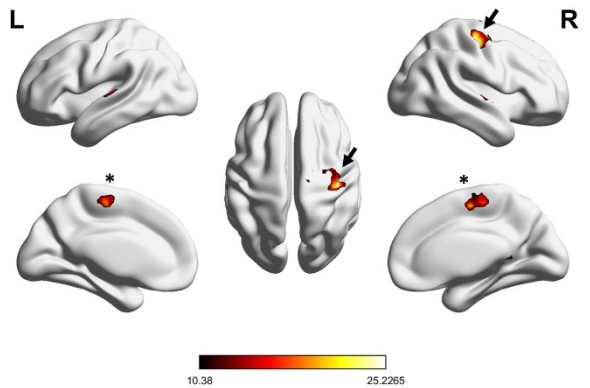
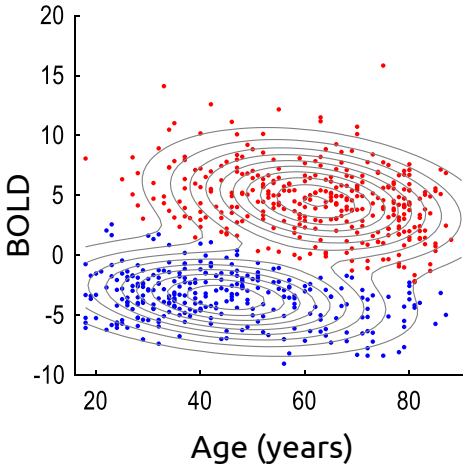
The ageing brain: ipsilateral M1

Main effect of age



N=635 participants aged 18–88 (Cam-CAN)

Subjects clustered into groups by rM1 response

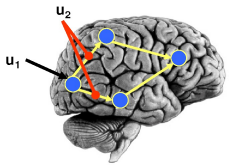


Tak, Y.W., Knights, E., Henson, R. and Zeidman, P., 2021. Ageing and the ipsilateral M1 BOLD response: a connectivity study. Brain sciences, 11(9), p.1130.

The ageing brain: DCM

Dynamic Causal Modelling (DCM) for fMRI

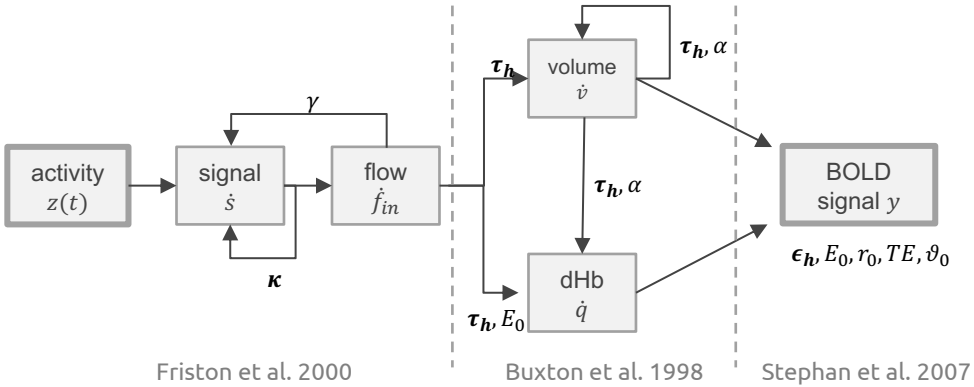
Neural model



Bilinear state equation

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

Haemodynamic Model



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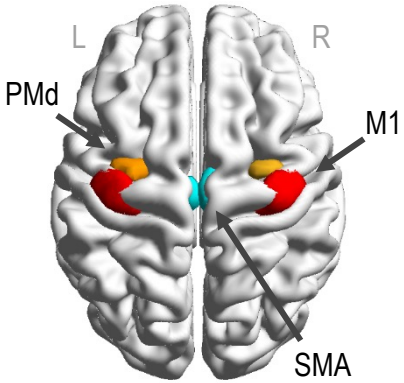
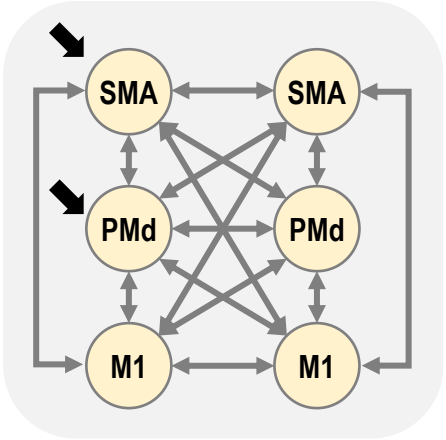
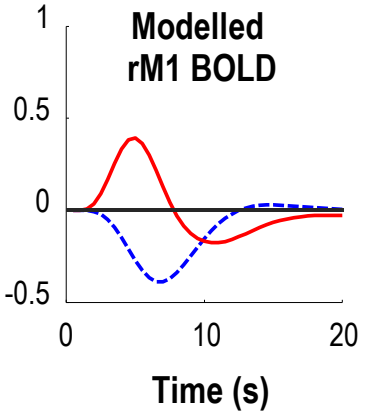
The ageing brain: model structure





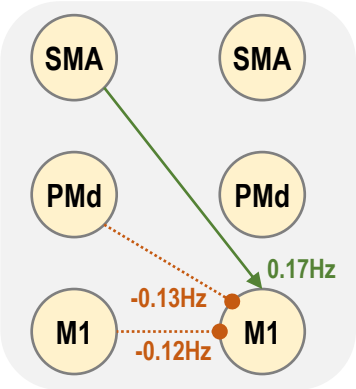


The model successfully captured the difference in the right M1 BOLD response between younger and older responders.

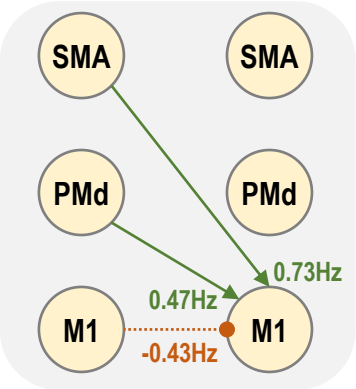
Tak, Y.W., Knights, E., Henson, R. and Zeidman, P., 2021. Ageing and the ipsilateral M1 BOLD response: a connectivity study. Brain sciences, 11(9), p.1130.

The ageing brain: model parameters

Younger subjects

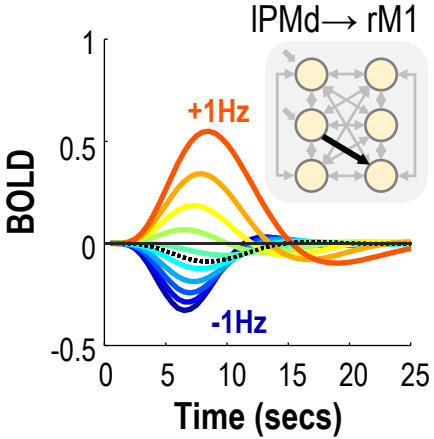


Older subjects



Positive connection Negative connection

In silico experiment



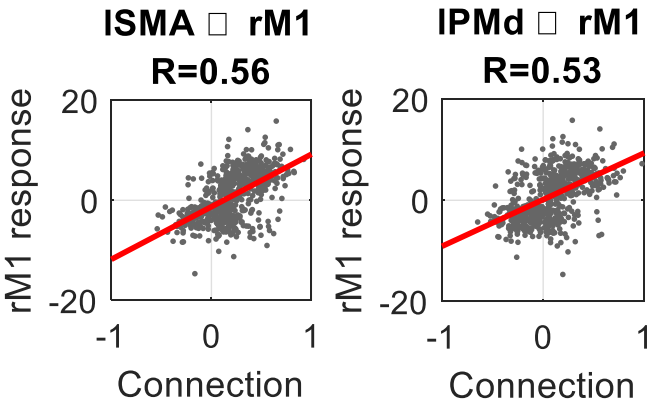
Increasing lSMA → rM1, lPMd → rM1 or lM1 → rM1 connection strengths *in silico* could flip the sign of the BOLD response, mirroring the ageing process.

Tak, Y.W., Knights, E., Henson, R. and Zeidman, P., 2021. Ageing and the ipsilateral M1 BOLD response: a connectivity study. Brain sciences, 11(9), p.1130.

The ageing brain: cross-validation

Only the lSMA → rM1 and lPMd → rM1 connections correlated with rM1 BOLD across subjects.

Total variance explained: 44%



Tak, Y.W., Knights, E., Henson, R. and Zeidman, P., 2021. Ageing and the ipsilateral M1 BOLD response: a connectivity study. Brain sciences, 11(9), p.1130.

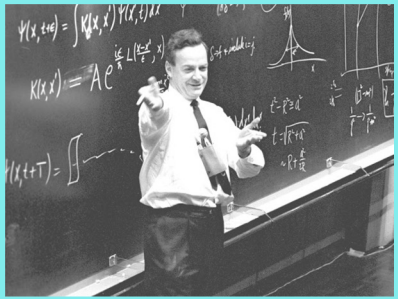
Eight steps to DCM success

1. Write down some **hypotheses**
2. **Design** an experiment
3. Data collection and **pre-processing**
4. Functional **localisation**
5. First-level **DCM**
6. Group analysis using Parametric Empirical Bayes (**PEB**)
7. Bayesian **model comparison**
8. Assess **predictive** validity

Further reading

“What I cannot create I do not understand.”

—Richard Feynman



Tutorial papers:

Zeidman, P., Jafarian, A., Corbin, N., Seghier, M.L., Razi, A., Price, C.J., Friston, K.J. **A guide to group effective connectivity analysis, part 1: First level analysis with DCM for fMRI**. NeuroImage, 200, pp. 174-190. 2019.

Zeidman, P., Jafarian, A., Seghier, M.L., Litvak, V., Cagnan, H., Price, C.J., Friston, K.J. **A guide to group effective connectivity analysis, part 2: Second level analysis with PEB.** NeuroImage, 200, pp. 12-25. 2019.

Technical papers:

Friston, K., Parr, T. and Zeidman, P., 2018. **Bayesian model reduction**. arXiv:1805.07092.

Friston, K.J., Litvak, V., Oswal, A., Razi, A., Stephan, K.E., Van Wijk, B.C., Ziegler, G. and Zeidman, P., 2016. **Bayesian model reduction and empirical Bayes for group (DCM) studies**. Neuroimage, 128, pp.413-431.

Zeidman, P., Friston, K. and Parr, T., 2022. **A primer on Variational Laplace**. https://doi.org/10.31219/osf.

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