DCM for resting state fMRI

SPM Course May 2017

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OUTLINE

Introduction and background
(Spectral) Dynamic Causal Modelling

Technical / Mathematical Content

Worked example using SPM

DMN connectivity

What's new?

Large DCMs

Applications

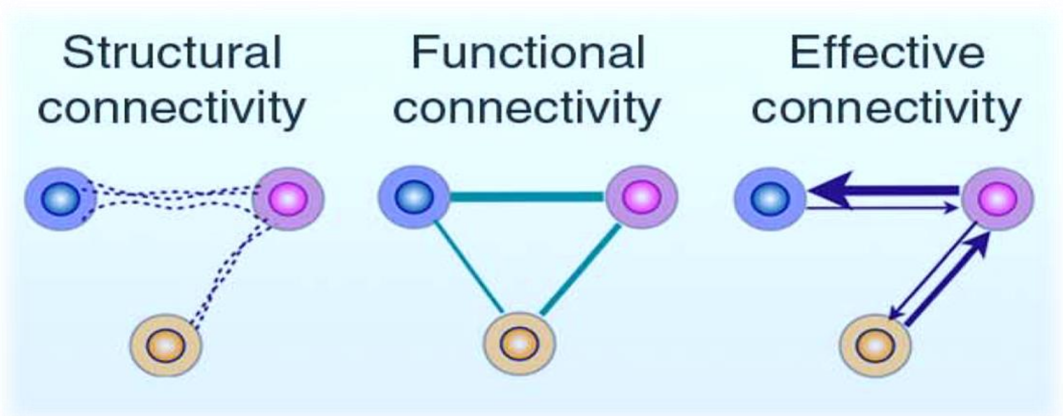
Cognitive / Psychiatric

OUTLINE

Introduction and background (Spectral) Dynamic Causal Modelling	Technical / Mathematical Content
Worked example using SPM	DMN connectivity
What’s new?	Large DCMs
Applications	Cognitive / Psychiatric

Brain connectivity

structural, functional and effective



Structural connectivity
presence of axonal connections

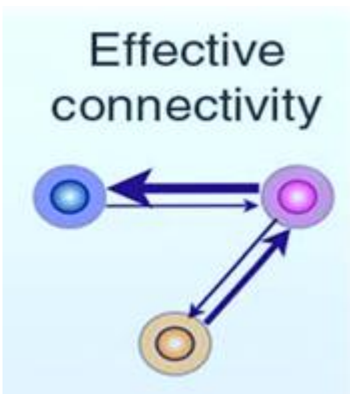
Functional connectivity
statistical dependencies between regional time series

Effective connectivity
causal (directed) influences between neuronal populations

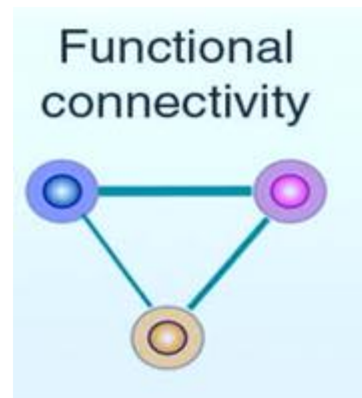
Brain connectivity

structural, functional and effective

- Relationship between functional and effective connectivity



Mapping



Hidden causes

Measured consequences

DCM for task fMRI

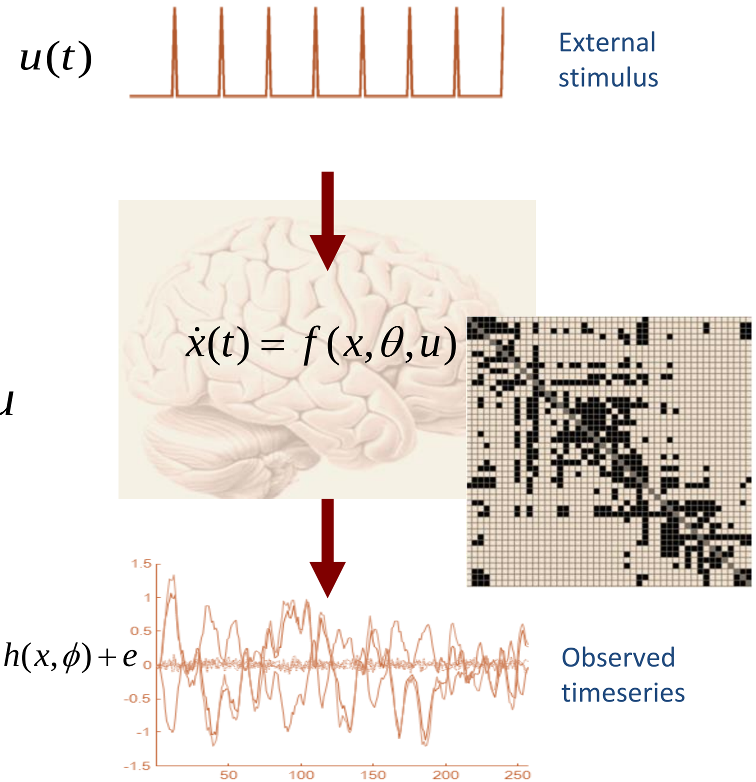
classic DCM

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)

DCM for task fMRI

classic DCM

The forward (dynamic causal) model

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

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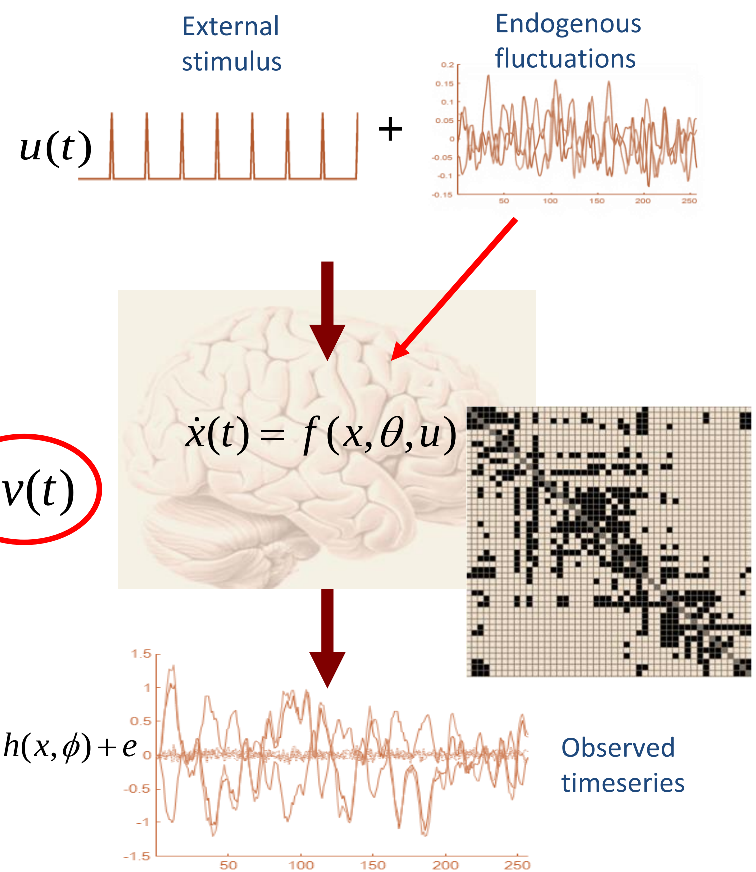

Stochastic system
Stochastic differential equation (SDE)

DCM for resting state fMRI

classic DCM

The forward (dynamic causal) model

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

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

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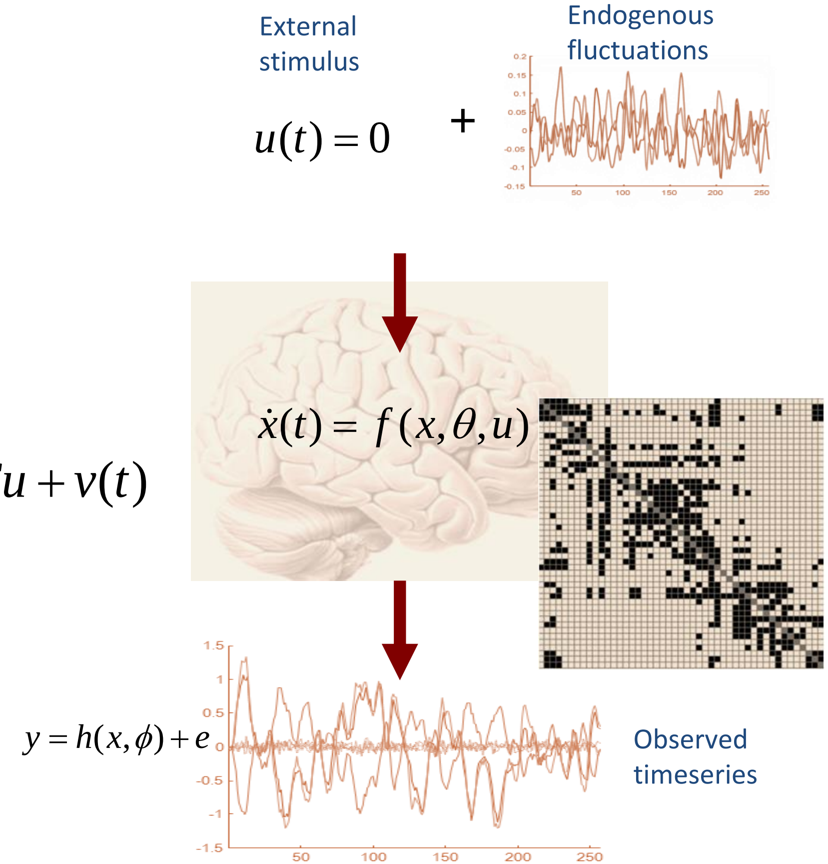


DCM for resting state fMRI

classic DCM

The forward (dynamic causal) model

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

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

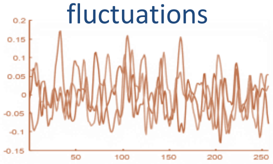
$$y(t) = h(x(t), \phi) + e(t)$$

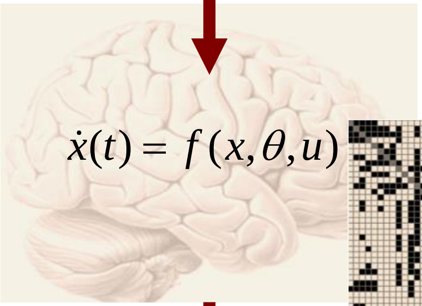
External stimulus

$$u(t) = 0$$

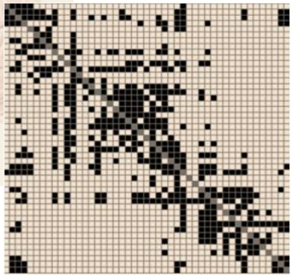
+

Endogenous fluctuations

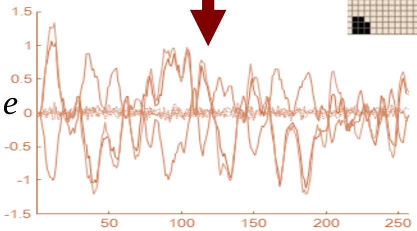




$$\dot{x}(t) = f(x, \theta, u)$$



$$y = h(x, \phi) + e$$



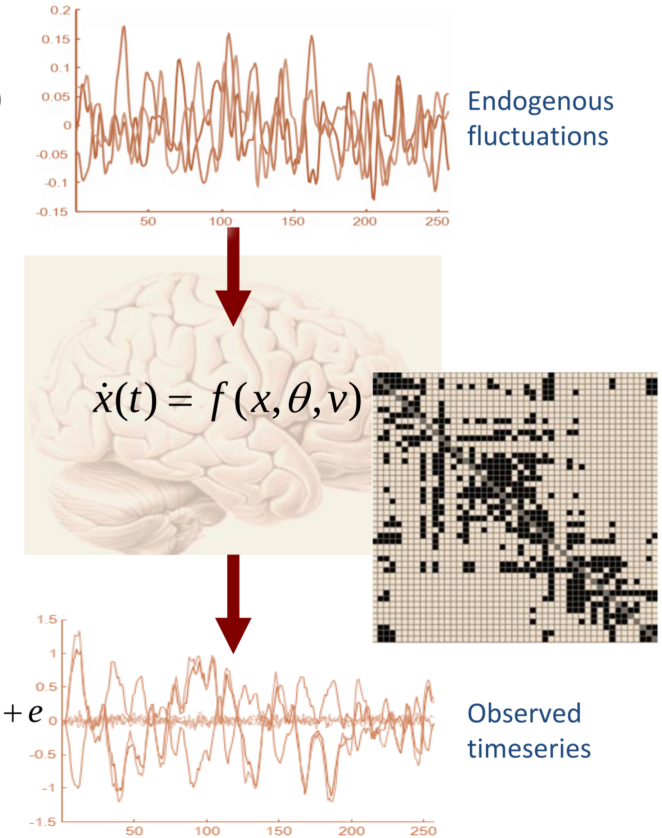
Observed timeseries

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

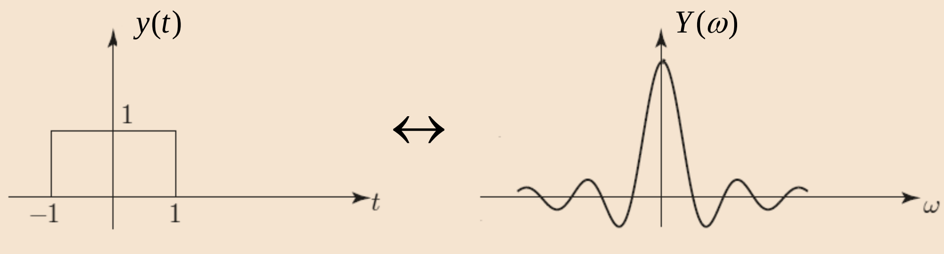
Slow estimation!

Quick detour..

Fourier transform, cross covariance, cross spectra

$$Y(\omega) = \mathbf{F}(y(t)) = \int_{-\infty}^{+\infty} y(t)e^{-i\omega t}dt$$

$$y(t) \leftrightarrow Y(\omega)$$



Sinc function

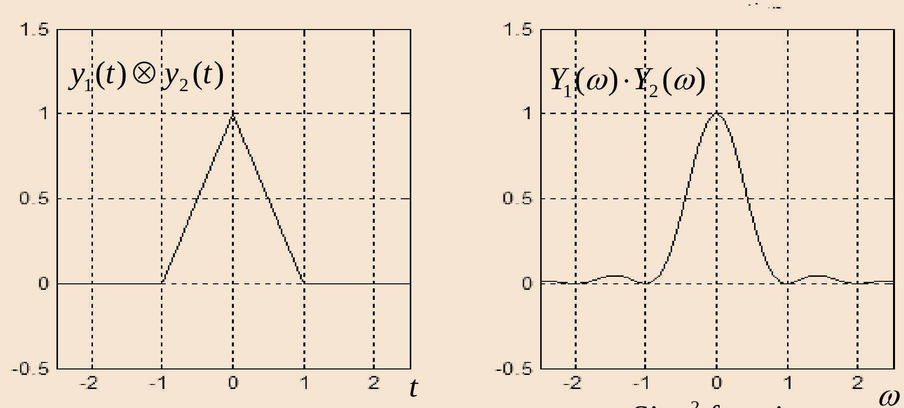
Some properties…

Linearity:

$$ay_1(t) + by_2(t) \leftrightarrow aY_1(\omega) + bY_2(\omega)$$

Convolution:

$$y_1(t) \otimes y_2(t) \leftrightarrow Y_1(\omega) \cdot Y_2(\omega)$$

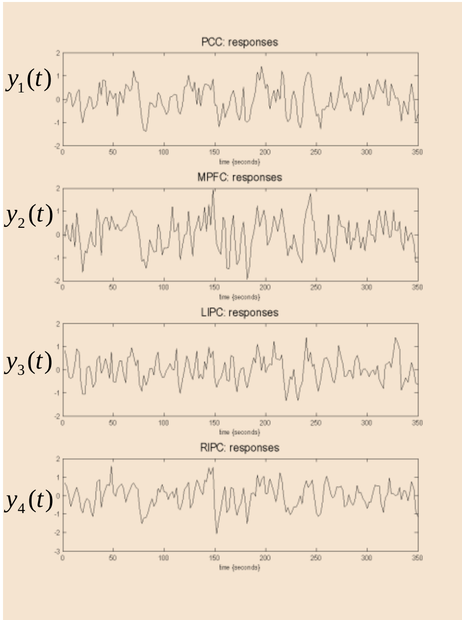


Sinc^2 function

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



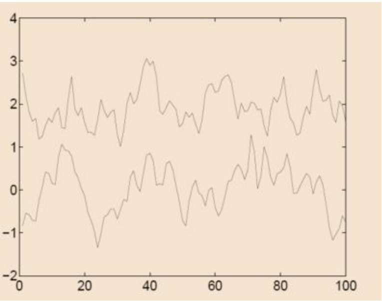
Cross covariance

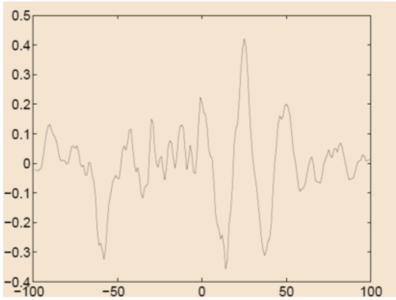
$$\Sigma_{y_1y_2}(\tau) = \mathrm{E}[y_1(\tau)y_2(t-\tau)]$$

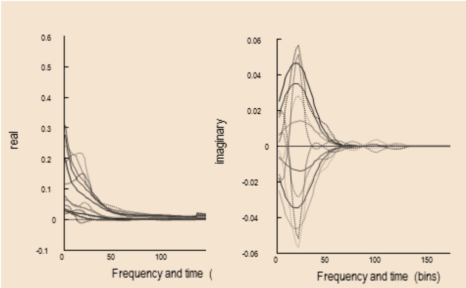
$$\leftrightarrow$$

Cross spectral density

$$g_{y_1y_2}(\omega) = \mathbf{E}[Y_1(\omega)Y_2^*(\omega)]$$







Cross correlation

$$\sigma_{y_1y_2}(\tau) = \frac{\Sigma_{y_1y_2}(\tau)}{\sqrt{\Sigma_{y_1y_1}(0)\Sigma_{y_2y_2}(0)}}$$

$$\leftrightarrow$$

Coherence

$$C_{y_1y_2}(\omega) = \frac{\left|g_{y_1y_2}(\omega)\right|^2}{g_{y_1y_1}(\omega)g_{y_2y_2}(\omega)}$$

Measures of functional connectivity

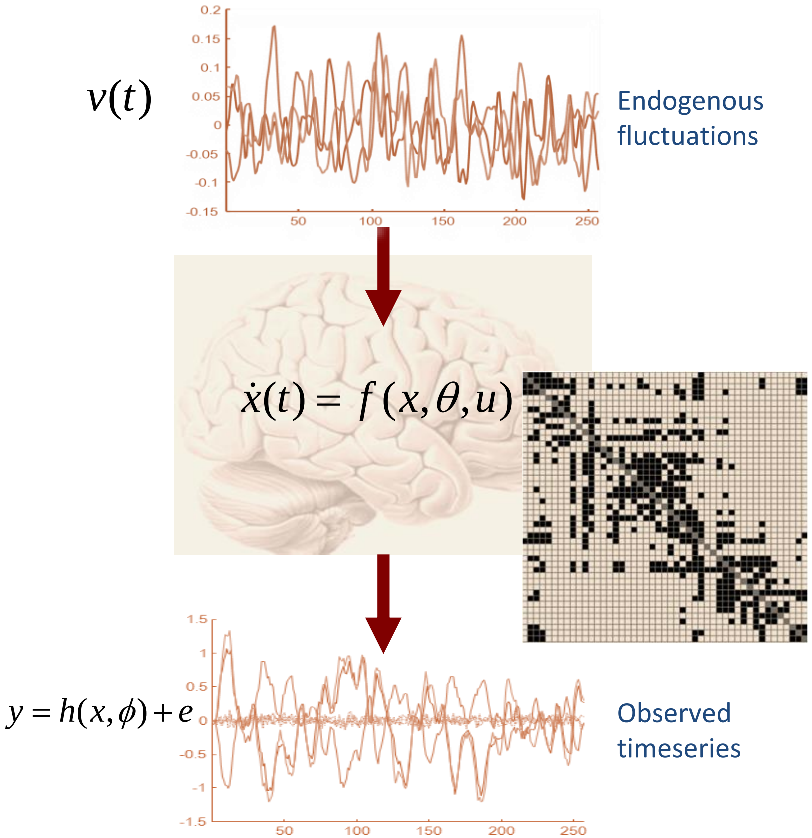
DCM for resting state fMRI

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

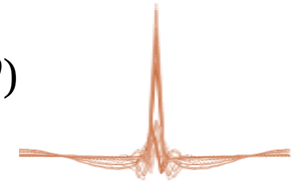
classic DCM

The forward (dynamic causal) model

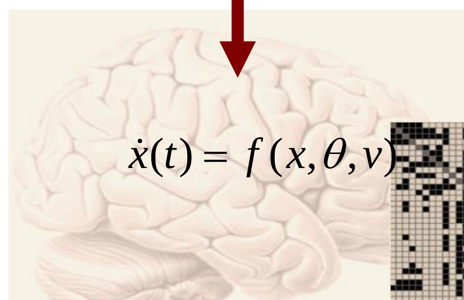
$$\dot{x}(t) = Ax(t) + v(t)$$

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

$$\Sigma_v(\tau, \theta)$$



Endogenous fluctuations



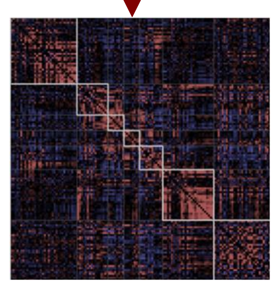
$$\dot{x}(t) = f(x, \theta, v)$$

$$\kappa(\tau) = \partial_x h \cdot \exp(\tau \partial_x f)$$

$$y(t) = \kappa(t) \otimes v(t) + e(t)$$

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

$$\Sigma_y(\tau, \theta)$$



DCM for resting state fMRI

spectral DCM

The forward (dynamic causal) model

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

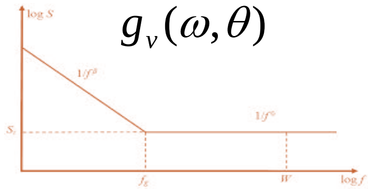
$$y(t) = h(x(t), \phi) + e(t)$$

$$g_v(\omega,\theta) = \alpha_v \omega^{-\beta_v}$$

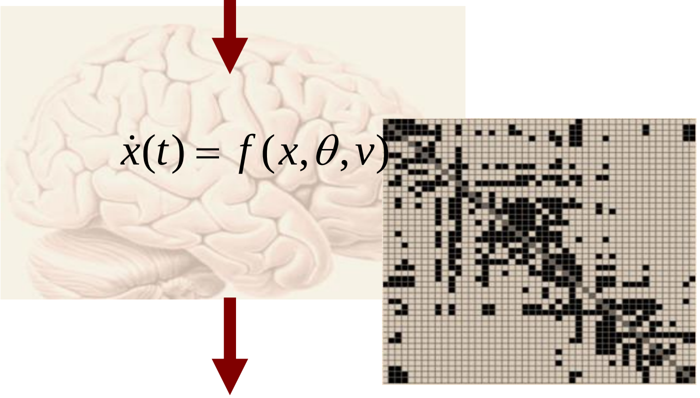
$$g_e(\omega,\theta) = \alpha_e \omega^{-\beta_e}$$

$$\theta \supset \{A, C, \alpha, \beta\}$$

$$g_v(\omega,\theta)$$



Endogenous fluctuations

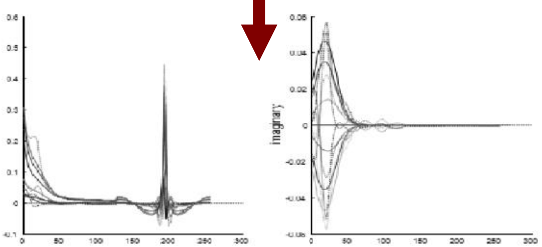


$$\dot{x}(t) = f(x,\theta,v)$$

$$K(\omega) = \mathbf{F}(\kappa(t))$$

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

$$g_y(\omega)$$



Complex cross-spectra

Power law
With amplitude and exponent
Fast estimation

DCM for resting state fMRI

spectral DCM

The forward (dynamic causal) model

$$g_v(\omega,\theta)$$

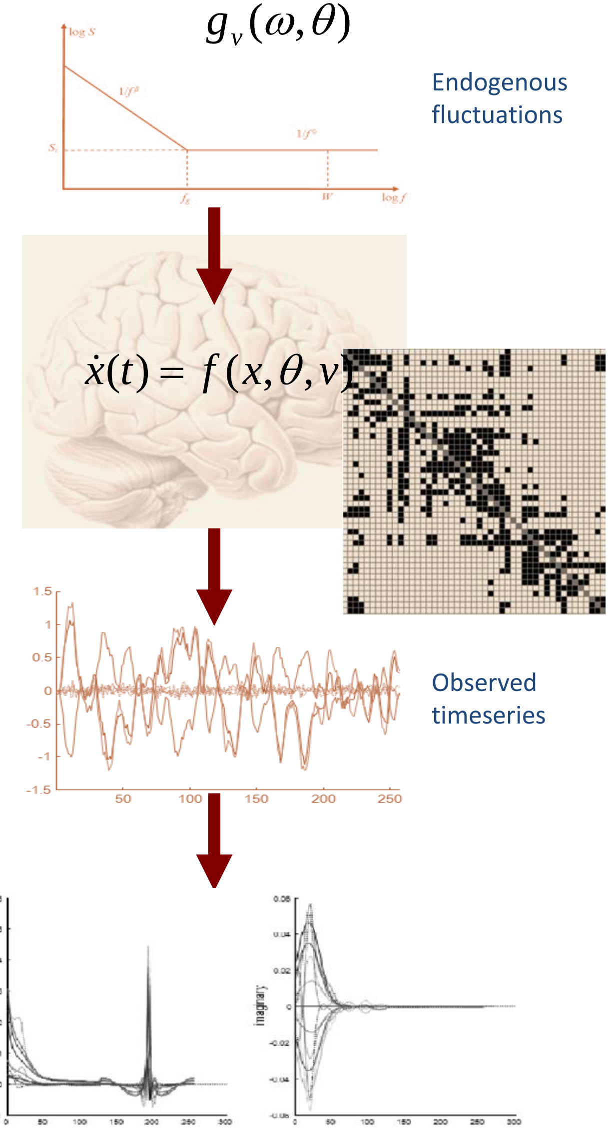
Endogenous fluctuations

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

$$y = h(x,\phi) + e$$

Observed timeseries

$$g_y(\omega,\theta)$$



Effective connectivity

Functional connectivity

DCM for resting state fMRI

spectral DCM

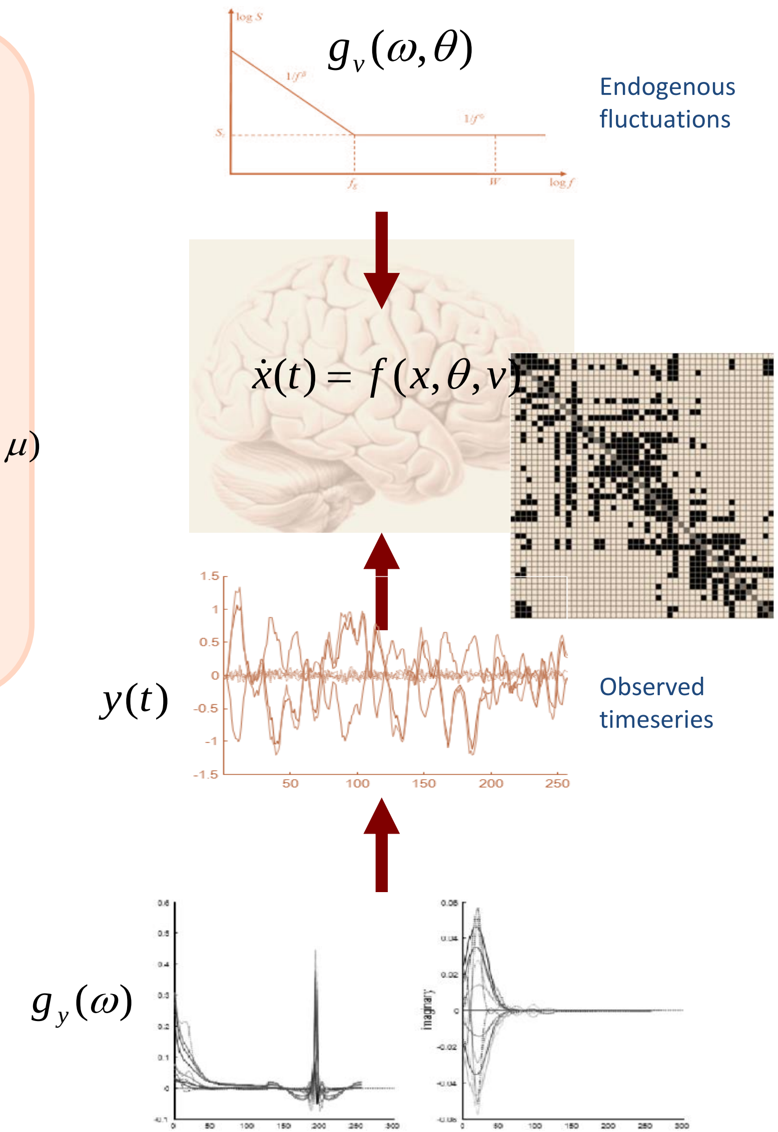
Bayesian model inversion

Posterior density

$$\mathbf{p}(\theta \mid g_y(\omega), m) \approx q(\theta \mid \mu)$$

$$\ln \mathbf{p}(g_y(\omega) \mid m) \approx F(g_y(\omega), \mu)$$

Log model evidence



Effective connectivity

$$\mu = \arg\min F(g_y(\omega), \mu)$$

Functional connectivity

DCM for resting state fMRI

spectral DCM

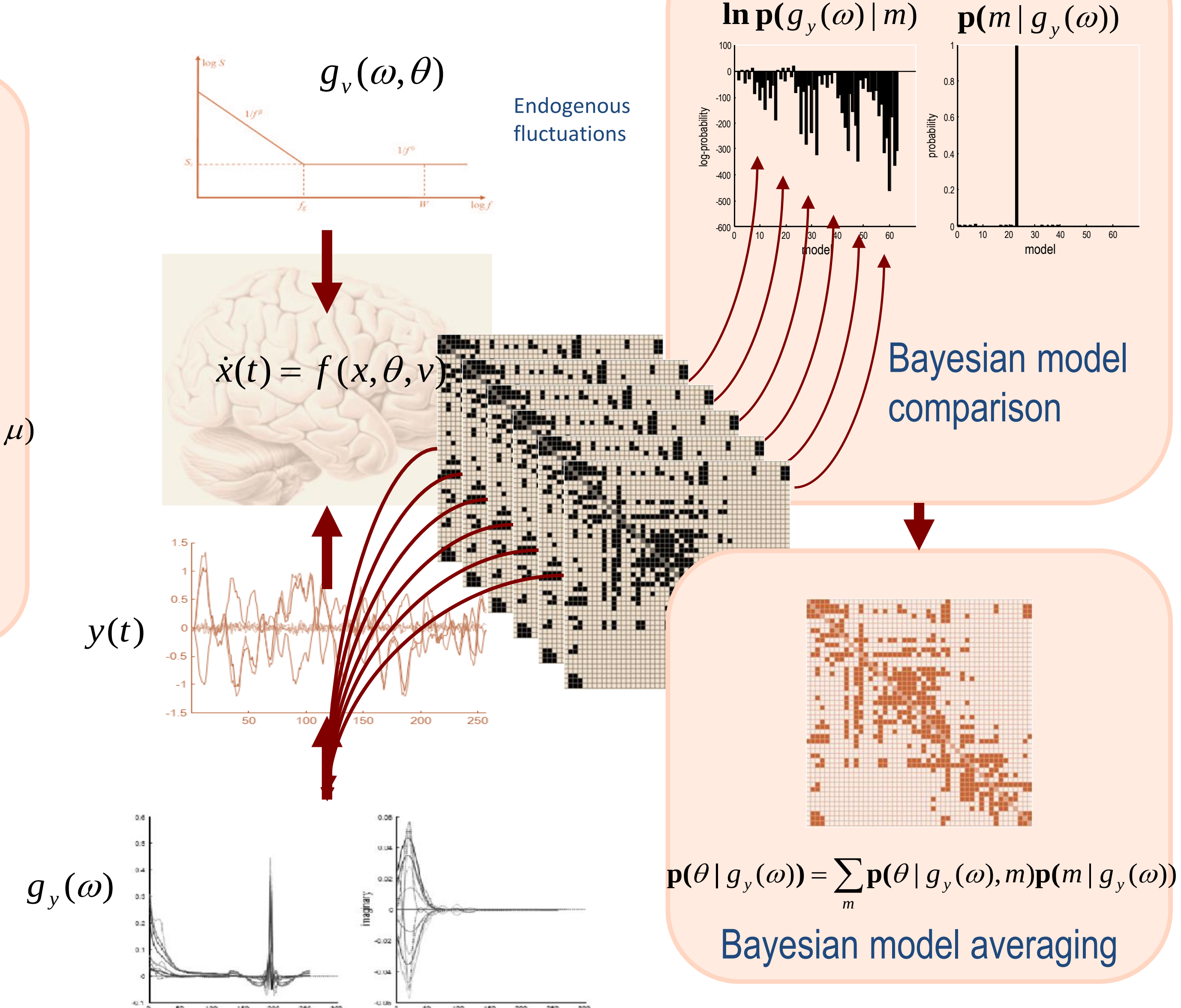
Bayesian model inversion

Posterior density

$$\mathbf{p}(\theta \mid g_y(\omega), m) \approx q(\theta \mid \mu)$$

$$\ln \mathbf{p}(g_y(\omega) \mid m) \approx F(g_y(\omega), \mu)$$

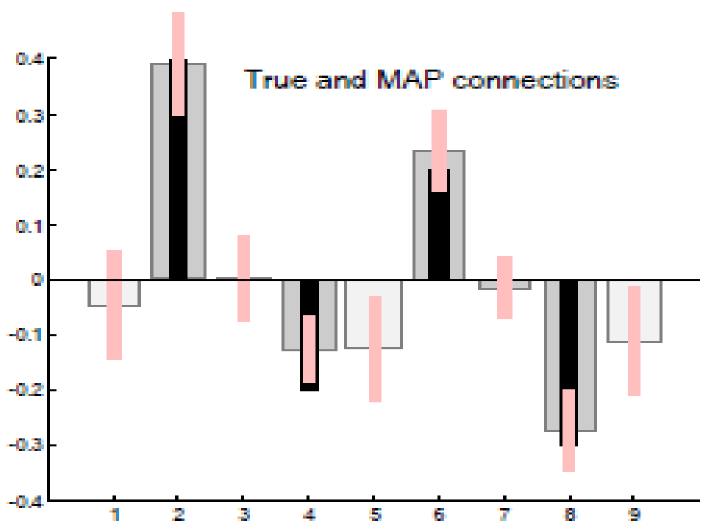
Log model evidence

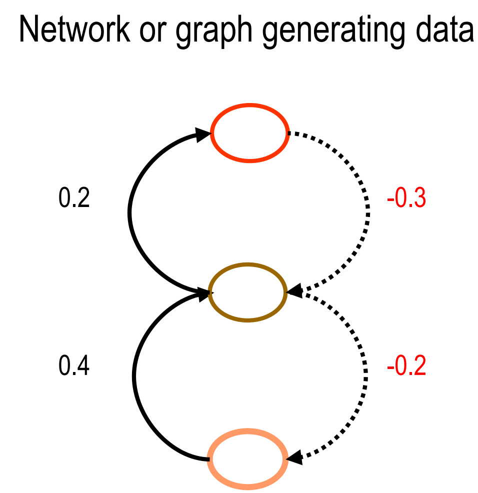


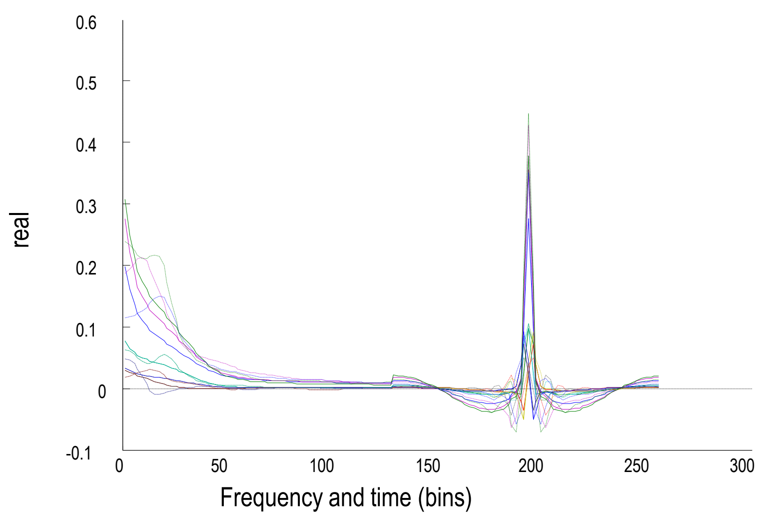
DCM for resting state fMRI

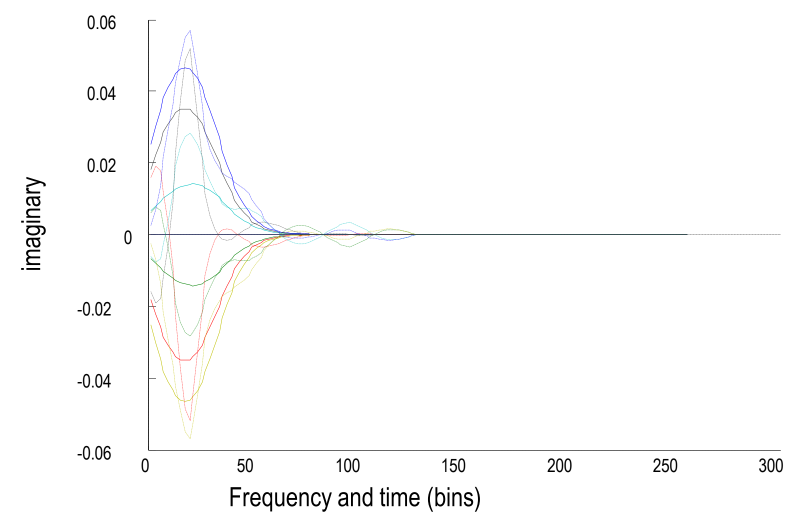
Friston, Kahan, Biswal, Razi, NeuroImage, 2014

face validity



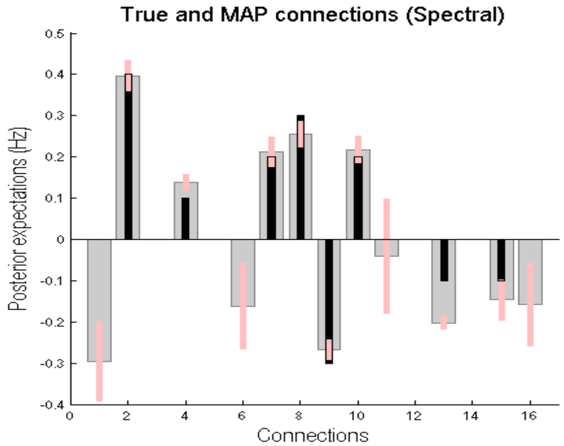


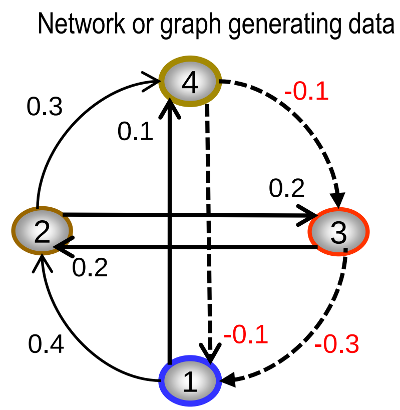


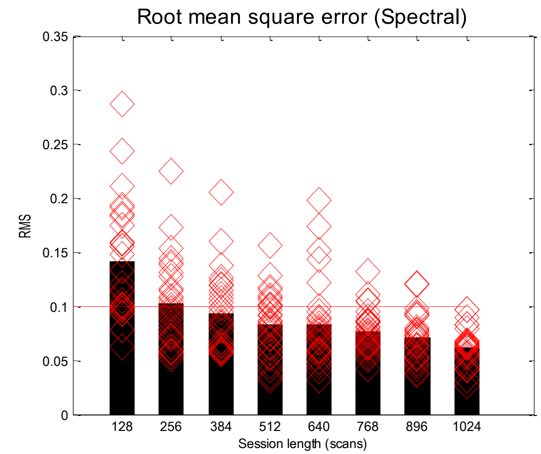


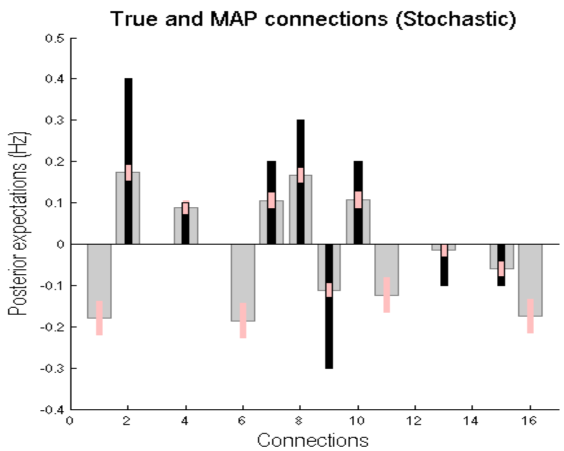
DCM for resting state fMRI

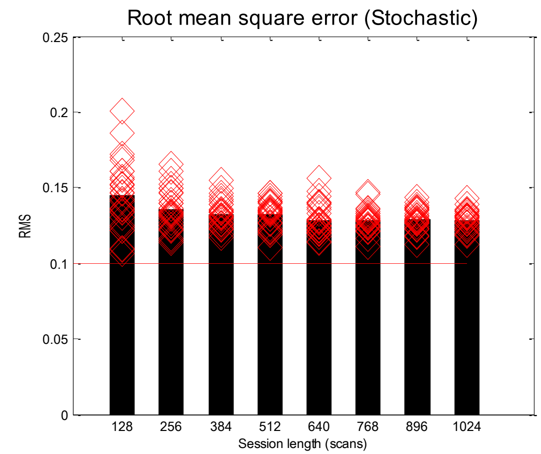
construct validity







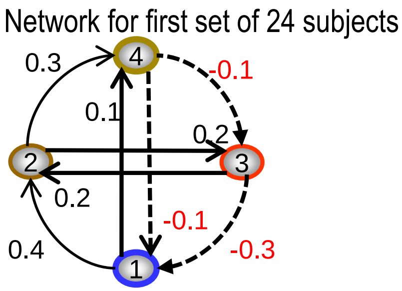


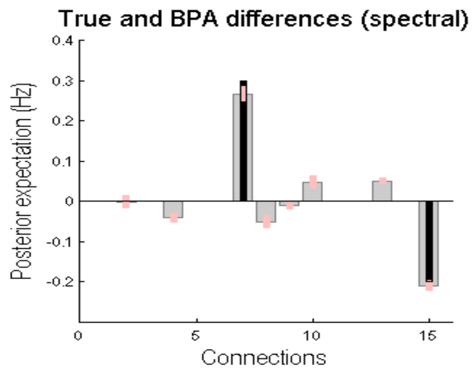


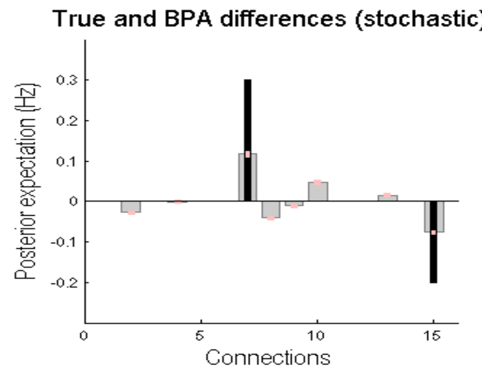
Razi, Kahan, Rees, Friston, NeuroImage, 2015

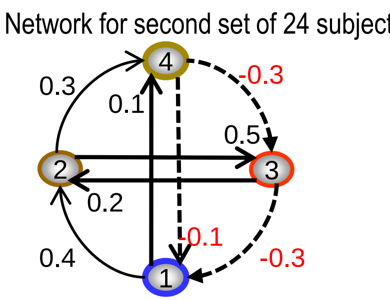
DCM for resting state fMRI

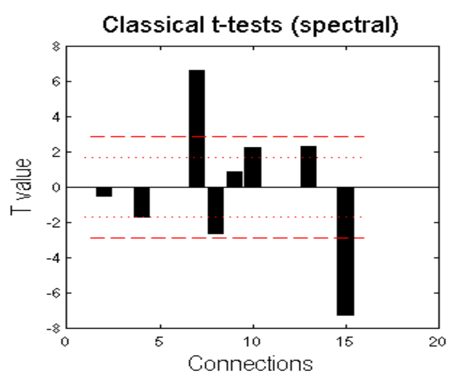
construct validity

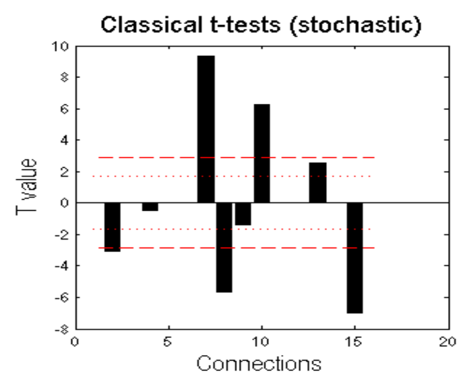












Razi, Kahan, Rees, Friston, NeuroImage, 2015

Brain connectivity

measures of connectivity

Razi and Friston. IEEE Sig. Proc. Mag, 2016

Transformation under assumptions

(Inverse) Fourier Transform

$$\tilde{Y} = \begin{bmatrix} 0 & & \\ y(t-1) & 0 & \\ y(t-2) & y(t-1) & 0 \\ \vdots & \ddots & \ddots \end{bmatrix}$$

$$\tilde{\mathbf{A}} = \begin{bmatrix} 0 & & \\ a_1 & 0 & \\ a_2 & a_1 & 0 \\ \vdots & \ddots & \ddots \end{bmatrix}$$

State-space model

$$\dot{\mathbf{x}}(t) = f(\mathbf{x}(t), \boldsymbol{\theta}) + \mathbf{w}(t)$$
$$\mathbf{y}(t) = h(\mathbf{x}(t), \boldsymbol{\theta}) + \mathbf{e}(t)$$
$$\boldsymbol{\Sigma}_{\mathbf{w}}(\mathrm{t}) = \langle \mathbf{w}(t)\mathbf{w}(t-\tau)^T \rangle \text{ and } \boldsymbol{\Sigma}_{\mathbf{e}}(t) = \langle \mathbf{e}(t)\mathbf{e}(t-\tau)^T \rangle$$

E.g., Bilinear DCM: $\dot{\mathbf{x}}(t) = \left(\mathbf{A} + \sum_j \mathbf{u}_j \mathbf{B}^j\right)\mathbf{x} + \mathbf{C}u + \mathbf{w}(t)$

Structural equation models (SEM)

(assuming $\mathbf{x}(t) = \mathrm{y}(t)$ and $\dot{\mathrm{y}}(t) = 0$ $\mathbf{u}(t) = 0$)

$$\dot{\mathbf{y}}(t) = \mathbf{A}\mathbf{y}(t) + \mathbf{w}(t) = (\boldsymbol{\Theta} - \mathbf{I})\mathbf{y}(t) + \mathbf{e}(t)$$
$$\mathbf{y}(t) = \boldsymbol{\Theta}\mathbf{y}(t) + \mathbf{e}(t)$$

Convolution kernel

$$\mathbf{y}(t) = \boldsymbol{\kappa}(\tau) * \mathbf{w}(t) + \mathbf{e}(t)$$
$$\boldsymbol{\kappa}(\tau) = \partial_{\mathbf{x}} h \,.\, \exp\left(\tau\, \partial_{\mathbf{x}} f\right)$$

Cross covariance

$$\boldsymbol{\Sigma}(\tau) = \langle \mathbf{y}(t).\mathbf{y}(t-\tau)^T \rangle = \boldsymbol{\kappa}(t) * \boldsymbol{\Sigma}_{\mathbf{w}}(t) * \boldsymbol{\kappa}(-t) + \boldsymbol{\Sigma}_{\mathbf{e}}(t)$$

Cross correlation

$$c_{ij}(\tau) = \frac{\Sigma_{jk}(\tau)}{\sqrt{\Sigma_{jj}(0)\Sigma_{kk}(0)}}$$

Spectral representations

Convolution theorem

$$\boldsymbol{Y}(\omega) = \boldsymbol{K}(\omega)\boldsymbol{W}(\omega) + \boldsymbol{E}(\omega)$$
$$\boldsymbol{K}(\omega) = \mathrm{FT}\big(\boldsymbol{\kappa}(\tau)\big)$$

Cross spectral density

$$\boldsymbol{g}_{\mathbf{y}}(\omega) = \langle \boldsymbol{Y}(\omega)\boldsymbol{Y}(\omega)^\dagger \rangle$$
$$= \boldsymbol{K}(\omega).\boldsymbol{g}_{\mathbf{w}}(\omega).\boldsymbol{K}(\omega)^\dagger + \boldsymbol{g}_{\mathbf{e}}(\omega)$$

Coherence

$$C_{ij}(\omega) = \frac{\left|g_{jk}(\omega)\right|^2}{g_{jj}(\omega)g_{kk}(\omega)}$$

Convolution theorem

$$\boldsymbol{Y}(\omega) = \boldsymbol{A}(\omega).\boldsymbol{Y}(\omega) + \boldsymbol{Z}(\omega)$$
$$\boldsymbol{A}(\omega) = \mathrm{FT}(a_1, a_2 .. a_N)$$

Directed transfer functions

$$\boldsymbol{Y}(\omega) = \boldsymbol{S}(\omega).\boldsymbol{Z}(\omega)$$
$$\boldsymbol{S}(\omega) = (\mathbf{I} - \boldsymbol{A}(\omega))^{-1}$$

Granger causality

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

Vector autoregressive model (VAR)

(assuming $\mathbf{x}(t) = \mathbf{y}(t)$)

$$\mathbf{y}(t) = \sum_{i=1}^{N} a_i \mathbf{y}(t-i) + \mathbf{z}(t)$$

Auto-regression coefficients

$$\tilde{\mathbf{A}} = \langle \tilde{\mathbf{Y}}^{\mathrm{T}}\tilde{\mathbf{Y}} \rangle^{-1} \langle \tilde{\mathbf{Y}}^{\mathrm{T}}\tilde{\mathbf{Y}} \rangle$$
$$= \boldsymbol{\rho}^{-1}\left[\boldsymbol{\rho}_1, \ldots\, \boldsymbol{\rho}_{\mathbf{p}}\right]^T$$

Auto- correlation

$$c_{ii} = (\mathbf{I} - \tilde{\mathbf{A}})^{-1}(\mathbf{I} - \tilde{\mathbf{A}}^T)^{-1}$$

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

OUTLINE

Introduction and background
(Spectral) Dynamic Causal Modelling

Technical / Mathematical Content

Worked example using SPM

DMN connectivity

What's new?

Large DCMs

Applications

Cognitive / Psychiatric

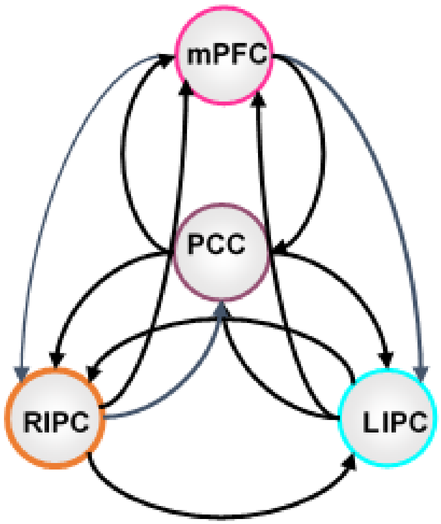
Worked example

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).

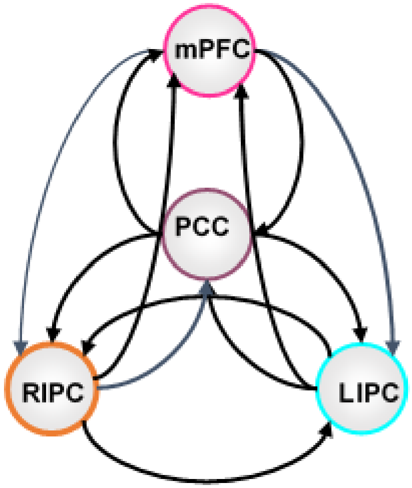
38.1 Theoretical background



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]



Di & Biswal, NeuroImage 2014 and Razi et al NeuroImage, 2015

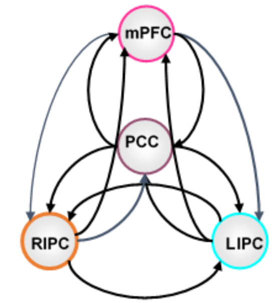
Worked example

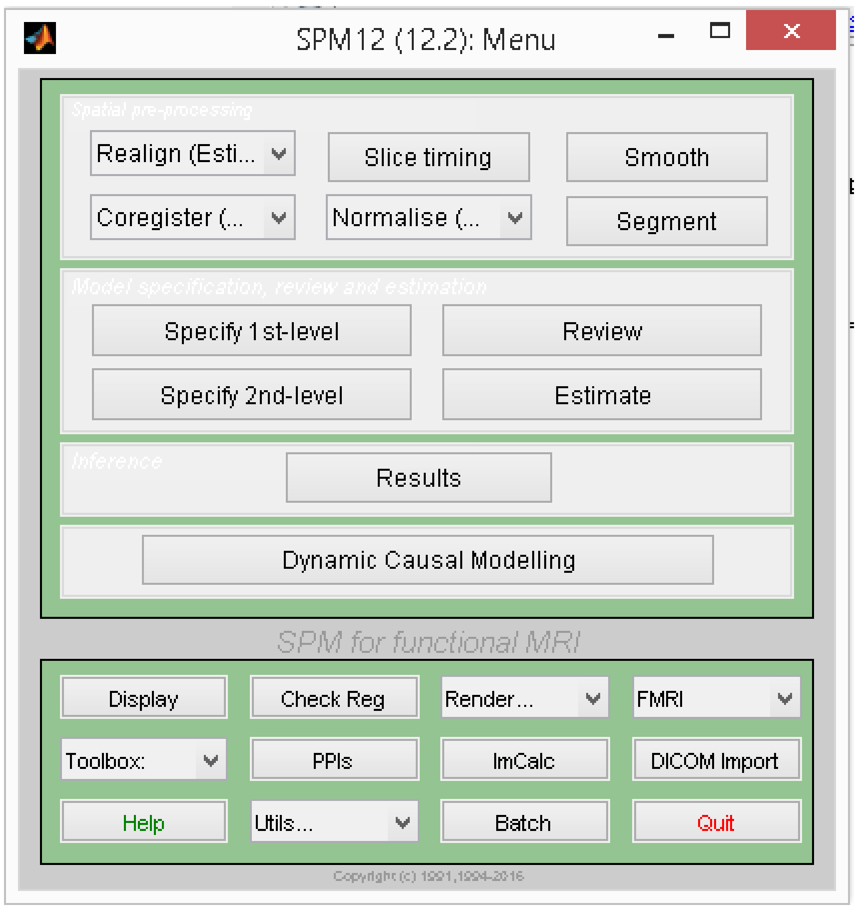
1. GLM estimation – to get SPM.mat
2. CSF/WM signal extraction
3. GLM estimation – to remove confounds
4. Extraction of time series from ROIs

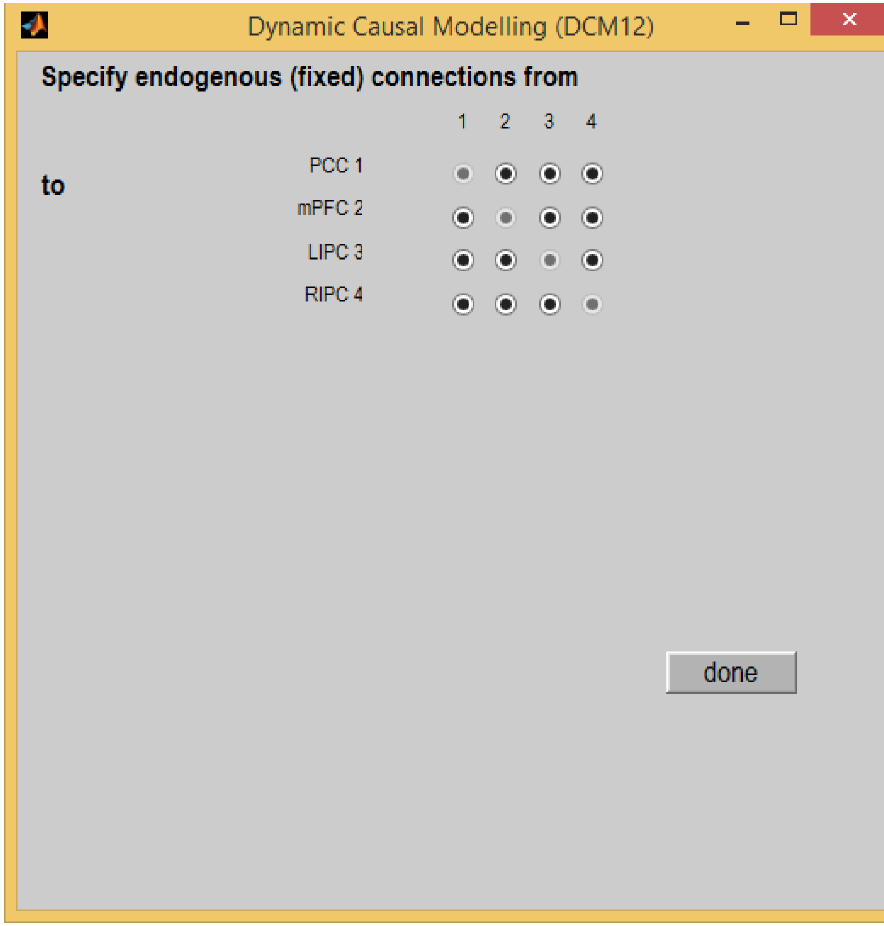
5. Specify DCM
6. Estimate DCM
7. Review DCM

Worked example

Default mode network

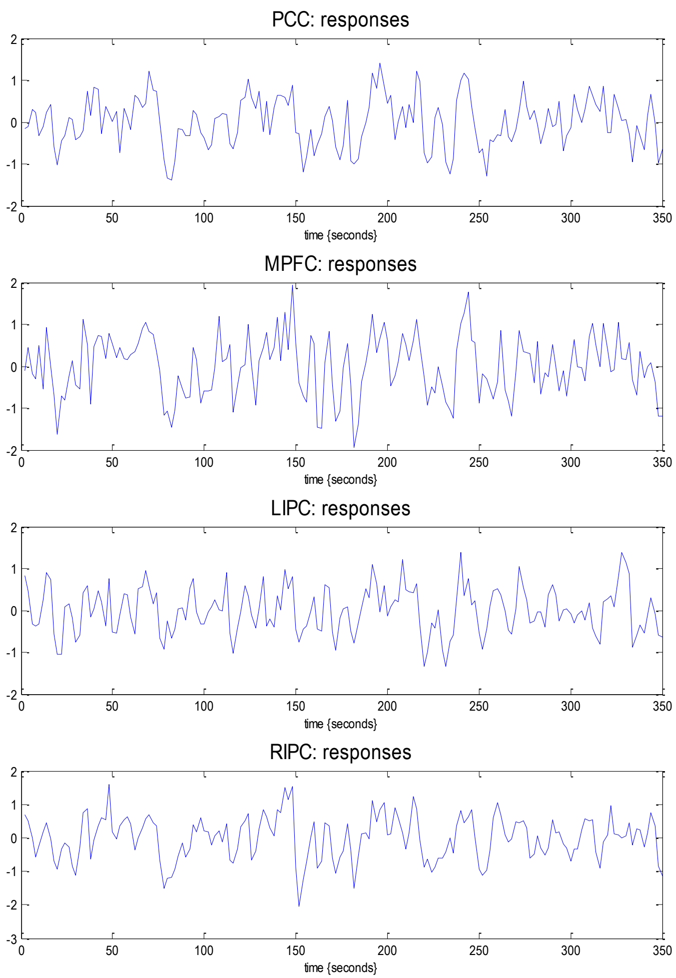




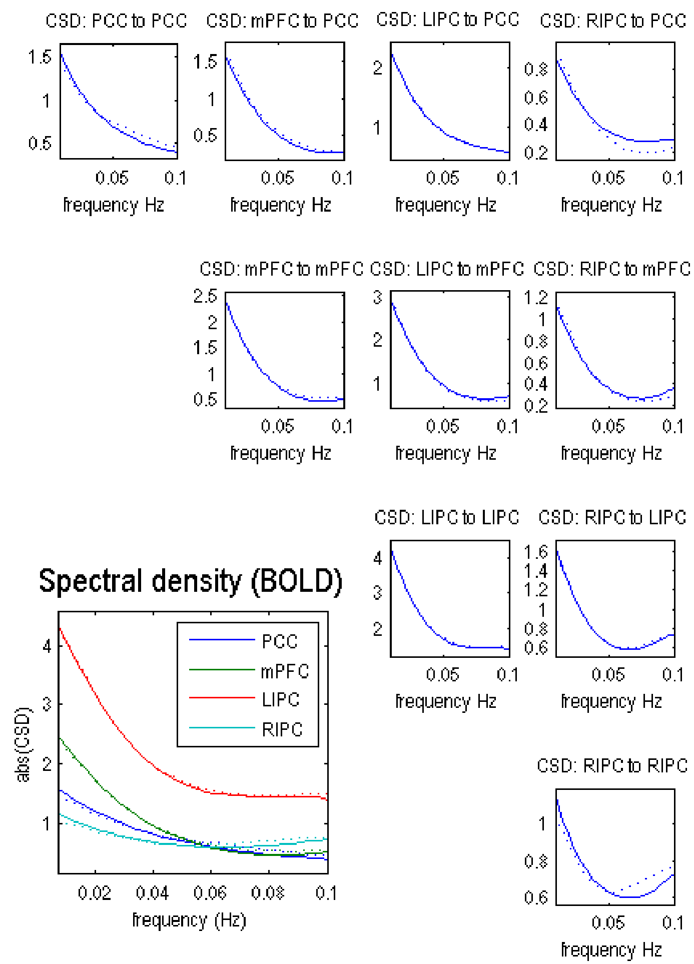


Worked example

Default mode network



Input time series

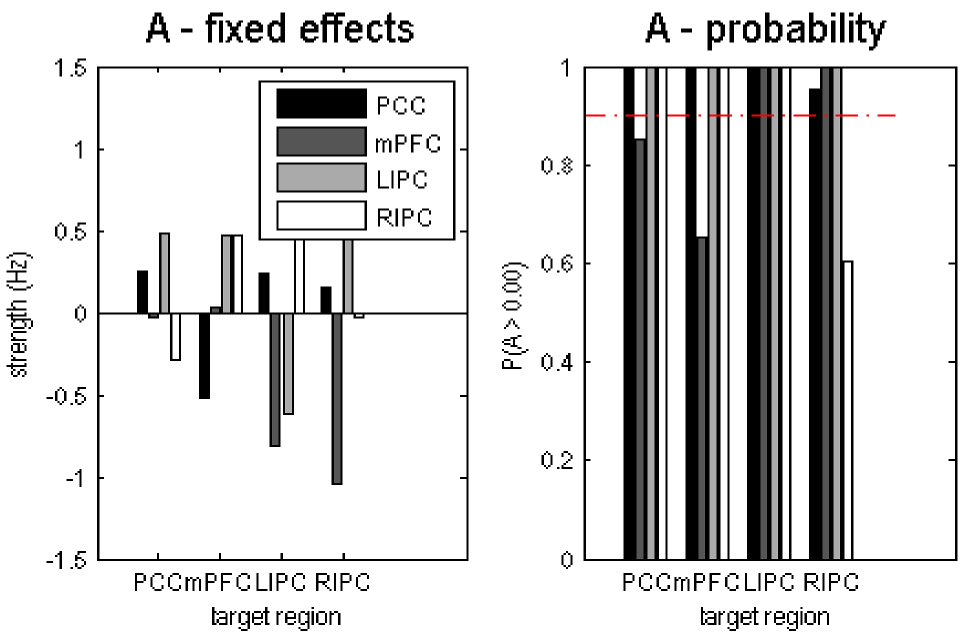


Data fits for CSD

Worked example

Default mode network

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




```
>> 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
```

UCL

OUTLINE

Introduction and background
(Spectral) Dynamic Causal Modelling

Technical / Mathematical Content

Worked example using SPM

DMN connectivity

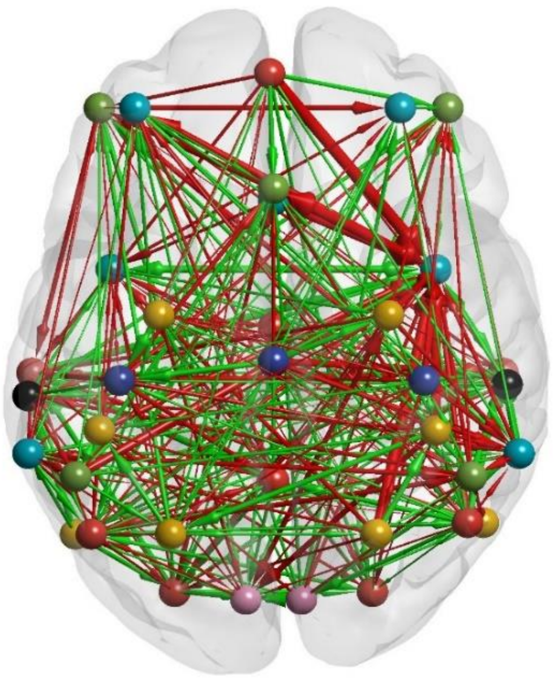
What's new?

Large DCMs

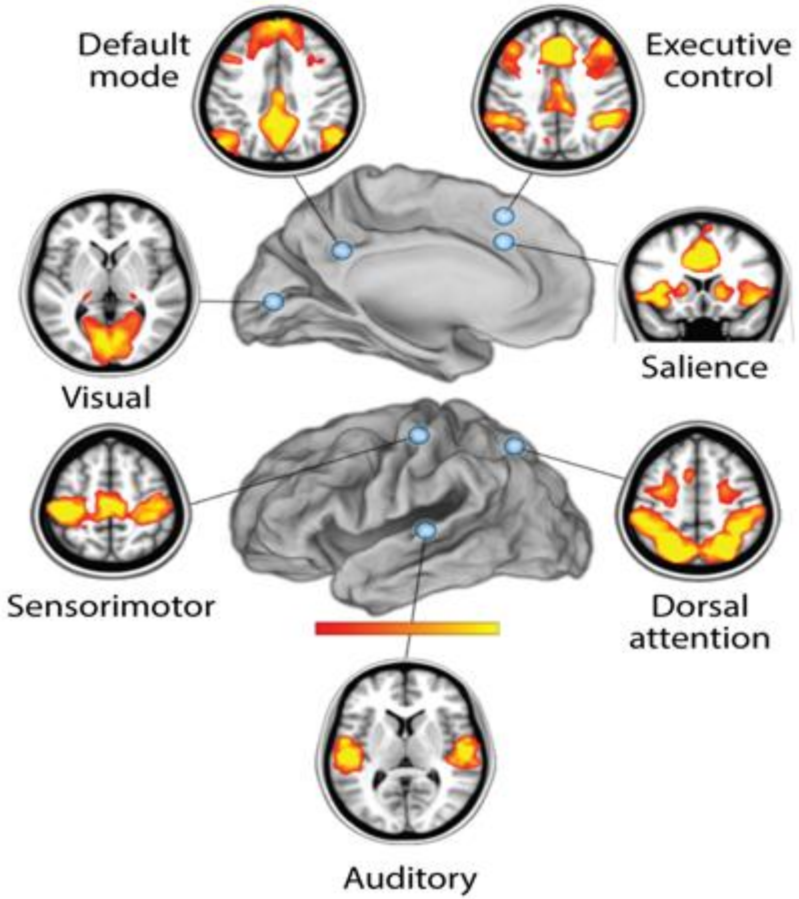
Applications

Cognitive / Psychiatric

Large-scale DCMs for resting state fMRI

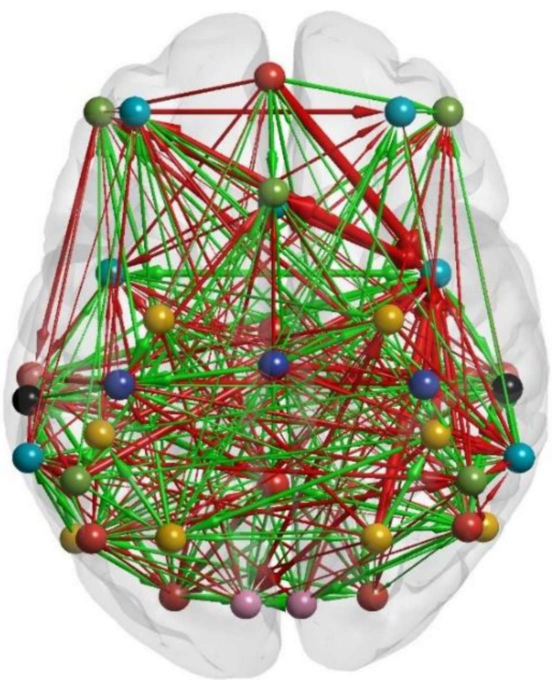


36 nodes network



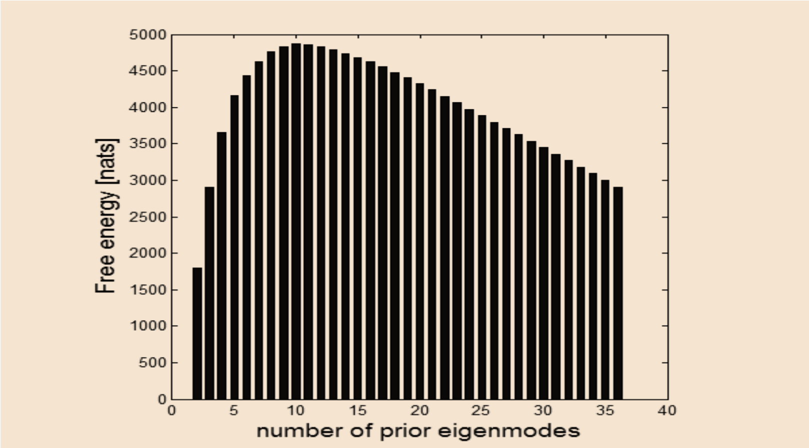
Raichle Annual Reviews, 2015

Large-scale DCMs for resting state fMRI

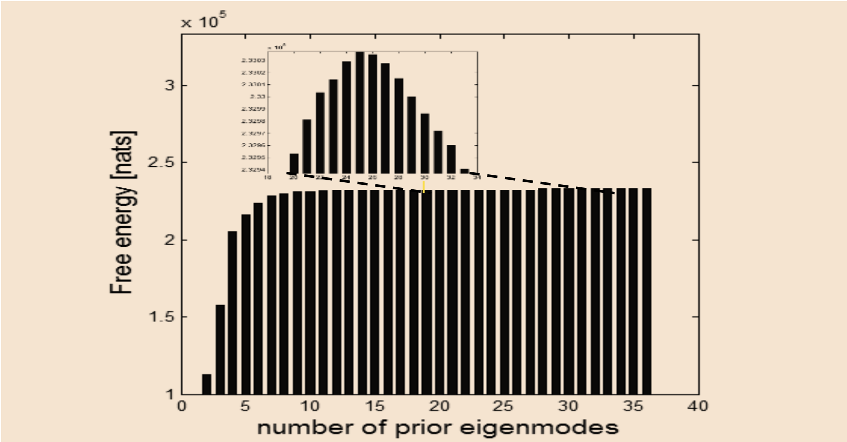


36 nodes network

Stochastic DCM



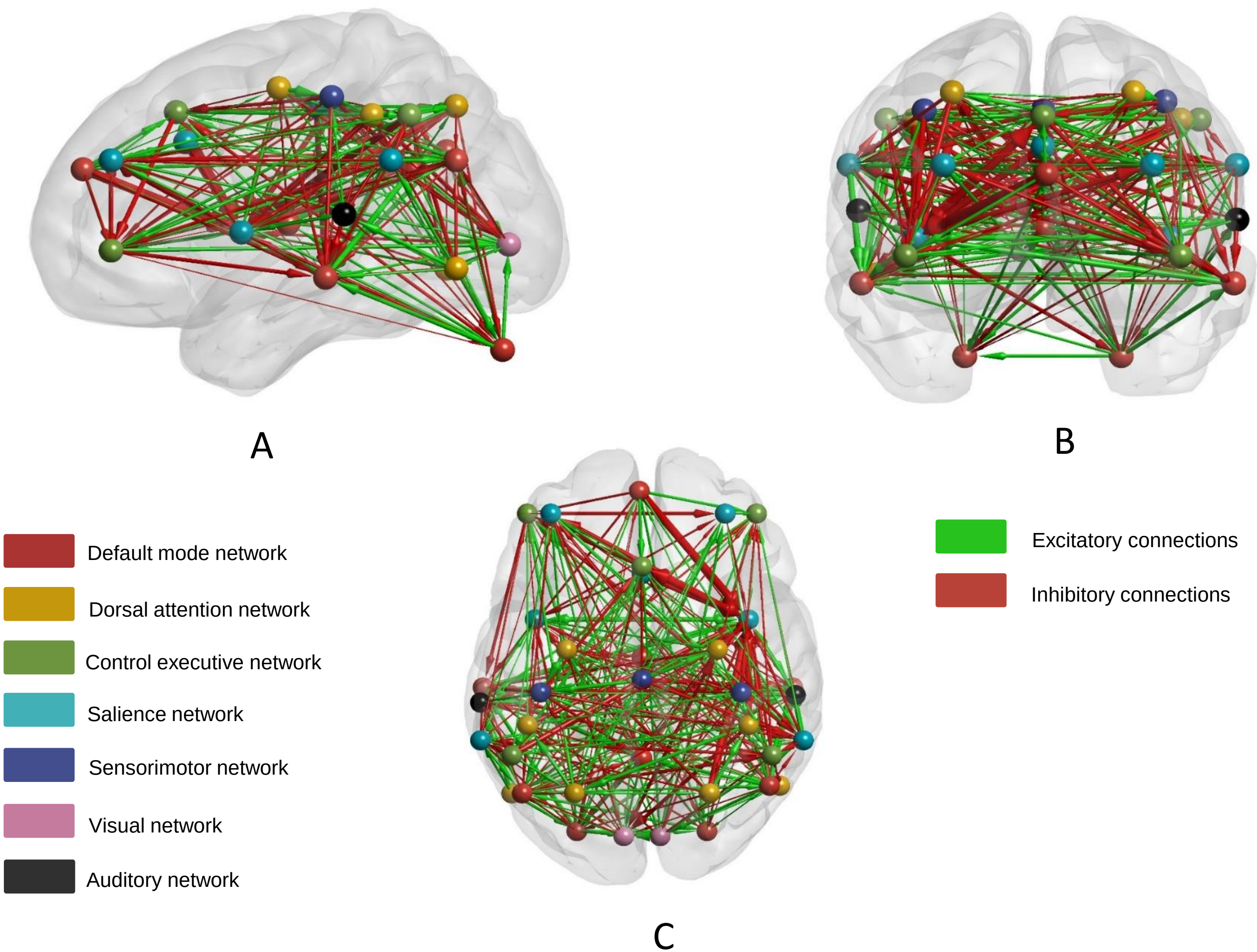
Spectral DCM



Number of modes (m)

Razi, Seghier, Yuan, McColgan, Zeidman, Park, Sporns, Rees, Friston, Net. Neurosci. In press

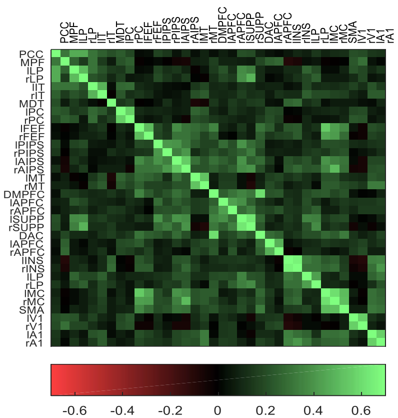
Large-scale DCMs for resting state fMRI



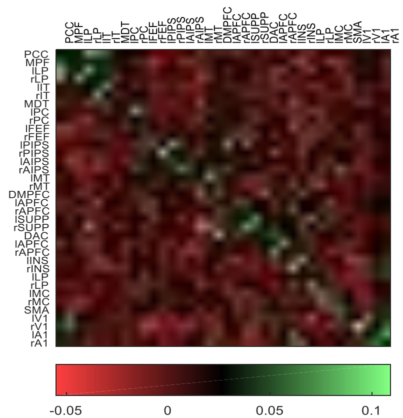
Razi, Seghier, Yuan, McColgan, Zeidman, Park, Sporns, Rees, Friston, Net. Neurosci. In press

Large-scale DCMs for resting state fMRI

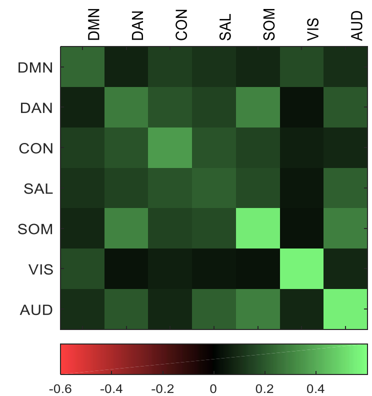
Averaged functional connectivity



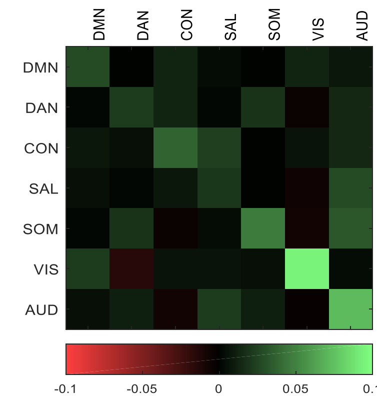
Averaged effective connectivity

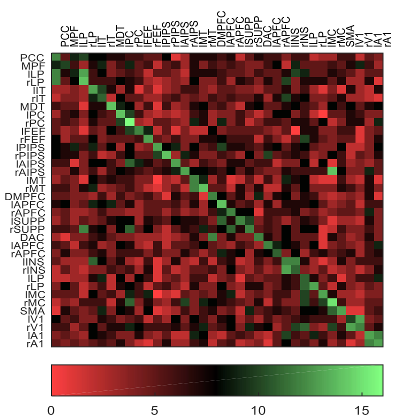


Averaged functional connectivity

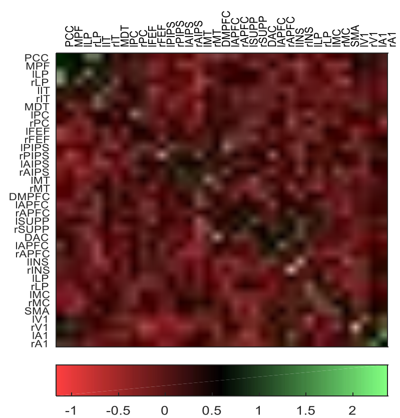


Averaged effective connectivity

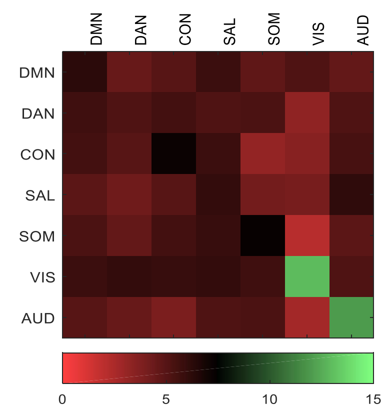




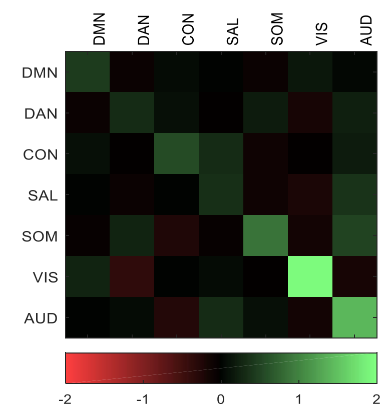
Averaged binarized adjacency matrix after BMR



Averaged weighted adjacency matrix after BMR



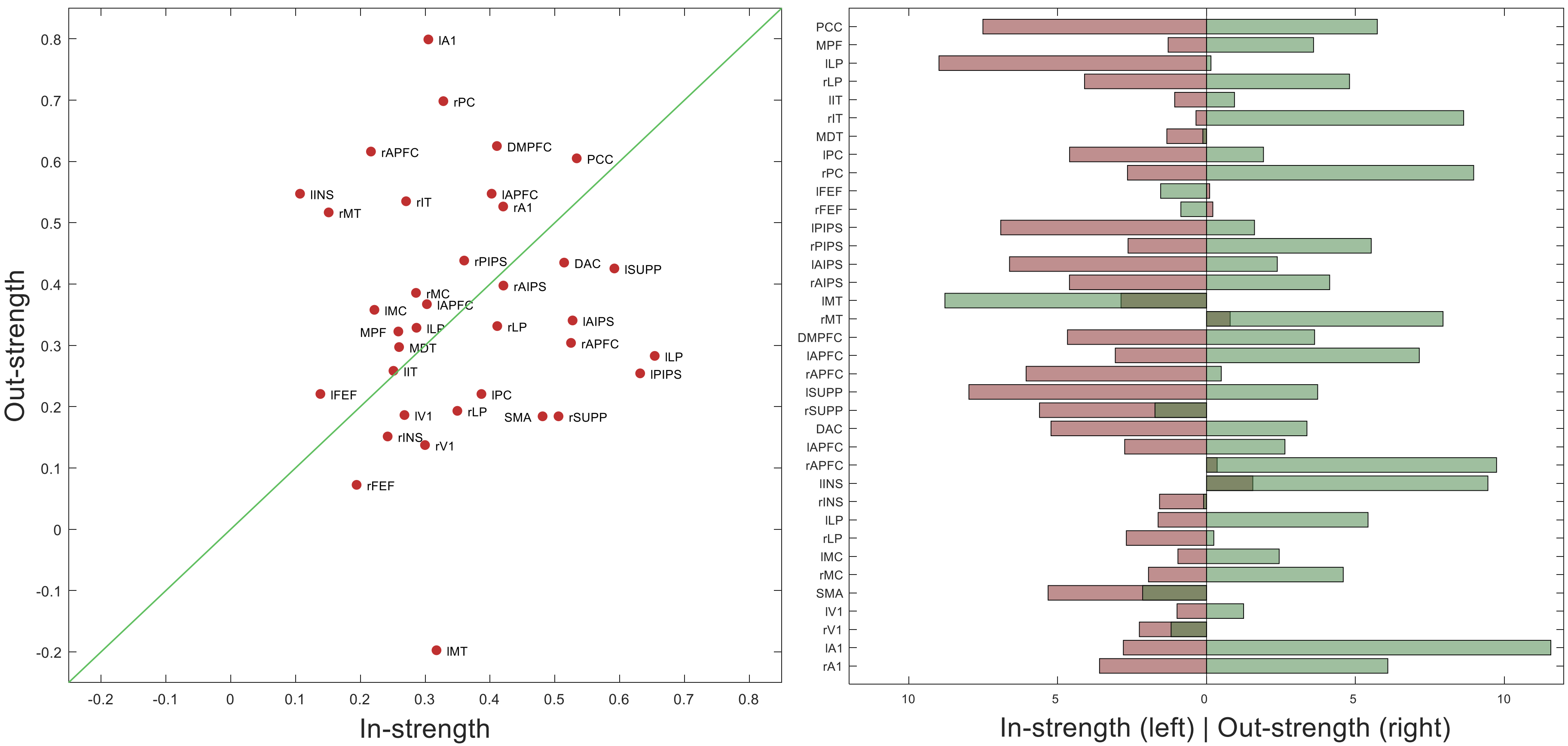
Averaged binarised after BMR



Averaged weighted after BMR

Razi, Seghier, Yuan, McColgan, Zeidman, Park, Sporns, Rees, Friston, Net. Neurosci. In press

Large-scale DCMs for resting state fMRI



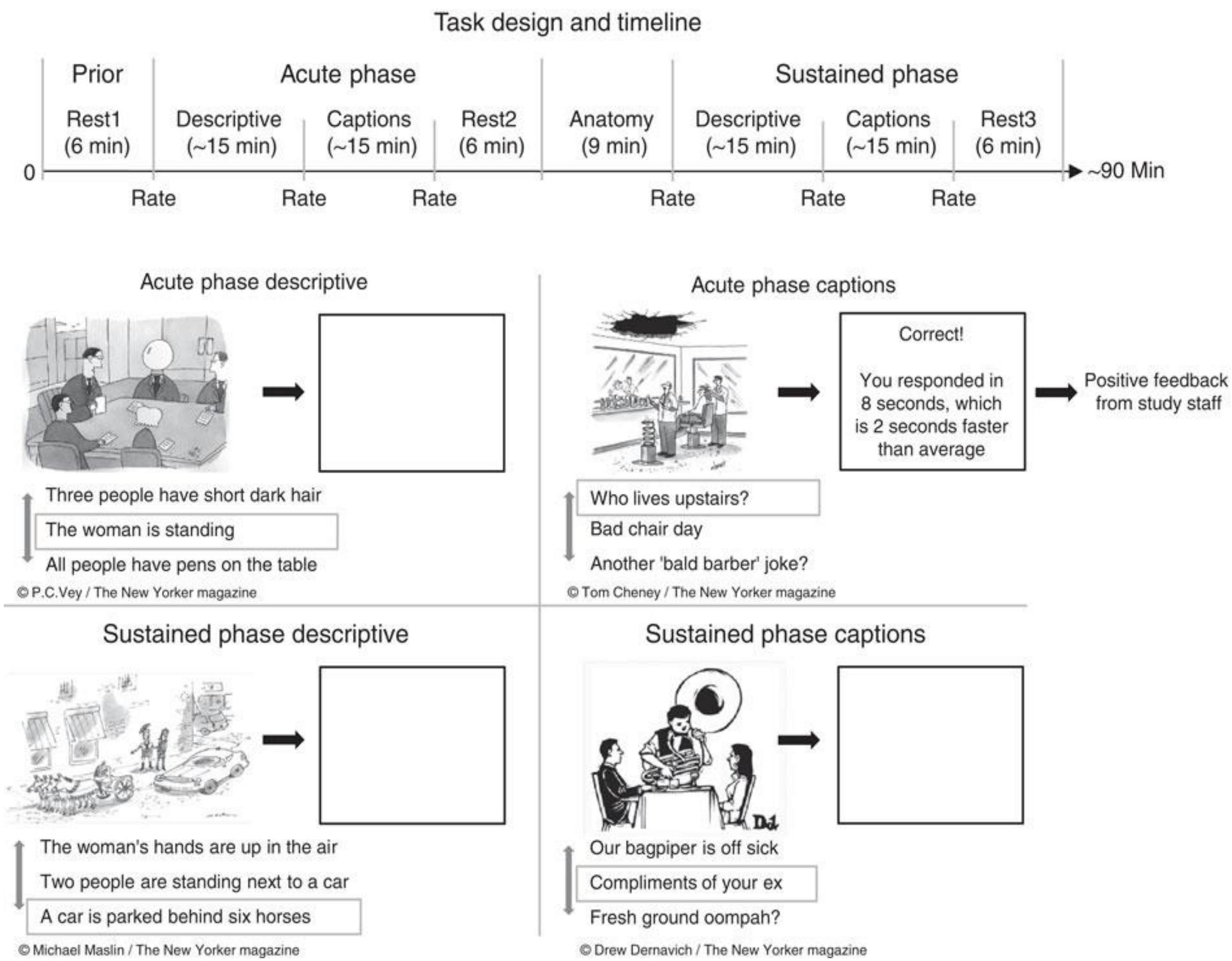
Razi, Seghier, Yuan, McColgan, Zeidman, Park, Sporns, Rees, Friston, Net. Neurosci. In press

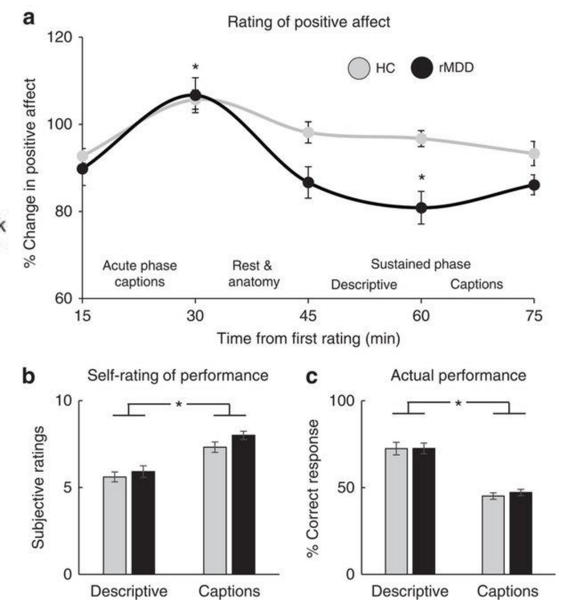
OUTLINE

Introduction and background (Spectral) Dynamic Causal Modelling	Technical / Mathematical Content
Worked example using SPM	DMN connectivity
What’s new?	Large DCMs
Applications	Cognitive / Psychiatric

Major Depressive Disorder

Natural time course of positive mood





Admon & Pizzagalli,(2016) *Nat. Comm.*

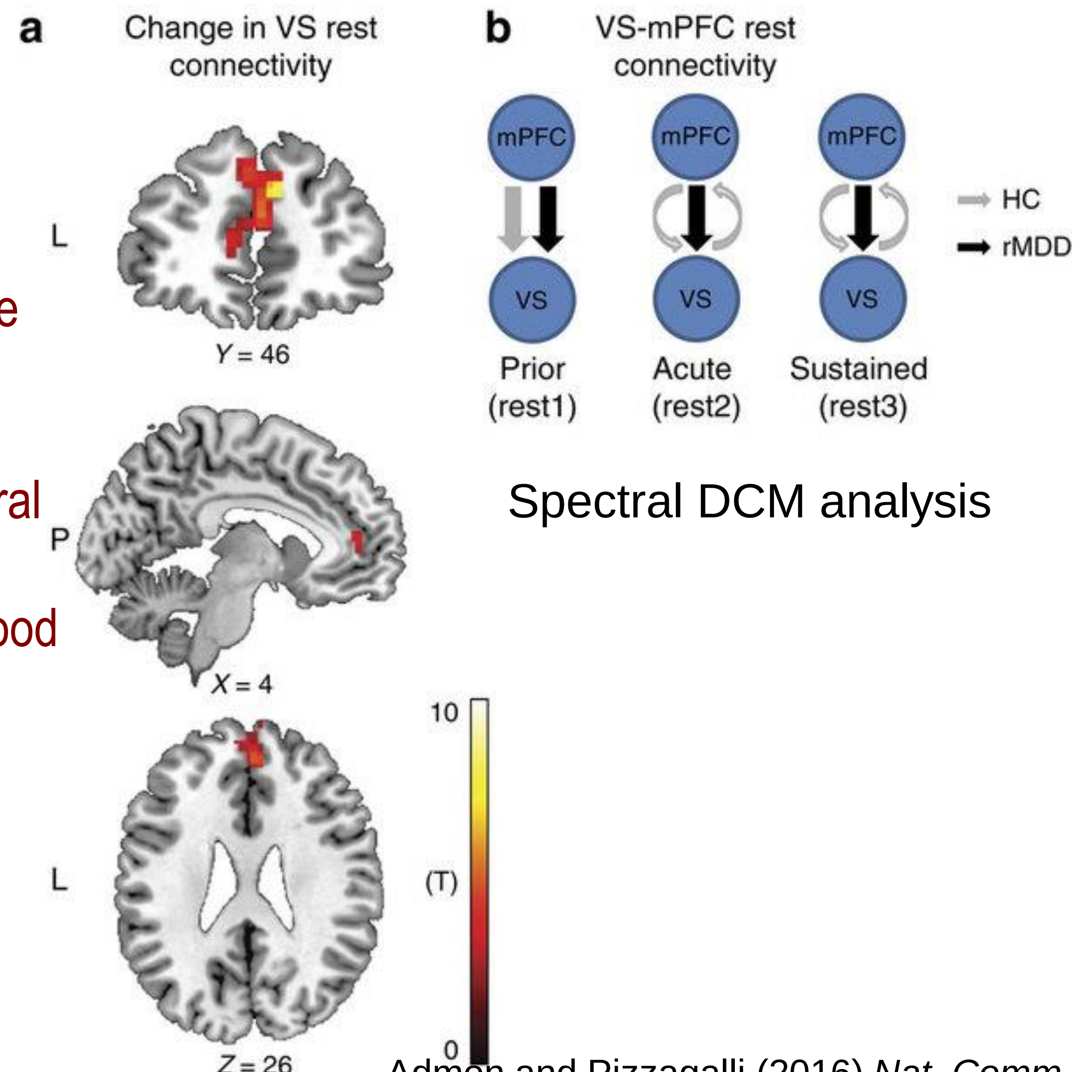
Major Depressive Disorder

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



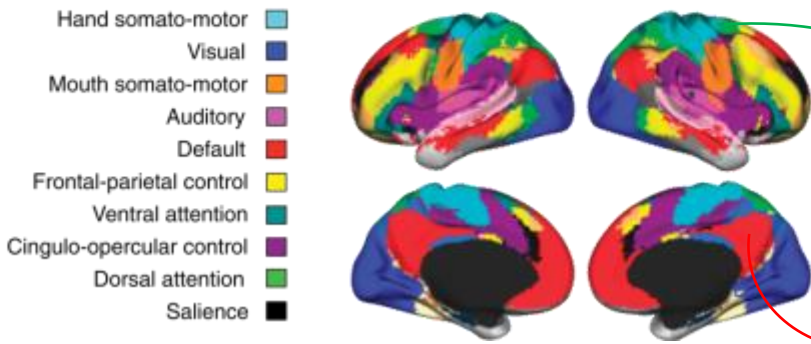
Spectral DCM analysis

Admon and Pizzagalli,(2016) *Nat. Comm.*

Hierarchical organization of intrinsic brain modes

anticorrelated brain modes

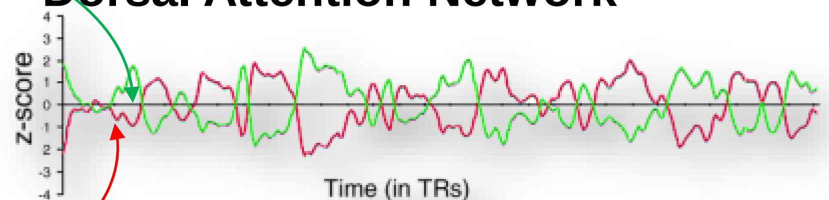
– Functional network organization



Power et al. 2011

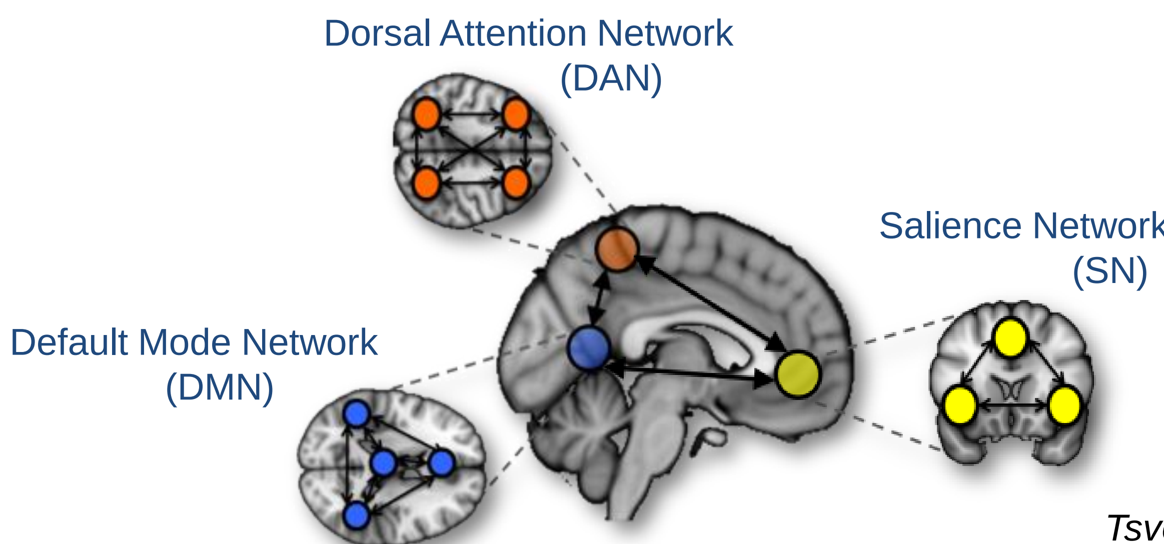
– Network interactivity important for cognitive function

Dorsal Attention Network



Default Mode Network

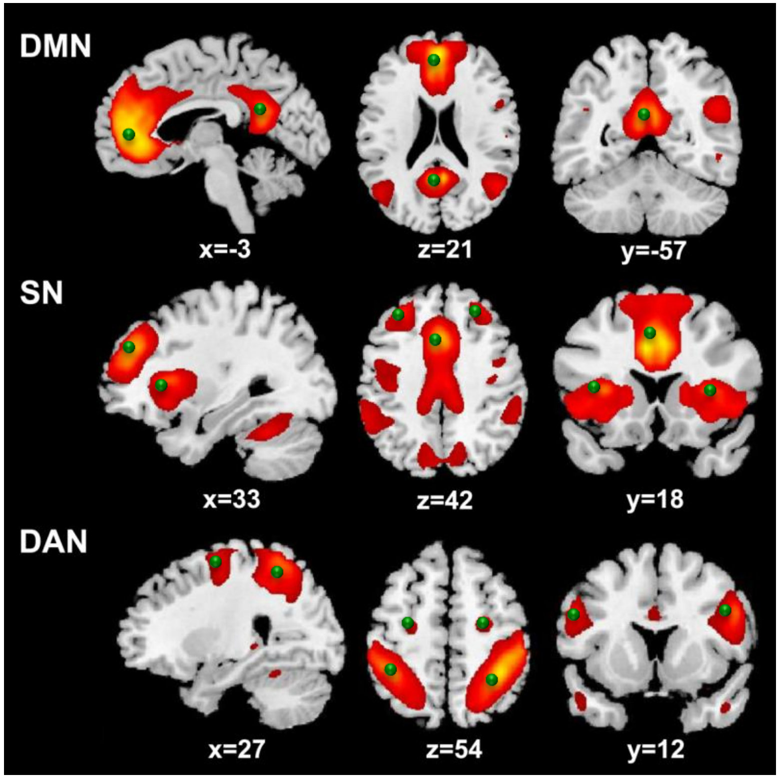
Kelly et al. 2008



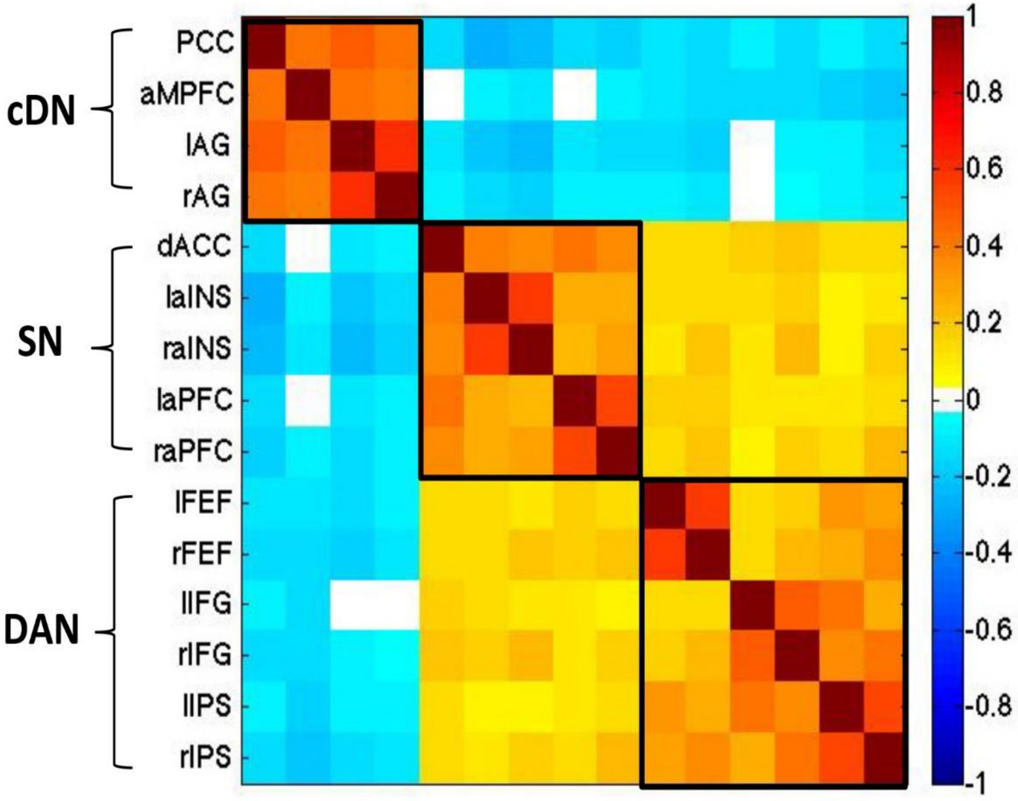
Tsvetanov et al. 2016

Hierarchical organization of intrinsic brain modes

anticorrelated brain modes



Functional connectivity matrix



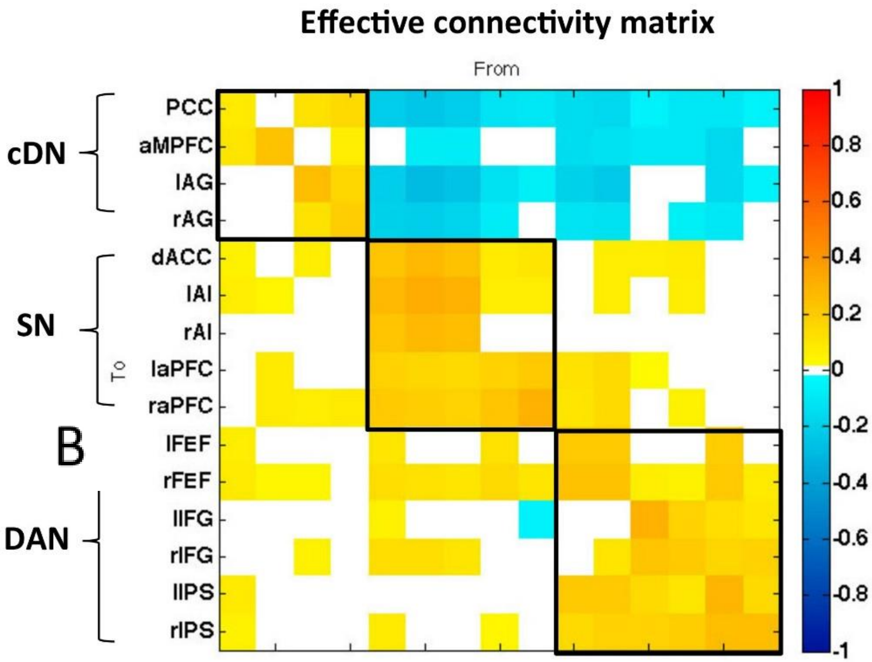
VOIs identified using spatial independent component analysis (ICA) (N=404)

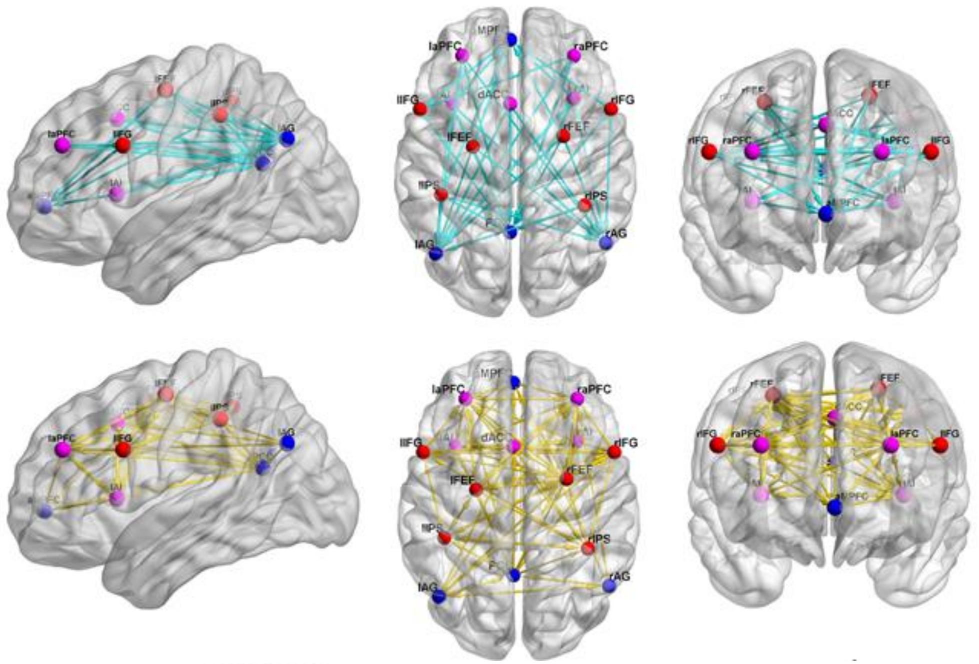
Functional connectivity

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

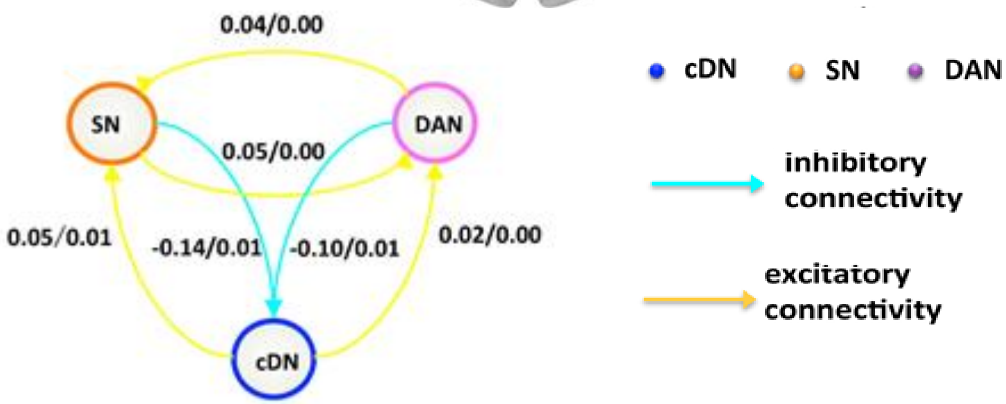
Hierarchical organization of intrinsic brain modes

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