DCM for resting state fMRI

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Introduction and background
(Spectral) Dynamic Causal Modelling

Technical / Mathematical Content

Worked example using SPM
DMN connectivity

What’s new?
Large DCMs

Applications
Cognitive / Psychiatric
Introduction and background (Spectral) Dynamic Causal Modelling

What’s new?

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DMN connectivity

Large DCMs

Cognitive / Psychiatric
Brain connectivity

*structural, functional and effective*

**Structural connectivity**

Presence of axonal connections

**Functional connectivity**

Statistical dependencies between regional time series

**Effective connectivity**

Causal (directed) influences between neuronal populations
Brain connectivity

*structural, functional and effective*

- Relationship between functional and effective connectivity

Hidden causes | Measured consequences
DCM for task fMRI

**classic DCM**

The forward (dynamic causal) model

\[
\dot{x}(t) = f(x(t), \theta, u)
\]

\[
= (A + \sum_{j=1}^{m} u_j B^j) x(t) + Cu
\]

\[
y(t) = h(x(t), \phi) + e(t)
\]

Deterministic system

Ordinary differential equation (ODE)
The forward (dynamic causal) model

\[ \dot{x}(t) = f(x(t), \theta, u, v) \]

\[ = (A + \sum_{j=1}^{m} u_j B^j)x(t) + Cu + v(t) \]

\[ y(t) = h(x(t), \phi) + e(t) \]

Stochastic system
Stochastic differential equation (SDE)
DCM for resting state fMRI

**classic DCM**

The forward (dynamic causal) model

\[
\dot{x}(t) = f(x(t), \theta, u, v)
\]

\[
= (A + \sum_{j=1}^{m} u_j B^j) x(t) + Cu + v(t)
\]

\[
y(t) = h(x(t), \phi) + e(t)
\]

External stimulus \( u(t) = 0 \) + Endogenous fluctuations

\[
\dot{x}(t) = f(x, \theta, u)
\]

Observed timeseries

\[
y = h(x, \phi) + e
\]
DCM for resting state fMRI

classic DCM

The forward (dynamic causal) model

\[
\dot{x}(t) = f(x(t), \theta, u, v) \\
= (A + \sum_{j=1}^{m} u_j B^j) x(t) + Cu + v(t) \\
y(t) = h(x(t), \phi) + e(t)
\]

\[
y = h(x, \phi) + e
\]
The forward (dynamic causal) model

\[
\begin{align*}
\dot{x}(t) &= Ax(t) + v(t) \\
y(t) &= h(x(t), \phi) + e(t)
\end{align*}
\]

Stochastic system
Stochastic differential equation (SDE)
More parameters to estimate
Slow estimation!

DCM for resting state fMRI

*classic DCM*

Endogenous fluctuations

Observed timeseries

Stochastic system
Stochastic differential equation (SDE)
More parameters to estimate
Slow estimation!
Quick detour..

*Fourier transform, cross covariance, cross spectra*

\[ Y(\omega) = F(y(t)) = \int_{-\infty}^{+\infty} y(t)e^{-i\omega t} \, dt \]

\[ y(t) \leftrightarrow Y(\omega) \]

Some properties…

**Linearity:**

\[ ay_1(t) + by_2(t) \leftrightarrow aY_1(\omega) + bY_2(\omega) \]

**Convolution:**

\[ y_1(t) \otimes y_2(t) \leftrightarrow Y_1(\omega) \cdot Y_2(\omega) \]
Quick detour..

**Fourier transform, cross covariance, cross spectra**

Now we are interested in situation where we have multiple time series and explore relationship between them

Cross covariance

\[
\Sigma_{y_1 y_2}(\tau) = \mathbb{E}[y_1(\tau)y_2(t-\tau)] \leftrightarrow g_{y_1 y_2}(\omega) = \mathbb{E}[Y_1(\omega)Y_2^*(\omega)]
\]

Cross spectral density

Cross correlation

\[
\sigma_{y_1 y_2}(\tau) = \frac{\Sigma_{y_1 y_2}(\tau)}{\sqrt{\Sigma_{y_1 y_1}(0)\Sigma_{y_2 y_2}(0)}} \leftrightarrow C_{y_1 y_2}(\omega) = \frac{|g_{y_1 y_2}(\omega)|^2}{g_{y_1 y_1}(\omega)g_{y_2 y_2}(\omega)}
\]

Measures of functional connectivity
DCM for resting state fMRI

classic DCM

The forward (dynamic causal) model

\[ \dot{x}(t) = Ax(t) + v(t) \]
\[ y(t) = h(x(t), \phi) + e(t) \]

Stochastic system
Stochastic differential equation (SDE)
More parameters to estimate
Slow estimation!
DCM for resting state fMRI

**classic DCM**

The forward (dynamic causal) model

\[
\dot{x}(t) = Ax(t) + v(t)
\]

\[
y(t) = h(x(t), \phi) + e(t)
\]

\[
\Sigma_y(\tau, \theta) = \kappa(\tau) \otimes \Sigma_v(\tau) \otimes \kappa(-\tau) + \Sigma_e(\tau)
\]

Endogenous fluctuations
DCM for resting state fMRI

**spectral DCM**

The forward (dynamic causal) model

\[ \dot{x}(t) = Ax(t) + v(t) \]
\[ y(t) = h(x(t), \phi) + e(t) \]

\[ g_v(\omega, \theta) = \alpha_v \omega^{-\beta_v} \]
\[ g_e(\omega, \theta) = \alpha_e \omega^{-\beta_e} \]
\[ \theta \supset \{A, C, \alpha, \beta\} \]

\[ g_y(\omega) = K(\omega) \cdot g_v(\omega) \cdot K^*(\omega) + g_e(\omega) \]

Power law
With amplitude and exponent
Fast estimation

Endogenous fluctuations

Complex cross-spectra
DCM for resting state fMRI

*spectral DCM*

The forward (dynamic causal) model

\[ x(t) = f(x, \theta, v) \]

\[ y = h(x, \phi) + e \]

Endogenous fluctuations

Observed timeseries

Effective connectivity

Functional connectivity
DCM for resting state fMRI

*spectral DCM*

Bayesian model inversion

Posterior density

\[ p(\theta | g_y(\omega), m) \approx q(\theta | \mu) \]

\[ \ln p(g_y(\omega) | m) \approx F(g_y(\omega), \mu) \]

Log model evidence

Endogenous fluctuations

Observed timeseries

Effective connectivity

\[ \mu = \arg \min F(g_y(\omega), \mu) \]

Functional connectivity
DCM for resting state fMRI

*spectral DCM*

Bayesian model inversion

Posterior density

\[ p(\theta \mid g_y(\omega), m) \approx q(\theta \mid \mu) \]

Log model evidence

\[ \ln p(g_y(\omega) \mid m) \approx F(g_y(\omega), \mu) \]

`\dot{x}(t) = f(x, \theta, v)`

Endogenous fluctuations

\[ y(t) \]

\[ g_y(\omega) \]

\[ \ln p(g_y(\omega) \mid m) \]

\[ p(m \mid g_y(\omega)) \]

Bayesian model comparison

\[ p(\theta \mid g_y(\omega)) = \sum_m p(\theta \mid g_y(\omega), m)p(m \mid g_y(\omega)) \]

Bayesian model averaging

DCM for resting state fMRI

spectral DCM

Bayesian model inversion

Posterior density

\[ p(\theta \mid g_y(\omega), m) \approx q(\theta \mid \mu) \]

Log model evidence

\[ \ln p(g_y(\omega) \mid m) \approx F(g_y(\omega), \mu) \]

`\dot{x}(t) = f(x, \theta, v)`

Endogenous fluctuations

\[ y(t) \]

\[ g_y(\omega) \]

\[ \ln p(g_y(\omega) \mid m) \]

\[ p(m \mid g_y(\omega)) \]

Bayesian model comparison

\[ p(\theta \mid g_y(\omega)) = \sum_m p(\theta \mid g_y(\omega), m)p(m \mid g_y(\omega)) \]

Bayesian model averaging
DCM for resting state fMRI

*face validity*

Friston, Kahan, Biswal, Razi, *NeuroImage*, 2014

Network or graph generating data

![Graph](image)

![Real and Imaginary Plots](image)
DCM for resting state fMRI

**construct validity**

![Graph 1: True and MAP connections (Spectral)](image1)

![Graph 2: True and MAP connections (Stochastic)](image2)

![Graph 3: Network or graph generating data](image3)

![Graph 4: Root mean square error (Spectral)](image4)

![Graph 5: Root mean square error (Stochastic)](image5)

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**Construct validity**

Network for first set of 24 subjects

Network for second set of 24 subjects

**True and BPA differences (spectral)**

**True and BPA differences (stochastic)**

**Classical t-tests (spectral)**

**Classical t-tests (stochastic)**

Brain connectivity
measures of connectivity

State-space model
\[
\begin{align*}
\dot{x}(t) &= f(x(t), \Theta) + w(t) \\
y(t) &= h(x(t), \Theta) + e(t) \\
\Sigma_w(t) &= \{w(t)w(t-t)^T\} \quad \text{and} \quad \Sigma_e(t) = \{e(t)e(t-t)^T\}
\end{align*}
\]

E.g., Bilinear DCM: \( \dot{x}(t) = (A + \sum_j u_j B_j)x + C u + w(t) \)

Structural equation models (SEM) (assuming \( x(t) = y(t) \) and \( y(t) = 0 \) \( u(t) = 0 \))
\[
\begin{align*}
y(t) &= Ay(t) + w(t) = (\Theta - I)y(t) + e(t) \\
y(t) &= \Theta y(t) + e(t)
\end{align*}
\]

Convolution kernel
\[
y(t) = \kappa(t) * w(t) + e(t) \\
\kappa(t) = \partial_x h \cdot \exp(\partial_x f)
\]

Cross covariance
\[
\Sigma_x(t) = \{y(t) y(t-t)^T\} \\
= \kappa(t) * \Sigma_w(t) * \kappa(-t) + \Sigma_e(t)
\]

Cross correlation
\[
c_{ij}(t) = \frac{\Sigma_{jk}(t)}{\sqrt{\Sigma_{jj}(0)\Sigma_{kk}(0)}}
\]

Coherence
\[
C_{ij}(\omega) = \frac{|g_{jk}(\omega)|^2}{g_{jj}(\omega)g_{kk}(\omega)}
\]

Directed transfer functions
\[
Y(\omega) = S(\omega)Z(\omega) \\
S(\omega) = (I - A(\omega))^{-1}
\]

Cross spectral density
\[
g_{xy}(\omega) = \{Y(\omega)Y(\omega)^T\} \\
= K(\omega) g_{w}(\omega) K(\omega)^T + g_{e}(\omega)
\]

Granger causality
\[
G_{jk}(\omega) = -\ln \left(1 - \frac{|S_{jk}(\omega)|^2}{g_{jj}(\omega)}\right)
\]

Auto-regression coefficients
\[
\hat{A} = \{Y(\omega)^T\}^{-1}\{Y(\omega)^T\} \\
= \rho^{-1}\{\rho_1 ... \rho_p\}^T
\]

Auto-correlation
\[
c_{ii} = (I - \hat{A})^{-1}(I - \hat{A}^T)^{-1}
\]
DCM for resting state fMRI

*interim summary*

- State space models – all connectivity measures can be derived from them as approximations
- Effective connectivity as what causes observations (functional connectivity)
- Spectral DCM is accurate, (computationally) efficient and sensitive relative to stochastic DCM
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(Spectral) Dynamic Causal Modelling

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DMN connectivity

What’s new?

Large DCMs

Cognitive / Psychiatric

Worked example using SPM
Worked example

Chapter 38

Dynamic Causal Modelling for resting state fMRI

This chapter provides an extension to the framework of Dynamic Causal Modelling (DCM) for modelling intrinsic dynamics of a resting state network [41, 99]. This DCM estimates the effective connectivity among coupled populations of neurons, which subtends the observed functional connectivity in the frequency domain. We refer to this as spectral DCM (spDCM).

38.1 Theoretical background

38 Dynamic Causal Modelling for resting state fMRI
   38.1 Theoretical background
   38.2 Practical example
      38.2.1 Defining the GLM
      38.2.2 Extracting time series
      38.2.3 Specifying and estimating the DCM
Worked example

1. GLM estimation – to get SPM.mat
2. CSF/WM signal extraction
3. GLM estimation – to remove confounds
4. Extraction of time series from ROIs

- PCC [0 -52 26]
- mPFC [3 54 -2]
- L-IPC [-50 -63 32]
- R-IPC [48 -69 35]

Worked example

1. GLM estimation – to get SPM.mat
2. CSF/WM signal extraction
3. GLM estimation – to remove confounds
4. Extraction of time series from ROIs

5. Specify DCM
6. Estimate DCM
7. Review DCM
Worked example

Default mode network
Worked example

Default mode network

PCC: responses

MPFC: responses

LIPC: responses

RIPC: responses

Input time series

Data fits for CSD
Worked example

Default mode network

Connectivity parameters: DCM.Ep.A
Neural fluctuation parameters: DCM.Ep.a

```matlab
>> load('DCM_DMN.mat')
>> DCM.Ep.A
ans =
0.2451  -0.0359   0.4764  -0.2926
-0.5201   0.0349   0.4647   0.4746
 0.2431  -0.8065  -0.6187   1.1881
 0.1499  -1.0462   0.8346  -0.0293

>> DCM.Ep.a
ans =
-0.6714  -0.5323   4.2406  -0.5629
-1.3155  -1.1841  -2.2338  -0.8349
```
OUTLINE

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(Spectral) Dynamic Causal Modelling

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Worked example using SPM
DMN connectivity

Cognitive / Psychiatric
Large-scale DCMs for resting state fMRI

36 nodes network
Large-scale DCMs for resting state fMRI

36 nodes network

Large-scale DCMs for resting state fMRI

Large-scale DCMs for resting state fMRI

Averaged functional connectivity

Averaged effective connectivity

Averaged binarized adjacency matrix after BMR

Averaged weighted adjacency matrix after BMR

Large-scale DCMs for resting state fMRI
Introduction and background
(Spectral) Dynamic Causal Modelling

What's new?

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Cognitive / Psychiatric

Worked example using SPM
DMN connectivity

What's new?
Large DCMs
Major Depressive Disorder

Natural time course of positive mood

**Task design and timeline**

<table>
<thead>
<tr>
<th>Prior</th>
<th>Acute phase</th>
<th>Sustained phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest1 (6 min)</td>
<td>Descriptive (~15 min)</td>
<td>Anatomy (9 min)</td>
</tr>
<tr>
<td>Rate</td>
<td>Captions (~15 min)</td>
<td>Descriptive (~15 min)</td>
</tr>
<tr>
<td>Rate</td>
<td>Rest2 (6 min)</td>
<td>Captions (~15 min)</td>
</tr>
<tr>
<td>Rate</td>
<td>Rate</td>
<td>Rest3 (6 min)</td>
</tr>
<tr>
<td>Rate</td>
<td>Rate</td>
<td>~90 Min</td>
</tr>
</tbody>
</table>

**Acute phase descriptive**

Three people have short dark hair

The woman is standing

All people have pens on the table

© P.C. Vey / The New Yorker magazine

**Acute phase captions**

Correct!

You responded in 8 seconds, which is 2 seconds faster than average

Who lives upstairs?

Bad chair day

Another ‘bald barber’ joke?

© Tom Cheney / The New Yorker magazine

**Sustained phase descriptive**

The woman’s hands are up in the air

Two people are standing next to a car

A car is parked behind six horses

© Michael Maslin / The New Yorker magazine

**Sustained phase captions**

Our bagpiper is off sick

Compliments of your ex

Fresh ground compah?

© Drew Dernavich / The New Yorker magazine

Major Depressive Disorder

Natural time course of positive mood

These findings suggest:

1) that corticostriatal pathways contribute to the natural time course of positive mood fluctuations

2) and that disturbances of those neural interactions may characterize individuals with a past history of mood disorders

Spectral DCM analysis

Hierarchical organization of intrinsic brain modes

anticorrelated brain modes

- Functional network organization
- Network interactivity important for cognitive function

Power et al. 2011

Dorsal Attention Network

Default Mode Network

Kelly et al. 2008

Dorsal Attention Network (DAN)

Default Mode Network (DMN)

Salience Network (SN)

Tsvetanov et al. 2016
Hierarchical organization of intrinsic brain modes

VOIs identified using spatial independent component analysis (ICA) (N=404)

Functional connectivity matrix

Yuan, Friston, Zeidman, Chen, Li, Razi, Submitted
Hierarchical organization of intrinsic brain modes

anticorrelated brain modes

1. Regions belonging to the same network grouped together
2. The task-positive mode (SN, DAN) inhibits the cDN
3. The task negative mode (cDN) excites the task positive mode (SN, DAN)

Yuan, Friston, Zeidman, Chen, Li, Razi, Submitted
Thank you

And thanks to

FIL Methods Group