Dynamic Causal Modelling (DCM)

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With Thanks to and Slides from

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System analyses in functional neuroimaging

Analyses of regionally specific effects: which areas constitute a neuronal system?

= the temporal correlation between spatially remote neurophysiological events

Analyses of inter-regional effects: what are the interactions between the elements of a given neuronal system?

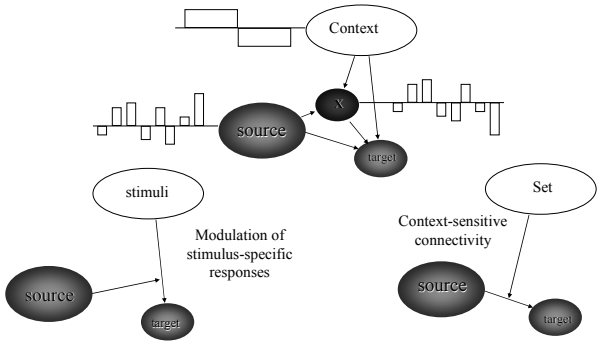
= the influence that the elements of a neuronal system exert over another

MODEL-dependent

[redacted]

- **Functional Connectivity**
  - Eigenimage analysis and PCA
  - Nonlinear PCA
  - ICA
- **Effective Connectivity**
  - Psychophysiological Interactions
  - MAR and State space Models
  - Structure Equation Models
  - Volterra Models
  - Dynamic Causal Models

Psychophysiological interactions



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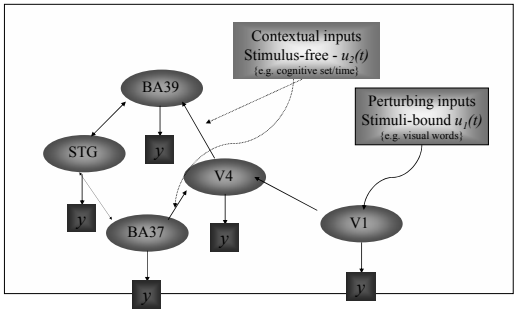
Overview

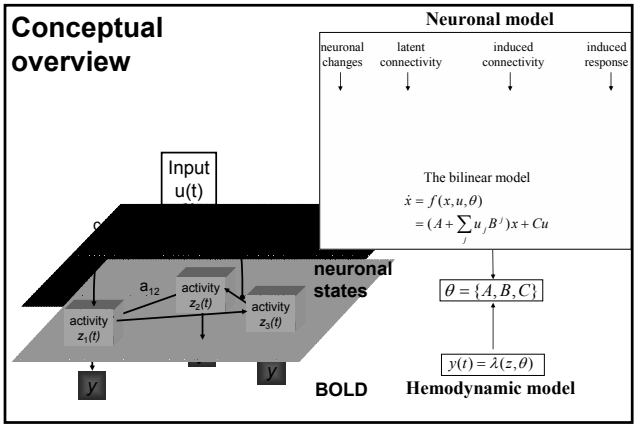
- DCM – Conceptual overview
- Neural and hemodynamic levels in DCM
- Parameter estimation
  - Priors in DCM
  - Bayesian parameter estimation in non-linear systems
- Interpretation of parameters
- Bayesian model selection
- Practical steps of a DCM study
- Example: attention to visual motion

The aim

Functional integration and the modulation of specific pathways



Conceptual overview



Conceptual overview

Models of
•Responses in a single region
•Neuronal interactions

Constraints on
•Connections
•Biophysical parameters

$$p(y \mid \theta) \qquad p(\theta)$$

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

Bayesian estimation

posterior ∝ likelihood · prior

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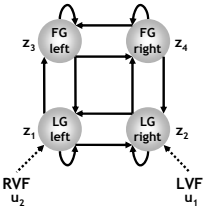
Example: linear dynamic system



LG = lingual gyrus
FG = fusiform gyrus

Visual input in the
- left (LVF)
- right (RVF)
visual field.

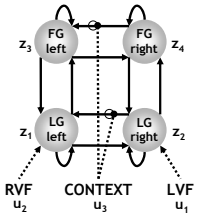
state changes | effective connectivity | system state | input parameters | external inputs

$$\dot{z} = Az + Cu$$

$$\theta = \{A, C\}$$

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

Extension: bilinear dynamic system



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

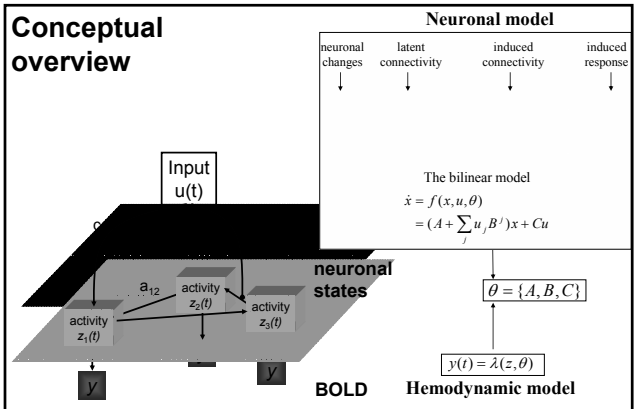
Bilinear state equation in DCM

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

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

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

Conceptual overview



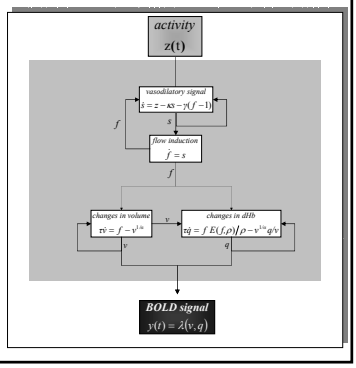
The hemodynamic "Balloon" model

- 5 hemodynamic parameters:

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

important for model fitting, but of no interest for statistical inference

- Empirically determined *prior* distributions.
- Computed separately for each area (like the neural parameters).



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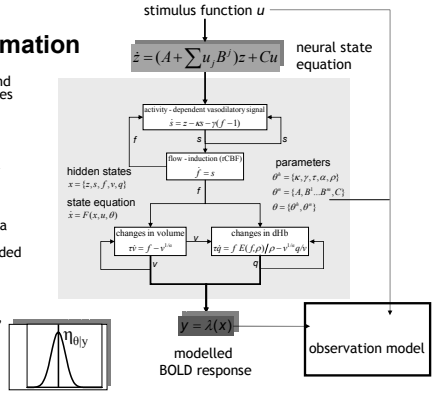
Overview: parameter estimation

- Combining the neural and hemodynamic states gives the complete forward model.
- An observation model includes measurement error e and confounds X (e.g. drift).
- Bayesian parameter estimation by means of a Levenberg-Marquardt gradient ascent, embedded into an EM algorithm.
- Result: Gaussian a posteriori parameter distributions, characterised by mean $\eta_{\theta|y}$ and covariance $C_{\theta|y}$.



Overview: parameter estimation

Models of
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Constraints on
- Connections
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$p(y \mid \theta)$ $\qquad$ $p(\theta)$

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

posterior $\propto$ likelihood $\cdot$ prior

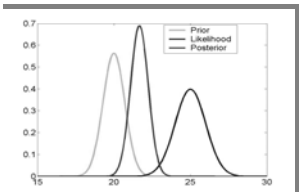
Bayesian estimation

Priors in DCM

Bayes Theorem

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

posterior ∝ likelihood · prior



- needed for Bayesian estimation, embody constraints on parameter estimation
- express our prior knowledge or "belief" about parameters of the model
- hemodynamic parameters: empirical priors
- temporal scaling: principled prior
- coupling parameters: shrinkage priors

Priors in DCM

- Principled priors:
  - System stability: in the absence of input, the neuronal states must return to a stable mode
  - Constraints on prior variance of intrinsic connections (A): Probability <0.001 of obtaining a non-negative Lyapunov exponent (largest real eigenvalue of the intrinsic coupling matrix)
  - Self-inhibition: Priors on the decay rate constant σ ($\eta\sigma$=1, $C\sigma$=0.105); these allow for neural transients with a half life in the range of 300 ms to 2 seconds

- Shrinkage priors for coupling parameters (η=0) → conservative estimates!

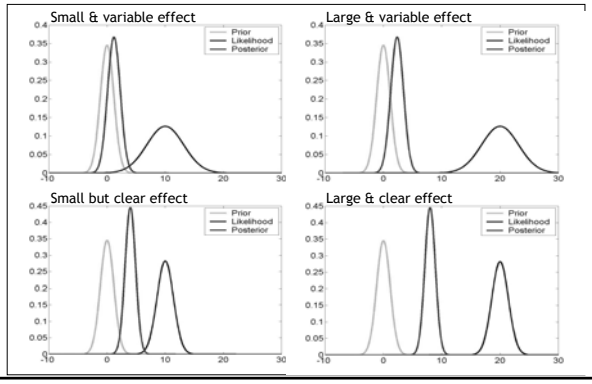
$$\theta = \begin{bmatrix} \sigma \\ a_{ij} \\ b_{ij}^k \\ c_{ik} \\ \theta^h \end{bmatrix}, \quad \eta_\theta \rightarrow \begin{bmatrix} 1 \\ 0 \\ 0 \\ 0 \\ \eta_\theta \end{bmatrix}, \quad C_\theta = \begin{bmatrix} 0.105 & \cdots & 0 \\ & C_A & \\ \vdots & & C_B \quad \vdots \\ & & 1 \\ 0 & \cdots & C_h \end{bmatrix}$$

$$A \rightarrow \sigma A = \sigma \begin{bmatrix} -1 & a_{12} & \cdots \\ a_{21} & -1 & \\ \vdots & & \ddots \end{bmatrix}$$

- Temporal scaling:

  Identical in all areas by factorising A and B with σ (a single rate constant for all regions) : all connection strengths are relative to the self-connections.

Shrinkage Priors



Bayesian estimation: univariate Gaussian case

Normal densities

$$p(\theta) = N(\theta; \eta_p, \sigma_p^2)$$

$$p(y \mid \theta) = N(y; \theta x, \sigma_e^2)$$

$$p(\theta \mid y) = N(\theta; \eta_{\theta|y}, \sigma_{\theta|y}^2)$$

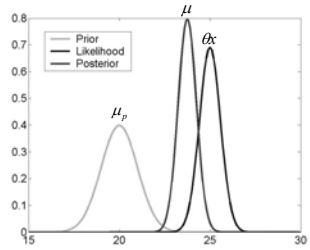
$$\frac{1}{\sigma_{\theta|y}^2} = \frac{x^2}{\sigma_e^2} + \frac{1}{\sigma_p^2}$$

$$\eta_{\theta|y} = \sigma_{\theta|y}^2 \left(\frac{x}{\sigma_e^2} y + \frac{1}{\sigma_p^2} \eta_p \right)$$

Relative precision weighting

Univariate linear model

$$y = \theta x + e$$



Bayesian estimation: multivariate Gaussian case

Normal densities

$$p(\boldsymbol{\theta}) = N(\boldsymbol{\theta}; \boldsymbol{\eta}_p, \mathbf{C}_p)$$

$$p(\mathbf{y} \mid \boldsymbol{\theta}) = N(\mathbf{y}; \mathbf{X}\boldsymbol{\theta}, \mathbf{C}_e)$$

$$p(\boldsymbol{\theta} \mid y) = N(\boldsymbol{\theta}; \boldsymbol{\eta}_{\theta|y}, \mathbf{C}_{\theta|y})$$

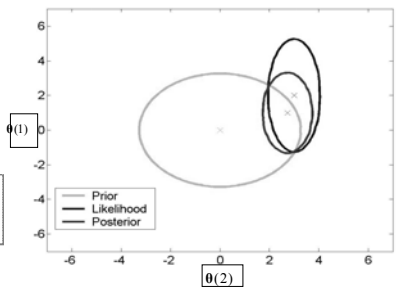
$$\mathbf{C}_{\theta|y}^{-1} = \mathbf{X}^T \mathbf{C}_e^{-1} \mathbf{X} + \mathbf{C}_p^{-1}$$

$$\boldsymbol{\eta}_{\theta|y} = \mathbf{C}_{\theta|y} \left(\mathbf{X}^T \mathbf{C}_e \mathbf{y} + \mathbf{C}_p^{-1} \boldsymbol{\eta}_p \right)$$

One step if $\mathbf{C}_e$ is known.

General Linear Model

$$\mathbf{y} = \mathbf{X}\boldsymbol{\theta} + \mathbf{e}$$



Bayesian estimation: nonlinear case

Local linearization by 1st order Taylor:

$$\mathbf{y} = h(\boldsymbol{\theta}) + \mathbf{e}$$

$$h(\boldsymbol{\theta}) = h(\boldsymbol{\eta}_{\theta|y}^i) + \frac{\partial h(\boldsymbol{\eta}_{\theta|y}^i)}{\partial \boldsymbol{\theta}} (\boldsymbol{\theta} - \boldsymbol{\eta}_{\theta|y}^i)$$

$$\mathbf{J} = \frac{\partial h(\boldsymbol{\eta}_{\theta|y}^i)}{\partial \boldsymbol{\theta}}$$

$$\Delta\boldsymbol{\theta} = \boldsymbol{\theta} - \boldsymbol{\eta}_{\theta|y}^i$$

$$\mathbf{r}^i = \mathbf{y} - h(\boldsymbol{\eta}_{\theta|y}^i) = \mathbf{J}\Delta\boldsymbol{\theta} + e$$

Current estimates

$$\boldsymbol{\eta}_{\theta|y}^i, \mathbf{C}_{\theta|y}^i$$

Prior density

$$p(\boldsymbol{\theta}) = N(\boldsymbol{\theta}; \boldsymbol{\eta}_p, \mathbf{C}_p)$$

$$p(\Delta\boldsymbol{\theta}) = N(\Delta\boldsymbol{\theta}; \boldsymbol{\eta}_p - \boldsymbol{\eta}_{\theta|y}^i, \mathbf{C}_p)$$

Likelihood

$$p(\mathbf{y} \mid \boldsymbol{\theta}) = N(\mathbf{y}; h(\boldsymbol{\theta}), \mathbf{C}_e)$$

$$p(\mathbf{r} \mid \Delta\boldsymbol{\theta}) = N(\mathbf{r}; \mathbf{J}\Delta\boldsymbol{\theta}, \mathbf{C}_e)$$

Gradient ascent (Fisher scoring) with priors

$$(\mathbf{C}_{\theta|y}^{i+1})^{-1} = \mathbf{J}^T \mathbf{C}_e^{-1} \mathbf{J} + \mathbf{C}_p^{-1}$$

$$\boldsymbol{\eta}_{\theta|y}^{i+1} = \boldsymbol{\eta}_{\theta|y}^i + \mathbf{C}_{\theta|y}^{i+1} \left(\mathbf{J}^T \mathbf{C}_e^{-1} \mathbf{r} + \mathbf{C}_p^{-1} \left(\boldsymbol{\eta}_p - \boldsymbol{\eta}_{\theta|y}^i \right) \right)$$

Friston (2002) Neuroimage, 16: 513-530.

EM and gradient ascent

- Bayesian parameter estimation by means of expectation maximisation (EM)
  - **E-step:**
    gradient ascent (Fisher scoring & Levenberg-Marquardt regularisation) to compute
    - (i) the conditional mean $\boldsymbol{\eta}_{\theta|y}$ (= expansion point of gradient ascent),
    - (ii) the conditional covariance $\mathbf{C}_{\theta|y}$
  - **M-step:**
    Estimation of hyperparameters $\boldsymbol{\lambda}_i$ for error covariance components $\mathbf{Q}_i$:

$$\mathbf{C}_e = \sum \lambda_i \mathbf{Q}_i$$

- Note: Gaussian assumptions about the posterior (Laplace approximation)

Parameter estimation: output in command window (new)

```
E-Step: 1   F: -1.514001e+003   dp: 8.299907e-002
E-Step: 2   F: -1.200724e+003   dp: 9.638851e-001
E-Step: 3   F: -1.115951e+003   dp: 2.703493e-001
E-Step: 4   F: -1.077757e+003   dp: 2.002973e-002
E-Step: 5   F: -1.075699e+003   dp: 4.219233e-003
E-Step: 6   F: -1.075663e+003   dp: 1.030322e-003
E-Step: 7   F: -1.075661e+003   dp: 3.595806e-004
E-Step: 8   F: -1.075661e+003   dp: 2.273264e-006
```

$$dp = \left\| \Delta\boldsymbol{\theta} \right\|_2$$

Change of the norm of the parameter vector (= magnitude of update)

objective function

$$F = \frac{1}{2}\left(-(\mathbf{y}-h(\boldsymbol{\theta}))^T\mathbf{C}_e^{-1}(\mathbf{y}-h(\boldsymbol{\theta})) - (\boldsymbol{\theta}_{\theta|y}-\boldsymbol{\theta}_p)^T\mathbf{C}_p^{-1}(\boldsymbol{\theta}_{\theta|y}-\boldsymbol{\theta}_p) - \log|\mathbf{C}_e| - \log|\mathbf{C}_p| + \log|\mathbf{C}_{\theta|y}|\right)$$

Parameter estimation in DCM

- Combining the neural and hemodynamic states gives the complete forward model:

$$\begin{aligned} x &= \{z, s, f, v, q\} \\ \theta &= \theta^n + \theta^h \\ \dot{x} &= f(x, u, \theta) \\ y &= \lambda(x) = h(u, \theta) \end{aligned}$$

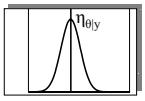
- The observation model includes measurement error ε and confounds X (e.g. drift):

$$y = h(u,\theta) + X\beta + \varepsilon$$

- Bayesian parameter estimation under Gaussian assumptions by means of EM and gradient ascent.

$$y - h(u, \eta_{\theta|y}) \rightarrow \min$$

- Result:
  Gaussian *a posteriori* parameter distributions with mean $\eta_{\theta|y}$ and covariance $C_{\theta|y}$.



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DCM parameters = rate constants

Generic solution to the ODEs in DCM:

$$\frac{dz}{dt} = az \quad \Rightarrow \quad z(t) = \exp(at) + c$$

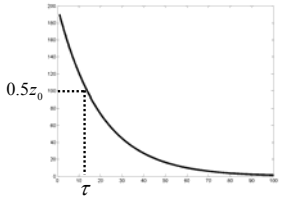
Decay function:

$$z(t) = z_0 \exp(-at)$$

Half-life τ:

$$\begin{aligned} z(\tau) &= 0.5 z_0 \\ &= z_0 \exp(-a\tau) \end{aligned}$$

$$\Rightarrow \quad \boxed{a = \ln 2 / \tau}$$



Interpretation of DCM parameters

- Dynamic model (differential equations)
  → neural parameters correspond to rate constants (inverse of time constants → Hz!)
  → speed at which effects take place

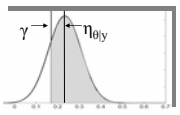
$$\theta^n = \{A, B, C, \sigma\}$$

$$p = \ln 2 / \tau_p$$

- Identical temporal scaling in all areas by factorising A and B with σ:
  all connection strengths are relative to the self-connections.

$$A \rightarrow \sigma A = \sigma \begin{bmatrix} -1 & a_{12} & \cdots \\ a_{21} & -1 & \\ \vdots & & \ddots \end{bmatrix}$$

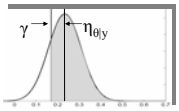
- Each parameter is characterised by the mean ($\eta_{\theta|y}$) and covariance of its *a posteriori* distribution. Its mean can be compared statistically against a chosen threshold γ.



Inference about DCM parameters: single-subject analysis

- Bayesian parameter estimation in DCM: Gaussian assumptions about the *a posteriori* distributions of the parameters
- Use of the cumulative normal distribution to test the probability by which a certain parameter (or contrast of parameters $c^T\eta_{\theta|y}$) is above a chosen threshold γ:

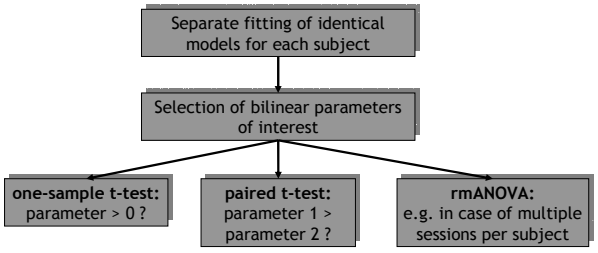
$$p = \phi_N\left(\frac{c^T\eta_{\theta|y} - \gamma}{\sqrt{c^T C_{\theta|y} c}}\right)$$



- γ can be chosen as a function of the expected half life of the neural process, e.g. $\gamma = \ln 2 / \tau$

Inference about DCM parameters: group analysis

- In analogy to "random effects" analyses in SPM, 2nd level analyses can be applied to DCM parameters:



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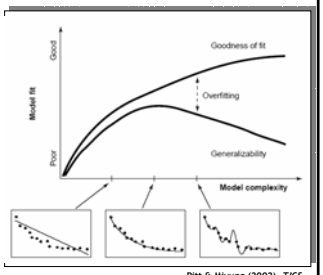
Model comparison and selection

Given competing hypotheses on structure & functional mechanisms of a system, which model is the best?

For which model *i* does $p(y|m_i)$ become maximal?

Which model represents the best balance between model fit and model complexity?



Pitt & Miyung (2002), *TICS*

Bayesian Model Selection

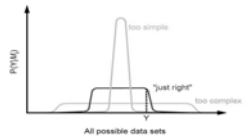
Bayes theorem:

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

Model evidence:

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

Occam's Razor:



Ghahramani, *Unsupervised Learning*, 2004

Bayesian Model Selection

Model evidence:

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

Laplace approximation:

$$F = accuracy(m) - complexity(m)$$
$$= -\frac{1}{2}\log|\mathbf{C}_\varepsilon| - \frac{1}{2}(\mathbf{y} - h(\boldsymbol{\theta}))^T \mathbf{C}_\varepsilon^{-1}(\mathbf{y} - h(\boldsymbol{\theta}))$$
$$-\frac{1}{2}(\boldsymbol{\theta}_{\theta|y} - \boldsymbol{\theta}_p)^T \mathbf{C}_p^{-1}(\boldsymbol{\theta}_{\theta|y} - \boldsymbol{\theta}_p) - \frac{1}{2}\log|\mathbf{C}_p| + \frac{1}{2}\log|\mathbf{C}_{\theta|y}|$$

The log model evidence can be represented as:

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

Approximations to model evidence

Bayesian information criterion (BIC):

$$BIC(y \mid m) = accuracy(m) - \frac{p}{2}\log N_S$$

Akaike information criterion (AIC):

$$AIC(y \mid m) = accuracy(m) - p$$

Bayes factor:

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

Penny et al. 2004, *NeuroImage*

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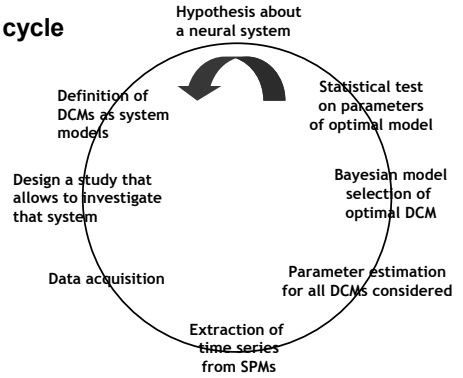
The DCM cycle

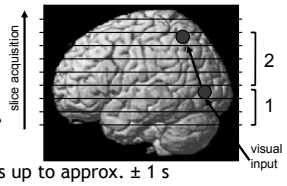


Planning a DCM-compatible study

- Suitable experimental design:
  - preferably multi-factorial (e.g. 2 x 2)
  - e.g. one factor that varies the driving (sensory) input
  - and one factor that varies the contextual input
- Hypothesis and model:
  - define specific *a priori* hypothesis
  - Which alternative models?
  - which parameters are relevant to test this hypothesis?
- TR:
  - as short as possible (optimal: < 2 s)

Timing problems at long TRs

- Two potential timing problems in DCM:
  1. wrong timing of inputs
  2. temporal shift between regional time series because of multi-slice acquisition
- DCM is robust against timing errors up to approx. ± 1 s
  - compensatory changes of σ and θ^h
- Possible corrections:
  - restriction of the model to neighbouring regions
  - in both cases: adjust temporal reference bin in SPM defaults (defaults.stats.fmri.t0)



Practical steps of a DCM study - I

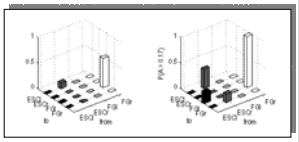
1. Conventional SPM analysis (subject-specific)
   - DCMs are fitted separately for each session
     → consider concatenation of sessions or adequate 2nd level analysis
2. Extraction of time series, e.g. via VOI tool in SPM
   - cave: anatomical & functional standardisation important for group analyses!

Practical steps of a DCM study - II

3. Possibly definition of a new design matrix, if the "normal" design matrix does not represent the inputs appropriately.
   - NB: DCM only reads timing information of each input from the design matrix, no parameter estimation necessary.
4. Definition of model
   - via DCM-GUI or directly in MATLAB

Practical steps of a DCM study - III

5. DCM parameter estimation
   - cave: models with many regions & scans can crash MATLAB!
6. Model comparison and selection:
   - Which of all models considered is the optimal one?
     → Bayesian model selection tool
7. Testing the hypothesis
   Statistical test on the relevant parameters of the optimal model



Overview

- DCM – Conceptual overview
- Neural and hemodynamic levels in DCM
- Parameter estimation
  - Priors in DCM
  - Bayesian parameter estimation in non-linear systems
- Interpretation of parameters
- Bayesian model selection
- Practical steps of a DCM study
- Example: attention to visual motion

Attention to motion in the visual system

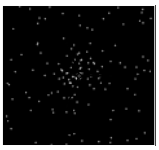
Stimuli 250 radially moving dots at 4.7 degrees/s

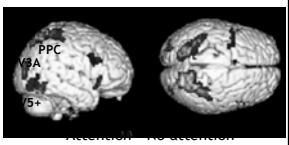
Pre-Scanning
5 x 30s trials with 5 speed changes (reducing to 1%)
Task - detect change in radial velocity

Scanning (no speed changes)
6 normal subjects, 4 x 100 scan sessions;
each session comprising 10 scans of 4 different conditions

F A F N F A F N S .....

F - fixation point only
A - motion stimuli with attention (detect changes)
N - motion stimuli without attention
S - no motion





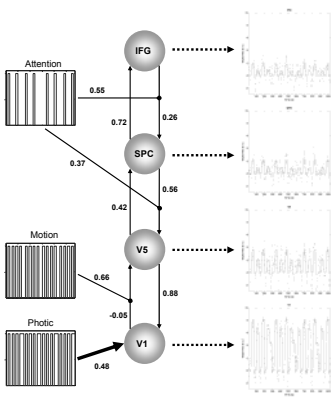
Attention – No attention

Büchel & Friston 1997, Cereb. Cortex
Büchel et al. 1998, Brain

A simple DCM of the visual system

- Visual inputs drive V1, activity then spreads to hierarchically arranged visual areas.
- Motion modulates the strength of the V1→V5 forward connection.
- The intrinsic connection V1→V5 is insignificant in the absence of motion (a_{21}=-0.05).
- Attention increases the backward-connections IFG→SPC and SPC→V5.

Re-analysis of data from Friston et al., NeuroImage 2003

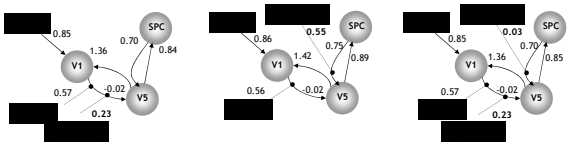


Comparison of three simple models

Model 1:
attentional modulation of V1→V5

Model 2:
attentional modulation of SPC→V5

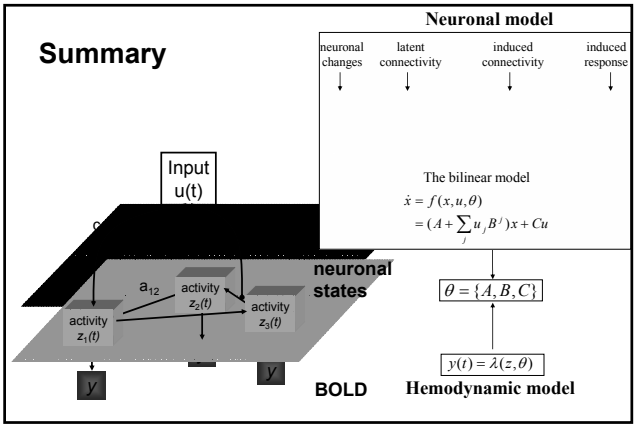
Model 3:
attentional modulation of V1→V5 and SPC→V5



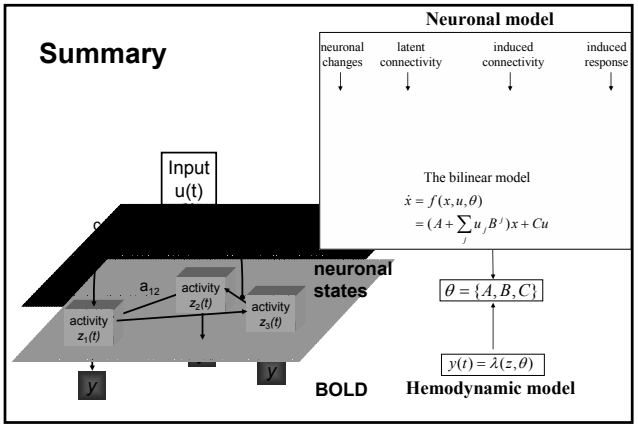
Bayesian model selection: Model 1 better than model 2, model 1 and model 3 equal

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

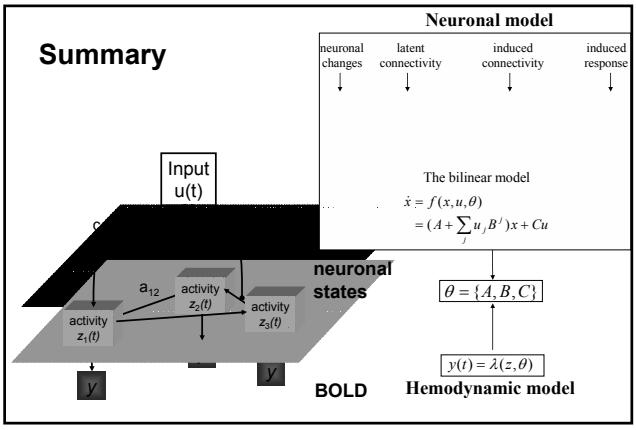
Summary



Summary

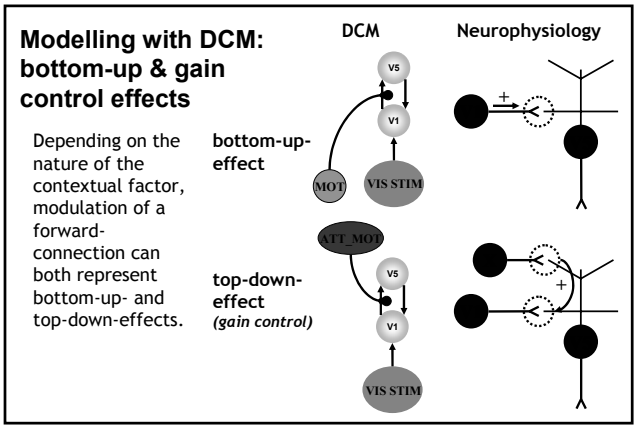


Summary



Modelling with DCM: bottom-up & gain control effects

Depending on the nature of the contextual factor, modulation of a forward-connection can both represent bottom-up- and top-down-effects.



Modelling with DCM: baseline shifts

Model A:
tests the existence of a baseline shift (BS) under ATT_MOT in V5

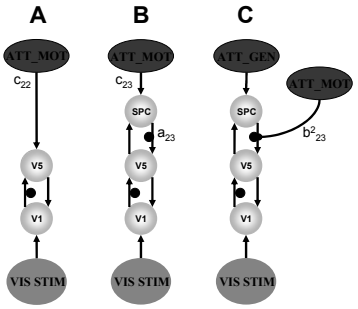
Hypothesis: $c_{22} > \gamma$

Model B:
tests whether there is a BS under ATT_MOT in SPC that is conveyed to V5 via the backward connection

Hypothesis: $c_{23} > \gamma_1$, $a_{23} > \gamma_2$

Model C:
tests whether a general attentional BS occurs in SPC that is conveyed to V5 via the backward connection during ATT_MOT

Hypothesis: $b^2_{23} > \gamma$



VIS STIM = visual stimuli (u_1)
ATT_MOT = attention to motion (u_2)
ATT_GEN = general attention of arbitrary modality (u_3)
γ = chosen statistical threshold