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Granger causality
Dynamic causal modelling

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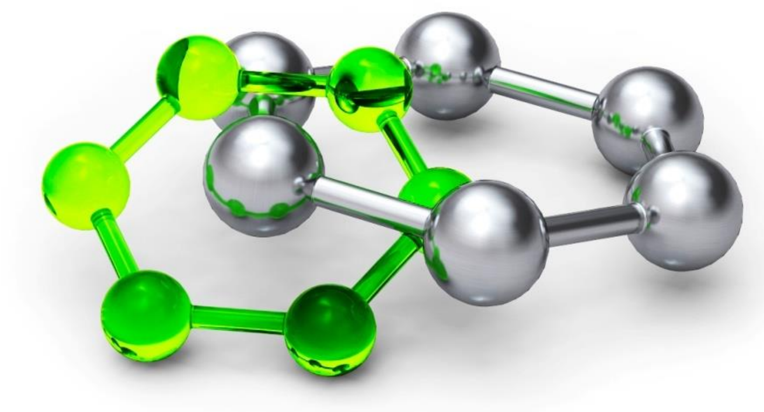

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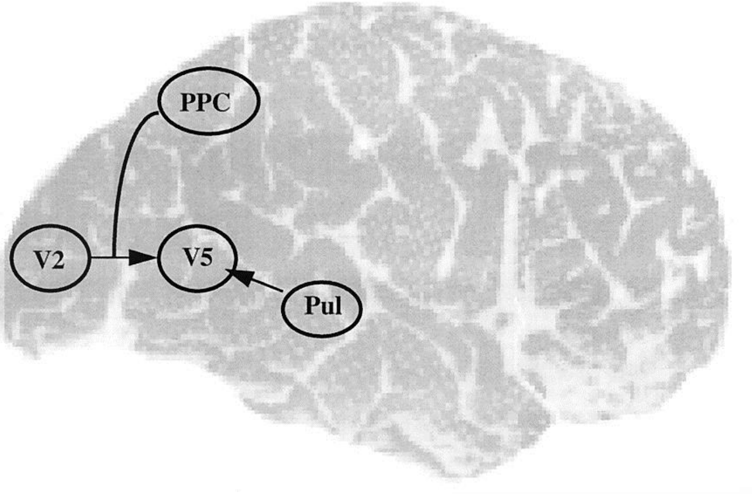
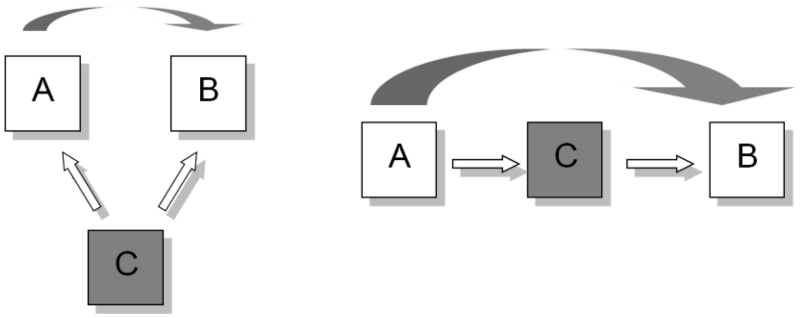
Granger causality

- Originally for economy
  - observing flow of information
    - (1969, Sir Clive William John Granger; 2003 Nobel Prize for Economic Sciences)
- Explain direction and significance of connection
- How good can signal from one area predict signal in another brain area
- Uses autoregressive models



Granger causality

- Prior knowledge about model of interactions is needed



- Inaccuracies:
  - Omitting important areas in model or including „noisy areas“
  - Regional variability of hemodynamic response
  - GC doesn‘t consider any neurobiological relevant model of neural dynamics

Granger causality

- „A classic example is to look at a drunk walking her dog. Both the drunk and her dog follow a random path, but they still try to stay close to each other. The paths are not actually correlated. Instead we say the 2 paths are **Co-Integrated**."
- Causation is not correlation

- https://charlesmartin14.wordpress.com/2013/05/27/causation-vs-correlation-granger-causality/

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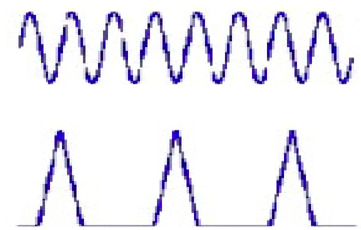
Granger causality

$$\mathbf{x}(n) = -\sum_{i=1}^{p} \mathbf{A}_x(i)\mathbf{x}(n-i) + \mathbf{u}(n)$$

$$\mathbf{y}(n) = -\sum_{i=1}^{p} \mathbf{A}_y(i)\mathbf{y}(n-i) + \mathbf{v}(n)$$



$$\mathbf{q}(n) = \begin{bmatrix} \mathbf{x}(n) \\ \mathbf{y}(n) \end{bmatrix} \qquad \boldsymbol{q}(n) = -\sum_{i=1}^{p} A_q(i)\boldsymbol{q}(n-i) + w(n)$$

$$\Sigma_1 = var(\mathrm{u}(n)) \quad T_1 = var(\mathrm{v}(n))$$

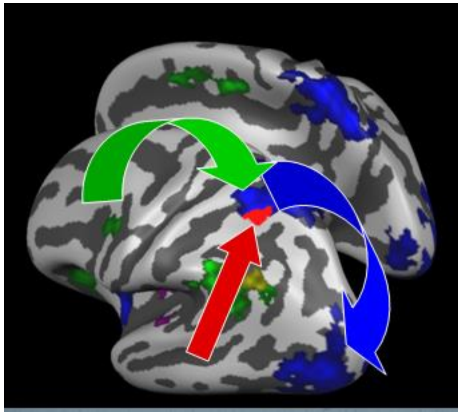
$$\mathrm{Y} = var(\mathbf{w}(n)) = \begin{bmatrix} \Sigma_2 & \mathrm{C} \\ \mathrm{C}^{\mathrm{T}} & \mathrm{T}_2 \end{bmatrix}$$

$$F_{x \to y} = \ln\left(\frac{|var(\mathbf{v}(n))|}{|T_2|}\right)$$

$$F_{y \to x} = \ln\left(\frac{|var(\mathbf{u}(n))|}{|\Sigma_2|}\right)$$

Granger causality

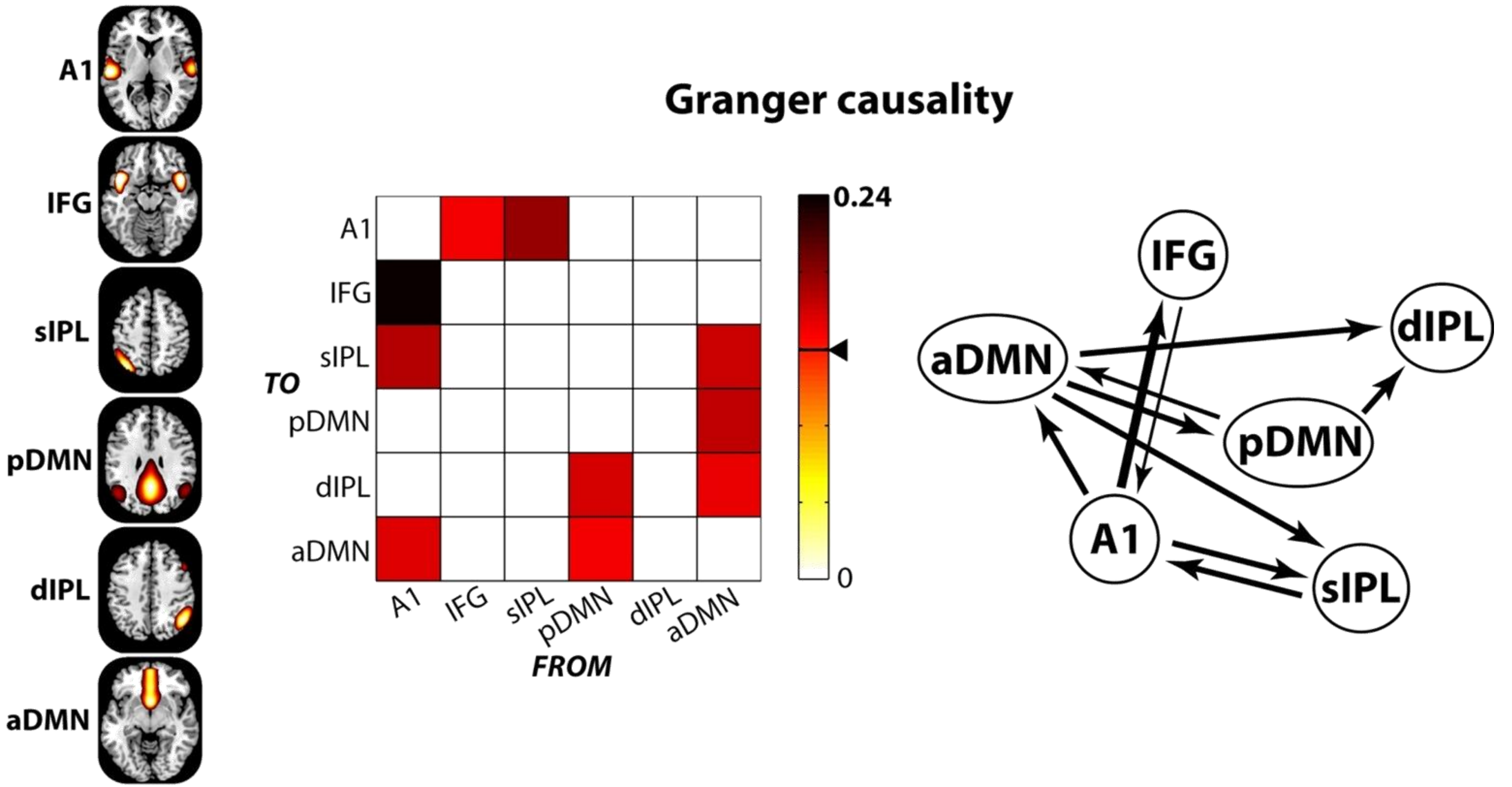
- Applicable on block data, event related design and task free data
- Structural model is not strictly required
- Domain
  - Time representation
  - Frequency (normalized) representation



- Application:
  - „Seed based“ – for pairs of voxels (two dimensional)
  - Don‘t need structural model (Exploratory)
  - Between functional networks (identified by e.g. ICA)

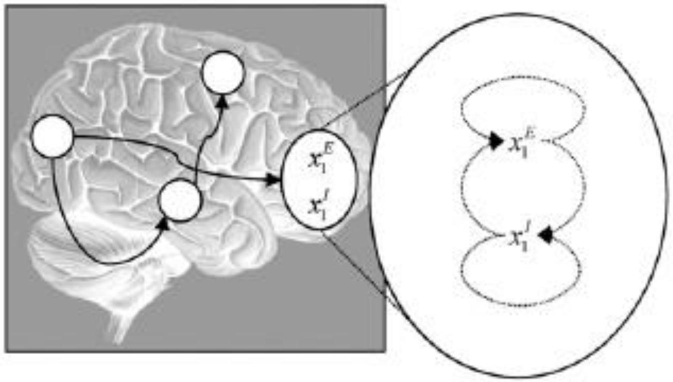
Granger causality

- GC between time series of spatially independent components



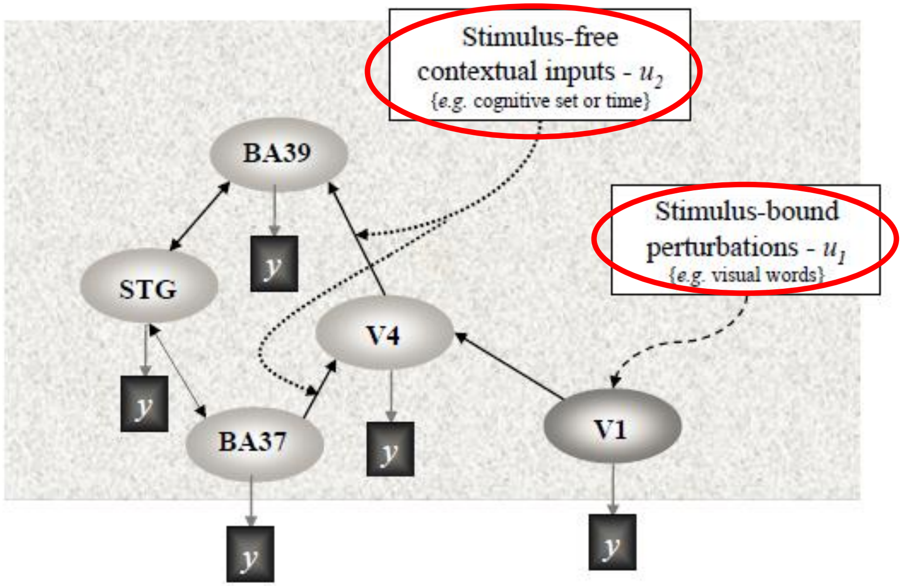
Dynamic causal modelling - DCM

- Developed for fMRI (2003)
- Extended for EEG, MEG, FNIRS, …
- Idea to treat the brain as a deterministic nonlinear dynamic system that is subject to inputs and produces outputs (Friston, 2003)



Dynamic causal modelling - DCM

- Brain as input-state-output system
- Two types of inputs:
  - Influence on specific anatomical regions (nodes) – u_1
  - Modulation of coupling among regions (nodes) – u_2
- E.g. visual input:



Dynamic causal modelling - DCM

- Uses state space for description of the system to model intrinsic dynamics
- Input – experimental stimuli (psychological conditions)
- Output – time series of measured signal
- Intrinsic states – states of neural populations

$$z(t) = \begin{bmatrix} z_1(t) \\ \vdots \\ z_n(t) \end{bmatrix}$$

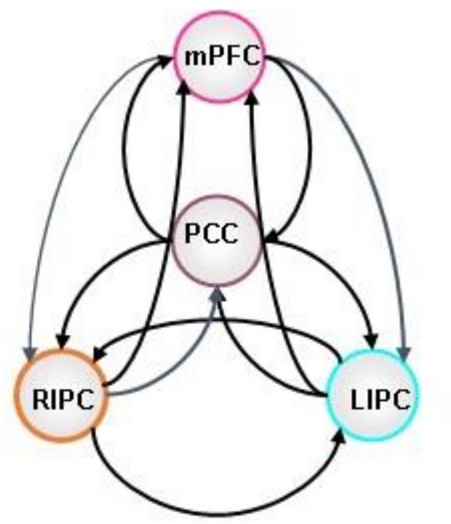
State variables of the system

$$\begin{bmatrix} \dot{z}_1 \\ \vdots \\ \dot{z}_n \end{bmatrix} = \begin{bmatrix} f_1(z_1 \ldots z_n, u, \theta_1) \\ \vdots \\ f_n(z_1 \ldots z_n, u, \theta_n) \end{bmatrix}$$

$$\dot{z} = F(z, u, \theta)$$

Dynamic causal modelling - DCM

- Uses neurobiological relevant model of neural populations dynamics combined with biophysical relevant forward model describing transformation of neural activity to measured signal
- Interactions are modelled on neuronal level
- Can quantify strength of connections



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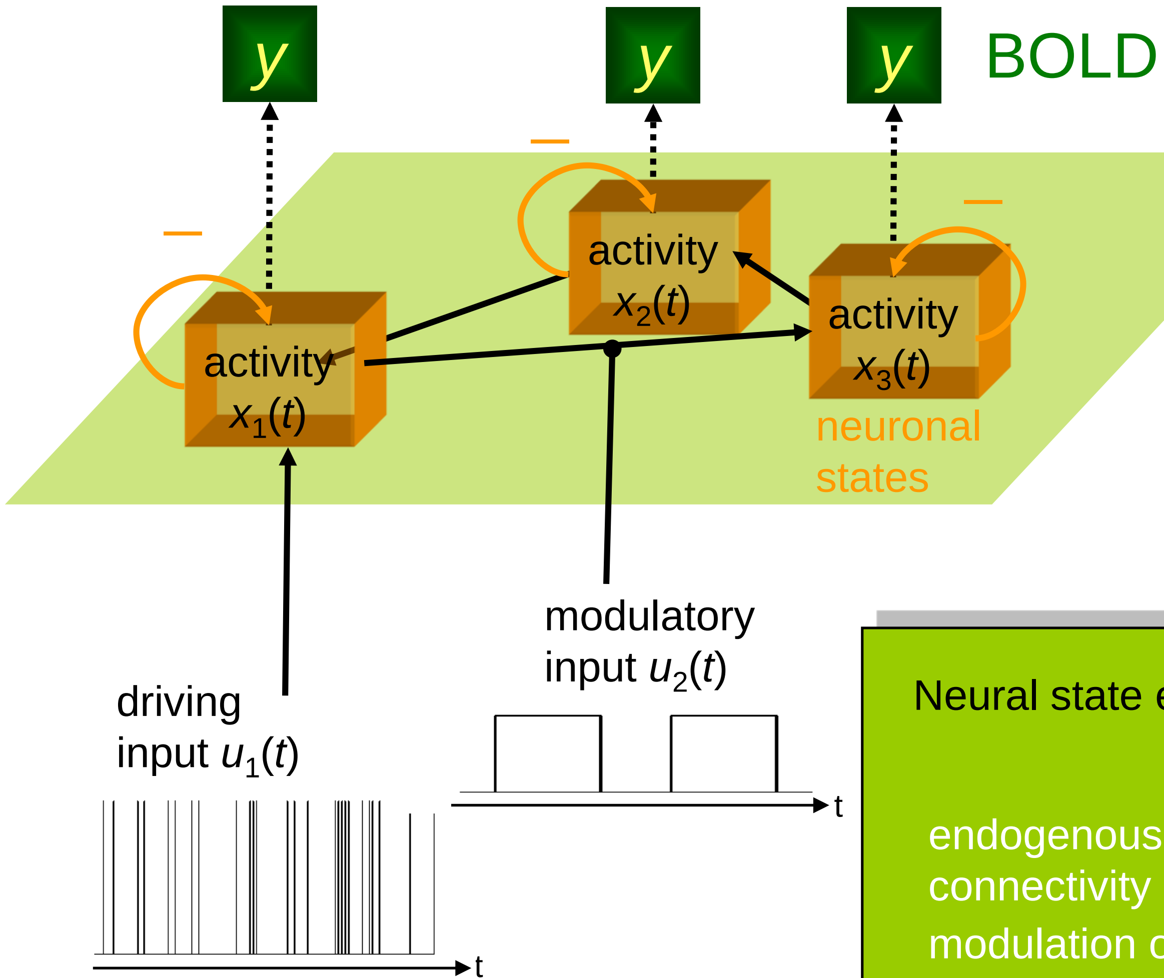
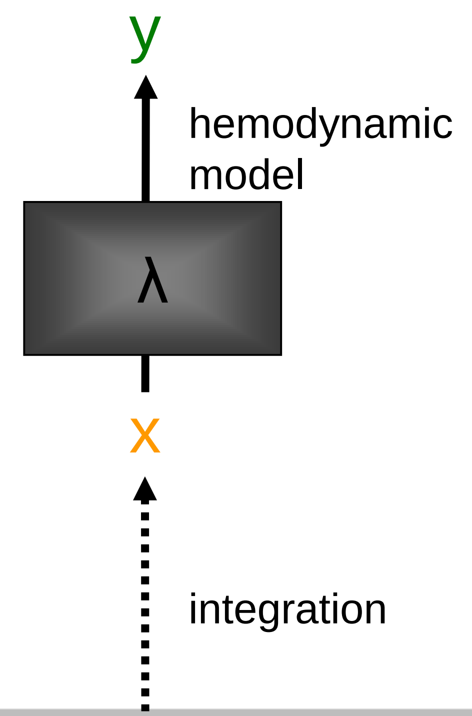
Dynamic causal modelling - DCM





Neural state equation $\dot{x} = (A + \sum u_j B^{(j)})x + Cu$

endogenous connectivity → $A = \frac{\partial \dot{x}}{\partial x}$

modulation of connectivity → $B^{(j)} = \frac{\partial}{\partial u_j} \frac{\partial \dot{x}}{\partial x}$

direct inputs → $C = \frac{\partial \dot{x}}{\partial u}$

The classical DCM:
a deterministic, one-state, bilinear model

Source: Klaas Enno Stephan, Zurich SPM Course 2014

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DCM - Bilinear state equation

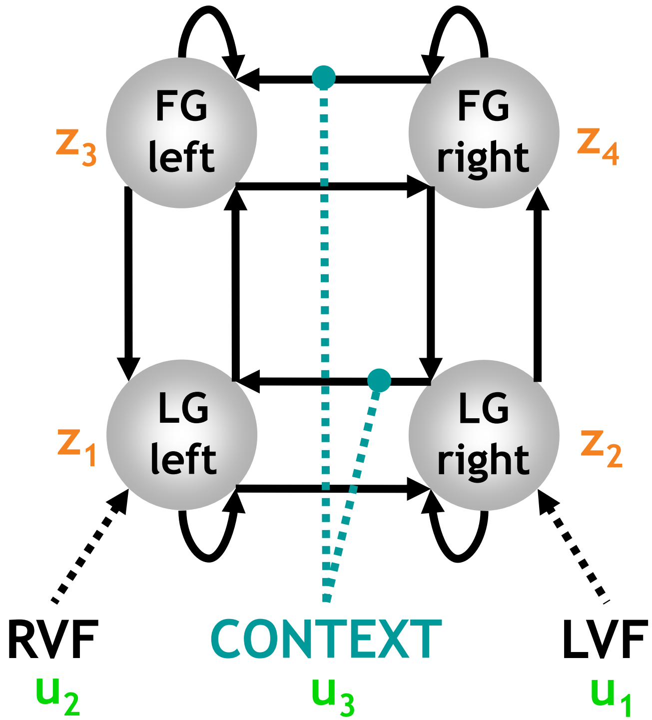
state changes | intrinsic connectivity | modulation of connectivity | system state | direct inputs | *m* external inputs

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

$$
\dot{z} = (A + \sum_{j=1}^{m} u_j B^{j}) z + Cu \Longrightarrow \theta^{n} = \{A, B^{1} \ldots B^{m}, C\}
$$

Source: Klaas Enno Stephan, Connectivity Workshop Melbourne, 2005

DCM - Bilinear state equation



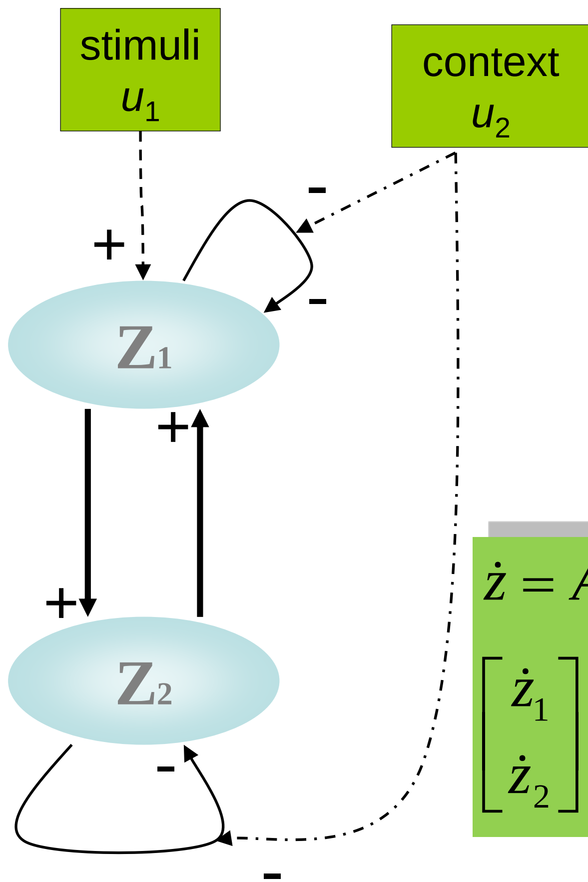
$$\dot{z} = (A + \sum_{j=1}^{m} u_j B^j) z + Cu$$

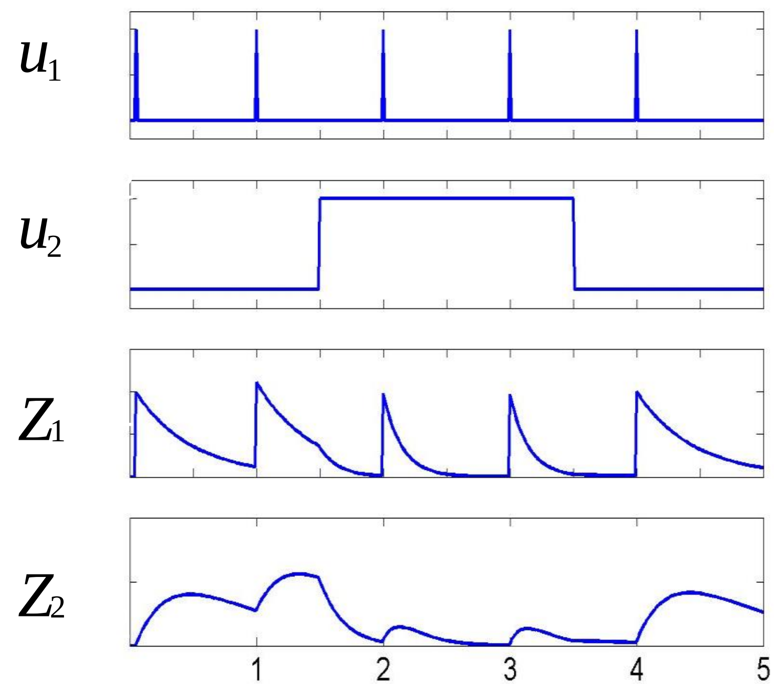
$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \\ \dot{z}_3 \\ \dot{z}_4 \end{bmatrix} = \left\{ \begin{bmatrix} a_{11} & a_{12} & a_{13} & 0 \\ a_{21} & a_{22} & 0 & a_{24} \\ a_{31} & 0 & a_{33} & a_{34} \\ 0 & a_{42} & a_{43} & a_{44} \end{bmatrix} + u_3 \begin{bmatrix} 0 & b_{12}^3 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & b_{34}^3 \\ 0 & 0 & 0 & 0 \end{bmatrix} \right\} \begin{bmatrix} z_1 \\ z_2 \\ z_3 \\ z_4 \end{bmatrix} + \begin{bmatrix} 0 & c_{12} & 0 \\ c_{21} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} u_1 \\ u_2 \\ u_3 \end{bmatrix}$$

Source: Klaas Enno Stephan, Connectivity Workshop Melbourne, 2005

DCM - Bilinear state equation

Example:
generated neural data





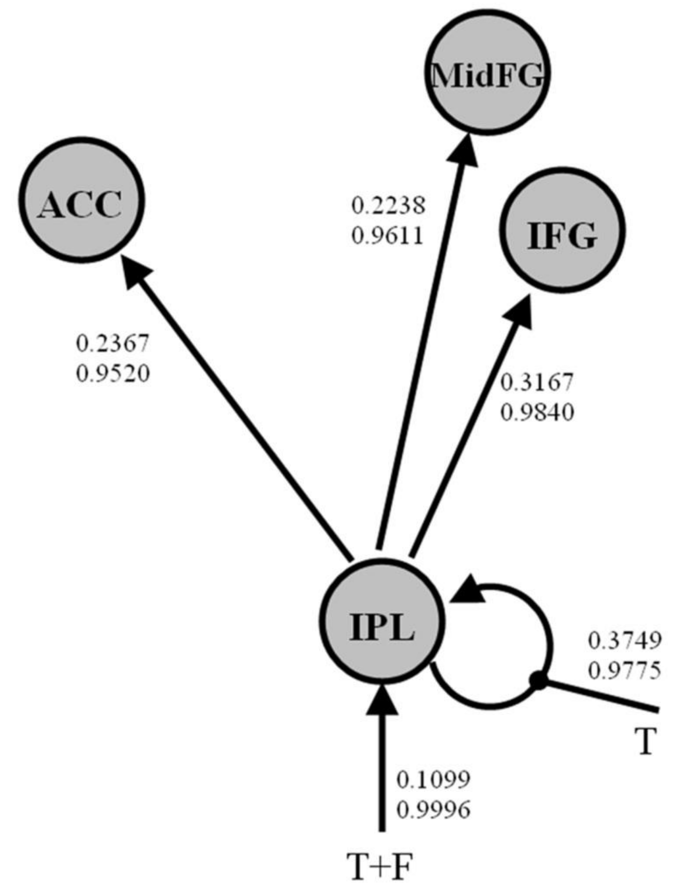
$$\dot{z} = Az + u_2 B^2 z + Cu_1$$

$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = \begin{bmatrix} \sigma & a_{12} \\ a_{21} & \sigma \end{bmatrix} z + u_2 \begin{bmatrix} b^2_{11} & 0 \\ 0 & b^2_{22} \end{bmatrix} z + \begin{bmatrix} c_1 & 0 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$$

Source: Klaas Enno Stephan, Connectivity Workshop Melbourne, 2005

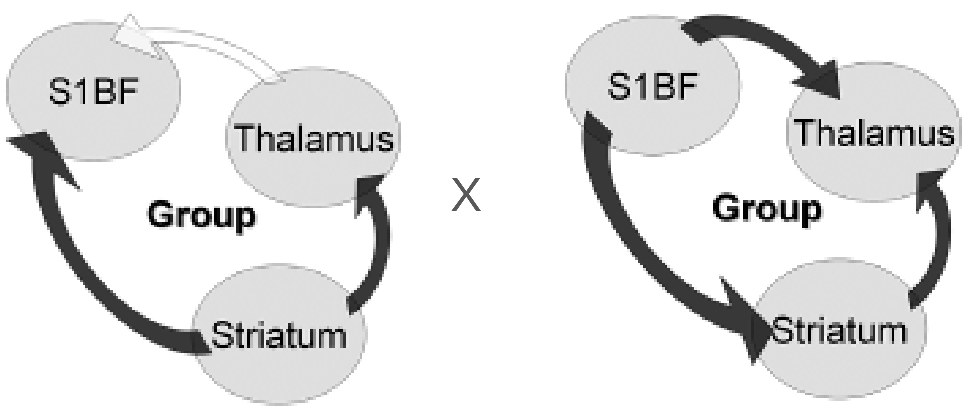
Dynamic causal modelling - DCM

- Not exploratory
- For testing very specific hypotheses (need to be precisely specified)
- Estimation of parameters – EM algorithm with priors
- Finally are estimated posterior probabilities, concerning if connection strengths are stronger than selected threshold



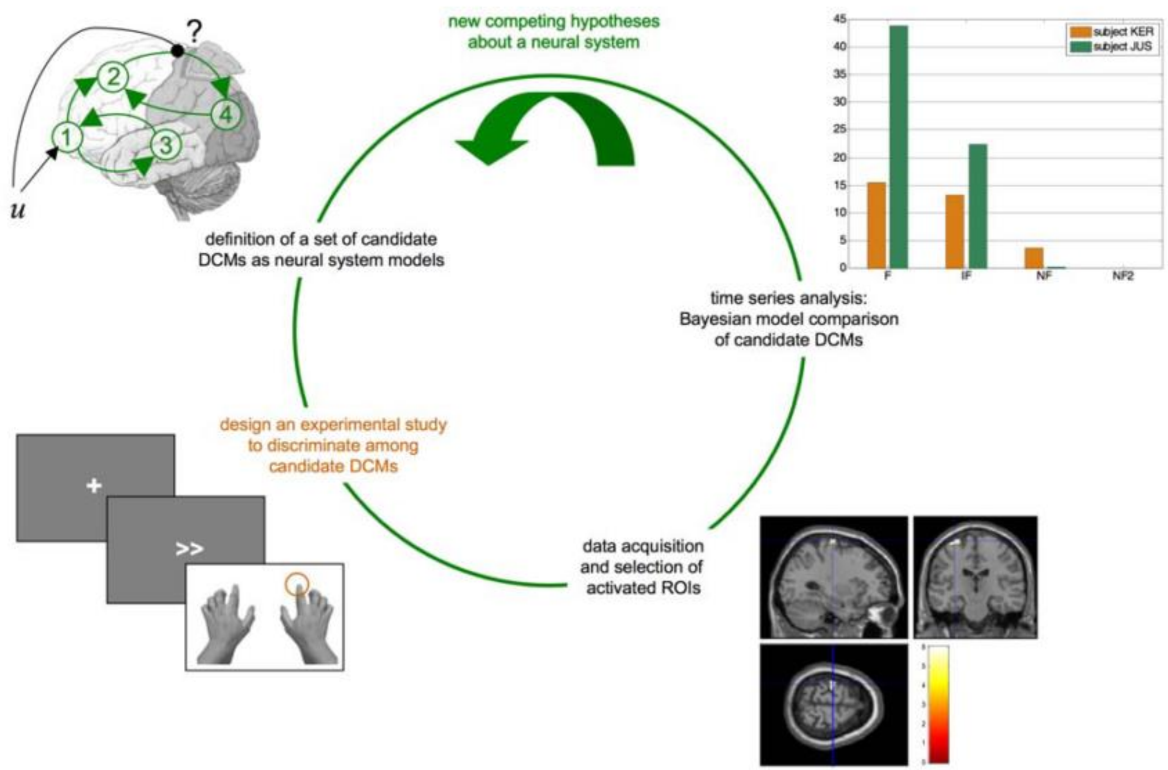
Dynamic causal modelling - DCM

- Hypotheses for testing:
- **Significance of specified connections** (explained by posterior probability)
- Comparison of **suitability of several specified models** with differences are in structure and allowed connections. Most suitable model is selected by Bayesian selection (BMS).



DCM – planning a study

- DCM can be applied to most datasets analysed using a GLM.



- BUT! there are certain parameters that can be optimised for a DCM study. (Daunizeau, J. et al (2011). Optimizing experimental design for comparing models of brain function.)

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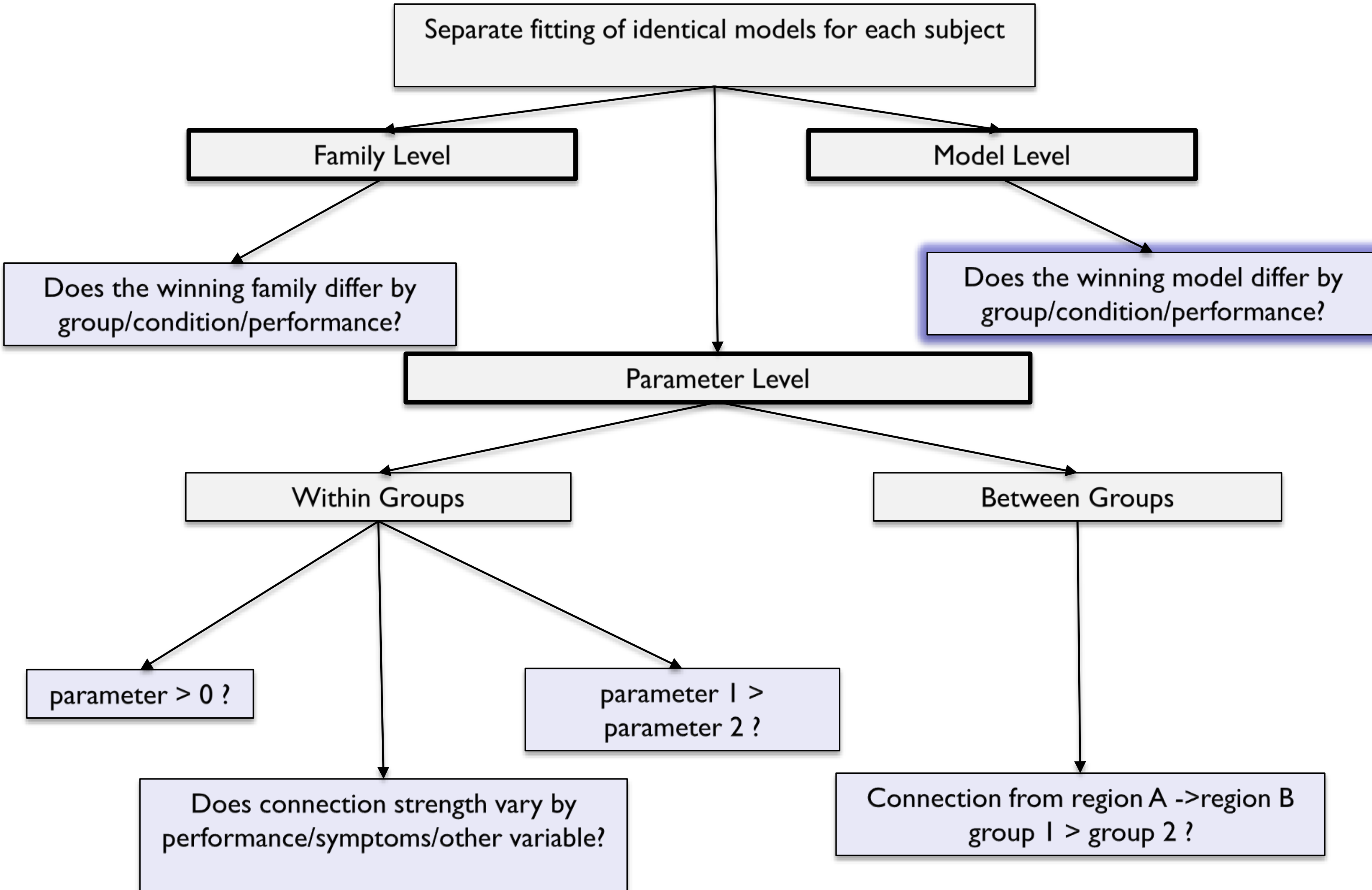
DCM – analysis

1. Define your contrast (e.g. task vs. rest) and extract the time-series for the areas of interest.
   - The areas need to be the same for all subjects.
   - There needs to be significant activation in the areas that you extract - DCM predicts responses to experimental manipulations
2. Defining the model space - depend largely on your hypotheses
3. Model Estimation
4. Inference

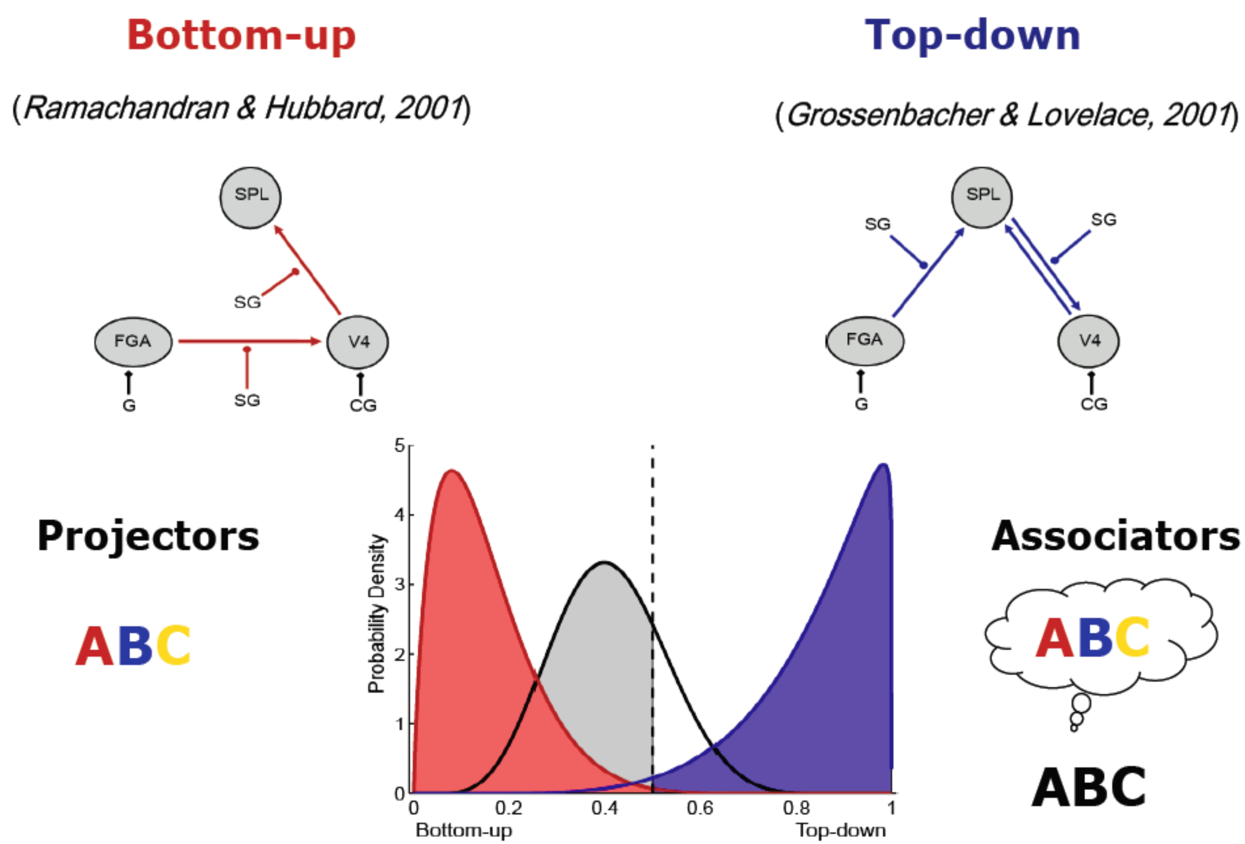
DCM – analysis



Source: Klaas Enno Stephan, Zurich SPM Course 2014

DCM application

- Classification of two patients groups with synesthesia graph – color (perception of one evokes sensation of different sense)



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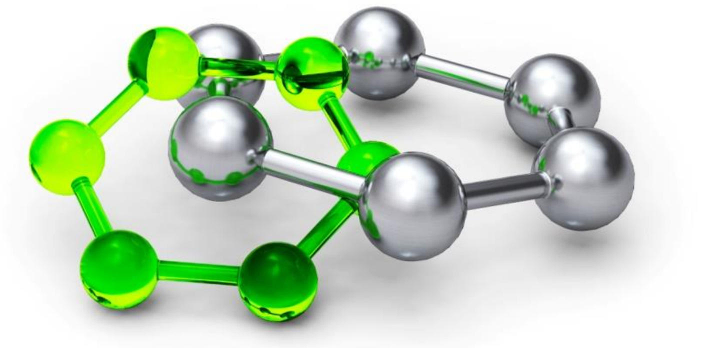

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