Dynamic Causal Modelling for fMRI

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Overview

Brain connectivity: types & definitions

- Anatomical connectivity
- Functional connectivity
- Effective connectivity

Dynamic causal models (DCMs)

- Neuronal model
- Hemodynamic model

Estimation: Bayesian framework

Applications & extensions of DCM to fMRI data
Principles of Organisation

Functional specialization

Functional integration
Structural, functional & effective connectivity

- **anatomical/structural connectivity**
  = presence of axonal connections

- **functional connectivity**
  = statistical dependencies between regional time series

- **effective connectivity**
  = causal (directed) influences between neurons or neuronal populations

Sporns 2007, Scholarpedia
Anatomical connectivity

**Definition:**

*presence of axonal connections*

- neuronal communication via synaptic contacts
- Measured with
  - tracing techniques
  - diffusion tensor imaging (DTI)
Knowing anatomical connectivity is not enough...

- Context-dependent recruiting of connections:
  - Local functions depend on network activity

- Connections show synaptic plasticity
  - Change in the structure and transmission properties of a synapse
  - Even at short timescales

→ Look at functional and effective connectivity
Functional connectivity

*Definition: statistical dependencies between regional time series*

- Seed voxel correlation analysis
- Coherence analysis
- Eigen-decomposition (PCA, SVD)
- Independent component analysis (ICA)
- any technique describing statistical dependencies amongst regional time series
Seed-voxel correlation analyses

• hypothesis-driven choice of a seed voxel
• extract reference time series
• voxel-wise correlation with time series from all other voxels in the brain
Pros & Cons of functional connectivity analysis

• Pros:
  – useful when we have no experimental control over the system of interest and no model of what caused the data (e.g. sleep, hallucinations, etc.)

• Cons:
  – interpretation of resulting patterns is difficult / arbitrary
  – no mechanistic insight
  – usually suboptimal for situations where we have a priori knowledge / experimental control

→ Effective connectivity
Effective connectivity

Definition: **causal** (directed) influences between neurons or neuronal populations

- *In vivo* and *in vitro* stimulation and recording

- Models of causal interactions among neuronal populations
  - explain *regional effects* in terms of *interregional connectivity*
Some models for computing effective connectivity from fMRI data

- Structural Equation Modelling (SEM)
  McIntosh et al. 1991, 1994; Büchel & Friston 1997; Bullmore et al. 2000

- regression models
  (e.g. psycho-physiological interactions, PPIs)
  Friston et al. 1997

- Volterra kernels
  Friston & Büchel 2000

- Time series models (e.g. MAR, Granger causality)
  Harrison et al. 2003, Goebel et al. 2003

- Dynamic Causal Modelling (DCM)
  \textit{bilinear}: Friston et al. 2003; \textit{nonlinear}: Stephan et al. 2008
• bilinear model of how the psychological context $A$ changes the influence of area $B$ on area $C$:

$$B \times A \rightarrow C$$

• A PPI corresponds to differences in regression slopes for different contexts.
Pros & Cons of PPIs

• Pros:
  – given a single source region, we can test for its context-dependent connectivity across the entire brain
  – easy to implement

• Cons:
  – only allows to model contributions from a single area
  – operates at the level of BOLD time series (SPM 99/2).
    SPM 5/8 deconvolves the BOLD signal to form the proper interaction term, and then reconvolves it.
  – ignores time-series properties of the data

*Dynamic Causal Models*

needed for more robust statements of effective connectivity.
Overview

Brain connectivity: types & definitions
- Anatomical connectivity
- Functional connectivity
- Effective connectivity

Dynamic causal models (DCMs)
- Basic idea
- Neuronal model
- Hemodynamic model
- Parameter estimation, priors & inference

Applications & extensions of DCM to fMRI data
DCM allows us to look at how areas within a network interact:

Investigate functional integration & modulation of specific cortical pathways

- Temporal dependency of activity within and between areas (causality)
Temporal dependence and causal relations

Seed voxel approach, PPI etc.

Dynamic Causal Models

timeseries (neuronal activity)
Basics of Dynamic Causal Modelling

DCM allows us to look at how areas within a network interact:

Investigate functional integration & modulation of specific cortical pathways

- Temporal dependency of activity within and between areas (causality)
- Separate neuronal activity from observed BOLD responses
Cognitive system is modelled at its underlying neuronal level (not directly accessible for fMRI).

The modelled neuronal dynamics \( Z \) are transformed into area-specific BOLD signals \( y \) by a hemodynamic model \( \lambda \).

The aim of DCM is to estimate parameters at the neuronal level such that the modelled and measured BOLD signals are optimally similar.
Neuronal systems are represented by differential equations.

A System is a set of elements \( z_n(t) \) which interact in a spatially and temporally specific fashion.

State changes of the system states are dependent on:
- the current state \( z \)
- external inputs \( u \)
- its connectivity \( \theta \)
- time constants & delays

\[
\frac{dz}{dt} = F(z, u, \theta)
\]
DCM parameters = rate constants

Generic solution to the ODEs in DCM:

\[
\frac{dz_1}{dt} = -sz_1
\]

\[z_1(t) = z_1(0) \exp(-st), \quad z_1(0) = 1\]

Half-life \(\tau\)

\[z_1(\tau) = 0.5 z_1(0) = z_1(0) \exp(-s\tau)\]

\[s = \ln 2 / \tau\]

Decay function

\[\tau = \ln 2 / s\]
DCM parameters = rate constants

Generic solution to the ODEs in DCM:

\[
\frac{dz_1}{dt} = -sz_1 \quad \Rightarrow \quad z_1(t) = z_1(0) \exp(-st), \quad z_1(0) = 1
\]

If A→B is 0.10 s\(^{-1}\) this means that, per unit time, the increase in activity in B corresponds to 10% of the activity in A.
Linear dynamics: 2 nodes

\[ \dot{z}_1 = -sz_1 \]
\[ \dot{z}_2 = s(a_{21}z_1 - z_2) \]

\[ z_1(0) = 1 \]
\[ z_2(0) = 0 \]

\[ z_1(t) = \exp(-st) \]
\[ z_2(t) = sa_{21}t \exp(-st) \]

\[ a_{21} > 0 \]
Neurodynamics: 2 nodes with input

\[
\begin{bmatrix}
\dot{z}_1 \\
\dot{z}_2
\end{bmatrix}
= \begin{bmatrix}
-1 & 0 \\
a_{21} & -1
\end{bmatrix}
\begin{bmatrix}
z_1 \\
z_2
\end{bmatrix}
+ \begin{bmatrix}
c
0
\end{bmatrix} u_1
\]

where \( a_{21} > 0 \)

activity in \( z_2 \) is coupled to \( z_1 \) via coefficient \( a_{21} \)
Neurodynamics: positive modulation

\[
\begin{bmatrix}
\dot{z}_1 \\
\dot{z}_2 \\
\end{bmatrix} = s \begin{bmatrix}
-1 & 0 \\
0 & -1 \\
\end{bmatrix} \begin{bmatrix}
z_1 \\
z_2 \\
\end{bmatrix} + u_2 \begin{bmatrix}
0 & 0 \\
b_{21}^2 & 0 \\
0 & 0 \\
\end{bmatrix} \begin{bmatrix}
z_1 \\
z_2 \\
\end{bmatrix} + \begin{bmatrix}
c \\
0 \\
\end{bmatrix} u_1
\]

modulatory input \( u_2 \) activity through the coupling \( a_{21} \)

index, not squared

\( b_{21}^2 > 0 \)
Neurodynamics: reciprocal connections

\[
\begin{bmatrix}
\dot{z}_1 \\
\dot{z}_2
\end{bmatrix} =
\begin{bmatrix}
-1 & a_{12} \\
{a}_{21} & -1
\end{bmatrix}
\begin{bmatrix}
z_1 \\
z_2
\end{bmatrix}
+ u_2
\begin{bmatrix}
0 & 0 \\
0 & b_{21}
\end{bmatrix}
\begin{bmatrix}
z_1 \\
z_2
\end{bmatrix}
+ c
\begin{bmatrix}
u_1
\end{bmatrix}
\]

reciprocal connection disclosed by \( u_2 \)

\( a_{12}, a_{21}, b_{21}^2 > 0 \)
Haemodynamics: reciprocal connections

$h(u, \theta)$ represents the BOLD response (balloon model) to input
Haemodynamics: reciprocal connections

\[ y = h(u, \theta) + e \]

\( y \) represents simulated observation of BOLD response, i.e. includes noise.
Bilinear state equation in DCM for fMRI

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

\[\dot{z} = (A + \sum_{j=1}^{m} u_j B^j) z + Cu\]
Neuronal state equation: \( \dot{z} = F(z, u, \theta^n) \)

The bilinear model: \( \dot{z} = (A + \sum u_j B^j) z + C u \)

- effective connectivity
- modulation of connectivity
- direct inputs

Friston et al. 2003, *NeuroImage*
The hemodynamic “Balloon” model

Friston et al. 2000, *NeuroImage*
Stephan et al. 2007, *NeuroImage*
DCM roadmap

- Neuronal dynamics
- Hemodynamics
- State space Model
- Model inversion using Expectation-maximization
- Priors
- fMRI data
- Posterior densities of parameters
- Model selection
Estimation: Bayesian framework

Models of
• Haemodynamics in a single region
• Neuronal interactions

Constraints on
• Haemodynamic parameters
• Connections

$p(y | \theta)$

likelihood term

$p(\theta)$

prior

Bayesian estimation

$p(\theta | y) \propto p(y | \theta) p(\theta)$
Overview: parameter estimation

- Specify model (neuronal and haemodynamic level)

- Make it an observation model by adding measurement error $e$ and confounds $X$ (e.g. drift).

- Bayesian parameter estimation using expectation-maximization.

- Result: (Normal) posterior parameter distributions, given by mean $\eta_{\theta | y}$ and Covariance $C_{\theta | y}$.

- $y = h(x, u, \theta) + X \beta + e$

where $h(x, u, \theta)$ is the modeled BOLD response.
Parameter estimation: an example

Simulated response

Input coupling, $c_1$

Forward coupling, $a_{21}$

Prior density  ---  Posterior density  ---  true values
Inference about DCM parameters

Bayesian single subject analysis

• The model parameters are distributions that have a mean $\eta_{\theta|y}$ and covariance $C_{\theta|y}$.
  
  – Use of the cumulative normal distribution to test the probability that a certain parameter is above a chosen threshold $\gamma$:

Classical frequentist test across groups

• Test summary statistic: mean $\eta_{\theta|y}$
  
  – One-sample t-test: Parameter $> 0$?

  – Paired t-test: parameter 1 $>$ parameter 2?

  – rmANOVA: e.g. in case of multiple sessions per subject

Bayesian parameter averaging
Model comparison and selection

Given competing hypotheses, which model is the best?

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

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

Pitt & Miyung (2002), *TICS*
Inference on model space

Model evidence: The optimal balance of fit and complexity

Comparing models

• Which is the best model?
Inference on model space

Model evidence: The optimal balance of fit and complexity

Comparing models
• Which is the best model?

Comparing families of models
• What type of model is best?
  • Feedforward vs feedback
  • Parallel vs sequential processing
  • With or without modulation
Inference on model space

Model evidence: The optimal balance of fit and complexity

Comparing models
• Which is the best model?

Comparing families of models
• What type of model is best?
  • Feedforward vs feedback
  • Parallel vs sequential processing
  • With or without modulation

Only compare models with the same data
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Applications & extensions of DCM to fMRI data
Attention to motion in the visual system

We used this model to assess the site of **attention modulation** during **visual motion processing** in an fMRI paradigm reported by Büchel & Friston.

- fixation only
- observe static dots + photic $\rightarrow$ V1
- observe moving dots + motion $\rightarrow$ V5
- task on moving dots + attention $\rightarrow$ V5 + parietal cortex

Friston et al. 2003, *NeuroImage*
Comparison of two simple models

Model 1: attentional modulation of V1→V5

Model 2: attentional modulation of SPC→V5

Bayesian model selection:

→ Decision for model 1:

Model 1 better than model 2

\[ \log p(y | m_1) \gg \log p(y | m_2) \]

in this experiment, attention primarily modulates V1→V5
**Extension I: Slice timing model**

- Potential timing problem in DCM: temporal shift between regional time series because of multi-slice acquisition

- **Solution:**
  - Modelling of (known) slice timing of each area.

Slice timing extension now allows for any slice timing differences!

**Long TRs (> 2 sec) no longer a limitation.**

(Kiebel et al., 2007)
Extension II: Two-state model

Single-state DCM

\[ \frac{\partial x}{\partial t} = (A + uB)x + Cu \]

\[ A = \begin{bmatrix} A_{11} & \cdots & A_{1N} \\ \vdots & \ddots & \vdots \\ A_{N1} & \cdots & A_{NN} \end{bmatrix} \quad x(t) = \begin{bmatrix} x_1 \\ \vdots \\ x_N \end{bmatrix} \]

\[ \dot{z} = Az + \sum u_j B_j z + Cu \]

Two-state DCM

\[ \frac{\partial x}{\partial t} = (AB^u)x + Cu \]

Extrinsic (between-region) coupling

\[ A = \begin{bmatrix} -e^{A_{1E}} & -e^{A_{1I}} & \cdots & e^{A_N} & 0 \\ e^{A_{1E}} & -e^{A_{1I}} & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ e^{A_{N1}} & 0 & \cdots & -e^{A_{NE}} & -e^{A_{NI}} \\ 0 & 0 & \cdots & e^{A_{NE}} & -e^{A_{NI}} \end{bmatrix} \]

Intrinsic (within-region) coupling

\[ x(t) = \begin{bmatrix} x_1^E \\ x_1^I \\ \vdots \\ x_N^E \\ x_N^I \end{bmatrix} \]
DCM for Büchel & Friston

Example: Two-state Model Comparison
Extension III: Nonlinear DCM for fMRI

Bilinear state equation

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

Nonlinear state equation

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

Here DCM can model activity-dependent changes in connectivity; how connections are enabled or gated by activity in one or more areas.
Can V5 activity during attention to motion be explained by allowing activity in SPC to modulate the V1-to-V5 connection?

The posterior density of $D_{V5,V1}^{(SPC)}$ indicates that this gating existed with 97% confidence.

(The $D$ matrix encodes which of the $n$ neural units gate which connections in the system)
So, DCM….

- enables one to **infer hidden neuronal processes** from fMRI data
- allows one to **test mechanistic hypotheses** about observed effects
  - uses a deterministic differential equation to model neuro-dynamics (represented by matrices A, B and C).
- is informed by anatomical and physiological principles.
- uses a **Bayesian framework** to estimate model parameters
- is a generic approach to modelling experimentally perturbed dynamic systems.
  - provides an observation model for neuroimaging data, e.g. fMRI, M/EEG
  - DCM is **not model or modality specific** (Models will change and the method extended to other modalities e.g. ERPs, LFPs)
Some useful references


Thank you for your attention!!!