Estimating effective connectivity in linear brain network models

G. Prando, M. Zorzi, A. Bertoldo, A. Chiuso

Department of Information Engineering - University of Padova

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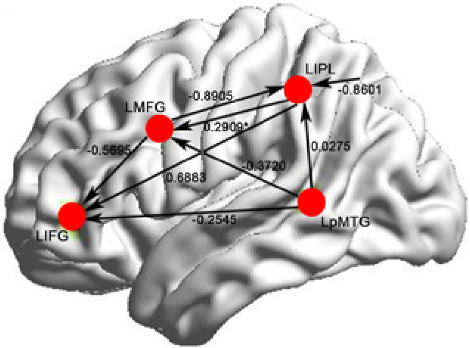
What is effective connectivity?

What

- It describes the causal influences that neural units exert over another, either at a synaptic or population level
- It is described by a causal model of interactions between the elements of the neural system



Effective Connectivity

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Why do we need system identification?

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How is effective connectivity estimated?

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- Using fMRI data
- Using EEG data

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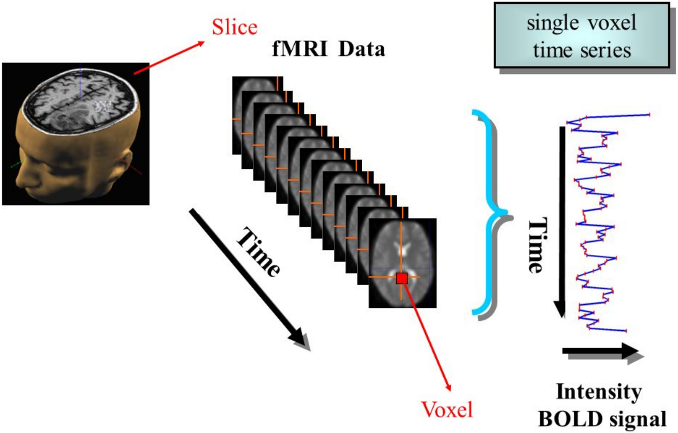
fMRI signal

- fMRI has
  - high spatial resolution (1-5 mm)
  - low temporal resolution (sampling time $T_R \approx sec$)
- fMRI measures the BOLD signal (*Blood Oxygenation Level Dependent* signal)



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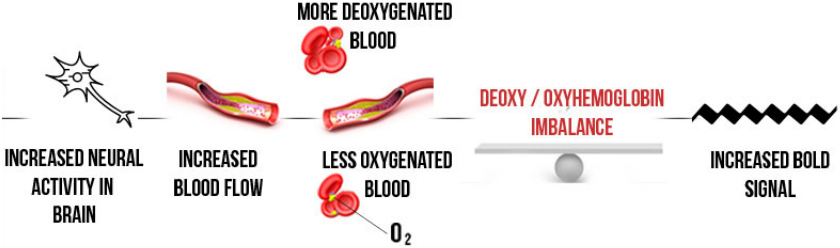

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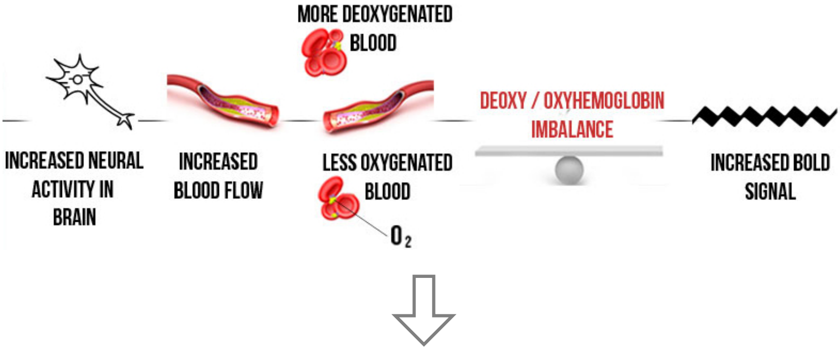

To estimate effective connectivity we need a generative model of the fMRI signal

Condition: Task

$[u_t^{(1)} \; \cdots \; u_t^{(m)}]^T = u_t$ **stimulus**

neuronal state equation

$$\dot{x}_t = \left(A + \sum_j u_t^{(j)} B^{(j)}\right) x_t + C u_t$$

Balloon model

$[x_t^{(1)} \; \cdots \; x_t^{(n)}]^T = x_t$ **neuronal activity**

hemodynamics state equation

$$\dot{r}_t = -\kappa r_t - \gamma(f_t - 1) + x_t^{(i)}$$

$$\dot{f}_t = r_t$$

$$\tau \dot{v}_t = f_t - v_t^{1/\xi}$$

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BOLD signal

$$b_t^{(i)} = V_0 \left[k_1(1 - q_t) + k_2\left(1 - \frac{q_t}{v_t}\right) + k_3(1 - v_t)\right]$$

fMRI signal $y_t = b_t + e_t$

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$$\theta_h = \{\kappa, \gamma, \tau, \xi, \rho\}$$

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Effective Connectivity Estimation

$\equiv$

Estimation of A, B, C, θ_h

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x_t **neuronal activity**

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Effective Connectivity Estimation

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Estimation of

A, θ_h,

$\{x_t\}$,

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1. Postulate a set of candidate models $\mathrm{m}^{(\ell)}$ (connectivity patterns)

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2. Use Variational Bayes

$$\ln p(y|\mathrm{m}^{(\ell)}) = \underbrace{\mathcal{F}\left(q(\theta|\mathrm{m}^{(\ell)})\right)} + KL\left(q(\theta|\mathrm{m}^{(\ell)}) \mid\mid p(\theta|y,\mathrm{m}^{(\ell)})\right)$$

$$\mathcal{F}\left(q(\theta|\mathrm{m}^{(\ell)})\right) := \int q(\theta|\mathrm{m}^{(\ell)}) \frac{\ln p(y,\theta)}{\ln q(\theta|\mathrm{m}^{(\ell)})}\, d\theta$$

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$$q(\theta|\mathrm{m}^{(\ell)}) = \prod_i q_i(\theta_i|\mathrm{m}^{(\ell)}) \quad \Longrightarrow \quad q_i^*(\theta_i|\mathrm{m}^{(\ell)}) = \frac{1}{C}\exp\left(\mathbb{E}_{j\neq i} \ln[p(y,\theta)]\right)$$

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$$p(\theta_i|y) \sim \mathcal{N}(\hat{\theta}_i, \hat{\Sigma}_i), \quad q_i(\theta_i|\mathrm{m}^{(\ell)}) \sim \mathcal{N}(\mu, P) \quad \Longrightarrow \quad q_i^* \sim \mathcal{N}(\hat{\theta}_i, \hat{\Sigma}_i)$$

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Model

Parameters Estimation

- Condition: rest

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Parameters Estimation

- Sparsity inducing prior on the connectivity matrix
    - Reweighted method to estimate it
- RTS smoother to estimate the neuronal state $\{x_k\}$
- EM algorithm to estimate model parameters

Condition: Rest

$$w_t \sim \mathcal{N}(0, \sigma^2 I_n)$$

neuronal state equation

$$\dot{x}_t = A\, x_t + w_t$$

Balloon model

x_t **neuronal activity**

hemodynamics state equation

$$\dot{r}_t = -\kappa r_t - \gamma(f_t - 1) + x_t$$

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fMRI signal $\quad y_t = b_t + e_t$

Our model

Condition: Rest

$$w_k \sim \mathcal{N}\left(0, \sigma^2 \int_0^{T_R} e^{A\tau} e^{A^T\tau} d\tau\right)$$

neuronal state equation

$$x_{k+1} = e^{A T_R} x_k + w_k$$

x_k **neuronal activity**

linearized Balloon model

$$b_k = \sum_{\ell=0}^{s-1} \boldsymbol{h}_\ell \, x_{k-\ell}$$

$$= \left[\boldsymbol{h}^T \otimes I_n\right] \begin{bmatrix} x_k \\ x_{k-1} \\ \vdots \\ x_{k-s+1} \end{bmatrix}$$

Discretization + Linearization

fMRI signal $y_k = b_k + e_k \quad e_k \sim \mathcal{N}(0, \lambda^2 I_n)$

Condition: Rest

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Linear Stochastic State-Space Model

$$\mathbf{x}_{k+1} = \begin{bmatrix} e^{AT_R} & \mathbf{0} \\ I_{n(s-1)} & \mathbf{0} \end{bmatrix} \mathbf{x}_k + \begin{bmatrix} w_k \\ \mathbf{0} \end{bmatrix}$$

$$b_k = \left[\boldsymbol{h}^T \otimes I_n\right] \mathbf{x}_k$$

Parameters:

A, $\boldsymbol{\sigma}$, $\boldsymbol{h}$, $\boldsymbol{\lambda}$

fMRI signal $y_k = b_k + e_k$ $\quad e_k \sim \mathcal{N}(0, \boldsymbol{\lambda}^2 I_n)$

$$\boldsymbol{\theta_h} \sim \mathcal{N}(\bar{\theta}, \bar{\Sigma}_\theta)$$

Empirical prior reported in
Friston, Harrison, and Penny 2003

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\end{aligned}$$

$$\rightarrow b_t^{(i)}$$

$$\approx$$

$$x_t^{(i)} \rightarrow \boxed{\boldsymbol{h}} \rightarrow b_t^{(i)}$$

$$\boldsymbol{h} \sim \mathcal{N}(\bar{h}, \bar{\Sigma}_h)$$

MAP Estimator

$$\hat{\eta} = \arg\max_{\eta} \; p(Y|\eta)p(\eta)$$

$$\eta = \{A, \boldsymbol{\sigma}, \; \boldsymbol{h}, \boldsymbol{\lambda}\}$$

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Likelihood

$$p(Y|\eta) = \int p(\mathbf{X}, Y|\eta) \, \mathrm{d}\mathbf{X}, \qquad \mathbf{X} := [\mathbf{x}^T(0) \; \cdots \; \mathbf{x}^T(N)]^T$$

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Prior

$$p(\eta) \;\propto\; p(A)\; p(\boldsymbol{\sigma})\; p(\boldsymbol{h})\; p(\boldsymbol{\lambda})$$

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- Use EM algorithm to maximize $\ln p(Y|\eta) + \ln p(\eta)$

EM Algorithm

Initialization: Choose $\eta^{(0)}$ and set $l = 0$

1: **repeat**

2: E-step: Evaluate $p(\mathbf{X}|Y, \eta^{(l)})$

3: M-step: $\eta^{(l+1)} = \arg\max_{\eta \in \Omega} \; \mathcal{Q}(\eta, \eta^{(l)}) + \ln \; p(\eta)$

4: $l = l + 1$

5: **until** $\|\eta^{(l)} - \eta^{(l-1)}\| / \|\eta^{(l)}\|$ is sufficiently small

Outputs: $\eta^{(l)}$

$$\mathcal{Q}(\eta, \eta^{(l)}) = \int p(\mathbf{X}|Y, \eta^{(l)}) \ln p(\mathbf{X}, Y|\eta) \, \mathrm{d}\mathbf{X}$$

Parameters Estimation: EM

Need to apply RTS smoother to evaluate
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Modified EM Algorithm

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E-step: Apply RTS smoother to evaluate $p(\mathbf{X}|Y, \eta^{(l)})$

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$\Gamma^{(l+1)} =$ Update hyper-parameters Γ of prior $p(\text{vec}(A))$

$l = l + 1$

until $\|A^{(l)} - A^{(l-1)}\|_F / \|A^{(l)}\|_F$ is sufficiently small

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2: E-step: Apply RTS smoother to evaluate $p(\mathbf{X}|Y, \eta^{(l)})$

3: M-step: $\eta^{(l+1)} = \arg\max_{\eta \in \Omega} \; \mathcal{Q}(\eta, \eta^{(l)}) + \ln p(\eta)$

4: $\Gamma^{(l+1)} =$ Update hyper-parameters Γ of prior $p(\text{vec}(A))$

5: $l = l + 1$

6: **until** $\|A^{(l)} - A^{(l-1)}\|_F / \|A^{(l)}\|_F$ is sufficiently small

Outputs: $\eta^{(l)}$

Iterative Reweighted Method on Nonlinear model

NonLinear Regression Model

$$x_{k+1} = e^{A T_R} x_k + w_k, \qquad w_k \sim \mathcal{N}(0, Q)$$

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Aim

Estimate A sparse

NonLinear Regression Model	$x_{k+1} = e^{A T_R} x_k + w_k, \qquad w_k \sim \mathcal{N}(0, Q)$
Aim	Estimate A sparse
Prior	$\mathrm{vec}(A) \sim \mathcal{N}(0, \mathrm{diag}(\gamma_1, \cdots, \gamma_{n^2}))$

NonLinear Regression Model	$x_{k+1} = e^{AT_R} x_k + w_k, \qquad w_k \sim \mathcal{N}(0, Q)$
Aim	Estimate A sparse
Prior	$\mathrm{vec}(A) \sim \mathcal{N}(0, \mathrm{diag}\,(\gamma_1, \cdots, \gamma_{n^2}))$
Reweighted Algorithm	Iterate until A converges: • $\mathrm{vec}\left(A^{(l+1)}\right) = \mathbb{E}[\mathrm{vec}(A) \mid Y, \gamma^{(l)}]$ • $\gamma_i^{(l+1)} =$ Update using linearization $e^{AT_R} \simeq I + AT_R$

Simulated Data

- True effective connectivity matrix

$$A = \begin{bmatrix} -0.5 & 0 & 0 & 0 & -0.2 & 0 & 0 \\ 0 & -0.5 & 0 & -0.45 & -0.3 & 0 & 0 \\ 0 & 0 & -0.5 & 0.8 & 0 & 0 & 0 \\ 0 & 0.6 & 0 & -0.5 & -0.1 & 0.6 & 0 \\ 0.3 & 0 & -0.55 & 0 & -0.5 & 0.2 & 0 \\ 0 & 0 & 0 & 0 & 0.3 & -0.5 & 0.45 \\ 0.15 & 0 & 0.2 & 0 & 0 & 0 & -0.5 \end{bmatrix}$$

- 20 Monte-Carlo runs with different realizations of w_k, $\sigma^2 = 0.01$
- $N = 600$ data per each MC run
- Output SNR=10
- $T_R = 2$ sec

Experiment: Data and Performance Metrics

Simulated Data

- True effective connectivity matrix

$$A = \begin{bmatrix} -0.5 & 0 & 0 & 0 & -0.2 & 0 & 0 \\ 0 & -0.5 & 0 & -0.45 & -0.3 & 0 & 0 \\ 0 & 0 & -0.5 & 0.8 & 0 & 0 & 0 \\ 0 & 0.6 & 0 & -0.5 & -0.1 & 0.6 & 0 \\ 0.3 & 0 & -0.55 & 0 & -0.5 & 0.2 & 0 \\ 0 & 0 & 0 & 0 & 0.3 & -0.5 & 0.45 \\ 0.15 & 0 & 0.2 & 0 & 0 & 0 & -0.5 \end{bmatrix}$$

- 20 Monte-Carlo runs with different realizations of w_k, $\sigma^2 = 0.01$
- $N = 600$ data per each MC run
- Output SNR=10
- $T_R = 2$ sec

Root Mean Squared Error

$$RMSE(\widehat{A}) = \frac{\|\underline{A} - \underline{\hat{A}}\|_F}{\sqrt{n(n-1)}}$$

$\underline{A}$ denotes the matrix A with its diagonal set to 0

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- True effective connectivity matrix

$$A = \begin{bmatrix} -0.5 & 0 & 0 & 0 & -0.2 & 0 & 0 \\ 0 & -0.5 & 0 & -0.45 & -0.3 & 0 & 0 \\ 0 & 0 & -0.5 & 0.8 & 0 & 0 & 0 \\ 0 & 0.6 & 0 & -0.5 & -0.1 & 0.6 & 0 \\ 0.3 & 0 & -0.55 & 0 & -0.5 & 0.2 & 0 \\ 0 & 0 & 0 & 0 & 0.3 & -0.5 & 0.45 \\ 0.15 & 0 & 0.2 & 0 & 0 & 0 & -0.5 \end{bmatrix}$$

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Errors in the sparsity pattern

No. false positives $+$ No. false negatives

Experiment: Comparison with Existing Methods

Compare proposed EM algorithm with:

- Spectral DCM (Variational Bayes on frequency-domain data)
- Generalized Filtering (Variational Bayes on time-domain data using generalized coordinates)

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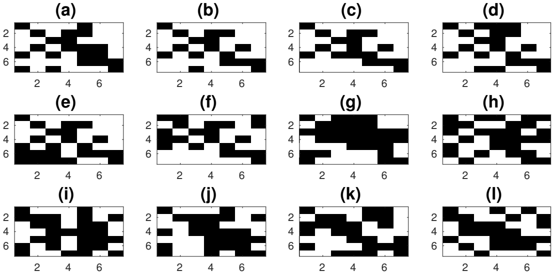

Candidate sparsity patterns provided to Variational Bayes methods

Experiment: Comparison with Existing Methods

		sDCM		GF	
	$ERR(\widehat{A})$	$\#Chosen$	$RMSE(\widehat{A})$	$\#Chosen$	$RMSE(\widehat{A})$
(a)	0	2	0.09	0	0.22
(b)	4	0	0.28	0	0.22
(c)	6	0	0.27	0	0.22
(d)	6	2	0.13	0	0.22
(e)	8	0	0.25	0	0.22
(f)	10	0	0.31	0	0.23
(g)	19	1	0.35	0	0.24
(h)	22	**15**	**0.30**	0	0.23
(i)	19	0	0.38	**20**	**0.24**
(j)	15	0	0.33	0	0.23
(k)	21	0	0.34	0	0.23
(l)	17	0	0.32	0	0.23

Our Method

	$\#$ MC $runs$	$RMSE(\widehat{A})$
$ERR(\widehat{A}) \leq 4$	5	0.09
$5 \leq ERR(\widehat{A}) \leq 8$	8	0.10
$9 \leq ERR(\widehat{A}) \leq 11$	5	0.13
$ERR(\widehat{A}) \geq 12$	2	0.44

Conclusions

We propose an algorithm to

estimate brain effective connectivity

from fMRI data

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Key Features

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- Linear state-space model as generative model for fMRI data

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Key Features

- Linear state-space model as generative model for fMRI data
- EM algorithm for parameters estimation
- Sparsity inducing prior + reweighted method to avoid combinatorial search over candidate connectivity patterns

Thank you

References I

Karl J Friston, Lee Harrison, and Will Penny. "Dynamic causal modelling". In: *Neuroimage* 19.4 (2003), pp. 1273–1302.

Karl Friston et al. "Variational free energy and the Laplace approximation". In: *Neuroimage* 34.1 (2007), pp. 220–234.

Karl J Friston et al. "A DCM for resting state fMRI". In: *Neuroimage* 94 (2014), pp. 396–407.

Stefan Frässle et al. "Regression DCM for fMRI". In: *NeuroImage* (2017).

Karl J Friston, N Trujillo-Barreto, and Jean Daunizeau. "DEM: a variational treatment of dynamic systems". In: *Neuroimage* 41.3 (2008), pp. 849–885.

Baojuan Li et al. "Generalised filtering and stochastic DCM for fMRI". In: *Neuroimage* 58.2 (2011), pp. 442–457.

David Wipf and Srikantan Nagarajan. "Iterative Reweighted ℓ_1 and ℓ_2 Methods for Finding Sparse Solutions". In: *IEEE Journal of Selected Topics in Signal Processing* 4.2 (2010), pp. 317–329.